EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Veterinary Medicinal Products

Scientific advice under Article 114(3) of Regulation (EU) 2019/6 on veterinary medicinal products - List of substances used in veterinary medicinal products authorised in the Union for use in food-producing terrestrial animal species or substances contained in medicinal products for human use authorised in the Union, which may be used in food-producing aquatic species in accordance with Article 114(1)

Introduction

Article 114(3) of Regulation (EU) 2019/6[1] requires the European Commission to establish, by means of implementing acts, a list of substances used in veterinary medicinal products authorised in the Union for use in food-producing terrestrial animal species or substances contained in a medicinal product for human use authorised in the Union in accordance with Directive 2001/83/EC or Regulation (EC) No 726/2004[2], which may be used in food-producing aquatic species in accordance with Article 114(1) of Regulation (EU) 2019/6. Only the substances on this list may be allowed for use in food-producing aquatic species in accordance with Article 114(1).

In a letter dated 12 April 2023, the European Commission requested[3] the European Medicines Agency (EMA) to provide scientific advice on the substances that may be considered for inclusion in the list.

To prepare the scientific advice, the EMA's Committee for Veterinary Medicinal Products (CVMP) formed an expert group, which was composed of 9 experts selected from the European network of experts on the basis of recommendations from Member States' national competent authorities or ministries, or the EMA. In view of the criteria to be considered in the scientific assessment pursuant to Article 114(3) of Regulation (EU) 2019/6 and as described in further detail below, the group's composition covered the following areas of expertise or knowledge:

[1] Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC, available from: https://eur-lex.europa.eu/eli/reg/2019/6/oj/eng
[2] Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (Text with EEA relevance), available from https://eur-lex.europa.eu/eli/reg/2004/726/oj/eng
[3] The request for scientific advice from the European Commission related to the adoption of implementing measures under Article 114(3) of Regulation (EU) 2019/6 is available from this link, and is reported in section 1.1 of this scientific advice

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- medicines for food-producing aquatic species in the different production systems;
- assessment of environmental risk associated with use of medicines in the different aquaculture production systems;
- antimicrobials;
- EMA's scientific advice to the Commission under Article 107(6) of Regulation (EU) 2019/6 for the establishment of a list of antimicrobials (AM) which shall not be used in accordance with Articles 112, 113 and 114 of the same Regulation, or which shall only be used in accordance with these articles subject to certain conditions[4];
- production systems used in aquaculture.

A number of scientific staff members of the EMA with expertise in toxicology, medicines and data analysis contributed to the development of the advice, and Commission representatives attended expert group meetings.

The CVMP was regularly informed of the progress of the work and provided input as needed.

The initial deadline for the scientific advice was 30 November 2024. However, in order to accommodate the assessment of the high number of eligible substances (more than 600 excluding the immunological substances) as well as the methodological amendments recommended by CVMP during the process, EMA requested a 6-month extension, to 31 May 2025, which was granted by the Commission.

A draft of this scientific advice was submitted to the CVMP on 1 April 2025 for comments.

The CVMP adopted the scientific advice on 15 May 2025.

Considerations and rationale for the recommendations

As requested by the European Commission, the Agency based the assessment on the criteria laid down in Article 114(3) of Regulation (EU) 2019/6:

'(a) risks to the environment if the food-producing aquatic species are treated with those substances;

(b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6);

(c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species.'

The Agency also took into account the considerations and the clarifications provided by the European Commission as described in further detail in section 1.

In the case of non-immunological substances, the substances identified by the aquaculture sector as important for the treatment of fish underwent a detailed assessment, while the substances not identified as such underwent a high-level assessment. The methodology is addressed in sections 3.1.1, 3.1.2 and 3.1.3.

In the case of immunological substances, only substances that target pathogens relevant for food-producing aquatic species were considered.

[4] EMA/CVMP/151584/2021, 'Scientific advice under Article 107(6) of Regulation (EU) 2019/6 for the establishment of a list of antimicrobials which shall not be used in accordance with Articles 112, 113 and 114 of the same Regulation or which shall only be used in accordance with these articles subject to certain conditions, available from: https://www.ema.europa.eu/system/files/documents/regulatory-procedural-guideline/vet_reg_cascade_list_report_en.pdf.

Overview of recommendations

Based on the evaluations presented in sections 2 and 3 of this scientific advice, 359 non-immunological substances and no immunological substance are recommended for inclusion in the list. Please refer to the table of section 4.

Points for further consideration

(i) This work is based on the information available and identified at the time of the assessment. It is anticipated that new information may be available in the future. For example, the authorisation of a first veterinary medicinal product for food-producing terrestrial species, or the authorisation of a first medicinal product for human use, may make eligible a substance currently not eligible for assessment. The same may result from the establishment of MRLs for new substances. On the contrary, the withdrawal of an authorisation of the only medicinal product containing the active substance concerned may make not eligible a substance currently eligible for assessment. Finally, new information on the environmental risk of an eligible substance may become available, that would raise the possibility of a change to the overall assessment against the criteria of Article 114(3) of Regulation (EU) 2019/6 and hence to the recommendation to include or not include in the list, or to recommend a specific risk mitigation measure. For these reasons, it is considered that the list would need to be revised in the future.

(ii) This work is based on the criteria set out in Article 114(3) of Regulation (EU) 2019/6 and on the other elements set out in the mandate from the Commission. These criteria do not formally include as such the usefulness of the substance for food-producing aquaculture[5] [6]. Consequently, a number of substances recommended for inclusion in the list do not have an identified use in food-producing aquatic species. Nevertheless, this report does indicate which substances have been identified by the aquaculture sector as important for the treatment of food-producing aquatic species.

(iii) The assessment against criterion (a) (risks to the environment) has been considered using accessible available information, however this assessment is not considered equivalent to a full environmental risk assessment described in Annex II of Regulation (EU) 2019/6.

[5] However, as indicated above, criterion (c) addresses the availability of other medicinal products
[6] However, as indicated above, the immunological substances were considered where the pathogens concerned are relevant for food-producing aquatic species

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1. Terms of reference and scope

1.1. Mandate from the European Commission to the EMA to provide scientific advice on the substances that may be considered for inclusion in the list

According to Article 114(3) of Regulation (EU) 2019/6 ('VMP Regulation'), the Commission is to establish, by means of implementing acts, a list of substances used in veterinary medicinal products authorised in the Union for use in food-producing terrestrial animal species or substances contained in a medicinal product for human use authorised in the Union in accordance with Directive 2001/83/EC or Regulation (EC) No 726/2004, which may be used in food-producing aquatic species in accordance with Article 114(1)('the list').

The Agency is requested to provide scientific advice on the substances that may be considered for inclusion in the list. The Agency's assessment of those substances must be based on the criteria laid down in article 114(3):

'(a) risks to the environment if the food-producing aquatic species are treated with those substances;

(b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6);

(c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species.'

Criterion (a) is about the risks associated with harmful effects that uses of a substance in accordance with Article 114(1) may cause to the environment. In the case of antimicrobials, the development of resistance as a result of exposure of the environment and the related risks for animal and public health are outside the scope of criterion (a). This aspect is considered under Article 107(6).

Criterion (b) is about the impact on animal and public health where food-producing aquatic species cannot be treated with antimicrobials which might not be allowed for use on the basis of Article 107(6).

Criterion (c) aims to underline the importance of the availability of treatment for food-producing aquatic species, which in the case of antimicrobial substances might also be impacted by any prohibition or conditions of use recommended in the Agency's scientific advice in relation to Article 107(6).

When performing the assessment, the Agency should take into account the following elements:

1. The overall objective of the VMP Regulation is to increase the availability of veterinary medicinal products, while guaranteeing the highest level of public and animal health and environmental protection.
2. Substances included in the Annex to Commission Implementing Regulation (EU) No 2022/1255 designating antimicrobials or groups of antimicrobials reserved for treatment of certain infections in humans[7] are prohibited for use in animals and outside the scope of this mandate.
3. Pursuant to Article 114(6), pharmacologically active substances included in the medicinal product used in accordance with paragraph 1 of that article need to be allowed in accordance with Regulation (EC) No 470/2009[8] and any acts adopted on its basis. Therefore, only the substances

[7] Commission Implementing Regulation (EU) 2022/1255 of 19 July 2022 designating antimicrobials or groups of antimicrobials reserved for treatment of certain infections in humans, in accordance with Regulation (EU) 2019/6 of the European Parliament and of the Council, available from: https://eur-lex.europa.eu/eli/reg_impl/2022/1255/oj/eng

[8] Regulation (EC) No 470/2009 of the European Parliament and of the Council of 6 May 2009 laying down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin, repealing Council Regulation (EEC) No 2377/90 and amending Directive 2001/82/EC of the European Parliament and of the

included in Table 1[9] of the Annex to Commission Regulation (EU) No 37/2010[10] and used in veterinary medicinal products authorised in the Union or contained in a medicinal product for human use authorised in the Union in accordance with Directive 2001/83/EC or Regulation (EC) No 726/2004 should be assessed against the criteria laid down in Article 114(3) and considered for the Agency's scientific advice. The substances included in Table 2 of that Annex are outside the scope of this mandate.

4. Antimicrobial substances that could be recommended for a prohibition or conditions of use in food-producing aquatic animals in the Agency's scientific advice requested by the Commission in relation to Article 107(6) should be assessed under the criteria laid down in Article 114(3).

5. Any scientific and technical evidence available that is relevant for the assessment of risks to the environment if the food-producing aquatic species are treated with the substances concerned.

6. Various productions systems in the EU, such as sea cages, ponds, raceways, on land recirculating aquaculture systems, and their specificities, as well as various routes of administration or pharmaceutical forms should also be taken into account when assessing substances under this mandate. In this respect, conditions of use and risk mitigation measures for the protection of the environment could be proposed in relation to the substances recommended for inclusion in the list.

Article 114(3) requires the Commission to adopt the implementing act at the latest by 27 January 2027.

The scientific advice was initially requested by the Commission by 30 November 2024. A 6-month extension was granted by the Commission, postponing the deadline to 31 May 2025.

1.2. Clarifications

Clarifications on the mandate were provided by the European Commission to the Agency and to the expert group. These clarifications are reported below.

General scope of the mandate

All eligible substances (please see the below clarification points, as well as section 2.1 Eligibility analysis) were considered within the scope of this mandate and then needed to be addressed, even when no need or use was identified for food-producing aquaculture.

Active substances contained in VMPs authorised in the Union for food-producing aquatic species.

According to Article 114(7), Article 114shall apply also when an authorised VMP is not available in the relevant Member State (e.g. due to shortages). The order laid down in Article 114(1) has to be respected. Only once the options under one paragraph of that article have been exhausted, may the options in the next paragraph be used.

However, since availability issues due to e.g. shortages are interconnected, it can also happen that VMPs for the same or another food-producing aquatic species, for the same indication or another indication are not available in the other Member States where they are authorised either. When the

Council and Regulation (EC) No 726/2004 of the European Parliament and of the Council (Text with EEA relevance), available from: https://eur-lex.europa.eu/eli/reg/2009/470/oj/eng

[9] All along this report, any reference to 'Table 1' should be understood to relate to Table 1 of the annex to Regulation (EU) No 37/2010

[10] Commission Regulation (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin (Text with EEA relevance), available from: https://eur-lex.europa.eu/eli/reg/2010/37(1)/oj/eng

options under Article 114(1)(a) have been exhausted, and in order to avoid animal welfare or animal health issues, veterinarians are allowed to use VMPs authorised for food-producing terrestrial species as described in Article 114(1)(b).

In practical terms, this means that veterinarians may also need to make recourse to veterinary medicinal products authorised in the EU for food-producing terrestrial animals or to medicinal products for human use authorised in the EU, containing substances that are also contained in (a) veterinary medicinal product(s) authorised in the EU for food-producing aquatic species.

Therefore, for the purposes of the scientific advice requested, the Agency needed to consider all active substances contained in VMPs authorised in any Member State for food-producing aquatic species where these substances are also contained in a VMP authorised in the EU for food-producing terrestrial animals or in a medicinal product authorised in the EU for humans, as required in Article 114(3).

Homeopathic substances

Homeopathic substances are within the scope of this mandate. Active substances of homeopathic veterinary medicinal products authorised, if any, in the Union for use in food-producing terrestrial animal species or of homeopathic medicinal products for human use authorised, if any, in the Union in accordance with Directive 2001/83/EC or Regulation (EC) No 726/2004 were to be considered by the expert group in their recommendations under the mandate, as long as these substances are allowed in accordance with Regulation (EC) No 470/2009 and any acts adopted on its basis. Active substances included in homeopathic veterinary medicinal products registered in the Union for use in food-producing terrestrial animal species or of homeopathic medicinal products for human use registered in accordance with Directive 2001/83/EC or Regulation (EC) No 726/2004, were considered outside the scope of this mandate.

Herbal substances

Herbal substances are within the scope of this mandate. The legislation of veterinary medicinal products does not envisage a special procedure for the placing on the market of traditional herbal products. Herbal substances used as active substances in veterinary medicinal products authorised in the Union for use in food-producing terrestrial animal species or contained as active substances in herbal medicinal products for human use authorised, if any, in the Union in accordance with Directive 2001/83/EC or Regulation (EC) No 726/2004 were to be considered by the expert group in their recommendations under the mandate, as long as these substances are allowed in accordance with Regulation (EC) No 470/2009 and any acts adopted on its basis.

Food additives

Food additives are within the scope of this mandate. Substances which are classified as food additives and are used as active substances in veterinary medicinal products authorised in the Union for use in food-producing terrestrial animal species or contained as active substances in medicinal products for human use authorised in the Union in accordance with Directive 2001/83/EC or Regulation (EC) No 726/2004 were to be considered by the expert group in their recommendations under the mandate, as long as these substances are allowed in accordance with Regulation (EC) No 470/2009 and any acts adopted on its basis.

Active substances versus excipients

Substances that are only allowed for use as excipients in accordance with Regulation (EC) No 470/2009 and any acts adopted on its basis are considered outside the scope of the mandate.

Substances whose use is not limited to excipients only and which are used as active substances in veterinary medicinal products authorised in the Union for use in food-producing terrestrial animal species or contained as active substances in medicinal products for human use authorised in the Union in accordance with Directive 2001/83/EC or Regulation (EC) No 726/2004 were to be considered by the expert group in their recommendations under the mandate, as long as these substances are allowed in accordance with Regulation (EC) No 470/2009 and any acts adopted on its basis.

Active substances of immunological medicinal products

Regulation (EC) 470/2009 does not apply to active principles of biological origin intended to produce active or passive immunity or to diagnose a state of immunity, used in immunological veterinary medicinal products [Article 1(2)]. Therefore, these active principles do not require an MRL assessment to be used in food-producing animals.

Immunological medicinal products fall within the scope of Article 114(1) and (2) as evident also from paragraph 4 of that Article.

Therefore, the active substances of immunological medicinal products were to be considered by the expert group as part of the mandate.

However, immunological medicinal products are linked to particular pathogens and pathogens are often species-specific. Therefore, the expert group had to consider active substances of immunological medicinal products for assessment only when the pathogens concerned affect food-producing aquatic species.

Beta-agonists

Beta-agonists are included in Annex II, List B of Directive 96/22/EC[11] , therefore they are prohibited substances with derogations. According to the same Directive, the derogations are the following:

- to induce tocolysis in cows when calving;
- to treat respiratory problems, navicular disease and laminitis and to induce tocolysis in Equidae.

The administration of beta-agonists to food-producing aquatic animals is illegal treatment. Therefore, these substances are considered outside of the scope of the mandate.

2. Eligibility analysis

Prior to the assessment of substances against the criteria laid down in Article 114(3), it was necessary to identify the substances that would be eligible for assessment. This section describes the methodology used for the eligibility analysis as well as the outcome of this analysis. The assessment of eligible substances is presented in section 3 of this report.

[11] Council Directive 96/22/EC of 29 April 1996 concerning the prohibition on the use in stockfarming of certain substances having a hormonal or thyrostatic action and of beta-agonists, and repealing Directives 81/602/EEC, 88/146/EEC and 88/299/EEC', available from: https://eur-lex.europa.eu/eli/dir/1996/22/oj/eng.

2.1. Non-immunological substances

2.1.1. Methodology for eligibility analysis

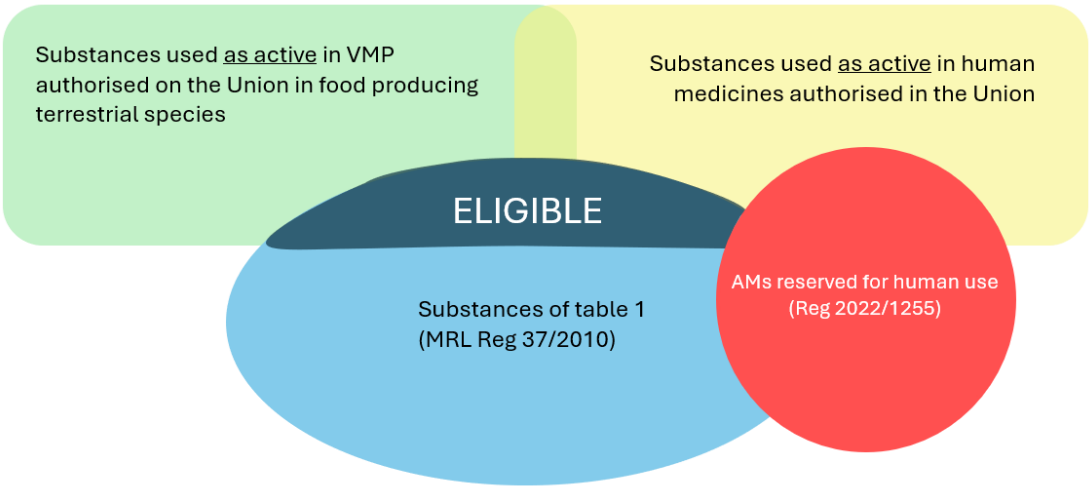
As per the mandate and the clarifications provided by the European Commission on the interpretation of this mandate, the substances to be assessed against the criteria laid down in article 114(3) need to meet three conditions:

(i) be in Table 1 (allowed substances) of the Annex to Commission Regulation (EU) No 37/2010 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin[12] [13] [14] [15], and

(ii) be active substances of veterinary medicinal products authorised in the Union for use in food-producing terrestrial animal species or be active substances of medicinal product for human use authorised in the Union, and

(iii) not be included in the Annex to Commission Implementing Regulation (EU) 2022/1255 designating antimicrobials or groups of antimicrobials reserved for treatment of certain infections in humans.

Consequently, the first step carried out was to determine which substances meet the three above conditions, i.e. which substances are eligible for assessment.



The point of departure was the Table 1 of the Annex to Commission Regulation (EU) No 37/2010. Indeed, all the eligible substances need to be in Table 1. The number of entries in this Table 1 (663) is much lower than the number of veterinary medicinal products (more than 45.000) or the number of medicinal products for human use (more than 157.000) or the number of active substances in these products (more than 3.900 active substances for veterinary use, more than 13.700 active substances for human use). Each of the 663 entries of Table 1 was considered. The information from Table 1 that was used was the column entitled 'Pharmacologically active substance'. The column entitled 'Other

[12] Table 1 of the Annex to Commission Regulation (EU) No 37/2010. Last accessed: November 2023 (consolidated version of 12 November 2023)
[13] Substances that are only allowed for use as excipients in accordance with Regulation (EC) No 470/2009 and any acts adopted on its basis are considered outside the scope of this mandate.
[14] Substances included in the 'list of chemical-unlike biological substances considered as not requiring an MRL evaluation as per Regulation (EU) No. 2018/782 with regard to residues of veterinary medicinal products in foodstuffs of animal origin' are considered within the scope of this mandate - if they also meet conditions (ii) and (iii)
[15] Active substances of immunological products are also considered within the scope of this mandate

Provisions'[16] was considered where appropriate for the eligibility analysis, i.e. where these other provisions had an impact on the decision to retain a substance as eligible for assessment: substance excluded since used as excipients or preservative only, substances excluded from the group entry for food additives, and substances identified as for use in homeopathic products only (see below approach when addressing questions (1) and (2). It is considered that the other 'Other Provisions' do not have any impact on the eligibility.

The entries that relate to a single substance were used directly.

The entries that were group entries were developed into several substances [except the group entry 'Substances used in homeopathic veterinary medicines']:

The group entry 'Food additives (substances with a valid E number approved as additives in foodstuffs for human consumption)' was developed into individual substances, according to Table 3 of Regulation (EC) No 1333/2008[17] of the European Parliament and of the Council which provides a Union list of food additives. The 'Other Provisions' column in Table 1 state 'Only substances approved as additives in foodstuffs for human consumption, with the exception of preservatives listed in part C of Annex III to European Parliament and Council Directive 95/2/EC', meaning that some food additives with E number are excluded from the group entry. These excluded food additives were not included unless they had a specific individual entry in Table 1. The food additives not excluded as per this exception were considered individually.

The group entry 'Sulfonamides ('all substances belonging to the sulfonamide group') was developed into 44 individual sulfonamide substances based on WHO ATC (ATCDDD - ATC/DDD Index) and WHO ATCVet indexes (ATCDDD - ATCvet).

The group entry 'Iodine and iodine inorganic compounds including: — Sodium and potassium iodide — Sodium and potassium iodate — Iodophors including polyvinylpyrrolidone-iodine' was developed into three individual substances, iodine, potassium iodide, and povidone iodinated.

The group entry 'stem cells' – from the list of chemical-unlike biological substances considered as not requiring an MRL evaluation as per Regulation (EU) No. 2018/782 with regard to residues of veterinary medicinal products in foodstuffs of animal origin - was developed into the relevant individual substances.

In total, the 663 entries in Table 1 lead to 985 substances (corresponding to 985 lines in the eligibility analysis table available in section 5.1). Each of these 985 substances was analysed to determine whether the substance is eligible for assessment.

Substances that are only allowed for use as excipients in accordance with Regulation (EC) No 470/2009 and any acts adopted on its basis are considered outside the scope of the mandate. Consequently, the 14 entries corresponding to the substances allowed as excipients only, as well as the 4 entries corresponding to preservatives only (which are by definition excipients) were considered not eligible for assessment. These 18 excipients are identified as 'out of scope' in the eligibility analysis table (see section 5.1).

Beta-agonists are included in Annex II, List B of Directive 96/22/EC[18], therefore they are prohibited substances with derogations. These derogations do not cover the use in food-producing aquatic species. Consequently, clenbuterol is identified as 'out of scope' in the eligibility analysis table (see

[16] All along this report, the reference to the 'Other Provisions' column should be understood to relate to the column of Table 1 of the annex to Regulation (EU) No 37/2010
[17] Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives, available from: https://eur-lex.europa.eu/eli/reg/2008/1333/oj/eng
[18] Council Directive 96/22/EC of 29 April 1996 concerning the prohibition on the use in stockfarming of certain substances having a hormonal or thyrostatic action and of beta-agonists, and repealing Directives 81/602/EEC, 88/146/EEC and 88/299/EEC', available from: https://eur-lex.europa.eu/eli/dir/1996/22/oj/eng

section 5.1) and considered not eligible for assessment. No other prohibited substances were identified.

For each of the remaining 966 substances, it was determined:

(1) whether it is an active substance in veterinary medicinal products authorised in the Union for use in food-producing terrestrial animal species as per the Union Product Database (UPD)[19]. In case of a positive answer, an example of such a veterinary medicinal product was mentioned.

(2) whether it is an active substance of medicinal products for human use authorised in the Union as per the Article 57 database[20]. In case of a positive answer, an example of such a medicinal product for human use was mentioned.

(3) whether it is a substance included in the Annex to Commission Implementing Regulation (EU) 2022/1255 designating antimicrobials or groups of antimicrobials reserved for treatment of certain infections in humans. Since this Annex refers not only to individual substances but also to groups of substances, the groups of substances were developed into individual substances. In practice, the only substances of this Annex which are also in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 are in the group of antimicrobials 'Combinations of cephalosporins with beta-lactamase inhibitors'.

The responses to questions (1) (2) and (3) were used to determine the eligibility for assessment as follows.

Table 1. Determination of eligibility

(1) Active substance in VMP in the EU for use in food-producing terrestrial animal species?	(2) Active substance in medicinal product for human use in the EU?	(3) Antimicrobial or groups of antimicrobials reserved for treatment of certain infections in humans?	Eligibility for assessment
Yes	Yes	No	**Yes**
Yes	No	No	**Yes**
No	Yes	No	**Yes**
No	No	-	**No**
-	-	Yes	**No**

Note: "-" means "Yes" or "No". Indeed, whatever the value of this field, the eligibility is not changed.

The response to the above questions (1) (2) and (3) were automated (scripts).

[19] The Union Product Database (UPD) serves as a single source of information on all authorised veterinary medicines and their availability in European Union (EU) and European Economic Area (EEA). EMA sets up and maintains the veterinary medicines information website and the Union Product Database, in collaboration with the Member States and the European Commission. Legal basis: Articles 56-57 of Regulation (EU) 2019/6. Available from: https://www.ema.europa.eu/en/veterinary-regulatory-overview/veterinary-medicinal-products-regulation/union-product-database

[20] EMA publishes data from the Article 57 database on all medicines authorised in the European Economic Area (EEA). Marketing authorisation holders must submit and maintain this information in accordance with EU legislation. Legal basis: Article 57 of Regulation (EC) No. 726/2004. Available from: https://www.ema.europa.eu/en/human-regulatory-overview/post-authorisation/data-medicines-iso-idmp-standards-post-authorisation/public-data-article-57-database

A preliminary manual step was conducted before the automated analysis in order to harmonise the substance names between Table 1 and databases or between databases. Indeed, the same substance may have different names in these different data sources.

Finally, the results of the automated analysis were manually checked and corrected as needed. The public interface of the Union Product Database[21] and the Article 57 database as publicly available[22] were the basis of the manual check for active substances in veterinary medicinal products authorised in the Union for use in food-producing terrestrial species and for active substances in human medicinal products authorised in the Union, respectively.

Mistakes identified and corrected during the manual review included:

- Listing of homeopathic medicinal products as examples for pharmaceutical or herbal/non-homeopathic active substances.
- Listing of non-authorised veterinary medicinal products.
- Listing of products in which the active substance is different than the one under eligibility analysis.
- Listing of products authorised in the United Kingdom only.
- Listing of products in which an excipient was mistakenly identified as an active substance.
- Incomplete information in medicinal product entry, with only dosages provided instead of the product itself.

For the substances used in homeopathic products, further to the responses to questions (1), (2), (3[23]), in determining the eligibility, consideration was given on identifying *authorised* (as opposed to *registered*) homeopathic products, as per the mandate and as clarified by the European Commission. This step was done manually. In doing so, for veterinary homeopathic products for use in food-producing terrestrial species, the entitlement type in the Union Product Database was checked. Products listed under the entitlement 'Homeopathic Registration' were considered registered (not authorised). For those listed under the entitlement 'Marketing Authorisation', the authorisation status was confirmed with National Competent Authorities (NCAs) via their website or via email. Human homeopathic products were considered authorised if listed in Article 57 database for active substances in human medicinal products authorised in the Union and not recorded by EMA as registered human homeopathic products.

As indicated above, when a substance was identified as an active substance in veterinary medicinal products authorised in the Union for use in food-producing terrestrial animal species or as an active substance of medicinal product for human use authorised in the Union, an example of such medicinal product was mentioned. This example of medicinal product is used only to illustrate the eligibility of the substance, not to recommend the use of this specific medicinal product in accordance with Article 114(1). Moreover, some of the medicinal products given as illustration contain a combination of active substances, and for this reason or another reason (e.g. pharmaceutical form, concentration) may not be suitable (or even not be allowed in case of combination of an eligible substance with non-eligible substance(s)) for the use in accordance with Article 114(1). Finally, the 'Other Provisions' in Table 1 of the Annex to Commission Regulation (EU) No 37/2010 were not considered when giving an example of medicinal product, except for the entry 'Food additives (substances with a valid E number approved as additives in foodstuffs for human consumption)' and for the entry 'Substances used in homeopathic

[21] Union Product Database. Last accessed: 2024, available from: https://www.ema.europa.eu/en/veterinary-regulatory/overview/veterinary-medicines-regulation/union-product-database.
[22] Article 57 product data. Last accessed: 2024, available from: https://www.ema.europa.eu/en/human-regulatory-overview/post-authorisation/data-medicines-iso-idmp-standards-post-authorisation/public-data-article-57-database.
[23] The response to Q3 was always no for homeopathics.

veterinary medicines'. It is up to the responsible veterinarian to select the appropriate medicinal product for use in accordance with Article 114(1).

When addressing questions (1) and (2), the below approach was followed:

- When the substance was identified as included in non-homeopathic medicinal products, only non-homeopathic medicines (including herbal non-homeopathic medicines) were considered.
- When the substance was identified as included in homeopathic medicinal products as per the 'Other Provisions', only *authorised* homeopathic medicines were considered.
- The entry in Table 1 of the annex to Regulation (EU) No 37/2010 for 'Substances used in homeopathic veterinary medicines' was considered as a unique entity complementing the individual entries for substances with homeopathic provisions and was not developed into several substances. The example given in Annex 5.1 to illustrate the eligibility of this entry is a homeopathic veterinary medicinal product for food-producing terrestrial animal authorised in the Union, containing several substances which do not have an individual entry in table 1 of the Annex to Regulation (EU) No 37/2010 and which meet the condition of concentration mentioned in the 'Other Provisions' column: 'does not exceed one part per ten thousand'. Should this entry be used in accordance with Article 114(1), it would be up to the responsible veterinarian to choose the appropriate substance and the appropriate veterinary medicinal product. No example of medicinal product for human use (see mention 'Not Applicable' in the eligibility table) was given since this would depend on the substance chosen, but there is no impact on eligibility since the entry is validated by an example of medicinal product for food-producing terrestrial animal.
- When the only identified medicine(s) were tests for allergy or allergotherapy, they were still considered despite the fact they may not be appropriate to deliver the right quantity of active substance.
- When the identified medicine(s) were radioactive, they were not considered.
- When the identified medicine(s) were cell therapy products based on autologous human cells, they were not considered.
- The sodium salts, lactate salts, sulphate salts, acetates, hydrochlorides and hydrates of an active substance were considered to be the same active substance, since their safety and efficacy is expected to be the same. However, for the entries in Table 1 mentioning only a specific salt (e.g. sodium salt), only this specific salt was considered.
- The bromide salts of an active substance were considered to be a different active substance, since their safety and efficacy is expected to be different.
- 17β-oestradiol was not considered due to its removal from Table 1 of Regulation (EU) No 37/2010 during this work as per Commission Implementing Regulation (EU) 2024/860 of 18 March 2024 amending Regulation (EU) No 37/2010 as regards the substance 17β-oestradiol[24].

[24] Commission Implementing Regulation (EU) 2024/860 of 18 March 2024 amending Regulation (EU) No 37/2010 as regards the substance 17β-oestradiol', available from: https://eur-lex.europa.eu/eli/reg_impl/2024/860/oj.

2.1.2. Eligibility table

The complete eligibility table is available in annex 5.1 and consists of the following columns:

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AMB[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Abamectin	Abamectin	yes	BULMECTIN® 0,2% medicated premix for cattle, sheep and horses	no		no	**yes**
No		Absinthium extract	Absinthium extract	no		yes	WERMUTKRAUT ZUR ANWENDUNG BEI ERWACHSENEN UND	no	**yes**

Important or out of scope substance: this column indicates whether the substance is considered important or not for the treatment of food-producing aquatic species [not used for eligibility analysis, See section 3.1.1], and whether the substance is out of scope (i.e. used as excipient only, or beta-agonist) [used for eligibility analysis]. This information is expressed in a "*yes*" or "*no*" or "out of scope" format.

Reason for important or for out of scope: when the substances are considered important, this column mentions why they are considered important (See section 3.1.1). When the substances are out of scope, this column mentions why they are considered out of scope.

1st step: substances in Table 1 of Regulation (EU) No 37/2010: this column contains the name of the substances as listed in the Table 1 of the Annex to Regulation (EU) No 37/2010.

2nd step: cleaned substances names: this column contains the name of the substances in the previous column adjusted after mapping them with the names in the EMA Substances Management System, which is the system used to identify substances in the EMA databases (including UPD and Article 57 database).

3rd step: analysis results: this column has 4 sub-columns that provide information about whether the substances are used in Human and Veterinary medicinal products.

- **VMP FP terrestrial (y/n):** this column contains information about whether the substance is used as active substance in a veterinary medicinal product (VMP) for food-producing terrestrial species as per UPD. This information is expressed in a "*yes*" or "*no*" format. See also point (1) of section 2.1.1.
- **VMP name example:** this column contains information on the name of the VMP whenever in the previous column there is a "*yes*". This column remains empty when a "no" is indicated in the previous sub-column. See also point (1) of section 2.1.1.
- **HMP (y/n):** this column contains information about whether the substance is used as active substance in a human medicinal product (HMP) as per Article 57 database. This information is expressed in a "*yes*" or "*no*" format. See also point (2) of section 2.1.1.
- **HMP name example:** this column contains information on the name of the HMP whenever in the previous column there is a "*yes*". This column remains empty when a "no" is indicated in the previous sub-column. See also point (2) of section 2.1.1.

AM reserved for human use: this column contains information about whether the substance is an antimicrobial reserved for human use. This information is expressed in a "*yes in combination with beta-lactamase inhibitors*" or "*yes in combination with cephalosporins*" or "*no*" format. Indeed, there was not any substance with an absolute "yes". See also point (3) of section 2.1.1.

Substance eligible for assessment: this column contains the outcome of the eligibility analysis of the substance based on the criteria explained in section *2.1.1 Methodology for eligibility analysis*. This information is expressed in a "*yes*" or "yes (not *in combination with beta-lactamase inhibitor)*" or "yes (not *in combination with cephalosporin)*" or "*no*" format.

2.1.3. Result of the eligibility analysis

The eligibility analysis based on the methodology presented in sections 2.1.1 and 2.1.2 identified 620 non-immunological substances eligible for assessment. See section 5.1.

2.2. Immunological substances

The scope of the mandate received from the EC was originally understood as limited to substances included in Table 1 of the Annex to Regulation (EU) No 37/2010 and, as such, not to include active substances used in immunological veterinary medicinal products (IVMPs). However, the European Commission subsequently clarified that Article 114(1) of Regulation (EU) 2019/6 apply to active substances used in IVMPs and that, therefore, these active principles should be considered as part of the mandate. However, it was also noted that IVMPs are linked to particular pathogens which are often species specific. Considering that, it was clarified that only active substances of IVMPs for which the pathogens concerned affect food-producing aquatic species should be considered as eligible.

2.2.1. Methodology for eligibility analysis

The aim of the eligibility analysis for immunological substances was to identify the pathogenic agents that affect food-producing aquatic species and for which there could be vaccines available for food-producing terrestrial species or humans.

The point of departure was the list of vaccines for fish authorised in the Union[25]. The manual of autogenous vaccines[26] was also consulted since it was considered useful information to identify these pathogenic agents, noting autogenous vaccines are not considered in the scope of the mandate.

Table 2. Pathogenic agents that affect food producing aquatic species and for which vaccines exist

Pathogen	Fish species	Commercial name	Country
Aeromonas salmonicida	Atlantic salmon	Aquavac FNM plus	Portugal
Aeromonas salmonicida	Rainbow Trout	Autogenous	Italy
Aeromonas salmonicida + *Vibrio anguillarum O1, O2*	Atlantic salmon	Alphaject 3000	Denmark, Finland, Iceland, Norway,
Aeromonas salmonicida, L.anguillarum O1,	Atlantic salmon	Pentium forte plus	

[25] EMA/CMDv/650880/2018-Rev.5, 'Veterinary Medicinal Products intended for fish', available from: https://www.hma.eu/veterinary-medicines/cmdv/procedural-guidance/miscellaneous.html.
[26] European Manufacturers of Autogenous Vaccines & Sera (EMAV), 'Manual of Autogenous Vaccines (AV)', Munich, Germany, 2023, available from: https://www.emav.be/publications.

Pathogen	Fish species	Commercial name	Country
O2a, Vibrio salmonicida, Moritella viscosa			
Aeromonas salmonicida, L.anguillarum O1, O2a, Vibrio salmonicida, Moritella viscosa, IPN Virus serotype Sp e A2	Atlantic salmon	Alpha ject micro 6 e 6-2	Ireland, Norway, UK
Aeromonas veronii biov. sobria	Sea bass	Autogenous	Italy, Greece
Betanodavirus, strain 1103	Sea bass	ICHTIOVAC VNN	Croatia, Italy, Spain, France, Greece, Portugal
Francisella noatunensis subsp orientalis	Tilapia	Autogenous	UK*
Infectious Spleen and Kidney Necrosis Virus	Tilapia	Autogenous	UK*
Lactococcus garvieae	Rainbow trout	Icthiovac LG	France, Greece, Italy, Portugal, Spain
	Rainbow trout	Lacto fish - Vax	Italy
	Rainbow trout	Autogenous	Italy, Spain, France
Lactococcus garvieae	sea bass and bream	Autogenous	Italy
Moritella viscosa	Atlantic salmon	ALPHA JECT Moritella	Norway
Moritella viscosa	Atlantic salmon	Autogenous	Norway
Nervous Necrosis Virus (RGNNV)	Sea bass	ALPHA JECT MICRO 1 NODA	Croatia, Italy, Spain, France
	Sea bass	MARIMARK N	Greece
Pasteurella atlantica genomovar salmonicida	Salmon	Autogenous	Norway
	Sea bass	AQUAVAC photobac prime	Cyprus

Pathogen	Fish species	Commercial name	Country
Photobacterium damselae subsp. piscicida	Sea bass	ICTHIOVAC PD	France, Greece, Spain
	Sea bass	Autogenous	Italy
Salmon pancreas disease virus proteins	Salmon	CLYNAV	All Member States
Salmon pancreas disease virus	Salmon	ALPHAJECT MICRO 1 PD	Ireland, Norway
	Salmon	NORVAX compact PD	Ireland, Norway, UK
Salmon pancreas disease virus, Infectious pancreatic necrosis virus, Aeromonas salmonicida subsp. salmonicida	Salmon	AQUAVAC PD 3	Ireland, UK
Streptooccus agalactiae	Tilapia	Autogenous	UK*
Streptococcus parauberis	Turbot	ICTHIOVAC STR (immersion, injection)	France, Greece, Portugal, Spain
Tenacibaculum spp.	Turbot	ICTHIOVAC TM	Spain
Tilapia Lake Virus	Tilapia	Autogenous	UK*
Vibrio anguillarum + *Ph. piscicida*	sea bass	ALPHA JECT	Croatia, Italy,
	sea bass	Icthiovac VR/PD	Croatia, France, Italy, Greece,
	sea bass	ALPHA JECT 2000	Croatia, Greece, Spain
Vibrio anguillarum + *Vibrio ordalii*	Rainbow trout	AQUAVAC Vibrio (immersion, injection)	Cyprus, France, Greece, Italy
Vibrio anguillarum + *V.ribrio ordalii*	Rainbow trout	AQUAVAC Vibrio oral	Cyprus, France, Greece, Italy, Portugal, Spain
Vibrio anguillarum O1 strainAL 112	Sea bass	ALPHA DIP VIB (immersion)	Croatia, Greece, Portugal, Spain

Pathogen	Fish species	Commercial name	Country
Vibrio anguillarum O1,O2 V.salmonicida, Aeromonas salmonicida, Moritella viscosa+ IPN	Atlantic salmon	ALPHAJECT micro 6	Ireland, UK
Vibrio anguillarum O1,O2 Vibrio salmonicida, Aeromonas salmonicida, Moritella viscosa+ IPN+Infectious Salmon AnemiaVirus (ISAV)	Atlantic salmon		Norway
Vibrio anguillarum O1,O2α e O2β strain	Sea bass, turbot	ICTHIOVAC VR (immersion, injection)	France, Greece
Vibrio anguillarum, Photobacterium damselae subsp. piscicida, Aeromonas salmonicida	sea bass	ALPHA JECT 3 FPV	Spain
Vibrio anguillarum, V ibrio salmonicida, Aeromonas salmonicida, Moritella viscosa	Atlantic salmon	ALPHAJECT 3-5	
Vibrio anguillarum, Vibrio salmonicida, Aeromonas salmonicida, Moritella viscosa+ IPN	Atlantic salmon	ALPHAJECT 6-2	Norway
Vibrio anguillarum	Cod	Autogenous	Norway
Vibrio harveyi	Sea bass	Autogenous	Italy
Yersinia ruckeri biotype 1 and 2	Atlantic salmon, Rainbow trout	AQUAVAC RELERA,	Czech Republic, France, Finland, Germany, Italy, Norway, Portugal, Slovakia, Spain, UK
Yersinia ruckeri O1 b	Atlantic salmon, Rainbow trout	ALPHA ERM	Norway

Pathogen	Fish species	Commercial name	Country
	Atlantic salmon, Rainbow trout	AQUAVAC ERM	Czech Republic, France, Germany, Greece, Ireland, Italy, Norway, Poland, Portugal, Slovakia, UK
	Atlantic salmon, Rainbow trout	AQUAVAC ERM oral	Czech Republic, Greece

* Autogenous vaccine to be used in Third Countries according to cooperation projects

The corresponding pathogens were extracted, adding those identified in the literature [27] [28] [29] [30] [31] [32] [33]. The expert group considered whether the pathogens identified from literature would need to be considered in relation to the identification of substances to be included in the eligibility analysis. After careful consideration, most of them were disregarded in view of the scarce association between pathogens affecting food-producing aquatic species and availability of vaccines for those pathogens for terrestrial food-producing species or humans. This is the case of parasites of aquatic species as there would be no chance to identify an authorised vaccine for terrestrial animals or for humans targeting these pathogens. In other instances, there are viruses that only affect a specific aquatic species and therefore there is no reason to consider these either, as there are no vaccines developed for any other aquatic, terrestrial or human species. Furthermore, there are certain pathogens with zoonotic potential referred to in the literature, however some of them were not considered as the exact role that aquatic animals play as vector in the cycle of certain zoonotic diseases is not fully understood. Overall, only a couple of bacteria were added in the table of relevant pathogens.

The table below reports the outcome of this exercise. For each relevant pathogen identified that affects food-producing aquatic species, it was determined whether it is also pathogenic for terrestrial animals or for humans, and whether a vaccine is authorised in the Union for either terrestrial food-producing species or for humans.

[27] Ziarati, M., Zorriehzahra, M.-J., Hassantabar, F., Mehrabi, Z., Dhawan, M., Sharun, K., Emran, T.-B., Dhama, K., Chaicumpa, W., Shamsi, S., 'Zoonotic diseases of fish and their prevention and control', Vet Q, 2022, Vol. 42(1), pp. 95-118.
[28] Novotny, L., Dvroska, L., Lorencova, A., Beran, V., Pavlik, I., 'Fish: A potential source of bacterial pathogens for human beings', Vet Med, 2004, Vol. 9, pp. 342-358.
[29] Elsevier. 'Vibrio parahaemolyticus'. n.d. Accessed August 2024, available from: https://www.sciencedirect.com/topics/immunology-and-microbiology/vibrio-parahaemolyticus.
[30] Chen, Y., Ai, X., Yang, Y., 'Vibrio cholerae: a pathogen shared by human and aquatic animals', Lancet Microbe, 2022, Vol. 3(6)., e402.
[31] Baker-Austin, C., Oliver, J.-D., Alam, M., Ali, A., Waldor, M.-K., Qadri, F., Martinez-Urtaza, J., 'Vibrio spp. infections', Nat Rev Dis Primers, 2018, Vol. 4(1).
[32] Parlapani, F.-F., Boziaris, I.-S., Mireles DeWitt, C.-A., 'Pathogens and their sources in freshwater fish, sea finfish, shellfish, and algae', In Knowles, M.-E., Anelich, L.-E., Boobis, A.-R., Popping, B., (Eds.), Present Knowledge in Food Safety, Elsevier, 2023, pp. 471-492.
[33] Elsevier. 'Vibrio vulnificus. n.d. Accessed August 2024, available from: https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/vibrio-vulnificus .

Table 3. Aquatic species pathogens, their relevance for terrestrial species or humans and availability of relevant vaccines for terrestrial species or humans.

List of fish pathogens (vaccines available for fish)	Pathogens for terrestrial or humans	Vaccines available for terrestrial or humans
Aeromonas salmonicida subspecies salmonicida	No	No
Aeromonas veronii biovar sobria	Only for immunocompromised humans	No
Betanodavirus (see also VNN)	No	No
Infectious pancreatic necrosis virus	No	No
Infectious Spleen and Kidney Necrosis Virus	No	No
Lactococcus garvieae	Only for immunocompromised humans	No
Moritella viscosa	No	No
Nervous Necrosis Virus (RGNNV)	No	No
Pasteurella atlantica genomovar salmonicida	No	No
Photobacterium damselae subspecies piscicida	No	No
Salmon pancreas disease virus	No	No
Streptococcus agalactiae	Only for immunocompromised humans	Yes
Streptococcus parauberis	Only for immunocompromised humans	No
Tenacibaculum spp.	No	No
Tilapia Lake Virus	No	No
Vibrio (Listonella) anguillarum	No	No
Vibrio harveyi	Only for immunocompromised humans	No
Vibrio ordalii	No	No
Vibrio parahaemolyticus Comment: can be included in the list as pathogens but only autogenous vaccines are available for fish	Yes	No
Vibrio salmonicida	No	No
Vibrio vulnificus Comment: can be included in the list as pathogens but only autogenous vaccines are available for fish	Yes	No
Yersinia ruckeri biotype 1 and 2	No	No

2.2.2. Result of the eligibility analysis

Based on this analysis, *Streptococcus agalactiae* is the only pathogen which affects both aquatic and terrestrial food-producing animals or humans, and for which there are vaccines authorised in the Union for terrestrial food-producing animals or humans. Consequently, *Streptococcus agalactiae* would be the only immunological active substance that would be potentially eligible for the list. However, a closer

review of the vaccines available against *Streptococcus agalactiae* showed that these contain several other active immunological substances in combination (multivalent vaccines). The other agents contained in such combinations – e.g. *Escherichia coli*, *Staphylococcus aureus*, *Pasteurella multocida*, *Hemophilus influenzae*, *Staphylococcus aureus*, *Streptococcus Pneumoniae* - are not regarded as of interest for food-producing aquatic species. Thus, it cannot be concluded that *Streptococcus agalactiae* is eligible.

Overall, none of the immunological substances identified could be regarded as eligible for assessment.

2.2.3. General review on the appropriateness to use in food-producing aquatic species some vaccines developed for food-producing terrestrial species or for humans

A literature review was also conducted to consider the relevance of the use of non-aquatic species vaccines in food-producing aquatic species. The review covered finfish, molluscs and crustaceans. The scope included the immunological particularities of aquatic species, the diseases, the types of vaccines and methods of administration. It was concluded that the inclusion of active substances used in immunological medicinal products in the list would seem scientifically inappropriate and may even cause stakeholders to question the scientific validity of the list and the regulatory authorities. Please refer to section 3.2.2.

3. Assessment of eligible substances

3.1. Assessment of non-immunological substances

3.1.1. Distinction between substances identified as important for the treatment of food-producing aquatic species and substances not identified as such

Due to the high number of eligible non-immunological substances, it was agreed to handle them according to their identified importance:

- Eligible substances identified by the aquaculture sector as important for the treatment of food-producing aquatic species. These substances were selected from among the eligible substances based on their identified interest for food-producing aquaculture, as indicated by current use in veterinary medicines authorised for food-producing aquatic species in the Union, or by needs identified by the FishMedPlusCoalition survey in December 2017[34], or by needs expressed or reported to the Expert Group by the Aquaculture Advisory Council, National Competent Authorities, CVMP or Experts of the Group. 48 substances were identified[35] [36]:

Table 4. Substances identified as important for the treatment of food-producing aquatic species

Eligible substances identified by aquaculture sector as important for the treatment of food-producing aquatic species		
Albendazole	Erythromycin	Monensin

[34] FishMedPlus Coalition, 'Fish Diseases Lacking Treatment Gap Analysis Outcome', 2017, available from: https://fve.org/cms/wp-content/uploads/Gap-Analysis-Outcome-Final2.pdf.
[35] Cypermethrin was initially identified as important for the treatment of food-producing aquatic species since it is the active substance of authorised veterinary medicinal product for fish. However, considering that cypermethrin is listed in current version of Annex X 'List of priority substances in the field of water policy' [i.e. is a substance of concern] of the Water Framework Directive, the substance was downgraded to the 'other substances'.
[36] Clavulanic acid was included in this group of 48 substances due to possible combination with amoxicillin which is in this group

Eligible substances identified by aquaculture sector as important for the treatment of food-producing aquatic species		
Ammonium lauryl sulphate	Fenbendazole	Neomycin (incl. framycetin)
Amoxicillin	Florfenicol	Oxfendazole
Amprolium	Flubendazole	Oxolinic acid
Bambermycin	Flumequine	Oxytetracycline
Benzocaine	Formaldehyde	Praziquantel
Bronopol	Gentamicin	Sodium chloride
Buserelin	Gonadorelin	Spectinomycin
Caryophylli aetheroleum (clove oil)	Human chorionic gonadotropin	Sulfadiazine
Chlortetracycline	Hydrogen peroxide	Sulfadoxine
Clavulanic acid	Isoeugenol	Thiamphenicol
Cooper sulphate	Ivermectin	Toltrazuril
Decoquinate	Levamisole	Tosylchloramide sodium
Deltamethin	Lincomycin	Trimethoprim
Doxycycline	Magnesium sulphate	Tylosin
Enrofloxacin	Menbendazole	Vitamin B1 (thiamine)

- The remaining substances, i.e. the 572 eligible substances not identified by aquaculture sector as important for the treatment of food-producing aquatic species.

Both groups of substances underwent an assessment that followed the same methodological approach but with differences in the level of detail. The difference arises because, with due note of the high number of substances included in the sub-group of substances not identified as important for food-producing aquatic species, and, in particular, as these substances are not considered important for aquaculture, they can be excluded from the list without the need to consider the appropriateness of risk mitigation measures if they pose a risk to the aquatic environment. On the other hand, for substances that are important for treatment of aquatic species, further consideration of the need for the substance and of possible risk mitigation measures is required in those cases where a risk to the environment is identified. Further information is provided in sections 3.1.2 and 3.1.3.

3.1.2. Methodology for assessment of eligible substances identified by aquaculture sector as important for the treatment of food-producing aquatic species

Template for assessment

<Active substance>

Include a brief introduction about the substance e.g. 'Florfenicol is a fluorinated amphenicol. This is a wide spectrum synthetic antibacterial used in terrestrial animals and fish.'

Include ATCvet classification[37] as needed.

For antimicrobials, include AMEG[38] classification.

[37] ATCvet Index Veterinary Anatomical Therapeutic Chemical code, WHO Collaborating Centre for Drug Statistics Methodology, available from: https://atcddd.fhi.no/atcvet/atcvet_index/.
[38] AMEG Categorisation of antibiotics used in animals, available from: https://www.ema.europa.eu/en/documents/report/infographic-categorisation-antibiotics-use-animals-prudent-and-responsible-use_en.pdf.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

If yes: the name of the VMP was included. The authorisation date was considered. Those VMPs authorised after October 2005 are the relevant for the ERA considering the date of effect of guideline VICH GL38 Environmental impact assessments for veterinary medicinal products[39] - Phase II. To review the most recently authorised product in UPD: Home | UPD (europa.eu)

If no: proceed to question 2.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Include the name (one-two examples) of the VMP or HMP and any other relevant details (if any).

Main assessment regarding the mandate criteria:

a) risks to the environment if food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

If no: proceed directly to consideration of thresholds.

If yes: first review if environmental information/recommendations/mitigation measures are included in the SPC or are available in the PuAR (public assessment report), and then proceed to consideration of thresholds.

SPC and PuAR can be found here: Home | UPD (europa.eu).

Depending on the QRD version of the SPC the environmental information can be found under sections:

- 4.5, 5.3 Environmental properties and 6.6 disposal advice or
- 3.5, 4.3 Environmental properties and 5.5 disposal advice.

In addition, the authorisation date should be considered. Those VMPs authorised after October 2005 are relevant for the ERA since only ERA carried out after 2005 could be considered as meeting the current ERA standards, considering the date of effect of guideline VICH GL38 Environmental impact assessments for veterinary medicinal products[33]- Phase II. This approach applies to both VMPs for aquatic animals and VMPs for terrestrial animals. Whenever possible, always review the most recently authorised product in UPD.

Additional thresholds to be considered:

The potential risks to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications….

Therefore, the environmental risk assessment under this mandate will be focused on the potential hazards of the substance due to its inherent properties.

[39] EMA/CVMP/ERA/418282/2005, 'Guideline on environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 and GL38', available from: https://www.ema.europa.eu/en/environmental-impact-assessment-veterinary-medicinal-products-support-vich-guidelines-gl6-gl38-scientific-guideline.

Sources of information

PuAR from the use of the substance in any authorised product in food-producing animals: https://medicines.health.europa.eu/veterinary/en

ECHA C&L inventory (the search is not intuitive, try different ways to include the name of the substance): https://echa.europa.eu/information-on-chemicals/cl-inventory-database (or substance search from https://echa.europa.eu/information-on-chemicals and then click C&L inventory)

ECHA chemTOX: https://chem.echa.europa.eu/

ECHA PBT: https://echa.europa.eu/pbt

PBT UBA list: List of putative PBT substances_UBA.xls

EFSA: EFSA | Science, safe food, sustainability (europa.eu)

EPA: CompTox Chemicals Dashboard (epa.gov)

NORMAN database: https://www.norman-network.com/nds/susdat/

PubMed: https://pubmed.ncbi.nlm.nih.gov/

PBT properties

Substances classified as PBT (persistant, bioaccumulative and toxic) or vPvB (very persistent and very bioaccumulative) are not to be included in the list because the use of such substance would require a full environmental assessment in context of marketing authorisation application in order to demonstrate the essentiality of the substance (Regulation (EU) 2019/6 – Article 37(2)(j)).

When the substance fulfils any of the individual criteria i.e. P, B or T, a potential risk to the environment cannot be excluded. The inclusion of the substance in the list would depend on the assessment against criteria b and c.

ED properties

Substances with recognized ED (endocrine disruption) properties can have potential serious risk for the environment due to their mechanism of action. However, some substances might be needed for the prevention or treatment of diseases or certain indications i.e. hormones, with regards to criterion c. In these cases, a potential risk for the environment might not be excluded, they should be assessed against criteria b (if applicable) and c. The final conclusion on hormones will depend on assessment against criterion c.

Other environmental hazards: CLP

To determine if the substance has been classified with any of the following hazard statements according to CLP regulation (Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures [40]).

H400 – Very toxic to aquatic life.

H410 – Very toxic to aquatic life with long lasting effects.

H411 – Toxic to aquatic life with long lasting effects.

[40] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006, available from: https://eur-lex.europa.eu/eli/reg/2008/1272/oj.

H412 – Harmful to aquatic life with long lasting effects.

H413 – May cause long lasting harmful effects to aquatic life.

The following hazard statements specific to GHS (Global Harmonised System[41]) should also be considered:

H401 – Toxic to aquatic life.

H402 – Harmful to aquatic life.

When the substance has been labelled with any of the above statements, a potential risk to the environment cannot be excluded. The inclusion of the substance in the list would depend on the assessment against criteria b and c.

Water Framework Directive (WFD)

If a substance is in the Annex X (Priority substances) of the Water framework directive (Directive 2000/60/EC establishing a framework for Community action in the field of water policy[42]) an environmental risk can be anticipated. The inclusion of the substance in the list would depend on the assessment against criteria b and c.

Specific precautions for some substances

Antiparasitics

According to VICH guidelines (GL6 and GL38), parasiticides should be assessed in phase II due to its ecotoxicological potential. When the substance is an antiparasitic a potential risk to the environment cannot be excluded. The inclusion of the substance in the list would depend on the assessment against criterion c.

Any other available information

Any other environmental information available in the scientific literature should be considered e.g. Pubmed.

Conclusion on the environmental risks

When any of the above triggers is fulfilled, the following conclusion should be reached:

- *An environmental risk cannot be excluded due to the intrinsic properties of the substance.*
- *If none of the above triggers is fulfilled the following conclusion should be reached:*
- *The information available does not allow to reach a conclusion on the environmental risks of the substance. The substance has no hazard classifications, and there is no other information that would indicate a risk to the environment when the substance is used as a veterinary medicine in aquatic species. Due to the inherent*

[41] United Nations Economic Commission for Europe (UNECE), 'Globally Harmonized System of Classification and Labelling of Chemicals (GHS)', United Nations, 2023, available from: https://unece.org/sites/default/files/2023-07/GHS%20Rev10e.pdf.
[42] Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy, available from: https://eur-lex.europa.eu/eli/dir/2000/60/oj.

properties of the substance, it is not expected that the use of the substance will pose an unacceptable risk for the environment.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

If no: no further consideration regarding criterion b needed.

If yes: include a reflection about the impact on animal and public health if the food-producing aquatic species affected cannot receive treatment with the substance.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107/6)?

If no: include the substance in the list.

If yes: proceed to question 2.

2. Is there an alternative substance (with lower risk for the environment)?

If no: consider whether additional information/recommendations/mitigation measures are needed and include the substance in the list with restriction/mitigations (if any).

If yes: proceed to question 3.

3. Is/Are the alternative substance/s enough to cover availability and avoid development of resistances (e.g. for antiparasitics – AMR resistance is not considered)?

If no: consider whether additional information/recommendations/mitigation measures are needed and include the substance in the list with restriction/mitigations (if any).

If yes: The substance CANNOT be included in the list.

When an environmental risk cannot be excluded the following should be considered:

- Possible options for reaching the conclusion that the substance cannot be included in the list:
  - *The substance is an antimicrobial and the Agency in its scientific advice under Article 107(6) recommended restrictions in the use of the substance in food-producing aquatic animals and the impact on animal and public health is [(not) significant/ negligible].*
  - *There are several treatment alternatives available. Only one or two alternatives are not considering enough to promote availability.*
- If any of the above options are fulfilled, the substance can be included in the list with mitigation measures. At least the following RMM should be included for <u>all substances</u> for which a potential environmental risk has been concluded:

<Substance X> is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[43] is required before discharge in the environment.

- Specific RMM from SPC or PuAR should be also considered.

Conclusion

Summarise the main conclusion (e.g. the substance is (not) proposed to be included in the list) and include the main mitigation measures/restrictions (if any) that should be associated to the substance.

Examples:

<Active substance> is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when <active substance> is used according to article 114 of Regulation (EU) 2019/6:

copy paste mitigation measures: general statement or specific statement.

<active substance> should not be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6 due to the following reasons:

<briefly describe the reasons for exclusion>

3.1.3. Methodology for assessment of eligible substances not identified by aquaculture sector as important for the treatment of food-producing aquatic species

The assessment of this group of substances followed the same methodological approach as outlined under section 3.1.2. However, with due note of the high number of substances included under this sub-group, and, in particular, as the substances are not considered important for aquaculture, there is less need to include them in the list if they pose a risk for the aquatic environment. Consequently, there was no need to consider possible risk mitigation measures.

[43] From EMA/CVMP/ERA/418282/2005, 'Guideline on environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 and GL38', available from: https://www.ema.europa.eu/en/environmental-impact-assessment-veterinary-medicinal-products-support-vich-guidelines-gl6-gl38-scientific-guideline.

3.1.3.1. Substances other than antiparasitics, antibacterials, antifungals and homeopathics

According to the mandate provided by the Commission, the overall objective of Regulation (EU) 2019/6 is to increase the availability of veterinary medicinal products, while ensuring the highest standards of public and animal health and environmental protection. When considering the criteria laid down in Article 114(3), any risks to the environment from the treatment of food-producing aquatic species (criterion (a)) is a key consideration for the assessment of eligible substances that have no identified important use in aquaculture. Criterion (b) as laid down in Article 114(3) becomes not applicable since no substance in this sub-group is an antimicrobial. With regards criterion (c), it is considered by default that for this sub-group of substances, there is not a lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species; therefore, criterion (c) was not considered further for these substances. This general approach with regards criterion (c), was considered not entirely applicable for hormonal substances identified within this sub-group as well as for the substances isoflurane and ketamine, as these substances might be potentially relevant to the aquaculture sector with regards criterion c) (see further details below).

Therefore, the overall key element for the assessment of these substances was the risk to the environment (criterion (a)). It is recognised that the potential risks to the environment as a consequence of the exposure of the environment due to the use of these substances in accordance with Article 114(1) cannot be addressed, as there are several data gaps that cannot be covered, e.g. dose and target species. Therefore, it was agreed that the environmental risk assessment would focus on the potential hazards of these substances due to their inherent properties. In the general case where criterion (c) was not considered further, only those substances for which an environmental risk is not identified based on the identification of hazard endpoints are recommended for inclusion in the list.

The detailed methodology for each of the criteria laid down in Article 114(3) is as follows:

- **Criterion (a) risk to environment**

As already indicated, the methodological approach for assessing these substances pertains to the environmental hazard identification. In doing so, each substance was searched for in the databases of ECHA (European Chemicals Agency), US EPA (Environmental Protection Agency)[44], and in safety data sheets (SDS), to determine whether it had been classified under any of the following statements according to CLP regulation[45]:

H400 – Very toxic to aquatic life.

H410 – Very toxic to aquatic life with long lasting effects.

H411 – Toxic to aquatic life with long lasting effects.

H412 – Harmful to aquatic life with long lasting effects.

H413 – May cause long lasting harmful effects to aquatic life.

The following statements specific to GHS were also considered:

H401 – Toxic to aquatic life.

H402 – Harmful to aquatic life.

[44] US EPA Environmental Protection Agency, CompTox Chemicals Dashboard, available from: https://comptox.epa.gov/dashboard/.
[45] With reference to the consolidated version of the Regulation (EC) No 1272/2008 on the classification, labelling and packaging of substances and mixtures (CLP Regulation).

PubChem[46] was used to find synonyms for the substances.

When the search in the above-mentioned databases did not retrieve a hazard endpoint, an additional (final) step for hazard identification involved searching the published literature with a view to identify any indication of potential risk of the substance to the aquatic environment.

As part of the environmental assessment, consideration was given to whether the substance is recognised as PBT or ED; indication of PBT properties would exclude the substance from the list; indication of ED properties for a substance not used as a hormone would exclude the substance from the list. For hormonal substances, ED properties can be assumed. However, in order to not discard hormonal substances of potential interest for aquaculture these substances were assessed against criterion (c) as below.

The above-mentioned search process stopped at the first indication of any environmental hazard.

- **Criterion (b) related to antimicrobials listed in accordance with Article 107(6)**

As already indicated, this criterion does not apply since none of these substances are antimicrobials.

- **Criterion (c) related to availability of alternatives**

With the exception of hormonal substances, and of ketamine and isoflurane, it was considered that these substances are not considered relevant for treating or preventing a disease or certain indication for which there is lack of availability of other treatments or measures since none of these substances had been identified as being immediately useful for the treatment of food-producing aquatic species. Consequently, when an issue related to criterion (a) was identified [i.e. a hazard to environment was identified], the conclusion would be negative [i.e. recommendation to not include in the list]. For hormonal substances, ketamine and isoflurane, consideration was given to whether the substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.

- **Conclusion**

With the exception of hormonal substances and of the substances isoflurane and ketamine, when an environmental hazard was declared/identified, the conclusion was as follows: "an environmental risk cannot be excluded", and the substance was recommended not to be included in the list. When no environmental hazard was declared/identified, the conclusion was as follows: "from the available information, a risk to the environment was not identified", and the substance was recommended for inclusion in the list.

For hormonal substances and for isoflurane and ketamine, a case-by-case decision was taken based on whether any of these would constitute an alternative treatment. Only in cases when the substance was deemed needed to treat or prevent a disease or certain indication for which there is lack of availability of other treatments or measures, the result would be positive [i.e. substance would be recommended for inclusion on the list]. For these substances, when it was concluded to recommend the inclusion in the list, risk management measures were considered.

- **Further clarifications**
  - **Limited data or no data available**

Given the high-level nature of this evaluation and the attention paid to the availability of medicinal products, in the absence of information or absence of evidence of aquatic hazard, the approach was to

[46] PubChem, available from: https://pubchem.ncbi.nlm.nih.gov/.

recommend the substance for inclusion in the list. In the following cases, it was considered that no hazard is declared/identified for the substance and the substance was proposed for inclusion in the list:

- Substance appears in ECHA, EPA, SDS database(s) with no hazard for aquatic environment but with other CLP/GHS notifications and literature search did not identify any aquatic hazard.
- Substance appears in ECHA, EPA database(s) but with no CLP, GHS notification information (i.e. substance with no hyperlink in the below table) and SDS database and literature search did not identify any aquatic hazard.
- Substance does not appear at ECHA, EPA, SDS databases and literature search did not identify any aquatic hazard.

– **Hazard indication from literature**

For a small number of substances (7 in total) no hazard was declared in ECHA, EPA, SDS databases but the literature search suggested a hazard for the aquatic environment. For these substances, the concentrations used in the studies, when those were available, were compared to the thresholds for classifying substances as hazardous to the aquatic environment as per the CLP regulation. The nature of the effects was also considered, i.e. whether they fall under the criteria for aquatic toxicity in the CLP regulation. The outstanding cases (ketamine, isoflurane) underwent an ad-hoc assessment factoring the usefulness of the substance for food-producing aquatic species for treating or preventing a disease or certain indication for which there is lack of availability of other treatments or measures.

– **Herbal substances**

The herbal substances eligible for assessment may include various parts of the plant, such as leaves, flowers, whole herbs, essential oils, fruits, roots, bark, seeds, and extracts. In cases where no ECHA, EPA, or SDS database entry was available for the specific part of the plant indicated by its name, the substance was linked to the closest available entry in the database, whether it pertains to the whole plant or another specific part, or extracts derived from them.

– **Harmonised and notified classifications**

Harmonised classification under the CLP Regulation is an official, EU-wide system for classifying hazardous substances. It ensures consistent safety standards across all EU member states and is mandatory for manufacturers, importers, or users of these substances. These classifications are listed in Annex VI of the CLP Regulation. On the other hand, notified classifications are provided by manufacturers, importers, or users through C&L notifications or registration dossiers. While these classifications are not mandatory, they are shared with ECHA for reference and can be updated by the notifier. ECHA maintains the C&L Inventory but does not verify the accuracy of the information.

For substances listed in the C&L Inventory with both harmonised and notified classifications, both are included in the assessments, with hyperlinks provided for each classification type ('harmonised' and 'notified').

- **Assessment template**

These steps are summarised in the table below, which represents the assessment template:

Substance	**Data available on toxicity**	**Conclusion**	**Include in list**
<Substance> [general case]	Brief introduction:<text> - Hazard from ECHA - Hazard from EPA - Hazard from SDS - Hazard from published literature - Consider PBT or ED	<From the available information, a risk to the environment was not identified.> OR <An environmental risk cannot be excluded.>	<Yes> OR <No>
<Substance> [case of hormones, isoflurane and ketamine]	Brief introduction:<text> - Hazard from ECHA - Hazard from EPA - Hazard from SDS - Hazard from published literature - Consider PBT or ED Ad-hoc assessment in relation to criterion c)	<Despite the potential risk(s) due to XX identified under criterion a), the substance is needed with regards criterion c).> OR <Potential risk(s) due to XX are identified under criterion a), and the substance is not needed with regards criterion c).>	<Yes and add RMM if needed > OR <No>

3.1.3.2. Antiparasitic, antibacterial and antifungal substances

According to the mandate provided by EC, the overall objective of Regulation (EU) 2019/6 is to increase the availability of veterinary medicinal products, while guaranteeing the highest standards of public and animal health and environmental protection. When considering the criteria laid down in Article 114(3), any risks to the environment from the treatment of food-producing aquatic species (criterion (a)) is a key consideration for the assessment of eligible substances that have no identified important use in aquaculture. It is recognised that the potential risks to the environment as a consequence of the exposure of the environment due to the use of these substances in accordance with Article 114(1) cannot be addressed, as there are several data gaps that cannot be covered (e.g. dose and target species). Therefore, it was agreed that the environmental risk assessment would be focused on the potential hazards of these substances due to their inherent properties. Criterion (b) as laid down in Article 114(3) is applicable for the antibacterials in this sub-group of substances. With regards to criterion (c), this sub-group of substances is deemed of relevance for treating or preventing a disease or certain indication for which there is lack of availability of other treatments or measures, as even though they are not recognised as important for treatment of food-producing aquatic species, their pharmacological activity indicates potential usefulness for such purpose.

The detailed methodology for each criterion laid down in Article 114(3) is as follows:

- **Criterion (a) risk to the environment**

The methodological approach for assessing these substances against criterion (a) is in line with the methodological approach followed for substances other than antiparasitics, antibacterials, antifungals and homeopathics (for the detailed methodological approach see section 3.1.3.1).

For this group of substances, as part of environmental assessment, consideration was given to whether the substance is recognised as PBT or ED; indication of such properties would exclude the substance from the list.

For the antiparasitics, it was agreed that there is no need to assess against thresholds, since a risk of these substances for the environment cannot be excluded due to the nature of the antiparasitic activity. However, for information purposes only, the stepwise approach for hazard identification, as outlined in section 3.1.3.1, was applied in the assessment of antiparasitics. It should be noted that the CLP statements on aquatic toxicity (H400, H410, H411, H412, H413, H401, H402) are based on toxicity observed in three types of organisms: fish, crustaceans and algae. They do not capture the toxicity of anthelmintics for worms. As a result, some anthelmintics may not have been assigned hazard classifications, though this does not exclude an environmental risk from these substances.

- **Criterion (b) related to antimicrobials listed in accordance with Article 107(6)**

Some antibacterials in this sub-group of substances are either not recommended for use under Article 114 of Regulation (EU) 2019/6 for food-producing aquatic species in the scientific advice under Article 107(6), or are recommended for use in individual animals only. A 'Yes' in the relevant column of the assessment against criterion (b) means the use of the antibacterial is subject to one of the two restrictions above. A 'No' means it is not.

- **Criterion (c) related to availability of alternatives**

When an issue related to criterion (a) [i.e. hazard to environment is identified] and/or (b) [i.e. the substance is recommended for restrictions in food-producing aquatic species in the scientific advice related to Article 107(6)] was identified, the substance was assessed against criterion (c) [i.e. availability of alternatives]. Such assessment was conducted by ATCvet groups rather than by individual substances.

- **Conclusion**

When there was no issue related to criteria (a) and (b), no further assessment with regards criterion (c) was warranted and the conclusion was proposed as follows: "From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under article 107(6)", and the substance is recommended to be included in the list. When there was an issue with criteria (a) and/or (b), the substance was assessed against criterion (c). The conclusion was then as follows: "Despite the risk(s) identified under <criterion a)> <criterion b)> <criteria a) and b)>, the substance is needed with regards criterion c)", and the substance was recommended for inclusion in the list with risk mitigation measures (RMM) if needed, or "Risk(s) are identified under <criterion a)> <criterion b)> <criteria a) and b)>, and the substance is not needed with regards criterion c)", and the substance is recommended to not be included in the list.

- **Assessment template**

The above-mentioned steps are summarised in the tables below, which represent the assessment templates:

Antibacterials

Substance	Assessment against mandate criteria		Conclusion	Include in list
<Substance>	<Brief introductory text>		If no issue with (a) nor (b): <From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under article 107(6).> If issue with (a) or (b): <Despite the risk(s) identified under <criterion a)> <criterion b)> <criteria a) and b)>, the substance is needed with regards criterion c).> OR <Risk(s) are identified under <criterion a)> <criterion b)> <criteria a) and b)>, and the substance is not needed with regards criterion c).>	<Yes> Or <Yes, and add RMM if needed> <No>
	<ATCvet>			
	<AMEG>			
	Criterion (a)	- Hazard from ECHA - Hazard from EPA - Hazard from SDS - Hazard from published literature - Consider PBT or ED.		
	Criterion (b)	<Yes> <No>		
	Criterion (c)	If issue with (a) or (b) assess against (c) per ATCVet group and mention the alternatives; otherwise, add 'N/A'.		

Antiparasitics

Substance	Assessment against mandate criteria		Conclusion	Include in list
<Substance>	<Brief introductory text>		<Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).> OR	<Yes, and add RMM if needed>
	<ATCvet>			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *- Hazard from* ECHA *- Hazard from* EPA *- Hazard from* SDS		

Substance	Assessment against mandate criteria		Conclusion	Include in list
		- *Hazard from published literature* - *Consider PBT or ED*	< Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.>	<No>
	Criterion (b)	N/A		
	Criterion (c)	Since there is always issue with (a), assess against (c) per ATCVet group and mention the alternatives		

Antifungals

Substance	Assessment against mandate criteria		Conclusion	Include in list
<Substance>	<Brief introductory text>		If no issue with (a): <From the available information, a risk to the environment was not identified.> If issue with (a): <Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).> OR <Risk(s) are identified under criterion a), and the substance is not needed with regards criterion c).>	<Yes> Or <Yes, and add RMM if needed> <No>
	<ATCvet>			
	Criterion (a)	- Hazard from ECHA - Hazard from EPA - Hazard from SDS - Hazard from published literature - Consider PBT or ED.		
	Criterion (b)	N/A		
	Criterion (c)	If issue with (a) assess against (c) per ATCVet group and mention the alternatives; otherwise, add 'N/A'.		

3.1.3.3. Homeopathic substances

- **Criterion (a) risk to environment**

Due to the high level of dilution of these substances in homeopathic veterinary medicinal products and in homeopathic medicinal product for human use, the concentrations of these substances in the environment are expected to be very low. Consequently, it is considered that there is negligible risk to the aquatic environment.

These substances shall be used under homeopathic conditions (specified in Table 1 of the Annex of Regulation (EU) No 37/2010) and consequently the exposure of the environment to these substances is very low. As a general principle, the 'Other Provisions' in Table 1 of Regulation (EU) No 37/2010 also apply to use under Article 114 of Regulation (EU) 2019/6. For homeopathic substances, these 'Other Provisions' restrict the use to homeopathic veterinary medicinal products and sometimes to concentration limits.

- **Criterion (b) related to antimicrobials listed in accordance with Article 107(6)**

None of these substances is an antimicrobial recommended for restrictions in the scientific advice of the Agency under Article 107(6).

- **Criterion (c) related to availability of alternatives**

Since there is no issue related to criterion (a) or (b) [i.e. no hazard to environment is expected, and there is no recommendation for restriction in the Agency's scientific advice related to Article 107(6)], there is no need to consider criterion (c), and the substances can be recommended for inclusion in the list.

- **Conclusion**

The conclusion is as follows: "the risk to the environment is considered negligible", and the substance is recommended for inclusion in the list.

The recommendation includes the following specific condition: The substance shall be used in line with the homeopathic conditions specified in table 1 of the Annex of Regulation (EU) No 37/2010.

Note: this recommendation to include the substance in the list does not factor the usefulness for food-producing aquaculture.

- **Assessment template**

The above is summarised in this tabulated assessment template:

Substance	Data available on toxicity	Conclusion	Include in list
<Substance>	<Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use>	<The risk to the environment is considered negligible.>	<Yes>

3.1.4. Result of assessment of eligible substances identified by aquaculture sector as important for the treatment of food-producing aquatic species

Based on the methodology presented in section 3.1.2:

- 45 non-immunological substances identified by aquaculture sector as important for the treatment of food-producing aquatic species are recommended to be included in the list: albendazole, ammonium laurylsulphate, amoxicillin, amprolium, benzocaine, bronopol, buserelin, *Caryophylli aetheroleum* (clove oil), chlortetracycline, copper sulphate, decoquinate, deltamethrin, doxycycline, enrofloxacin, erythromycin, fenbendazole, florfenicol, flubendazole, flumequine, formaldehyde, gentamicin, gonadorelin, human chorionic gonadotropin, hydrogen peroxide, isoeugenol, levamisole, lincomycin, magnesium sulfate, mebendazole, monensin, neomycin, oxfendazole, oxolinic acid, oxytetracycline, sodium chloride, praziquantel, spectinomycin, sulfadiazine, sulfadoxine, thiamphenicol, toltrazuril, tosylchloramide sodium, trimethoprim, tylosin and vitamin B1 (thiamine).
- 3 non-immunological substances identified by aquaculture sector as important for the treatment of food-producing aquatic species are recommended to not be included in the list: bambermycin, clavulanic acid, and ivermectin.

For further information including risk management measures, please refer to the recommendation table in section 4 Conclusion and recommendations, and to the assessment reports in section 5.2.1.

3.1.5. Result of assessment of eligible substances not identified by aquaculture sector as important for the treatment of food-producing aquatic species

3.1.5.1. Substances other than antiparasitics, antibacterials, antifungals and homeopathics

Based on the methodology presented in section 3.1.3.1:

- 216[47] non-immunological substances other than antiparasitics, antibacterials, antifungals and homeopathics and not identified by aquaculture sector as important for the treatment of food-producing aquatic species are recommended to be included in the list.
- 223 non-immunological substances other than antiparasitics, antibacterials, antifungals and homeopathics and not identified by aquaculture sector as important for the treatment of food-producing aquatic species are recommended to not be included in the list.

For further information including risk management measures, please refer to the recommendation table in section 4 Conclusion and recommendations, and to the assessment report in section 5.2.2.

3.1.5.2. Antiparasitic, antibacterial and antifungal substances

Based on the methodology presented in section 3.1.3.2:

- Antiparasitic substances not identified by aquaculture sector as important for the treatment of food-producing aquatic species
  - 2 antiparasitic substances are recommended to be included in the list: albendazole oxide and imidocarb
  - 33 antiparasitic substances are recommended to not be included in the list: abamectin, alphacypermethrin and cypermethrin, amitraz, clorsulon, closantel, coumafos, cyfluthrin, derquantel, diazinon, diclazuril, dicyclanil, doramectin, eprinomectin, febantel, flumethrin, fluralaner, halofuginone, monepantel, morantel, moxidectin, netobimin, nitroxinil,

[47] Including *Hamamelis virginiana* which is also eligible as homeopathic substance (see the relevant assessment concluding also to inclusion in the list)

oxibendazole, oxyclozanide, permethrin, phoxim, piperazine, pyrantel embonate, rafoxanide, tau-fluvalinate, thiabendazole, and triclabendazole

- Antibacterial substances not identified by aquaculture sector as important for the treatment of food-producing aquatic species
  - 57 antibacterial substances are recommended to be included in the list: ampicillin, apramycin, bacitracin, benzylpenicillin, cefacetrile, cefalexin, cefalonium, cefapirin, cefazolin, cefoperazone, cefquinome, ceftiofur, cloxacillin, danofloxacin, dicloxacillin, difloxacin, dihydrostreptomycin, gamithromycin, kanamycin, marbofloxacin, nafcillin, natamycin, novobiocin, oxacillin, paromomycin, penethamate, phenoxymethylpenicillin, pirlimycin, rifaximin, spiramycin, streptomycin, sulfamethizole, sulfadimidine, sulfapyridine, sulfafurazole, sulfanilamide, sulfathiazole, sulfamethoxazole, sulfadimethoxine, sulfamethoxypyridazine, sulfamerazine, sulfamethizole, sulfachlorpyridazine, sulfaquinoxaline, sulfamerazine, sulfamonomethoxine, sulfacetamide, formosulfathiazole, phthalylsulfathiazole, sulfaguanidine, tetracycline, tiamulin, tildipirosin, tilmicosin, tulathromycin, tylvalosin, and valnemulin
  - 2 antibacterial substances are recommended to not be included in the list: mecillinam and colistin
- Antifungal substances not identified by aquaculture sector as important for the treatment of food-producing aquatic species are recommended to be included in the list
  - 2 antifungal substances are recommended to be included in the list: enilconazole and parconazole
  - No antifungal substance is recommended to be excluded from the list

For further information including risk management measures, please refer to the recommendation table in section 4 Conclusion and recommendations, and to the assessment report in section 5.2.3.

3.1.5.3. Homeopathic substances

Based on the methodology presented in section 3.1.3.3, all the eligible homeopathic substances are recommended to be included in the list: *Adonis vernalis, Aesculus hippocastanum, Agnus castus, Ailanthus altissima, Allium cepa, Apocynum cannabinum, Artemisia abrotanum, Atropa belladonna, Bellis perennis, Calendula officinalis, Camphora, Cardiospermum halicacabum, Convallaria majalis, Crataegus, Echinacea, Eucalyptus globules, Euphrasia officinalis, Ginkgo biloba, Ginseng Hamamelis virginiana*[48]*, Harpagophytum procumbens, Harunga madagascariensis, Hypericum perforatum, Lobaria pulmonaria, Okoubaka aubrevillei, Phytolacca americana, Prunus laurocerasus, Selenicereus grandifloras, Serenoa repens, Silybum marianum, Solidago virgaurea,* Substances used in homeopathic veterinary medicines, *Syzygium cumini, Thuja occidentalis, Turnera diffusa, Urginea maritima, Virola sebifera,* and *Viscum album*.

The following condition is applicable to all eligible homeopathic substances: The substance shall be used in line with the homeopathic conditions as specified in Table 1 of the Annex of Regulation (EU) No 37/2010.

Please refer to the recommendation table in section 4 Conclusion and recommendations, and to the assessment report in section 5.2.4.

[48] *Hamamelis virginiana* is also eligible as herbal non-homeopathic substance (see the relevant assessment concluding also to inclusion in the list)

3.2. Assessment of immunological substances

3.2.1. Assessment of specific substances

As reported in section 2.2.1, the approach based on pathogens affecting both food-producing aquatic species and [food-producing terrestrial species or humans] lead to the conclusion that there is no immunological substance eligible for assessment.

3.2.2. General considerations on the appropriateness to use some vaccines developed for food-producing terrestrial species or for humans in food-producing aquatic species

Despite the clear outcome from the eligibility analysis, it was felt appropriate to conduct a literature review to discuss the relevance of the use of vaccines designed and authorised in non-aquatic species (i.e. food-producing terrestrial species or humans) in food-producing aquatic species. The review covered scientific evidence for finfish, molluscs and crustaceans. The scope of this review included the immunological particularities of aquatic species, the diseases, the types of vaccines and methods of administration.

In reflecting on the question of which pathogens infect aquatic species and might be targeted by vaccines authorised for food-producing terrestrial species and humans, it is noted that the target pathogen is only one of the factors to consider. Other critical factors include the comparability of immune systems between terrestrial and aquatic species, the influence of the aquatic species environment (e.g. temperature, salinity, pH), knowledge of relevant dosing regimens, and the routes by which IVMPs might be administered. Additionally, as most fish are vaccinated when they are quite small, there is a limit to the volume that can be safely injected.

In evolutionary terms, teleost (bony fish) fishes are animals where basic aspects of the immune system of higher vertebrates are observed for the first time. Fish acquired immune responses are characterized with less specificity, diversity and memory compared to those of mammals and, even among the relatively few fish species commercially farmed in the E.U. today, fish immunity does not behave homogenously between species. The number of fish species is also significantly higher (>30.000 teleosts) than the number of mammalian species (~5500) and the evolutionary distances, even between different teleost families, are considerably larger than between mammalian families, with the result that major differences are likely to exist in the way different aquatic species combat pathogens, and consequently in their response to vaccines.

Although significant progress has been made in the fields of fish immunology and vaccinology, vaccination strategies have remained largely unchanged over the last 10 years. As reviewed by Bedekar & Kole (2022), various challenges continue to impede development of fish vaccines, the most critical being the identification of protective antigens, which is complicated by the diversity of fish species. Most fish pathogens have a wide range of susceptible hosts, which may behave differently to each other from an immunological perspective. Lack of detailed knowledge of the immune systems in different fish species limits the possibilities to study both pathogen and vaccine-induced immunity. Variations observed in susceptibility and clinical signs of an infection caused by a pathogen from species to species are, primarily, due to differences in the immune defence mechanisms of different fish species. Several studies have emphasised that what we know of the pathogen–host association in one species can seldom be transferred to another fish species (Magnadottir, 2010).

Indeed, in a review of fish vaccines in use in aquaculture, Sommerset et al. (2005) report that, for bacterial vaccines, since different serotypes might be involved in disease outbreaks, vaccines designed for one fish species cannot automatically be used in another fish species; this is particularly true in

relation to transfer from non-marine to marine species, and vice versa. With regards to viral fish vaccines, current available vaccines for aquaculture are mostly based on inactivated virus or recombinant subunit proteins. Inactivated/killed viral vaccines are generally not efficacious unless delivered by injection and relatively high doses are needed to achieve protection; the selection of adjuvant is of the outmost importance for these. On the other hand, despite their ability to induce good protection in laboratory studies, live vaccines have generally been demonstrated to be unsafe for field use. For example, residual virulence and uncertainty about their effects on other aquatic species made attenuated vaccines against the infectious haematopoietic necrosis (IHN) of salmonids poor candidates for licensing (Winton, 1997); also, the level and duration of protection offered was inversely correlated with the degree of attenuation (Roberti et al., 1998). No parasite vaccines are commercially available as yet.

Another critical factor in successful fish vaccination is the role external factors like temperature, light, water quality, salinity and different stress inducers play in influencing the immune response in vaccinated fish (Magnadottir, 2010). In ectothermic or poikilothermic animals, environmental changes can have significant effects on the immune system. It is commonly stated that innate parameters are more active at low temperatures while parameters of the adaptive system tend to be suppressed. Another generally accepted paradigm is that stress, especially chronic stress, will suppress immune response and lower disease resistance.

The first fish immersion vaccines proved to be effective in the USA in the 1970s. Injectable vaccines containing adjuvants were developed in the early 1990s. Following years of testing with different vaccine adjuvants and a range of different antigen combinations, it became evident that administering multiple antigens in a single oil-adjuvanted vaccine was the preferred approach. For practical reasons, there is a reluctance to include more than one vaccination during a production cycle (e.g. one of the most extensively used vaccines for salmon contains antigens for six different pathogens) (Sommerset et al., 2005).

Progress made over the last four decades has led to developing and licensing fish vaccines which comprise whole killed, live-attenuated, peptide subunit, DNA and recombinant protein (Bedekar & Kole, 2022). However, the majority of successful commercial fish vaccines are based on killed whole-cell bacteria preparations in intraperitoneal injection formulations.

As for their terrestrial counterparts, vaccine design is typically based on the characteristics of the target pathogen as well as other practical considerations such as size and value of target species to which it is to be administered. The method of administration is a crucial step in the development and efficacious use of a fish vaccine. Three main routes of administration are described in fish (Bedekar & Kole, 2022): injection, immersion and oral.

- Injection vaccination is the conventional approach of vaccine delivery to fish, with the intraperitoneal route being preferred for most vaccines and the intra-muscular route preferred for DNA vaccines. The injection route is also the most potent and gives a high level of long-lasting immunity to the recipient host (believed to be dependent on the depot effect). It is labour-intensive and non-feasible for the smallest-sized fish (<20 g). The method is highly stressful for the animal.
- Immersion involves two methods: dip vaccination (high dose vaccine for a short time) and bath vaccination (diluted vaccine for a more extended period); wherein the antigens are taken up by the skin, gills or gut. It is the simplest form of vaccine delivery system for fish and has proved to be effective for mass vaccination. However, the uptake of antigens is limited compared to injection, which results in short-term immunity or moderate to low protection in most instances.

- Oral vaccination, while it might seem the ideal method of administration (it is non-stressful and can be used for vaccinating all fish sizes), the development of efficacious and safe oral vaccines has been a challenge due to significant limiting factors, e.g. ensuring even dose administration throughout the targeted population, or ensuring that antigens are stable in the highly acidic gut (stomach and foregut) environment without degradation before reaching the hindgut, wherein they can be processed by the immune cells.

The majority of vaccines authorised for food-producing terrestrial animals and humans are designed for subcutaneous or intramuscular administration, routes which may be impractical or impossible in aquatic species, while the impact of administration by alternative routes more adapted to use in aquatic species is entirely unknown. Appropriate dosing regimens for use in aquatic species would be equally unknown.

Overall, it is considered that uncertainties resulting from

- the differing immune systems of terrestrial species, humans and aquatic species
- the heterogeneity of aquatic species immune systems
- the influence of the aquatic environment (e.g. temperature, light, water quality, salinity) on the immune systems of aquatic species
- formulation factors (e.g. inclusion of an adjuvant)
- appropriate dosing regimens including routes of administration
- the practicalities of administering vaccines to aquatic species

mean that the likelihood of achieving clinically relevant results from administration of vaccines authorised for food-producing terrestrial species and humans to aquatic species is extremely low. Indeed, it is questionable whether such use could be considered "therapeutic" (it is noted that use of a product in accordance with Article 114(1) is focused in particular on avoiding unacceptable suffering to the treated animal). Administration of vaccines authorised for use in terrestrial species and humans to aquatic species might better be considered "experimental".

In light of the above, it is considered that inclusion of active principles used in immunological medicinal products in the list referred to in Article 114(3) would seem scientifically inappropriate and may even cause stakeholders to question the scientific validity of the list and the regulatory authorities. For bacterial diseases where no authorised fish vaccine is available, the veterinarian would use an inactivated immunological veterinary medicinal product manufactured from the relevant pathogen, as defined in Article 2(3) of Regulation (EU) 2019/6. Consequently, only vaccines against viral diseases in food-producing terrestrial animals or humans would be of even theoretical interest. However, it is also noteworthy that the likelihood of veterinarians actually using vaccines authorised for food-producing terrestrial species and humans in aquatic species is so low that the resulting environmental exposure and impact is expected to be extremely limited.

In line with this, the European Commission noted that immunological medicinal products are linked to particular pathogens that are often species-specific, and clarified that active substances of immunological medicinal products should be considered for assessment only when the pathogens concerned affect food-producing aquatic species. This review supports that no active substances of immunological medicinal products should be recommended for inclusion in the list.

3.3. Uncertainties and data gaps

Uncertainties and data gaps were identified in the process of developing the advice:

- There were limited data for the environmental risk assessment. The potential risks to the environment as a consequence of the exposure of the environment associated with the use of the substance according to Article 114(1) could not be comprehensively addressed as there are several gaps that cannot be covered i.e. dose, target species, indications. Therefore, the environmental risk assessment under this mandate was focused on the potential hazard of the substances due to their inherent properties - with the exception of the homeopathic substances since the exposure of the environment was considered very low in this case. Also, for most substances, the environmental toxicity reference values were not available (e.g. Predicted No Effect Concentrations - PNECs). Finally, when there was no information on aquatic hazard or no evidence of aquatic hazard, the approach was to consider that there was no issue in relation to criterion (a) risk to environment. Consequently, this assessment is not considered equivalent to a full environmental risk assessment as described in Annex II of Regulation (EU) 2019/6. The inclusion of a substance in the list does not exclude any environmental risks.
- This work is based on the information available and identified at the time of the assessment. It is anticipated that new information may be available in the future. For example, the authorisation of a first veterinary medicinal product for food-producing terrestrial species, or the authorisation of a first medicinal product for human use, may make eligible a substance currently not eligible for assessment. The same may result from the establishment of MRLs for a new substance. On the contrary, the withdrawal of an authorisation of the only medicinal product containing the active substance concerned may make not eligible a substance currently eligible for assessment. Finally, new information on the environmental risk of an eligible substance may become available and change the overall assessment against the criteria of Article 114(3) of Regulation (EU) 2019/6, and hence the recommendation to include or not include the substance in the list, or to recommend a specific risk mitigation measure. If an environmental risk mitigation measure is included in a SPC of a veterinary medicinal product authorised for food-producing aquatic species, this should be considered for the use of this substance under Article 114(1) of Regulation (EU) 2019/6. For these reasons, it is considered that the list may need to be revised in the future.

3.4. Aspects beyond the scope of this mandate

- This advice does not address the substances (listed in Table 1 of the Annex to Regulation (EU) No 37/2010) used as excipients or adjuvants only. Indeed, as requested by the mandate, the scope of the advice is limited to active substances. However, when selecting a medicinal product (immunological or non-immunological) for use under Article 114(1) of Regulation (EU) 2019/6, the responsible veterinarian will have to take into account the excipients, and other factors such as the formulation in relation to the administration route, the concentration and quantity of active substance in relation to the intended dose and use.
- This work is based on the criteria set out in Article 114(3) of Regulation (EU) 2019/6 and on the other elements set out in the mandate from the Commission. These criteria do not formally include as such the usefulness of the substance for food-producing aquaculture[49] [50]. Consequently, a number of substances recommended for inclusion in the list do not have an identified use in aquatic food-producing species. This report does specify which of these substances have been

[49] However, as indicated above, criterion (c) addresses the availability of other medicinal products
[50] However, as indicated above, the immunological substances were considered where the pathogens concerned are relevant for food-producing aquatic species

identified by aquaculture sector as important for the treatment of food-producing aquatic species (see substances marked by an asterisk in the tables from Section 4).

4. Conclusion and recommendations

The following substances are recommended for inclusion in the list[51].

Table 5. Substances recommended to be included in the list referred to in Article 114(3) of Regulation (EU) 2019/6

Classification	Substance	Conditions of use and risk mitigation measures Codes explained below the table
-	**Acetylcysteine**	O
-	**Acetylmethionine**	O
-	**Adenosine and its 5'-mono-, 5'- di-and 5' triphosphates**	O
Homeopathic	***Adonis vernalis***	H
Homeopathic	***Aesculus hippocastanum***	H
Homeopathic	***Agnus castus***	H
Homeopathic	***Ailanthus altissima***	H
-	**Alanine**	O
Hormonal	**Alarelin**	I
Antiparasitic	**Albendazole ***	B
Antiparasitic	**Albendazole oxide**	B
-	**Alfacalcidol**	O
-	**Allantoin**	O
Homeopathic	***Allium cepa***	H
Herbal non-homeopathic	***Aloe vera* gel and whole leaf extract of *Aloe vera***	O
Herbal non-homeopathic	**Aloes, Barbados and Capae, their standardised dry extract and preparations thereof**	O
-	**Aluminium phosphate**	O
-	**Aluminium salicylate, basic**	O
-	**Ammonium lauryl sulphate ***	O
Antibacterial	**Amoxicillin ***	B, C
Antibacterial	**Ampicillin**	B, C
Antiparasitic	**Amprolium ***	B
Herbal non-homeopathic	***Anisi stellati fructus*, standardised extracts and preparations thereof**	O
Homeopathic	***Apocynum cannabinum***	H
Antibacterial	**Apramycin**	B
-	**Arginine**	O
Herbal non-homeopathic	***Arnica montana* (*arnicae flos* and *arnicae planta tota*)**	O
Homeopathic	***Artemisia abrotanum***	H

[51] The substance names are listed by alphabetical order.

Classification	Substance	Conditions of use and risk mitigation measures Codes explained below the table
-	**Asparagine**	O
-	**Aspartic acid**	O
Homeopathic	***Atropa belladonna***	H
-	**Atropine**	O
Antibacterial	**Bacitracin**	B
Homeopathic	***Bellis perennis***	H
Anaesthetic/sedative	**Benzocaine ***	B
Antibacterial	**Benzylpenicillin**	B
-	**Betaine**	O
-	**Biotin**	O
-	**Bromelain**	O
Antifungal	**Bronopol ***	B
-	**Brotizolam**	O
Anaesthetic/sedative	**Bupivacaine**	O
Hormonal	**Buserelin ***	I
-	**Butafosfan**	O
-	**Butylscopolaminium bromide**	O
-	**Calcium borogluconate**	O
-	**Calcium citrate**	O
-	**Calcium glucoheptonate**	O
-	**Calcium glycerophosphate**	O
-	**Calcium hypophosphite**	O
-	**Calcium pantothenate**	O
-	**Calcium chloride**	O
-	**Calcium gluconate**	O
-	**Calcium glucono glucoheptonate**	O
-	**Calcium phosphate**	O
-	**Calcium propionate**	O
Homeopathic	***Calendula officinalis***	H
Herbal non-homeopathic	***Calendulae flos***	O
Homeopathic	***Camphora***	H
Herbal non-homeopathic	***Capsici fructus acer***	O
-	**Carazolol**	O
Homeopathic	***Cardiospermum halicacabum***	H
Herbal non-homeopathic	***Carlinae radix***	O
-	**Carnitine**	O
-	**Carprofen**	O
Herbal non-homeopathic	***Caryophilli aetheroleum*** **(clove oil) ***	O
Antibacterial	**Cefacetrile**	C

Classification	Substance	Conditions of use and risk mitigation measures Codes explained below the table
Antibacterial	**Cefalexin**	C
Antibacterial	**Cefalonium**	B, C
Antibacterial	**Cefapirin**	C
Antibacterial	**Cefazolin**	C
Antibacterial	**Cefoperazone**	B, S, C
Antibacterial	**Cefquinome**	B, S, C
Antibacterial	**Ceftiofur**	B, S, C
Herbal non-homeopathic	***Centellae asiaticae extractum***	O
Antibacterial	**Chlortetracycline ***	B
-	**Choline**	O
Herbal non-homeopathic	***Cimicifugae racemosae rhizoma***	O
Herbal non-homeopathic	***Cinchonae cortex*, standardised extracts and preparations thereof**	O
-	**Citrulline**	O
-	**Clodronic acid (in the form of disodium salt)**	O
Hormonal	**Cloprostenol**	I
Antibacterial	**Cloxacillin**	O
-	**Cobalt gluconate**	O
Herbal non-homeopathic	***Condurango cortex*, standardised extracts and preparations thereof**	O
Homeopathic	***Convallaria majalis***	H
	Copper sulphate *	B
-	**Copper methionate**	O
Homeopathic	***Crataegus***	H
-	**Cytidine and its 5'-mono-, 5'-di- and 5'-triphosphates**	O
Antibacterial	**Danofloxacin**	B
Antiparasitic	**Decoquinate ***	B, F
Antiparasitic	**Deltamethrin ***	B, D
-	**Dembrexine**	O
-	**Denaverine hydrochloride**	O
-	**Detomidine**	O
Hormonal	**Dexamethasone**	I
-	**Dexpanthenol**	O
Antibacterial	**Dicloxacillin**	O
Antibacterial	**Difloxacin**	B
Antibacterial	**Dihydrostreptomycin**	O
-	**Dimethicone**	O
Hormonal	**Dinoprost tromethamine**	I
Hormonal	**Dinoprostone**	I

Classification	Substance	Conditions of use and risk mitigation measures Codes explained below the table
-	**Diprophylline**	O
-	**Doxapram**	O
Antibacterial	**Doxycycline ***	B
Hormonal	**D-Phenylalanine (6) luteinising-hormone releasing hormone**	I
Homeopathic	***Echinacea***	H
Herbal non-homeopathic	***Echinacea purpurea***	O
Antifungal	**Enilconazole**	B
Antibacterial	**Enrofloxacin ***	B
Hormonal	**Epinephrine**	I
-	**Ergometrine maleate**	O
Antibacterial	**Erythromycin ***	B
-	**Etamsylate**	O
Homeopathic	***Eucalyptus globulus***	H
Homeopathic	***Euphrasia officinalis***	H
Antiparasitic	**Fenbendazole ***	B
-	**Fenpipramide hydrochloride**	O
Antibacterial	**Florfenicol ***	B
Antiparasitic	**Flubendazole ***	B
Antibacterial	**Flumequine ***	B
Hormonal	**Follicle stimulating hormone (natural FSH from all species and their synthetic analogues)**	I
Food additive	**Food additive E 1202 - Polyvinylpolypyrrolidone**	O
Food additive	**Food additive E 290 - Carbon dioxide**	O
Food additive	**Food additive E 967 - Xylitol**	O
Food additive	**Food additive E 322 - Lecithins**	O
Food additive	**Food additive E 522 - Aluminium potassium sulphate**	O
Food additive	**Food additive E 941 - Nitrogen**	O
Food additive	**Food additive E 434 - Polyoxyethylene sorbitan monopalmitate (polysorbate 40)**	O
Food additive	**Food additive E 577 - Potassium gluconate**	O
Food additive	**Food additive E 500 - Sodium carbonates**	O
Food additive	**Food additive E 435 - Polyoxyethylene sorbitan monostearate (polysorbate 60)**	O
Food additive	**Food additive E 340 - Potassium phosphates**	O
Food additive	**Food additive E 300 - Ascorbic acid**	O
Food additive	**Food additive E 336 - Potassium tartrates**	O
Food additive	**Food additive E 339 - Sodium phosphates**	O

Classification	Substance	Conditions of use and risk mitigation measures Codes explained below the table
Food additive	**Food additive E 464 - Hydroxypropyl methyl cellulose**	O
Food additive	**Food additive E 621 – Monosodium glutamate**	O
Food additive	**Food additive E 160d - Lycopene**	O
Food additive	**Food additive E 939 - Helium**	O
Food additive	**Food additive E 261 - Potassium acetate**	O
Food additive	**Food additive E 400 - Alginic acid**	O
Food additive	**Food additive E 948 - Oxygen**	O
Food additive	**Food additive E 302 - Calcium ascorbate**	O
Food additive	**Food additive E 579 - Ferrous gluconate**	O
Food additive	**Food additive E 576 - Sodium gluconate**	O
Food additive	**Food additive E 966 - Lactitol**	O
Food additive	**Food additive E 332 - Potassium citrates**	O
Food additive	**Food additive E 331 - Sodium citrates**	O
Food additive	**Food additive E 407 - Carrageenan**	O
Food additive	**Food additive E 420 - Sorbitols**	O
Food additive	**Food additive E 327 - Calcium lactate**	O
Food additive	**Food additive E 942 - Nitrous oxide**	O
Food additive	**Food additive E 422 - Glycerol**	O
Food additive	**Food additive E 100 - Curcumin**	O
Food additive	**Food additive E 131 - Patent Blue V**	O
Food additive	**Food additive E 351 - Potassium malate**	O
Food additive	**Food additive E 416 - Karaya gum**	O
Food additive	**Food additive E 345(i) - Trimagnesium dicitrate**	O
Food additive	**Food additive E 1210 - Carbomer**	O
Antiparasitic	**Formaldehyde ***	B
Herbal non-homeopathic	***Frangulae cortex*, standardised extracts and preparations thereof**	O
Antibacterial	**Gamithromycin**	O
Antibacterial	**Gentamicin ***	B
Herbal non-homeopathic	***Gentianae radix*, standardised extracts and preparations thereof**	O
Homeopathic	***Ginkgo biloba***	H
Homeopathic	***Ginseng***	H
Herbal non-homeopathic	***Ginseng*, standardised extracts and preparations thereof**	O
-	**Glutamic acid**	O
-	**Glutamine**	O
-	**Glycine**	O
Hormonal	**Gonadorelin ***	I

Classification	Substance	Conditions of use and risk mitigation measures Codes explained below the table
Herbal non-homeopathic	***Hamamelis virginiana***	O
Homeopathic	***Hamamelis virginiana***	H
Homeopathic	***Harpagophytum procumbens***	H
Homeopathic	***Harunga madagascariensis***	H
-	**Heparin and its salts**	O
-	**Heptaminol**	O
-	**Hesperidin**	O
-	**Hesperidin methyl chalcone**	O
-	**Hexetidine**	O
-	**Histidine**	O
Hormonal	**Human chorionic gonadotropin (HCG) ***	I
-	**Humic acids and their sodium salts**	O
Hormonal	**Hydrocortisone**	I
Antiparasitic	**Hydrogen peroxide ***	B
Herbal non-homeopathic	***Hyperici oleum***	O
Homeopathic	***Hypericum perforatum***	H
Antiparasitic	**Imidocarb**	B
-	**Inosine**	O
-	**Inositol**	O
-	**Iron dextran**	O
-	**Iron sulphate**	O
Anaesthetic/sedative	**Isoeugenol ***	B
-	**Isoleucine**	O
-	**Isopropanol**	O
Antibacterial	**Kanamycin**	O
Anaesthetic/sedative	**Ketamine**	I
-	**Ketanserin tartrate**	O
-	**Lanolin**	O
Hormonal	**Lecirelin**	I
-	**Leucine**	O
Antiparasitic	**Levamisole ***	B
Anaesthetic/sedative	**Lidocaine**	O
Antibacterial	**Lincomycin ***	B
Herbal non-homeopathic	***Lini oleum***	O
Homeopathic	***Lobaria pulmonaria***	H
Hormonal	**Luteinising hormone (natural LH from all species and their synthetic analogues)**	I
-	**Lysine**	O
-	**Magnesium acetate**	O
-	**Magnesium aspartate**	O

Classification	Substance	Conditions of use and risk mitigation measures Codes explained below the table
-	**Magnesium carbonate**	O
-	**Magnesium chloride**	O
-	**Magnesium citrate**	O
-	**Magnesium gluconate**	O
-	**Magnesium glycerophosphate**	O
-	**Magnesium hydroxide**	O
-	**Magnesium hypophosphite**	O
-	**Magnesium orotate**	O
-	**Magnesium phosphate**	O
-	**Magnesium sulfate ***	O
-	**Manganese gluconate**	O
-	**Manganese glycerophosphate**	O
-	**Mannitol**	O
Antibacterial	**Marbofloxacin**	B
Antiparasitic	**Mebendazole ***	B
Herbal non-homeopathic	***Medicago sativa extractum***	O
Hormonal	**Medroxyprogesterone acetate**	I
Anaesthetic/sedative	**Mepivacaine**	O
Antiparasitic	**Monensin ***	B
Antibacterial	**Nafcillin**	O
Antibacterial	**Natamycin**	O
Antibacterial	**Neomycin ***	B
-	**Nicoboxil**	O
-	**Nonivamide**	O
Antibacterial	**Novobiocin**	B
Homeopathic	***Okoubaka aubrevillei***	H
-	**Ornithine**	O
-	**Orotic acid**	O
Antibacterial	**Oxacillin**	O
Antiparasitic	**Oxfendazole ***	B
Antibacterial	**Oxolinic acid ***	B
Antibacterial	**Oxytetracycline ***	B
Hormonal	**Oxytocin**	I
-	**Pancreatin**	O
-	**Papain**	O
-	**Papaverine**	O
Antifungal	**Parconazole**	O
Antibacterial	**Paromomycin**	O
Antibacterial	**Penethamate**	O
-	**Pepsin**	O
Antibacterial	**Phenoxymethylpenicillin**	O
-	**Phenylalanine**	O

Classification	Substance	Conditions of use and risk mitigation measures Codes explained below the table
Homeopathic	***Phytolacca americana***	H
Antibacterial	**Pirlimycin**	O
-	**Poloxamer**	O
-	**Polysulfated glycosaminoglycan**	O
-	**Potassium DL-aspartate**	O
-	**Potassium glycerophosphate**	O
Antiparasitic	**Praziquantel ***	B
Hormonal	**Pregnant mare serum gonadotrophin (equine chorionic gonadotropin, PMSG)**	I
Anaesthetic/sedative	**Procaine**	O
Hormonal	**Progesterone**	I
-	**Proline**	O
-	**Propylene glycol**	O
Homeopathic	***Prunus laurocerasus***	H
Herbal non-homeopathic	***Quercus cortex***	O
-	***Quillaia* saponins**	O
Hormonal	**R-Cloprostenol**	I
Antibacterial	**Rifaximin**	B
-	**Romifidine**	O
Herbal non-homeopathic	***Ruscus aculeatus***	O
Herbal non-homeopathic	***Sambuci flos***	O
Homeopathic	***Selenicereus grandiflorus***	H
Homeopathic	***Serenoa repens***	H
-	**Serine**	O
Homeopathic	***Silybum marianum***	H
-	**Sodium chloride ***	O
-	**Sodium glycerophosphate**	O
-	**Sodium hypophosphite**	O
-	**Sodium thiosulfate**	O
-	**Sodium cromoglycate**	O
-	**Sodium propionate**	O
Homeopathic	***Solidago virgaurea***	H
-	**Sorbitan sesquioleate**	O
Antibacterial	**Spectinomycin ***	B
Antibacterial	**Spiramycin**	B
Antibacterial	**Streptomycin**	O
Homeopathic	**Substances used in homeopathic veterinary medicines**	H
-	**Sulfogaiacol**	O

Classification	Substance	Conditions of use and risk mitigation measures Codes explained below the table
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) – Sulfadiazine***	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) – Sulfadoxine***	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfamethizole**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfadimidine**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfapyridine**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfafurazole**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfanilamide**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfathiazole**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfamethoxazole**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfadimethoxine**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfamethoxypyridazine**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfamerazine**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfamethizole**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfachlorpyridazine**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfaquinoxaline**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfamerazine**	B

Classification	Substance	Conditions of use and risk mitigation measures Codes explained below the table
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfamonomethoxine**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfacetamide**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Formosulfathiazole**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Phthalylsulfathiazole**	B
Antibacterial	**Sulfonamides (all substances belonging to the sulfonamide group) - Sulfaguanidine**	B
Herbal non-homeopathic	***Symphyti radix***	O
Homeopathic	***Syzygium cumini***	H
Herbal non-homeopathic	***Terebinthinae laricina***	O
-	**Terpin hydrate**	O
Anaesthetic/sedative	**Tetracaine**	O
Antibacterial	**Tetracycline**	B
Antibacterial	**Thiamphenicol ***	B
Anaesthetic/sedative	**Thiopental sodium**	O
-	**Threonine**	O
Homeopathic	***Thuja occidentalis***	H
Antibacterial	**Tiamulin**	B
Antibacterial	**Tildipirosin**	O
Herbal non-homeopathic	***Tiliae flos***	O
Antibacterial	**Tilmicosin**	B
-	**Tiludronic acid (in the form of disodium salt)**	O
-	**Toldimfos**	O
-	**Tolfenamic acid**	O
Antiparasitic	**Toltrazuril ***	B
	Tosylchloramide sodium *	B
-	**Trichlormethiazide**	O
Antibacterial	**Trimethoprim ***	B
-	**Trimethylphloroglucinol**	O
Hormonal	**Triptorelin acetate**	I
-	**Tryptophan**	O
Antibacterial	**Tulathromycin**	B

Classification	Substance	Conditions of use and risk mitigation measures Codes explained below the table
Homeopathic	***Turnera diffusa***	H
Antibacterial	**Tylosin ***	B
Antibacterial	**Tylvalosin**	O
-	**Tyrosine**	O
Homeopathic	***Urginea maritima***	H
-	**Uridine and its 5'-mono-5'-di- and 5'-triphosphates**	O
Herbal non-homeopathic	***Urticae herba***	O
-	**Valine**	O
Antibacterial	**Valnemulin**	B
-	**Vedaprofen**	O
-	**Vetrabutine hydrochloride**	O
-	**Vincamine**	O
Homeopathic	***Virola sebifera***	H
Homeopathic	***Viscum album***	H
	Vitamin B1 (thiamine) *	O
-	**Vitamin B12**	O
-	**Vitamin B2**	O
-	**Vitamin B5**	O
-	**Probiotic components including bacteria and yeasts**	O
-	**Stem cells - Chondrogenic induced equine peripheral blood-derived mesenchymal stem cells – Alisvetcel**	O
-	**Stem cells - Equine umbilical cord-derived mesenchymal stem cells**	O
-	**Stem cells - Tenogenic primed equine allogeneic peripheral blood-derived mesenchymal stem cells - Tesrivetcel**	O

* Substance identified by aquaculture sector as important for the treatment of food-producing aquatic species.

Conditions of use and risk mitigation measures:

O: No condition of use or risk mitigation measure.

B: The substance is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system[52] with:

[52] This RMM does not restrict the use of the substance to closed systems, but strongly recommends to consider them whenever possible. For the purpose of this advice, a 'closed system' should be understood as a 'contained treatment system'—that is, any setup in which effluent containing the substance can be effectively confined, controlled, and treated before being released. This approach should be considered regardless of the type of aquaculture facility. For example, in

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1µg/L[53] is required before discharge in the environment.

C: The substance shall not be used in combination with beta-lactamase inhibitors.

D: Deltamethrin is toxic to aquatic and sediment living species and may cause adverse effects in the vicinity of treated sea cages. Also, at distances of up to 4 kilometers downstream short-term effects after treatment can be seen in sensitive organisms. Deltamethrin demonstrates high affinity to organic matter and particles in the water column and in sediments. Deltamethrin is very stable and slowly degradable when bound to sediments, both at aerobic and anaerobic conditions. The environmental risk assessment of deltamethrin, is based on the theoretical use of only a single (annual) application in a single cage at one site. More frequent use and/or use on a larger scale may pose an increased risk to the environment. In order to ensure safe use (including large scale and multiple treatments) of deltamethrin under a combination of different environmental conditions (e.g. low water current speeds, shallow waters, short distance to the shore etc.) local environmental regulations governing discharges, where applicable, must be adhered to. If there is any doubt about safe use, relevant competent authorities should be consulted or professional advice sought accordingly.

Other precautions: The substance is toxic to crustaceans and should not be used in sea farms where crabs or lobsters are kept in the close vicinity of the treated sea-cages (<200 m), or when local water-currents increase the likelihood of exposure. To prevent toxic effects on local aquatic organisms and to prevent toxic waste of deltamethrin to be washed into the littoral zone, bath treatment should be performed at outgoing tide or during periods with a local outgoing current.

S: The substance shall be used in individual animals only.

F: The substance shall be administered in feed only.

H: The substance shall be used in line with the homeopathic conditions specified in Table 1 of the Annex of Regulation (EU) No 37/2010**.**

I: The substance shall be administered by injection only.

The following substances are **recommended to be not included in the list[54]:**

Table 6. Substances recommended to be not included in the list referred to in Article 114(3) of Regulation (EU) 2019/6

Classification	Substance
Antiparasitic	Abamectin
Herbal non-homeopathic	*Absinthium* extract
-	Acetylsalicylic acid

semi-open facilities, temporary containment measures can be implemented during treatment to reduce environmental exposure or in raceways, individual raceway units can be isolated and treated separately to minimize the volume of treated water discharged into the environment.

[53] From EMA/CVMP/ERA/418282/2005, 'Guideline on environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 and GL38', available from: https://www.ema.europa.eu/en/environmental-impact-assessment-veterinary-medicinal-products-support-vich-guidelines-gl6-gl38-scientific-guideline.

[54] The substance names are listed by alphabetical order.

Classification	Substance
-	Acetylsalicylic acid DL-lysine
Hormonal	Alfaprostol
Antiparasitic	Alphacypermethrin and cypermethrin
Hormonal	Altrenogest
-	Aluminium distearate
-	Aluminium hydroxide
Antiparasitic	Amitraz
-	Ammonium chloride
Herbal non-homeopathic	*Angelicae radix aetheroleum*
Herbal non-homeopathic	*Anisi aetheroleum*
-	Azaperone
Herbal non-homeopathic	*Balsamum peruvianum*
Antibacterial	Bambermycin *
Hormonal	Beclomethasone dipropionate
-	Benzyl benzoate
-	Benzyl p-hydroxybenzoate
Hormonal	Betamethasone
-	Bismuth subsalicylate
-	Bismuth subgallate
-	Bismuth subnitrate
-	Bituminosulfonates, ammonium and sodium salts
Herbal non-homeopathic	*Boldo folium*
-	Boric acid and borates
-	Bromhexine
-	Bromide, potassium salt
-	Bromide, sodium salt
-	Butorphanole tartrate
-	Butyl 4-hydroxybenzoate
-	Cabergoline
-	Caffeine
-	Calcium acetate
-	Calcium oxide
-	Calcium carbonate
-	Calcium hydroxide
-	Calcium sulphate
-	Camphor
-	Carbasalate calcium
Hormonal	Carbetocin
Herbal non-homeopathic	Cardamon extract
Herbal non-homeopathic	*Carvi aetheroleum*
-	Cetostearyl alcohol
-	Cetrimide
-	Chlorhexidine
Hormonal	Chlormadinone
-	Chlorocresol
-	Chlorphenamine

Classification	Substance
-	Chymotrypsin
Hormonal	Ciclesonide
Herbal non-homeopathic	*Cinnamomi cassiae aetheroleum*
Herbal non-homeopathic	*Cinnamomi cassia cortex*, standardised extracts and preparations thereof
Herbal non-homeopathic	*Cinnamomi ceylanici aetheroleum*
Herbal non-homeopathic	*Citri aetheroleum*
Herbal non-homeopathic	*Citronellae aetheroleum*
Antibacterial	Clavulanic acid *
Antiparasitic	Clorsulon
Antiparasitic	Closantel
-	Cobalt dichloride
-	Copper chloride
Antibacterial	Colistin
-	Copper gluconate
Herbal non-homeopathic	*Coriandri aetheroleum*
Antiparasitic	Coumafos
Antiparasitic	Cyfluthrin
-	Cysteine
Antiparasitic	Derquantel
Antiparasitic	Diazinon
Antiparasitic	Diclazuril
-	Diclofenac
Antiparasitic	Dicyclanil
-	Dimethyl phthalate
-	Dimethyl sulphoxide
Antiparasitic	Doramectin
Antiparasitic	Eprinomectin
-	Ethylenediaminetetraacetic acid (EDTA) and salts
Hormonal	Etiproston tromethamine
Herbal non-homeopathic	*Eucalypti aetheroleum*
-	Eucalyptol
Antiparasitic	Febantel
-	Firocoxib
Hormonal	Flugestone acetate
Antiparasitic	Flumethrin
-	Flunixin
Antiparasitic	Fluralaner
Herbal non-homeopathic	*Foeniculi aetheroleum*
-	Folic acid
Food additive	Food additive E 470a - Sodium, potassium and calcium salts of fatty acids
Food additive	Food additive E 466 - Sodium carboxy methyl cellulose, Cellulose gum
Food additive	Food additive E 320 - Butylated hydroxyanisole (BHA)
Food additive	Food additive E 321 - Butylated hydroxytoluene (BHT)

Classification	Substance
Food additive	Food additive E 520 - Aluminium sulphate
Food additive	Food additive E 905 - Microcrystalline wax
Food additive	Food additive E 200 - Sorbic acid
Food additive	Food additive E 512 - Stannous chloride
Food additive	Food additive E 586 - 4-Hexylresorcinol
Food additive	Food additive E 514 - Sodium sulphates
Food additive	Food additive E 175 - Gold
Food additive	Food additive E 1203 - Polyvinyl alcohol (PVA)
Food additive	Food additive E 127 - Erythrosine
Food additive	Food additive E 432 - Polyoxyethylene sorbitan monolaurate (polysorbate 20)
Food additive	Food additive E 132 - Indigotine, Indigo carmine
Food additive	Food additive E 363 - Succinic acid
Food additive	Food additive E 553b - Talc
Food additive	Food additive E 501 - Potassium carbonates
Food additive	Food additive E 223 - Sodium metabisulphite
Food additive	Food additive E 440 - Pectins
Food additive	Food additive E 412 - Guar gum
Food additive	Food additive E 262 - Sodium acetates
Food additive	Food additive E 461 - Methyl cellulose
Food additive	Food additive E 211 - Sodium benzoate
Food additive	Food additive E 161b - Lutein
Food additive	Food additive E 218 - Methyl p-hydroxybenzoate
Food additive	Food additive E 260 - Acetic acid
Food additive	Food additive E 515 - Potassium sulphates
Food additive	Food additive E 325 - Sodium lactate
Food additive	Food additive E 401 - Sodium alginate
Food additive	Food additive E 524 - Sodium hydroxide
Food additive	Food additive E 210 - Benzoic acid
Food additive	Food additive E 301 - Sodium ascorbate
Food additive	Food additive E 551 - Silicon dioxide
Food additive	Food additive E 508 - Potassium chloride
Food additive	Food additive E 160a - Carotenes
Food additive	Food additive E 525 - Potassium hydroxide
Food additive	Food additive E 171 - Titanium dioxide
Food additive	Food additive E 1201 - Polyvinylpyrrolidone
Food additive	Food additive E 173 - Aluminium
Food additive	Food additive E 214 - Ethyl-p-hydroxybenzoate
Food additive	Food additive E 330 - Citric acid
Food additive	Food additive E 1521 - Polyethylene glycol
Food additive	Food additive E 513 - Sulphuric acid
Food additive	Food additive E 172 - Iron oxides and hydroxides
Food additive	Food additive E 914 - Oxidised polyethylene wax
Food additive	Food additive E 392 - Extracts of rosemary
Food additive	Food additive E 319 - Tertiary-butyl hydroquinone (TBHQ)
-	Formic acid

Classification	Substance
-	Furosemide
-	Glutaraldehyde
-	Guaiacol
Antiparasitic	Halofuginone
Herbal non-homeopathic	*Hippocastani semen*
Hormonal	Human menopausal urinary gonadotrophin
-	Hyaluronic acid
-	Hydrochlorothiazide
Hormonal	Hydrocortisone aceponate
-	Hydroxyethylsalicylate
-	Iodine
-	Potassium iodide
-	Povidone, iodinated
-	Iodoform
-	Iron fumarate
Anaesthetic/sedative	Isoflurane
Antiparasitic	Ivermectin *
Herbal non-homeopathic	*Juniperi fructus*
-	Ketoprofen
-	Lactic acid
Herbal non-homeopathic	*Lauri folii aetheroleum*
Herbal non-homeopathic	*Lavandulae aetheroleum*
-	Levomethadone
Hormonal	Levothyroxine
-	Lobeline
Hormonal	Luprostiol
-	Magnesium
-	Magnesium aluminium silicate
-	Magnesium oxide
-	Magnesium trisilicate
Herbal non-homeopathic	*Majoranae herba*
-	Manganese carbonate
-	Manganese chloride
-	Manganese sulphate
Herbal non-homeopathic	*Matricaria recutita* and preparations thereof
Herbal non-homeopathic	*Matricariae flos*
Antibacterials	Mecillinam
Hormonal	Melatonin
Herbal non-homeopathic	*Melissae aetheroleum*
Herbal non-homeopathic	*Melissae folium*
-	Meloxicam
-	Menadione
-	Menbutone
Herbal non-homeopathic	*Menthae piperitae aethe- roleum*
-	Menthol
-	Mercaptamine hydrochloride

Classification	Substance
-	Metamizole
-	Methionine
-	Methyl nicotinate
Hormonal	Methylprednisolone
-	Methyl salicylate
Herbal non-homeopathic	*Millefolii herba*
-	Mineral hydrocarbons, low to high viscosity including microcristalline waxes, approximately C10-C60, aliphatic, branched aliphatic and alicyclic compounds
Antiparasitic	Monepantel
Antiparasitic	Morantel
Antiparasitic	Moxidectin
Herbal non-homeopathic	*Myristicae aetheroleum*
-	Neostigmine
Antiparasitic	Netobimin
-	Nickel sulphate
-	Nickel gluconate
Antiparasitic	Nitroxinil
-	Octenidine dihydrochloride
-	Omeprazole
-	Oxalic acid
Antiparasitic	Oxibendazole
Antiparasitic	Oxyclozanide
-	Paracetamol
Hormonal	Peforelin
Hormonal	Pegylated bovine granu-locyte colony stimulating factor
Antiparasitic	Permethrin
-	Phenol
-	Phloroglucinol
Antiparasitic	Phoxim
-	Phytomenadione
Herbal non-homeopathic	*Piceae turiones recentes extractum*
Antiparasitic	Piperazine
-	Piperonyl butoxide
-	Policresulen
-	Polysorbate 80
-	Potassium nitrate
Hormonal	Prednisolone
Antiparasitic	Pyrantel embonate
Herbal non-homeopathic	*Pyrethrum* extract
Antiparasitic	Rafoxanide
Herbal non-homeopathic	*Rhei radix*, standardised extracts and preparations thereof
Herbal non-homeopathic	*Rosmarini aetheroleum*
Herbal non-homeopathic	*Rosmarini folium*
-	Salicylic acid
Herbal non-homeopathic	*Salviae folium*

Classification	Substance
-	Sodium chlorite
-	Sodium dichloroisocyanurate
-	Sodium nitrite
-	Sodium selenate
-	Sodium selenite
-	Sodium salicylate
-	Sulphur
-	*Tanninum albuminatum*
Antiparasitic	Tau fluvalinate
Herbal non-homeopathic	*Terebinthinae aetheroleum rectificatum*
-	Theophylline
Antiparasitic	Thiabendazole
-	Thioctic acid
Herbal non-homeopathic	*Thymi aetheroleum*
-	Thymol
Antiparasitic	Triclabendazole
-	Trypsin
-	Urea
-	Vitamin A
-	Vitamin B3
-	Vitamin B6
-	Vitamin D
-	Vitamin E
-	Wool alcohols
-	Xylazine hydrochloride
-	Zinc acetate
-	Zinc aspartate
-	Zinc chloride
-	Zinc gluconate
-	Zinc oxide
-	Zinc sulphate
-	2-Aminoethanol
-	8-Hydroxyquinoline

* Substance identified by aquaculture sector as important for the treatment of food-producing aquatic species.

** Substance considered similarly to * due to possible combination with amoxicillin which is identified by aquaculture sector as important for the treatment of food-producing aquatic species *.

Acronyms

AM	Antimicrobial
AMEG	Categorisation of antibiotics used in animals
AMR	Antimicrobial resistance
ATC	Anatomical therapeutic chemical classification system
ATCVet	Veterinary anatomical therapeutic chemical classification system
C&L	Classification & labelling
CLP	Classification, labelling and packaging of substances and mixtures
CVMP	Committee for veterinary medicinal products
DNA	Deoxyribonucleic acid
ECHA	European Chemicals Agency
ED	Endocrine disruptor
EDTA	Ethylenediamine tetraacetic acid
EMA	European Medicines Agency
EU	European Union
FSH	Follicle stimulating hormone
GHS	Globally harmonized system of classification and labelling of chemicals
HCG	Human chorionic gonadotropin
IHN	Infectious haematopoietic necrosis
IVMP	Immunological veterinary medicinal product
NCA	National competent authority
PBT	Persistent, bioaccumulative and toxic
PNEC	Predicted no effect concentration
PuAR	Public assessment report
RMM	Risk mitigation measure
SDS	Safety data sheet
SPC	Summary of product characteristics
UBA	German Environment Agency - UmweltBundesamt
US EPA	US Environmental Protection Agency
VICH	International cooperation on harmonisation of technical requirements for registration of veterinary medicinal products
VMP	Veterinary Medicinal Product
vPvB	Very persistent and very bioaccumulative
WFD	Water framework directive

References[55]

ATCvet Index Veterinary Anatomical Therapeutic Chemical code, WHO Collaborating Centre for Drug Statistics Methodology, available from: https://atcddd.fhi.no/atcvet/atcvet_index/.

Baker-Austin, C., Oliver, J.-D., Alam, M., Ali, A., Waldor, M.-K., Qadri, F., Martinez-Urtaza, J., 'Vibrio spp. infections', Nat Rev Dis Primers, 2018, Vol. 4(1).

Bedekar, M.-K., Kole, S., 'Fundamentals of Fish Vaccination', Methods Mol Biol, 2022, pp. 147-173.

Chen, Y., Ai, X., Yang, Y., 'Vibrio cholerae: a pathogen shared by human and aquatic animals', Lancet Microbe, 2022, Vol. 3(6)., e402.

[55] This list of references covers the references used in the main document. The references used in the annexed assessment reports are not included.

Elsevier. 'Vibrio parahaemolyticus'. n.d. Accessed August 2024, available from: https://www.sciencedirect.com/topics/immunology-and-microbiology/vibrio-parahaemolyticus.

Elsevier. 'Vibrio vulnificus. n.d. Accessed August 2024, available from: https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/vibrio-vulnificus.

EMA, AMEG Categorisation of antibiotics used in animals, available from: https://www.ema.europa.eu/en/documents/report/infographic-categorisation-antibiotics-use-animals-prudent-and-responsible-use_en.pdf.

EMA, Article 57 product data. Last accessed: 2024, available from: https://www.ema.europa.eu/en/human-regulatory-overview/post-authorisation/data-medicines-iso-idmp-standards-post-authorisation/public-data-article-57-database.

EMA/CMDv/650880/2018-Rev.5, 'Veterinary Medicinal Products intended for fish', available from: https://www.hma.eu/veterinary-medicines/cmdv/procedural-guidance/miscellaneous.html.

EMA/CVMP/151584/2021, 'Scientific advice under Article 107(6) of Regulation (EU) 2019/6 for the establishment of a list of antimicrobials which shall not be used in accordance with Articles 112, 113 and 114 of the same Regulation or which shall only be used in accordance with these articles subject to certain conditions, available from: https://www.ema.europa.eu/system/files/documents/regulatory-procedural-guideline/vet_reg_cascade_list_report_en.pdf.

EMA/CVMP/ERA/418282/2005, 'Guideline on environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 and GL38', available from: https://www.ema.europa.eu/en/environmental-impact-assessment-veterinary-medicinal-products-support-vich-guidelines-gl6-gl38-scientific-guideline.

EMA, Union Product Database. Last accessed: 2024, available from: https://www.ema.europa.eu/en/veterinary-regulatory/overview/veterinary-medicines-regulation/union-product-database.

European Commission, 'Commission Implementing Regulation (EU) 2022/1255 of 19 July 2022 designating antimicrobials or groups of antimicrobials reserved for treatment of certain infections in humans, in accordance with Regulation (EU) 2019/6 of the European Parliament and of the Council', available from: https://eur-lex.europa.eu/eli/reg_impl/2022/1255/oj/eng.

European Commission, 'Commission Implementing Regulation (EU) 2024/860 of 18 March 2024 amending Regulation (EU) No 37/2010 as regards the substance 17β-oestradiol', available from: https://eur-lex.europa.eu/eli/reg_impl/2024/860/oj.

European Commission, 'Commission Regulation (EU) No 37/2010 of 22 December 2009 on pharmacologically active substances and their classification regarding maximum residue limits in foodstuffs of animal origin', available from: https://eur-lex.europa.eu/eli/reg/2010/37(1)/oj/eng.

Council of the European Union, 'Council Directive 96/22/EC of 29 April 1996 concerning the prohibition on the use in stockfarming of certain substances having a hormonal or thyrostatic action and of beta-agonists, and repealing Directives 81/602/EEC, 88/146/EEC and 88/299/EEC', available from: https://eur-lex.europa.eu/eli/dir/1996/22/oj/eng.

European Parliament and Council of the European Union, 'Directive 2000/60/EC of the European Parliament and of the Council of 23 October 2000 establishing a framework for Community action in the field of water policy', available from: https://eur-lex.europa.eu/eli/dir/2000/60/oj.

European Parliament and Council of the European Union, 'Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the

authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency', available from: https://eur-lex.europa.eu/eli/reg/2004/726/oj/eng.

European Parliament and Council of the European Union, 'Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006, available from: https://eur-lex.europa.eu/eli/reg/2008/1272/oj.

European Parliament and Council, 'Regulation (EC) No 1333/2008 of the European Parliament and of the Council of 16 December 2008 on food additives', available from: https://eur-lex.europa.eu/eli/reg/2008/1333/oj/eng.

European Parliament and Council, 'Regulation (EC) No 470/2009 of the European Parliament and of the Council of 6 May 2009 laying down Community procedures for the establishment of residue limits of pharmacologically active substances in foodstuffs of animal origin, repealing Council Regulation (EEC) No 2377/90 and amending Directive 2001/82/EC of the European Parliament and of the Council and Regulation (EC) No 726/2004 of the European Parliament and of the Council', available from: https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX%3A32009R0470.

European Parliament and Council of the European Union, 'Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing Directive 2001/82/EC', available from: https://eur-lex.europa.eu/eli/reg/2019/6/oj.

European Manufacturers of Autogenous Vaccines & Sera (EMAV), 'Manual of Autogenous Vaccines (AV)', Munich, Germany, 2023, available from: https://www.emav.be/publications.

FishMedPlus Coalition, 'Fish Diseases Lacking Treatment Gap Analysis Outcome', 2017, available from: https://fve.org/cms/wp-content/uploads/Gap-Analysis-Outcome-Final2.pdf.

Magnadottir, B., 'Immunological control of fish diseases' Mar Biotechnol (NY), 2010, Vol. 12(4), pp. 361–379.

Novotny, L., Dvroska, L., Lorencova, A., Beran, V., Pavlik, I., 'Fish: A potential source of bacterial pathogens for human beings', Vet Med, 2004, Vol. 9, pp. 342-358.

PubChem, available from: https://pubchem.ncbi.nlm.nih.gov/.

Parlapani, F.-F., Boziaris, I.-S., Mireles DeWitt, C.-A., 'Pathogens and their sources in freshwater fish, sea finfish, shellfish, and algae', In Knowles, M.-E., Anelich, L.-E., Boobis, A.-R., Popping, B., (Eds.), Present Knowledge in Food Safety, Elsevier, 2023, pp. 471-492.

Roberti, K.-A., Rohovec, J.-S., Winton, J.-R., Vaccination of rainbow trout against Infectious Hematopoietic Necrosis (IHN) by using attenuated mutants selected by neutralizing monoclonal antibodies, 1998, Journal of Aquatic Animal Health, Vol. 10(4), pp. 328-337.

Sommerset, I., Krossøy, B., Biering, E., Frost, P., 'Vaccines for fish in aquaculture', Expert Rev Vaccines, 2005, Vol. 4(1), pp. 89-101.

United Nations Economic Commission for Europe (UNECE), 'Globally Harmonized System of Classification and Labelling of Chemicals (GHS)', Rev. 10, United Nations, 2023, available from: https://unece.org/sites/default/files/2023-07/GHS%20Rev10e.pdf.

US EPA Environmental Protection Agency, CompTox Chemicals Dashboard, available from: https://comptox.epa.gov/dashboard/.

Winton, J.-R., 'Immunization with viral antigens: Infectious haematopoietic necrosis', In Gudding, R., Lillehaug, A., Midtlyng, P.-J., Brown, F., (Eds.), Fish Vaccinology, Karger, Basel, Switzerland, 1997, pp. 211-220.

Ziarati, M., Zorriehzahra, M.-J., Hassantabar, F., Mehrabi, Z., Dhawan, M., Sharun, K., Emran, T.-B., Dhama, K., Chaicumpa, W., Shamsi, S., 'Zoonotic diseases of fish and their prevention and control', Vet Q, 2022, Vol. 42(1), pp. 95-118.

5. List of annexes

5.1. Eligibility table

5.2. Assessment reports of eligible substances:

5.2.1. Substances identified by aquaculture sector as important for the treatment of food-producing aquatic species

5.2.2. Substances not identified by aquaculture sector as important for the treatment of food-producing aquatic species: substances other than antiparasitic, antibacterial, antifungal and homeopathic substances

5.2.3. Substances not identified by aquaculture sector as important for the treatment of food-producing aquatic species: antiparasitic, antibacterial and antifungal substances

5.2.4. Substances not identified by aquaculture sector as important for the treatment of food-producing aquatic species: homeopathic substances

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SCIENCE MEDICINES HEALTH

Annex 5.1: Eligibility table

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Abamectin	Abamectin	yes	BULMECTIN® 0,2% medicated premix for cattle, sheep and horses	no		no	**yes**
No		Absinthium extract	Absinthium extract	no		yes	WERMUTKRAUT ZUR ANWENDUNG BEI ERWACHSENEN UND	no	**yes**

[1] AM: Antimicrobial
[2] A substance in the overlap is a substance of Table 1 which is either an active substance of VMP for food-producing (FP) terrestrial species or an active substance of HMP, with the exception of the AMs reserved for human use.
[3] SMS: Substance Management Service. SMS provides a central dictionary of substance data and supports the exchange of data between information systems across the European medicines regulatory network and across the pharmaceutical industry. https://spor.ema.europa.eu/smswi/#/
[4] VMP FP terrestrial: Veterinary medicinal product for food-producing terrestrial species
[5] HMP: Medicinal product for human use

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
							KINDERN AB 12 JAHREN SIDROGA		
No		Acetyl cysteine	Acetylcysteine	yes	KANAMUCIL	yes	ACC	no	**yes**
No		Acetylmethionine	Acetylmethionine	yes	SOLUZIONE GLUCOSATA 25% CON METIONINA, 250 mg/ml + 50 mg/ml, soluzione per infusione per bovini, equini, cani e gatti	no		no	**yes**
No		Acetylsalicylic acid	Acetylsalicylic acid	yes	Febrivex p, 650 mg/g pó oral para suínos e frangos de engorda.	yes	A.A.S.	no	**yes**
No		Acetylsalicylic acid DL-lysine	Lysine aspirin	no		yes	ACETILSALICILATO DE LISINA LABESFAL	no	**yes**
No		Adenosine and its 5'-mono-, 5'- di- and 5' trip-hosphates	Adenosine phosphate, sodium salt	yes	MYOTROFIL	yes	ADENYL 60 mg, comprimé	no	**yes**
No		Adonis vernalis	Adonis vernalis	yes	Scilla comp. PlantaVet	yes	Auxcillin Hm	no	**yes**
No		Aesculus hippocastanum	Aesculus hippocastanum	no		yes	Haemex	no	**yes**
No		Agnus castus	Agnus castus	no		yes	Mastodynon	no	**yes**
No		Ailanthus altissima	Ailanthus altissima	no		yes	Mercurius Cyanatus N Oligoplex	no	**yes**
No		Alanine	Alanine	yes	BOGRAS soluzione iniettabile per bovini	yes	AMINO-MEL NEPHRO	no	**yes**
No		Alarelin	Alarelin	yes	MRAbit	no		no	**yes**

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Yes	AAC	Albendazole	Albendazole	yes	Albendazole 300/Anafasis, 300mg/tab δισκία για πρόβατα	yes	ALBENDAZOL MICRO LABS	no	**yes**
No		Albendazole oxide	Albendazole oxide	yes	Gardal 10%	no		no	**yes**
No		Alfacalcidol	Alfacalcidol	no		yes	A-OSTIN-D3	no	**yes**
No		Alfaprostol	Alfaprostol	yes	ALFABEDYL 2 mg/ml	no		no	**yes**
No		Allantoin	Allantoin	no		yes	ALANTAN	no	**yes**
No		Allium cepa	Allium cepa	yes	Articulatio comp. N PlantaVet	yes	Neutrovent	no	**yes**
No		Aloe vera gel and whole leaf extract of Aloe vera	Aloe vera gel and whole leaf extract of Aloe vera	yes	PURGARUMINA TIPO FORTE	yes	IDEOLAXYL	no	**yes**
No		Aloes, Barbados and Capae, their standardised dry extract and preparations thereof	Aloes, Barbados and Capae, their standardised dry extract and preparations thereof	yes	PURGARUMINA TIPO FORTE	yes	Ideolaxyl	no	**yes**
No		Alphacyper-methrin	Alphacypermethrin	yes	ДИАЦИП DIACIP	no		no	**yes**
No		Altrenogest	Altrenogest	yes	Regumate Equine 2.2 mg/ml oral solution for horses	no		no	**yes**
No		Aluminium tris-tearate	Aluminium tristearate	no		no		no	**no**
No		Aluminium distearate	Aluminium distearate	no		yes	REMEDERM	no	**yes**
No		Aluminium hydroxide	Aluminium hydroxide	yes	CLASOVAX vaccino inattivato in sospensione iniettabile per	yes	ACIDO-GIT MAALOX	no	**yes**

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					bovini, ovini e caprini				
No		Aluminium hydroxide acetate	Aluminium hydroxide acetate	no		no		no	**no**
No		Aluminium monostearate	Aluminium monostearate	no		no		no	**no**
No		Aluminium phosphate	Aluminium phosphate	no		yes	GELATUM ALUMINII PHOSPHORICI PF ZIOLOLEK	no	**yes**
No		Aluminium salicylate, basic	Hydroxyaluminium disalicylate	yes	VETO-ANTI-DIAR	no		no	**yes**
No		Amitraz	Amitraz	yes	APIVAR	no		no	**yes**
No		Ammonium chloride	Ammonium chloride	no		yes	ADDEX-	no	**yes**
Yes	FMP survey	Ammonium lauryl sulphate	Ammonium dodecyl sulfate	yes	Helodip 3.1 % w/v Teat Dip Concentrate	yes	DERMOWAS	no	**yes**
Yes	FMP survey	Ammonium sulfate	Ammonium sulfate	no		no		no	**no**
Yes	CMDv list	Amoxicillin	Amoxicillin	yes	Lamoxsan 150 mg/ml suspension for injection for cattle and pigs	yes	ABBA	no	**yes**
No		Ampicillin	Ampicillin	yes	Vetamplius mucosol 100 g/500 ml polvere e solvente per soluzione iniettabile	yes	A-PEN	no	**yes**
Yes	AAC	Amprolium	Amprolium	yes	Coccibal, 400 mg/ml oplossing voor gebruik in drinkwater voor	no		no	**yes**

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					kippen en kalkoenen				
No		Angelicae radix aetheroleum	Angelica Archangelica Root	no		yes	MELISANA	no	**yes**
No		Anisi aethe- roleum	Anise oil	yes	Colosan, suspensie voor oraal gebruik	yes	ANIZYN	no	**yes**
No		Anisi stellati fructus, standardised extracts and preparations thereof	Anisi Stellati Fructus	no		yes	NAGY SVÉDCSEPP	no	**yes**
No		Apocynum cannabinum	Apocynum cannabinum	no		yes	Herztropfen	no	**yes**
No		Apramycin	Apramycin	yes	Apravet 100 000 NE/g gyógypremix sertések és házinyulak számára A.U.V	no		no	**yes**
No		Aqua levici	Aqua levici	no		no		no	**no**
No		Arginine	Arginine	yes	Ornipural solution	yes	AMINO-MEL NEPHRO	no	**yes**
No		Arnica montana (arnicae los and arnicae planta tota)	Arnica montana planta tota	no		yes	ARNICA BUMPS AND BRUISES	no	**yes**
No		Arnicae radix	Arnicae radix	no		no		no	**no**
No		Artemisia abrotanum	Artemisia abrotanum	yes	Weravet 2 Nymphosal S	yes	Abrotanum	no	**yes**
No		Asparagine	Asparagine	no		yes	AMINOPLASMAL HEPA	no	**yes**
No		Aspartic acid	Aspartic acid	yes	Metabolik	yes	AMINOPLASMAL	no	**yes**
No		Atropa belladonna	Atropa belladonna	yes	Weravet 6 Keratisal	yes	Angin-Heel	no	**yes**

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No		Atropine	Atropine	yes	VT doses atropine 1 pour cent	yes	ATROPIN ACTREVO	no	**yes**
No		Avilamycin	Avilamycin	no		no		no	**no**
No		Azagly-nafarelin	Azagly-nafarelin	no		no		no	**no**
Yes	CMDv list	Azamethiphos	Azamethiphos	no		no		no	**no**
No		Azaperone	Azaperone	yes	Azaporc 40 mg/ml solution for injection for pigs	no		no	**yes**
No		Bacitracin	Bacitracin	yes	Bacivet S 4200 IU/g Poeder voor gebruik in drinkwater	yes	ALTABACTIN	no	**yes**
No		Balsamum peru-vianum	Balsamum peruvianum	no		yes	SOCKETOL	no	**yes**
Yes	CMDv list	Bambermycin	Bambermycin	yes	Флавомицин 80	no		no	**yes**
No		Baquiloprim	Baquiloprim	no		no		no	**no**
No		Barium selenate	Barium selenate	no		no		no	**no**
No		Beclomethasone dipropionate	Beclometasone dipropionate	no		yes	AEROBEC	no	**yes**
No		Bellis perennis	Bellis perennis	yes	Trauma-logoplex forte injekció	yes	Bellis N Oligoplex	no	**yes**
Out of scope	Excipient only	Benzalkonium chloride	Benzalkonium chloride	no		yes	AFTAJUVENTUS	no	**no**
Yes	CMDv list	Benzocaine	Benzocaine	yes	Aureozásyp, 2%, Kožní zásyp	yes	AAA SORE THROAT	no	**yes**
Out of scope	Excipient only	Benzyl alcohol	Benzyl alcohol	no		yes	AUTODERM EXTRA	no	**no**
No		Benzyl benzoate	Benzyl benzoate	no		yes	ACARILBIAL	no	**yes**
No		Benzyl p-hydroxy-benzoate	Benzyl parahydroxybenzoate	no		yes	EPITEST 36	no	**yes**
No		Benzylpenicillin	Benzylpenicillin	yes	Repen suspensão injectável para	yes	BENZYLPENICILLIN SODIUM ROWEX	no	**yes**

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					bovinos, equinos, ovinos, suínos, cães e gatos				
No		Betaine	Betaine Anhydrous	yes	ORNIPURAL solução injetável para Bovinos, Equinos, Ovinos, Suínos, cães e gatos	yes	AMVERSIO	no	**yes**
No		Betaine glucuronate	Betaine glucuronate	no		no		no	**no**
No		Betamethasone	Betamethasone	yes	Penbex	yes	ALPIDER	no	**yes**
No		Biotin	Biotin	yes	Oxytetravit	yes	ACTIVAL EXTRA	no	**yes**
No		Bismuth subcarbonate	Bismuth subcarbonate	no		no		no	**no**
No		Bismuth subsalicylate	Bismuth subsalicylate	no		yes	INTESTAL	no	**yes**
No		Bismuth subgallate	Bismuth subgallate	no		yes	ANUSOL	no	**yes**
No		Bismuth subnitrate	Bismuth subnitrate	yes	ShutOut / Cepralock 2.6 g Intramammary Suspension for Dry Cows	yes	BISMUTH GRANIONS	no	**yes**
No		Bituminosulfonates, ammonium and sodium alts	Ammonium bituminosulfonate concentrate	no		yes	ICHTHO-BAD	no	**yes**
No		Boldo folium	Boldo folium	no		yes	ARTICHOKE-MILK THISTLE COMPLEX	no	**yes**
No		Boric acid and borates	Boric acid	yes	Borogluconat de calciu 38%, soluție injectabilă	yes	ACIDI BORICI FONO VIII. NATURLAND	no	**yes**
No		Bromelain	Bromelains	no		yes	ANANASE	no	**yes**

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No		Bromhexine	Bromhexine	yes	Vetamplius mucosol 4g/20 ml polvere e solvente per soluzione iniettabile	yes	ARDINE	no	**yes**
No		Bromide, potassium salt	Potassium bromide	yes	Kalmofarm	yes	DIBRO-BE MONO	no	**yes**
No		Bromide, sodium salt	Sodium bromide	no		yes	ELIXIRIUM THYMI COMPOSITUM FONO VII	no	**yes**
Yes	CMDv list	Bronopol	Bronopol	no		yes	BRONOPOL SMARTPRACTICE EUROPE	no	**yes**
No		Brotizolam	Brotizolam	yes	Mederantil, 0,2 mg/ml oplossing voor injectie voor runderen	yes	BROTIZOLAM AMDIPHARM	no	**yes**
No		Bupivacaine	Bupivacaine	yes	Equi-Solfen - solução cutânea para cavalos	yes	BUPIVACAINA ANGELINI	no	**yes**
Yes	CMDv list	Buserelin	Buserelin	yes	Бузерин	yes	METRELEF	no	**yes**
No		Butafosfan	Butafosfan	yes	Catophos, 100+0,05mg/ml, Solution for injection	no		no	**yes**
No		Butorphanole tartrate	Butorphanol tartrate	yes	Torbugesic vet 10 mg/ml solução injetável para cavalos, cães e gatos	no		no	**yes**
No		Butyl 4-hydroxy-benzoate	Butyl parahydroxybenzoate	no		yes	BUTYLHYDROXYBENZOAT	no	**yes**

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No		Butylscopolaminium bromide	HYOSCINE BUTYLBROMIDE	yes	Buscopan Compositum ad us. vet. 4 mg/ml + 500 mg/ml, Injektionslösung für Pferde, Kälber und Hunde	yes	ADDOFIX	no	**yes**
No		Cabergoline	Cabergoline	no		yes	ACTUALENE	no	**yes**
No		Caffeine	Caffeine	yes	КОФЕИН НАТРИЕВ БЕНЗОАТ 20% разтвор за инжекции	yes	ACETYLSALICYLIC ACID, PARACETAMOL, COFFEÏNE MAREL	no	**yes**
No		Calcium acetate	Calcium acetate	yes	SURCALCE	yes	CALCET	no	**yes**
No		Calcium borogluconate	Calcium borogluconate	yes	Калциев Бороглюконат 20% разтвор за инжекции	no		no	**yes**
No		Calcium citrate	Calcium citrate	no		yes	CITROKALCIUM	no	**yes**
No		Calcium glucoheptonate	Calcium glucoheptonate	yes	Solução de cálcio Braun solução injetável	yes	CALCIFORTE ÉDULCORÉE AU CYCLAMATE DE SODIUM ET À LA SACCHARINE SODIQUE	no	**yes**
No		Calcium gluconolactate	Calcium gluconolactate	no		no		no	**no**
No		Calcium glycerophosphate	Calcium glycerophosphate	yes	Primalen injekció A.U.V.	yes	ARPHOS	no	**yes**
No		Calcium hypophosphite	Calcium hypophosphite	yes	КАЛЦИВЕКС	yes	ERIGON	no	**yes**
No		Calcium malate	Calcium malate	no		no		no	**no**

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No		Calcium oxide	Calcium oxide	yes	Calcitat - Injektionslösung für Tiere	yes	ICHTOXYL	no	**yes**
No		Calcium pantothenate	Calcium pantothenate	yes	STIMULFOS soluzione iniettabile per bovini, ovini, equini, suini, cani e gatti	yes	APOVIT B-COMBIN STÆRK	no	**yes**
No		Calcium polyphosphates	Calcium polyphosphates	no		no		no	**no**
No		Calcium silicate	Calcium silicate	no		no		no	**no**
No		Calcium stearate	Calcium stearate	no		no		no	**no**
No		Calcium aspartate	Aspartate calcium	no		no		no	**no**
No		Calcium benzoate	Calcium benzoate	no		no		no	**no**
No		Calcium carbonate	Calcium carbonate	yes	CALCIUM, 20%, Injekční roztok	yes	AC-CALCIVITD3 BT	no	**yes**
No		Calcium chloride	Calcium chloride	yes	Soroplasma solução injetável para equinos, bovinos, cães e gatos.	yes	CALCIFORTE ÉDULCORÉE AU CYCLAMATE DE SODIUM ET À LA SACCHARINE SODIQUE	no	**yes**
No		Calcium gluconate	Calcium gluconate	yes	NOROCALCIN 20 CM INJECTION	yes	CALCIFORTE ÉDULCORÉE AU CYCLAMATE DE SODIUM ET À LA SACCHARINE SODIQUE	no	**yes**
No		Calcium glucono gluco- heptonate	Calcium gluconoglucoheptonate	yes	MAGNOPHOS	no		no	**yes**
No		Calcium glutamate	Calcium glutamate	no		no		no	**no**
No		Calcium hydroxide	Calcium hydroxide	yes	Calcitat 50, solution for	no		no	**yes**

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					infusion and injection in cattle				
No		Calcium phosphate	Calcium phosphate	no		yes	CALCIUM AND ERGOCALCIFEROL CRESCENT PHARMA	no	**yes**
No		Calcium propionate	Calcium propionate	yes	PRODIGESTAN perorálny prášok	no		no	**yes**
No		Calcium sulphate	Calcium sulfate	no		yes	CIRCOSAN	no	**yes**
No		Calendula officinalis	Calendula officinalis	yes	Trauma-logoplex forte injekció	yes	Calendumed	no	**yes**
No		Calendulae flos	Calendulae flos	no		yes	EPILOBIN PLANTA	no	**yes**
No		Camphor	Camphor	yes	Камфор-салициликов унгвент	yes	2 - DROP	no	**yes**
No		Camphora	Camphora	no		yes	Chamoca	no	**yes**
No		Capsici fructus acer	Capsici fructus acer	no		yes	SOR VIRGINIA	no	**yes**
No		Carazolol	Carazolol	yes	Simpanorm 0,5 mg/ml Roztwór do wstrzykiwań	no		no	**yes**
No		Carbasalate calcium	Carbasalate calcium	no		yes	ASCAL	no	**yes**
No		Carbetocin	Carbetocin	yes	Depotocin 70 µg/ml, oplossing voor injectie voor runderen en varkens	yes	CARBETOCIN	no	**yes**
No		Cardamon extract	Cardamon extract	no		yes	GALLEXIER KRÄUTERBITTER ELIXIER	no	**yes**
No		Cardiospermum halicacabum	Cardiospermum halicacabum	no		yes	POLLINOSAN HAYFEVER	no	**yes**
No		Carlinae radix	Carlinae radix	no		yes	NAGY SVÉDCSEPP	no	**yes**

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No		Carnitine	Carnitine	yes	METABOLASE FORTE, solution for injection for cattle, sheep, swine, horses	yes	VIGORUP	no	**yes**
No		Carprofen	Carprofen	yes	Carprosol 50 mg/ml solution for injection for cattle	no		no	**yes**
No		Carvi aetheroleum	Carvi aetheroleum	yes	Colosan - Lösung zum Eingeben für Tiere	yes	Milchbildungsöl	no	**yes**
Yes	AAC	Caryophylli aetheroleum	Caryophylli aetheroleum	yes	Melissengeist ademspray, neusspray voor herkauwers, paarden en varkens	yes	Osa Zahnungshilfe	no	**yes**
No		Cefacetrile	Cefacetrile	yes	CEFAXIMIN – L 100 mg/200 mg intramamálna emulzia	no		yes if combination with beta-lactamase inhibitor	**yes (not in combination with beta-lactamase inhibitor)**
No		Cefalexin	Cefalexin	yes	Ceporex vet 180 mg/ml suspensão injetável para bovinos, cães e gatos	yes	CEFALEKSIN BELUPO	yes if combination with beta-lactamase inhibitor	**yes (not in combination with beta-lactamase inhibitor)**
No		Cefalonium	Cefalonium	yes	Seclaris DC 250 mg intramamárna suspenzia pre	no		yes if combination with beta-	**yes (not in combination with beta-**

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					dojnice v období státia na sucho			lactamase inhibitor	**lactamase inhibitor)**
No		Cefapirin	Cefapirin	yes	Mastiplan lc, 300mg/20 mg (cefapirina/prednisolona), suspensão intramamária para vacas em lactação	no		yes if combination with beta-lactamase inhibitor	**yes (not in combination with beta-lactamase inhibitor)**
No		Cefazolin	Cefazolin	yes	Cefovet L 300 mg Suspension zur intramammären Anwendung für Rinder	yes	AZEPO	yes if combination with beta-lactamase inhibitor	**yes (not in combination with beta-lactamase inhibitor)**
No		Cefoperazone	Cefoperazone	yes	Pathozone 25 mg/ml Suspension intramammaire	yes	ACEFA	yes if combination with beta-lactamase inhibitor	**yes (not in combination with beta-lactamase inhibitor)**
No		Cefquinome	Cefquinome	yes	Cobactan LA 7.5% w/v suspension for injection for swine	no		yes if combination with beta-lactamase inhibitor	**yes (not in combination with beta-lactamase inhibitor)**
No		Ceftiofur	Ceftiofur	yes	Actionis 50 mg/ml, sospensione iniettabile per bovini e suini	no		yes if combination with beta-lactamase inhibitor	**yes (not in combination with beta-lactamase inhibitor)**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Centellae asiaticae extractum	Centellae asiaticae extractum	no		yes	Blastoestimulina	no	**yes**
No		Cetostearyl alcohol	Cetostearyl alcohol	no		yes	AQUEOUS BP	no	**yes**
No		Cetrimide	Cetrimide	yes	SPORYL	yes	ANTISEPTIC FIRST AID SAINSBURYS	no	**yes**
No		Chlorhexidine	Chlorhexidine	yes	HIBITANE IRRIGATION	yes	CHLORHEXIDINE/LIDOCAINE CHEMINEAU	no	**yes**
No		Chlormadinone	CHLORMADINONE ACETATE	yes	Anifertil N	yes	ALICE NIO	no	**yes**
No		Chlorocresol	Chlorocresol	yes	ACA CERULEN R, Spray auricolare per conigli	yes	ANBESOL	no	**yes**
Out of scope	Excipient only	Chloroform	Chloroform	no		no		no	**no**
No		Chlorphenamine	Chlorphenamine	yes	PEN-HISTA-STREP	yes	ALERJUVENTUS	no	**yes**
Yes	CMDv list	Chlortetracy- cline	Chlortetracycline	yes	Animedazon Spray 3,21 g kutanspray, suspension	yes	AUREOMYCINE COOPER 3 POUR CENT, pommade	no	**yes**
No		Choline	Choline	yes	BIOVEINE GLUCO-METHIO-CHOLINE	no		no	**yes**
No		Chrysanthemi cinerariifolii flos	Chrysanthemi cinerariifolii flos	no		no		no	**no**
No		Chymotrypsin	Chymotrypsin	yes	Nekro Veyxym injekčná suspenzia	yes	CHIMAR ORAL	no	**yes**
No		Ciclesonide	Ciclesonide	yes	Aservo EquiHaler 343 micrograms/actuation - Inhalation solution	yes	ALVESCO	no	**yes**
No		Cimicifugae racemosae rhizoma	Cimicifugae racemosae rhizoma	no		yes	DONNAFYTA MENO	no	**yes**

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		Original extracted name	**SMS[3] Substance name (cleaned)**	**VMP FP terres-trial[4] (y/n)**	**VMP name example**	**HMP[5] (y/n)**	**HMP name example**	**y/n**	
No		Cinchonae cortex, stan- dardised extracts and preparations thereof	Cinchonae cortex, stan-dardised extracts and preparations thereof	no		yes	AMARA	no	**yes**
No		Cinnamomi cassiae aethe- roleum	Cinnamomi cassiae aetheroleum	yes	Colosan - Lösung zum Eingeben für Tiere	yes	Кармолис	no	**yes**
No		Cinnamomi cassiae cortex, standardised extracts and preparations thereof	Cinnamomi cassiae cortex, standardised extracts and preparations thereof	yes	Colosan - Lösung zum Eingeben für Tiere	yes	Кармолис	no	**yes**
No		Cinnamomi ceylanici aethe-roleum	Cinnamomi ceylanici aethe-roleum	no		yes	AROMATOL	no	**yes**
No		Cinnamomi ceylanici cortex, standardised extracts and preparations thereof	Cinnamomi ceylanici cortex, standardised extracts and preparations thereof	no		no		no	**no**
No		Citri aetheroleum	Citri aetheroleum	yes	Melissengeist ademspray, neusspray voor herkauwers, paarden en varkens	yes	AMOL	no	**yes**
No		Citronellae aetheroleum	Citronellae aetheroleum	yes	Melissengeist ademspray, neusspray voor herkauwers, paarden en varkens	yes	AMOL	no	**yes**

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Citrulline	Citrulline	yes	NEATOX, solution for injection for cattle, horses, swine, dogs and cats	no		no	**yes**
Yes	Combination with Amoxicillin	Clavulanic acid	Clavulanic acid	yes	SYNULOX - SOSPENSIONE INIETTABILE	yes	ABBA	yes if combination with cephalosporin	**yes (not in combination with cephalosporin)**
No		Clazuril	Clazuril	no		no		no	**no**
Out of scope	Beta-agonist	Clenbuterol hydrochloride	Clenbuterol hydrochloride	yes	Subestin 25 microgram/ml oral solution for horses	yes	CLEMBROXOL	no	**no**
No		Clodronic acid (in the form of disodium salt)	Clodronate disodium tetrahydrate	yes	Osphos 51 mg/ml solution for injection for horses	yes	ACIDO CLODRONICO DOC GENERICI	no	**yes**
No		Cloprostenol	Cloprostenol	yes	Veteglan 0,075 mg/ml injektionsvæske, opløsning	no		no	**yes**
No		Clorsulon	Clorsulon	yes	TOPIMEC F, 10 mg/ml / 100 mg/ml, injekcinis tirpalas galvijams	no		no	**yes**
No		Closantel	Closantel	yes	TELCEN	no		no	**yes**
No		Cloxacillin	Cloxacillin	yes	Orbenin EDC 600 mg Suspension zur intramammären Anwendung	yes	ANACLOSIL	no	**yes**

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No		Cobalt dich- loride	Cobalt dichloride hexahydrate	yes	PRODIGESTAN perorálny prášok	yes	KIDIAMIX G	no	**yes**
No		Cobalt oxide	Cobalt oxide	no		no		no	**no**
No		Cobalt sulphate	Cobalt sulfate	no		no		no	**no**
No		Cobalt trioxide	Cobalt trioxide	no		no		no	**no**
No		Cobalt carbonate	Cobalt carbonate	no		no		no	**no**
No		Cobalt gluconate	Cobalt gluconate	yes	Fercobsang, solução injetável e oral para equinos, bovinos, ovinos, caprinos, suínos, cães e gatos	yes	COBALT OLIGOSOL LABCATAL	no	**yes**
Out of scope	Excipient only	Coco alkyl dimethyl betaines	Coco alkyl dimethyl betaines	no		no		no	**no**
No		Colistin	Colistin	yes	COLISTIN APSA 1 200 000 IU/g	yes	BAKTO-DIARÖNT	no	**yes**
No		Condurango cortex, stan- dardised extracts and preparations thereof	Condurango cortex, stan-dardised extracts and preparations thereof	yes	ZOOCOLAGOGO C.M.	yes	PASCOPANKREAT	no	**yes**
No		Convallaria majalis	Convallaria majalis	yes	Scilla comp. PlantaVet	yes	Presselin Hk Mischung	no	**yes**
No		Copper chloride	Copper chloride	yes	GAFERVIT, Injekční roztok	yes	NUTRITRACE	no	**yes**
No		Copper hept- anoate	Copper heptanoate	no		no		no	**no**
No		Copper oxide	Copper oxide	no		no		no	**no**
Yes	FMP survey	Copper sulphate	Copper sulfate	yes	MULTIVIT–MINERAL, injekcinis tirpalas	yes	AQUA CUPROZINCICA	no	**yes**
No		Copper carbonate	Copper carbonate	no		no		no	**no**

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No		Copper gluconate	Copper gluconate	yes	Hemo 15 soluzione iniettabile per cavalli bovini e suini	yes	ADDEL JUNIOR	no	**yes**
No		Copper methionate	Copper methionate	yes	B.V.P. COPPER WITH VITAMIN B12 INJECTION	no		no	**yes**
No		Coriandri aetheroleum	Coriandri aetheroleum	no		yes	ARGOL ESSENZA BALSAMICA	no	**yes**
No		Corticotropin	Corticotropin	no		no		no	**no**
No		Coumafos	Coumafos	yes	Perizin	no		no	**yes**
No		Crataegus	Crataegus	yes	Scilla comp. PlantaVet	yes	Pectapas Cpl.-Injektopas	no	**yes**
No		Cupressi aethe-roleum	Cupressi aethe-roleum	no		no		no	**no**
No		Cyfluthrin	Cyfluthrin	yes	Bayofly solução para unção contínua para bovinos	no		no	**yes**
No		Cyhalothrin	Cyhalothrin	no		no		no	**no**
No[6]		Cypermethrin	Cypermethrin	yes	ECTOPOR 2%W/V ΔΕΡΜΑΤΙΚΟ ΔΙΑΛΥΜΑ	no		no	**yes**
No		Cyromazine	Cyromazine	no		no		no	**no**
No		Cysteine	Cysteine	yes	DUPHALYTE injekčný roztok	yes	AMIPED	no	**yes**
No		Cytidine and its 5'-mono-, 5'-di-	Cytidine	no		yes	CENTRUM	no	**yes**

[6] Cypermethrin was initially identified as important for the treatment of food-producing aquatic species since it is the active substance of authorised veterinary medicinal product for fish. However, considering that cypermethrin is listed in current version of Annex X 'List of priority substances in the field of water policy' [i.e. is a substance of concern] of the Water Framework Directive, the substance was downgraded to the 'other substances'.

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
		and 5'-triphosphates							
No		Danofloxacin	Danofloxacin	yes	Advocid 2,5 %	no		no	**yes**
Yes	AEMPS	Decoquinate	Decoquinate	yes	Deccox 6 - Pré-mistura para alimento medicamentoso para bovinos e ovinos.	no		no	**yes**
Yes	CMDv list	Deltamethrin	Deltamethrin	yes	BUTOX PROTECT 7,5MG/ML ΕΝΑΙΩΡΗΜΑ ΕΠΙΧΥΣΗΣ	no		no	**yes**
No		Dembrexine	Dembrexine	yes	Venti Plus	no		no	**yes**
No		Denaverine hydrochloride	Denaverine hydrochloride	yes	Sensiblex 40 mg/ml solution for injection for cattle	no		no	**yes**
No		Derquantel	Derquantel	yes	Startect Dual Active Oral Solution for Sheep	no		no	**yes**
No		Deslorelin acetate	Deslorelin acetate	no		no		no	**no**
No		Detomidine	Detomidine	yes	Presedine 10 mg/ml solution for injection for horses and cattle	no		no	**yes**
No		Dexamethasone	Dexamethasone	yes	FATROCORTIN 0,2 mg/ml, soluzione iniettabile per bovini, suini, equini, cani e gatti	yes	AMELINOR	no	**yes**

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Dexpanthenol	Dexpanthenol	yes	MULTIVIT INJ., soluție injectabilă pentru cabaline, mânji, bovine, viței, miei, purcei, pui de găină, porumbei	yes	ACODIN 150 JUNIOR	no	**yes**
No		Diazinon	Diazinon	yes	Zooveca 150 mg/ml solução tópica para bovinos, ovinos e suínos	no		no	**yes**
No		Diclazuril	Diclazuril	yes	VECOXAN 2.5 MG/ML ORAL SUSPENSION FOR LAMBS AND CALVES	no		no	**yes**
No		Diclofenac	Diclofenac	yes	DOLOFENAC 50 mg/ml SOLUCION INYECTABLE	yes	ALMIRAL	no	**yes**
No		Dicloxacillin	Dicloxacillin	yes	CLOXALENE PLUS 200 mg + 200 mg/5 ml intramammárna masť	yes	DICLIN	no	**yes**
No		Dicopper oxide	Dicopper oxide	no		no		no	**no**
No		Dicyclanil	Dicyclanil	yes	CLIK 5% Pour-on Suspension for Sheep	no		no	**yes**
No		Diethyl sebacate	Diethyl sebacate	no		no		no	**no**
No		Diethyl phthalate	Diethyl phthalate	no		no		no	**no**
No		Diethylene glycol monethyl ether	Diethylene glycol monoethyl ether	no		no		no	**no**

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Difloxacin	Difloxacin	yes	Diflocin 100 mg/g oldat ivóvízbe keveréshez házityúkok, pulykák részére A.U.V.	no		no	**yes**
Yes	CMDv list	Diflubenzuron	Diflubenzuron	no		no		no	**no**
No		Dihydrostrep-tomycin	Dihydrostreptomycin	yes	CRODISTREPTO suspensão injetável para bovinos, ovinos, suínos e equinos	no		no	**yes**
No		Dimanganese trioxide	Dimanganese trioxide	no		no		no	**no**
No		Dimethicone	Dimethicone	yes	SICADEN-S	yes	Conotrane	no	**yes**
No		Dimethyl acetamide	Dimethylacetamide	no		no		no	**no**
No		Dimethyl phthalate	Dimethyl phthalate	no		yes	NOVASCABIN	no	**yes**
No		Dimethyl sulphoxide	Dimethyl sulfoxide	yes	TRAUFIN	yes	Osteogēls	no	**yes**
No		Dinoprost	Dinoprost	no		no		no	**no**
No		Dinoprost tromethamine	Dinoprost tromethamine	yes	ENZAPROST T	no		no	**yes**
No		Dinoprostone	Dinoprostone	no		yes	Cervidil	no	**yes**
No		Diprophylline	Diprophylline	yes	Analeptol 50 mg/ml + 50 mg/ml solution for injection for cattle, horses, pigs, dogs and cats	yes	ALERJUVENTUS EXPECTORANTE	no	**yes**
No		Doramectin	Doramectin	yes	Doramax 10 mg/ml Solution for Injection for	no		no	**yes**

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
					Cattle, Sheep and Pigs				
No		Double stranded ribonucleic acid homologous to viral ribonucleic acid coding for part of the coat protein and part of the intergenic region of the Israel Acute Paralysis Virus	Double stranded ribonucleic acid homologous to viral ribonucleic acid coding for part of the coat protein and part of the intergenic region of the Israel Acute Paralysis Virus	no		no		no	**no**
No		Doxapram	Doxapram	yes	DOPRAM-V INJECTABLE	yes	DOPRAM	no	**yes**
Yes	FMP survey	Doxycycline	Doxycycline	yes	DOXIPULVIS S.P. 500 mg/g POLVO PARA ADMINISTRACIÓN EN AGUA DE BEBIDA O LACTOREEMPLAZANTE	yes	ADJUSAN	no	**yes**
No		D-Phenylalanine (6) –luteinising-hormone releasing hormone	D-Phenylalanine (6) –luteinising-hormone releasing hormone	yes	GONADORELIN Bioveta, 0,05ml/ml, Injekční roztok	no		no	**yes**
No		Echinacea	Echinacea	yes	Endometrium comp. A PlantaVet	yes	Pectovowen	no	**yes**
No		Echinacea purpurea	Echinacea purpurea	yes	Traumeel S gel	yes	ESBERITOX N	no	**yes**
Yes	CMDv list	Emamectin	EMAMECTIN BENZOATE	no		no		no	**no**
No		Enilconazole	Enilconazole	yes	IMAVEROL	no		no	**yes**

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terres-trial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
Yes	CMDv list	Enrofloxacin	Enrofloxacin	yes	Enrolen 10% Solution for Injection	no		no	**yes**
No		Epinephrine	Epinephrine	yes	Multi-Solfen, solução cutânea para bovinos	yes	ADREANALIN TAKEDA	no	**yes**
No		Eprinomectin	Eprinomectin	yes	Eprivalan 5mg/ml pour-on solution for cattle	no		no	**yes**
No		Ergometrine maleate	Ergometrine maleate	yes	Biopartus 0,4 mg/ml Roztwór do wstrzykiwań	yes	ERGOMETRINE N.A.	no	**yes**
Yes	FMP survey	Erythromycin	Erythromycin	yes	Eritromicina 15% Chemifarma 150 mg/g, polvere orale per uso in acqua da bere, per polli da carne, tacchini e galline ovaiole	yes	ABBOTICIN	no	**yes**
No		Etamiphylline camsylate	Etamiphylline camsylate	no		no		no	**no**
No		Etamsylate	Etamsylate	yes	Hemosilate vet 125 mg/ml Roztwór do wstrzykiwań	yes	CYCLONAMINE	no	**yes**
Out of scope	Excipient only	Ethanol	Ethanol	no		yes	ALCOOL A USAGE MEDICAL	no	**no**
No		Ethyl lactate	Ethyl lactate	no		no		no	**no**
No		Ethyl oleate	Ethyl oleate	no		no		no	**no**
No		Ethylenedia-minetetraacetic acid and salts	Ethylenediaminetetraacetic acid and salts	no		yes	CHELATRAN	no	**yes**

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Etiproston tromethamine	Etiproston tromethamine	yes	Prostavet-C injekció A.U.V.	no		no	**yes**
No		Eucalypti aetheroleum	Eucalypti aetheroleum	yes	EucaComp PlantaVet	yes	Luuf Verkoudheidsbalsem	no	**yes**
No		Eucalyptol	Eucalyptol	yes	Apilife var tira para colmeias de abelhas	yes	Essence Algerienne	no	**yes**
No		Eucalyptus globulus	Eucalyptus globulus	no		yes	Aconitum-Homaccord	no	**yes**
No		Euphrasia officinalis	Euphrasia officinalis	yes	Weravet 6 Keratisal	yes	Adler Hom Yvosniff	no	**yes**
No		Febantel	Febantel	yes	Avicas 15 mg Comprimé	no		no	**yes**
Yes	Norway list	Fenbendazole	Fenbendazole	yes	Pigfen 40 mg/g premix for medicated feeding stuff for pigs	no		no	**yes**
No		Fenpipramide hydrochloride	Fenpipramide hydrochloride	yes	L-Polamivet vet injektioneste, liuos	no		no	**yes**
No		Fenvalerate	Fenvalerate	no		no		no	**no**
No		Fertirelin acetate	Fertirelin acetate	no		no		no	**no**
No		Firocoxib	Firocoxib	yes	Equioxx 8.2 mg/g - Oral paste	no		no	**yes**
Yes	CMDv list	Florfenicol	Florfenicol	yes	ФЛОРФЕНИКОЛ 20	no		no	**yes**
No		Fluazuron	Fluazuron	no		no		no	**no**
Yes	Sweden list	Flubendazole	Flubendazole	yes	Fludosol 200 mg/ml suspenzia na použitie v pitnej vode pre ošípané a kury domáce	yes	FLUVERMAL	no	**yes**
No		Flugestone acetate	Flugestone acetate	yes	CHRONOGEST CR	no		no	**yes**

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Yes	CMDv list	Flumequine	Flumequine	yes	Flumechina 20% Chemifarma, polvere per soluzione orale per polli e suini	no		no	**yes**
No		Flumethrin	Flumethrin	yes	PolyVar Yellow 275 mg bee-hive strip	no		no	**yes**
No		Flunixin	Flunixin	yes	Cyclofin 300 mg/ml + 20 mg/ml solution for injection for cattle	no		no	**yes**
No		Fluralaner	Fluralaner	yes	Exzolt 10 mg/ml - Solution for use in drinking water	no		no	**yes**
No		Foeniculi aethe-roleum	Foeniculi aethe-roleum	yes	Colosan, suspensie voor oraal gebruik	yes	Melissenöl	no	**yes**
No		Folic acid	Folic acid	yes	Multivit extra	yes	ACFOL	no	**yes**
No		Follicle stimu-lating hormone (natural FSH from all species and their synthetic analogues)	Follicle stimulating hormone	yes	PLUSET 500 IU/500 IU powder and solvent for solution for injection for cattle	yes	FERTINORM	no	**yes**
No		Food additives *	E 470b - Magnesium salts of fatty acids	no		no		no	**no**
No		Food additives *	E 470a - Sodium, potassium and calcium salts of fatty acids	yes	ARA PNEUMOPATHIE	no		no	**yes**
No		Food additives *	E 304 - Fatty acid esters of ascorbic acid	no		no		no	**no**

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No		Food additives *	E 559 - Aluminium silicate (Kaolin)	no		no		no	**no**
No		Food additives *	E 466 - Sodium carboxy methyl cellulose, cellulose gum	no		yes	CARMELOSA QUALIGEN	no	**yes**
No		Food additives *	E 469 - Enzymatically hydrolysed carboxy methyl cellulose, Enzymatically hydrolysed cellulose gum	no		no		no	**no**
No		Food additives *	E 120 - Cochineal, Carminic acid, Carmines	no		no		no	**no**
No		Food additives *	E 468 - Cross-linked sodium carboxy methyl cellulose, cross linked cellulose gum	no		no		no	**no**
No		Food additives *	E 160b(i) – Annatto bixin	no		no		no	**no**
No		Food additives *	E 160b(ii) – Annatto norbixin	no		no		no	**no**
No		Food additives *	E 1202 - Polyvinylpolypyrrolidone	no		yes	BOLINAN	no	**yes**
No		Food additives *	E 224 - Potassium metabisulphite	no		no		no	**no**
No		Food additives *	E 290 - Carbon dioxide	no		yes	BAD NIEDERNAUER RÖMERQUELLE	no	**yes**
No		Food additives *	E 462 - Ethyl cellulose	no		no		no	**no**
No		Food additives *	E 320 - Butylated hydroxyanisole (BHA)	no		yes	BUTYLHYDROXYANISOL SMARTPRACTICE EUROPE	no	**yes**
No		Food additives *	E 321 - Butylated hydroxytoluene (BHT)	no		yes	BUTYLHYDROXYTOLUOL SMARTPRACTICE EUROPE	no	**yes**
No		Food additives *	E 903 - Carnauba wax	no		no		no	**no**
No		Food additives *	E 385 - Calcium disodium ethylene diamine tetra-acetate (Calcium disodium EDTA)	no		no		no	**no**
No		Food additives *	E 404 - Calcium alginate	no		no		no	**no**
No		Food additives *	E 161g - Canthaxanthin	no		no		no	**no**
No		Food additives *	E 950 - Acesulfame K	no		no		no	**no**

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No		Food additives *	E 520 - Aluminium sulphate	no		yes	BOOTS STYPTIC PENCIL	no	**yes**
No		Food additives *	E 905 - Microcrystalline wax	no		yes	DERMAPHARM BASISSALBE	no	**yes**
No		Food additives *	E 967 - Xylitol	no		yes	AMINOMIX 4	no	**yes**
No		Food additives *	E 553a - Magnesium silicate	no		no		no	**no**
No		Food additives *	E 322 - Lecithins	no		yes	BUERLECITHIN	no	**yes**
No		Food additives *	E 558 - Bentonite	no		no		no	**no**
No		Food additives *	E 425 - Konjac	no		no		no	**no**
No		Food additives *	E 1518 - Glyceryl triacetate (triacetin)	no		no		no	**no**
No		Food additives *	E 556 - Calcium aluminium silicate	no		no		no	**no**
No		Food additives *	E 522 - Aluminium potassium sulphate	no		yes	CO-BUCAL	no	**yes**
No		Food additives *	E 123 - Amaranth	no		no		no	**no**
No		Food additives *	E 523 - Aluminium ammonium sulphate	no		no		no	**no**
No		Food additives *	E 503 - Ammonium carbonates	no		no		no	**no**
No		Food additives *	E 200 - Sorbic acid	no		yes	SORBINSÄURE SMARTPRACTICE EUROPE	no	**yes**
No		Food additives *	E 512 - Stannous chloride	no		yes	CARDIOSCAN	no	**yes**
No		Food additives *	E 626 - Guanylic acid	no		no		no	**no**
No		Food additives *	E 586 - 4-Hexylresorcinol	no		yes	4-HEXYLRESORCIN SMARTPRACTICE EUROPE	no	**yes**
No		Food additives *	E 355 - Adipic acid	no		no		no	**no**
No		Food additives *	E 337 - Sodium potassium tartrate	no		no		no	**no**
No		Food additives *	E 220 - Sulphur dioxide	no		no		no	**no**
No		Food additives *	E 222 - Sodium hydrogen sulphite	no		no		no	**no**
No		Food additives *	E 335 - Sodium tartrates	no		no		no	**no**

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No		Food additives *	E 514 - Sodium sulphates	no		yes	CASENGLICOL	no	**yes**
No		Food additives *	E 574 - Gluconic acid	no		no		no	**no**
No		Food additives *	E 175 - Gold	no		yes	D'OR GRANIONS	no	**yes**
No		Food additives *	E 133 - Brilliant Blue FCF	no		no		no	**no**
No		Food additives *	E 955 - Sucralose	no		no		no	**no**
No		Food additives *	E 954 - Saccharins	no		no		no	**no**
No		Food additives *	E 174 - Silver	no		no		no	**no**
No		Food additives *	E 585 - Ferrous lactate	no		no		no	**no**
No		Food additives *	E 1203 - Polyvinyl alcohol (PVA)	no		yes	ONUFRID	no	**yes**
No		Food additives *	E 127 - Erythrosine	no		yes	ENDEKAY DISCLOSING	no	**yes**
No		Food additives *	E 432 - Polyoxyethylene sorbitan monolaurate (polysorbate 20	no		yes	FLUISEDAL	no	**yes**
No		Food additives *	E 202 - Potassium sorbate	no		no		no	**no**
No		Food additives *	E 938 - Argon	no		no		no	**no**
No		Food additives *	E 297 - Fumaric acid	no		no		no	**no**
No		Food additives *	E 570 - Fatty acids	no		no		no	**no**
No		Food additives *	E 132 - Indigotine, Indigo carmine	no		yes	CARMIN D'INDIGO PROVINGO PROVEPHARM	no	**yes**
No		Food additives *	E 527 - Ammonium hydroxide	no		no		no	**no**
No		Food additives *	E 363 - Succinic acid	no		yes	ACTIVAL JUNIOR	no	**yes**
No		Food additives *	E 553b - Talc	no		yes	ALOPLASTINE	no	**yes**
No		Food additives *	E 1404 - Oxidised starch	no		no		no	**no**
No		Food additives *	E 310 - Propyl gallate	no		no		no	**no**
No		Food additives *	E 450 - Diphosphates	no		no		no	**no**
No		Food additives *	E 941 - Nitrogen	no		yes	AMINOPLASMAL PAEDIATRIC	no	**yes**
No		Food additives *	E 1505 - Triethyl citrate	no		no		no	**no**
No		Food additives *	E 434 - Polyoxyethylene sorbitan monopalmitate (polysorbate 40)	no		yes	DECODERM	no	**yes**
No		Food additives *	E 501 - Potassium carbonates	no		yes	ZOLFO E POTASSIO CARBONATO NEW.FA.DEM.	no	**yes**

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No		Food additives *	E 357 - Potassium adipate	no		no		no	**no**
No		Food additives *	E 577 - Potassium gluconate	no		yes	OLIGOSOL	no	**yes**
No		Food additives *	E 622 - Monopotassium glutamate	no		no		no	**no**
No		Food additives *	E 415 - Xanthan gum	no		no		no	**no**
No		Food additives *	E 219 - Sodium methyl p-hydroxybenzoate	no		no		no	**no**
No		Food additives *	E 904 - Shellac	no		no		no	**no**
No		Food additives *	E 500 - Sodium carbonates	yes	Effydral, compresse effervescenti per bovini (vitelli)	yes	ACCUSOL 35	no	**yes**
No		Food additives *	E 223 - Sodium metabisulphite	no		yes	NATRIUMDISULFIT SMARTPRACTICE EUROPE	no	**yes**
No		Food additives *	E 326 - Potassium lactate	no		no		no	**no**
No		Food additives *	E 338 - Phosphoric acid	no		no		no	**no**
No		Food additives *	E 959 - Neohesperidine DC	no		no		no	**no**
No		Food additives *	E 471 - Mono-and diglycerides of fatty acids	no		no		no	**no**
No		Food additives *	E 440 - Pectins	yes	DIAR STOP FORTE powder for oral use for calves, swine, pigs, dogs and cats	yes	DIARRHOESAN SAFT	no	**yes**
No		Food additives *	E 435 - Polyoxyethylene sorbitan monostearate (polysorbate 60)	no		yes	DERMAPHARM BASISCREME	no	**yes**
No		Food additives *	E 953 - Isomalt	no		no		no	**no**
No		Food additives *	E 965 - Maltitols	no		no		no	**no**
No		Food additives *	E 412 - Guar gum	no		yes	FIBRAGUAR	no	**yes**
No		Food additives *	E 952 - Cyclamates	no		no		no	**no**
No		Food additives *	E 493 - Sorbitan monolaurate	no		no		no	**no**
No		Food additives *	E 495 - Sorbitan monopalmitate	no		no		no	**no**
No		Food additives *	E 492 - Sorbitan tristearate	no		no		no	**no**

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No		Food additives *	E 262 - Sodium acetates	yes	ERGOGEN COMPLEX	yes	ACETATO SÓDICO FRESENIUS KABI	no	**yes**
No		Food additives *	E 406 - Agar	no		no		no	**no**
No		Food additives *	E 340 - Potassium phosphates	yes	LACTOLYTE	yes	HYPOTONAX 48	no	**yes**
No		Food additives *	E 461 - Methyl cellulose	no		yes	LACRIMART	no	**yes**
No		Food additives *	E 300 - Ascorbic acid	yes	MULTIVIT INJ., soluție injectabilă pentru cabaline, mânji, bovine, viței, miei, purcei, pui de găină, porumbei	yes	ABIDEC MULTIVITAMIN	no	**yes**
No		Food additives *	E 459 - Beta-cyclodextrin	no		no		no	**no**
No		Food additives *	E 460 - Cellulose	no		no		no	**no**
No		Food additives *	E 336 - Potassium tartrates	no		yes	NATI-K	no	**yes**
No		Food additives *	E 631 - Disodium inosinate	no		no		no	**no**
No		Food additives *	E 339 - Sodium phosphates	no		yes	CITORSAL	no	**yes**
No		Food additives *	E 463 - Hydroxypropyl cellulose	no		no		no	**no**
No		Food additives *	E 414 - Gum arabic (acacia gum)	no		no		no	**no**
No		Food additives *	E 901 - Beeswax, white and yellow	no		no		no	**no**
No		Food additives *	E 464 - Hydroxypropyl methyl cellulose	no		yes	ACUOLENS	no	**yes**
No		Food additives *	E 554 - Sodium aluminium silicate	no		no		no	**no**
No		Food additives *	E 621 - Monosodium glutamate	yes	DUPHALYTE, Injekční roztok	no		no	**yes**
No		Food additives *	E 211 - Sodium benzoate	yes	CAFFEINE AND SODIUM BENZOATE 20% solutio pro injectionibus	yes	CARIDENT	no	**yes**
No		Food additives *	E 1205 - Basic methacrylate copolymer	no		no		no	**no**
No		Food additives *	E 491 - Sorbitan monostearate	no		no		no	**no**

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No		Food additives *	E 160d - Lycopene	no		yes	ACTIVAL EXTRA	no	**yes**
No		Food additives *	E 215 - Sodium ethyl p-hydroxybenzoate	no		no		no	**no**
No		Food additives *	E 161b - Lutein	no		yes	ACTIVAL EXTRA	no	**yes**
No		Food additives *	E 153 - Vegetable carbon	no		no		no	**no**
No		Food additives *	E 939 - Helium	no		yes	APULCO	no	**yes**
No		Food additives *	E 218 - Methyl p-hydroxybenzoate	yes	MORANTEL TARTRATO 4% LIQUIDO, 40 mg/ml soluzione orale per bovini, ovini e caprini	yes	EPITEST 36	no	**yes**
No		Food additives *	E 1200 - Polydextrose	no		no		no	**no**
No		Food additives *	E 494 - Sorbitan monooleate	no		no		no	**no**
No		Food additives *	E 260 - Acetic acid	no		yes	APORIL	no	**yes**
No		Food additives *	E 515 - Potassium sulphates	no		yes	EZICLEN	no	**yes**
No		Food additives *	E 943a - Butane	no		no		no	**no**
No		Food additives *	E 261 - Potassium acetate	yes	ERGOGEN COMPLEX, injekcinis tirpalas	yes	ACETATO DE POTASIO B.BRAUN	no	**yes**
No		Food additives *	E 142 - Green S	no		no		no	**no**
No		Food additives *	E 325 - Sodium lactate	yes	Vetivex solution au ringer lactate pour perfusion pour bovins, chevaux, chiens	yes	ARDEAELYTOSOL D	no	**yes**
No		Food additives *	E 400 - Alginic acid	no		yes	GAVISCON	no	**yes**
No		Food additives *	E 401 - Sodium alginate	yes	MASTIPIS-S intramamálny gél	yes	ACIDEX	no	**yes**
No		Food additives *	E 124 - Ponceau 4R, Cochineal Red A	no		no		no	**no**
No		Food additives *	E 524 - Sodium hydroxide	yes	RINGER LATTATO ACME, soluzione perfusionale per	yes	AMINOMEL	no	**yes**

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					cavalli, bovini, cani e gatti				
No		Food additives *	E 1517 - Glyceryl diacetate (diacetin)	no		no		no	**no**
No		Food additives *	E 210 - Benzoic acid (1)	yes	DERMAFLON Crema per cani, gatti, cavalli, bovini e suini	yes	ACERBINE	no	**yes**
No		Food additives *	E 948 - Oxygen	no		yes	ACTYNOX	no	**yes**
No		Food additives *	E 356 - Sodium adipate	no		no		no	**no**
No		Food additives *	E 1452 - Starch aluminium octenyl succinate	no		no		no	**no**
No		Food additives *	E 302 - Calcium ascorbate	no		yes	BIO-C-VITAMIN	no	**yes**
No		Food additives *	E 579 - Ferrous gluconate	no		yes	ACIFER	no	**yes**
No		Food additives *	E 301 - Sodium ascorbate	yes	VITAMIN AD3EC oralna emulzija, za goveda, konje, svinje, ovce, koze, kuniće, nerčeve, činčile, kokoši, purane, golubove	yes	AMYXEDYL,	no	**yes**
No		Food additives *	E 551 - Silicon dioxide	no		yes	BUMINIFORM	no	**yes**
No		Food additives *	E 576 - Sodium gluconate	yes	Plasmalyte WET 5,26 g/1000 ml + 0,37 g/1000 ml + 0,3 g/1000 ml + 3,68 g/1000 ml + 5,02 g/1000 ml Roztwór do infuzji	yes	CRYSTALSOL	no	**yes**
No		Food additives *	E 966 - Lactitol	no		yes	IMPORTAL	no	**yes**
No		Food additives *	E 332 - Potassium citrates	yes	BIODIET ROSE	yes	ACALKA	no	**yes**

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No		Food additives *	E 508 - Potassium chloride	yes	Lactato de ringer Braun Vet, associação, solução injetável para bovinos, equinos, ovinos, caprinos, suínos, cães e gatos	yes	1 M KALIJEV KLORID HZTM	no	**yes**
No		Food additives *	E 160a - Carotenes	yes	Carofertin 10 mg/ml - Injektionslösung für Rinder, Schweine und Pferde	yes	ACTIVAL EXTRA	no	**yes**
No		Food additives *	E 525 - Potassium hydroxide	no		yes	ADDEX-KALIUM	no	**yes**
No		Food additives *	E 331 - Sodium citrates	yes	LECTADE PLUS, Prášek pro perorální roztok	yes	AURIMEL	no	**yes**
No		Food additives *	E 407 - Carrageenan	no		yes	TITANOREIN	no	**yes**
No		Food additives *	E 420 - Sorbitols	yes	Neatox solução injectável para bovinos, equinos, suínos, cães e gatos	yes	ARGININA-SORBITOL INFOMED FLUIDS	no	**yes**
No		Food additives *	E 327 - Calcium lactate	yes	Electrovit poeder voor toediening via drinkwater voor kalveren en biggen	yes	CITORSAL	no	**yes**
No		Food additives *	E 942 - Nitrous oxide	no		yes	ACTYNOX	no	**yes**
No		Food additives *	E 171 - Titanium dioxide	no		yes	HEMOFISSURAL, ASSOCIAÇÃO	no	**yes**
No		Food additives *	E 102 - Tartrazine	no		no		no	**no**

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No		Food additives *	E 1201 - Polyvinylpyrrolidone	yes	ANTIEMOR-K, 10 mg/ml + 30 mg/ml Soluzione iniettabile per Bovini, Equini, Suini, Ovini, Caprini, Cani e Gatti	yes	ALGODOL	no	**yes**
No		Food additives *	E 110 - Sunset Yellow FCF/Orange Yellow S	no		no		no	**no**
No		Food additives *	E 173 - Aluminium	yes	Aluspray 4% w/w Cutaneous Spray, Powder	yes	NOVALUZID	no	**yes**
No		Food additives *	E 422 - Glycerol	yes	Eimü-Doppeldip	yes	ADULAX	no	**yes**
No		Food additives *	E 214 - Ethyl-p-hydroxybenzoate	no		yes	EPITEST 36	no	**yes**
No		Food additives *	E 150a - Plain caramel (1)	no		no		no	**no**
No		Food additives *	E 140 - Chlorophylls and chlorophyllins	no		no		no	**no**
No		Food additives *	E 104 - Quinoline Yellow	no		no		no	**no**
No		Food additives *	E 151 - Brilliant Black BN, Black PN	no		no		no	**no**
No		Food additives *	E 122 - Azorubine, Carmoisine	no		no		no	**no**
No		Food additives *	E 330 - Citric acid	yes	Biopect, poeder voor gebruik in drinkwater/melk voor kalveren, lammeren en biggen	yes	CITRAFLEET	no	**yes**
No		Food additives *	E 100 - Curcumin	no		yes	CHOLAGOL	no	**yes**
No		Food additives *	E 150c - Ammonia caramel	no		no		no	**no**
No		Food additives *	E 129 - Allura Red AC	no		no		no	**no**
No		Food additives *	E 155 - Brown HT	no		no		no	**no**
No		Food additives *	E 1521 - Polyethylene glycol	no		yes	POLYETHYLENGLYKOL SALBE	no	**yes**

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							SMARTPRACTICE EUROPE		
No		Food additives *	E 405 - Propane-1, 2-diol alginate	no		no		no	**no**
No		Food additives *	E 131 - Patent Blue V	yes	Terramicina Spray para bovinos, ovinos, caprinos, equinos, suínos e coelhos	no		no	**yes**
No		Food additives *	E 163 - Anthocyanins	no		no		no	**no**
No		Food additives *	E 351 - Potassium malate	no		yes	POTASSION - SALI DI POTASSIO	no	**yes**
No		Food additives *	E 536 - Potassium ferrocyanide	no		no		no	**no**
No		Food additives *	E 957 - Thaumatin	no		no		no	**no**
No		Food additives *	E 1204 - Pullulan	no		no		no	**no**
No		Food additives *	E 627 - Disodium guanylate	no		no		no	**no**
No		Food additives *	E 473 - Sucrose esters of fatty acids	no		no		no	**no**
No		Food additives *	E 418 - Gellan gum	no		no		no	**no**
No		Food additives *	E 162 - Beetroot Red, betanin	no		no		no	**no**
No		Food additives *	E 1440 - Hydroxy propyl starch	no		no		no	**no**
No		Food additives * consumption)	E 221 - Sodium sulphite	no		no		no	**no**
No		Food additives *	E 141 - Copper complexes of chlorophylls, chlorophyllins	no		no		no	**no**
No		Food additives *	E 513 - Sulphuric acid	no		yes	OXOVASIN	no	**yes**
No		Food additives *	E 402 - Potassium alginate	no		no		no	**no**
No		Food additives *	E 172 - Iron oxides and hydroxides	no		yes	VELTIFER	no	**yes**
No		Food additives *	E 902 - Candelilla wax	no		no		no	**no**
No		Food additives *	E 1450 - Starch sodium octenyl succinate	no		no		no	**no**
No		Food additives *	E 431 - Polyoxyethylene (40) stearate	no		no		no	**no**

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No		Food additives *	E 436 - Polyoxyethylene sorbitan tristearate (polysorbate 65)	no		no		no	**no**
No		Food additives *	E 416 - Karaya gum	no		yes	NORMACOL	no	**yes**
No		Food additives *	E 427 - Cassia gum	no		no		no	**no**
No		Food additives *	E 150d - Sulphite ammonia caramel	no		no		no	**no**
No		Food additives *	E 410 - Locust bean gum	no		no		no	**no**
No		Food additives *	E 951 - Aspartame	no		no		no	**no**
No		Food additives *	E 555 - Potassium aluminium silicate	no		no		no	**no**
No		Food additives *	E 472a - Acetic acid esters of mono- and diglycerides of fatty acids	no		no		no	**no**
No		Food additives *	E 968 - Erythritol	no		no		no	**no**
No		Food additives *	E 961 - Neotame	no		no		no	**no**
No		Food additives *	E 914 - Oxidised polyethylene wax	no		yes	REMEDERM	no	**yes**
No		Food additives *	E 575 - Glucono-delta-lactone	no		no		no	**no**
No		Food additives *	E 630 - Inosinic acid	no		no		no	**no**
No		Food additives *	E 392 - Extracts of rosemary	no		yes	BOLDOFLORINE	no	**yes**
No		Food additives *	E 319 - Tertiary-butyl hydroquinone (TBHQ)	no		yes	TERT.-BUTYLHYDROCHINON SMARTPRACTICE EUROPE	no	**yes**
No		Food additives *	E 306 - Tocopherol-rich extract	no		no		no	**no**
No		Food additives *	E 465 - Ethyl methyl cellulose	no		no		no	**no**
No		Food additives *	E 472e - Mono- and diacetyl tartaric acid esters of mono- and diglycerides of fatty acids	no		no		no	**no**
No		Food additives *	E 445 - Glycerol esters of wood rosins	no		no		no	**no**
No		Food additives *	E 472c - Citric acid esters of mono- and diglycerides of fatty acids	no		no		no	**no**

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No		Food additives *	E 160c - Paprika extract, capsanthin, capsorubin	no		no		no	**no**
No		Food additives *	E 451 - Triphosphates	no		no		no	**no**
No		Food additives *	E 444 - Sucrose acetate isobutyrate	no		no		no	**no**
No		Food additives *	E 160e - Beta-apo-8'-carotenal (C 30)	no		no		no	**no**
No		Food additives *	E 354 - Calcium tartrate	no		no		no	**no**
No		Food additives *	E 228 - Potassium hydrogen sulphite	no		no		no	**no**
No		Food additives *	E 315 - Erythorbic acid	no		no		no	**no**
No		Food additives *	E 150b - Caustic sulphite caramel	no		no		no	**no**
No		Food additives *	E 309 - Delta-tocopherol	no		no		no	**no**
No		Food additives *	E 472b - Lactic acid esters of mono- and diglycerides of fatty acids	no		no		no	**no**
No		Food additives *	E 472f - Mixed acetic and tartaric acid esters of mono- and diglycerides of fatty acids	no		no		no	**no**
No		Food additives *	E 472d - Tartaric acid esters of mono- and diglycerides of fatty acids	no		no		no	**no**
No		Food additives *	E 308 - Gamma-tocopherol	no		no		no	**no**
No		Food additives *	949 - Hydrogen	no		no		no	**no**
No		Food additives *	E 1451 - Acetylated oxidised starch	no		no		no	**no**
No		Food additives *	E 640 - Glycine and its sodium salt	no		no		no	**no**
No		Food additives *	E 417 - Tara gum	no		no		no	**no**
No		Food additives *	E 1422 - Acetylated distarch adipate	no		no		no	**no**
No		Food additives *	E 212 - Potassium benzoate (1)	no		no		no	**no**
No		Food additives *	E 907 - Hydrogenated poly-1-decene	no		no		no	**no**

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No		Food additives *	E 521 - Aluminium sodium sulphate	no		no		no	**no**
No		Food additives *	E 624 - Monoammonium glutamate	no		no		no	**no**
No		Food additives *	E 350 - Sodium malates	no		no		no	**no**
No		Food additives *	E 482 - Calcium stearoyl-2-lactylate	no		no		no	**no**
No		Food additives *	E 632 - Dipotassium inosinate	no		no		no	**no**
No		Food additives *	E 535 - Sodium ferrocyanide	no		no		no	**no**
No		Food additives *	E 629 - Calcium guanylate	no		no		no	**no**
No		Food additives *	E 538 - Calcium ferrocyanide	no		no		no	**no**
No		Food additives *	E 633 - Calcium inosinate	no		no		no	**no**
No		Food additives *	E 481 - Sodium stearoyl-2-lactylate	no		no		no	**no**
No		Food additives *	E 380 - Triammonium citrate	no		no		no	**no**
No		Food additives *	E 403 - Ammonium alginate	no		no		no	**no**
No		Food additives *	E 628 - Dipotassium guanylate	no		no		no	**no**
No		Food additives *	E 226 - Calcium sulphite	no		no		no	**no**
No		Food additives *	E 180 - Litholrubine BK	no		no		no	**no**
No		Food additives *	E 541 - Sodium aluminium phosphate acidic	no		no		no	**no**
No		Food additives *	E 316 - Sodium erythorbate	no		no		no	**no**
No		Food additives *	E 476 - Polyglycerol polyricinoleate	no		no		no	**no**
No		Food additives *	E 962 - Salt of aspartame-acesulfame	no		no		no	**no**
No		Food additives *	E 227 - Calcium hydrogen sulphite	no		no		no	**no**
No		Food additives *	E 353 - Metatartaric acid	no		no		no	**no**
No		Food additives *	E 407a - Processed euchema seaweed	no		no		no	**no**
No		Food additives *	E 426 - Soybean hemicellulose	no		no		no	**no**
No		Food additives *	E 1442 - Hydroxy propyl distarch phosphate	no		no		no	**no**

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Food additives *	E 479b - Thermally oxidised soya bean oil interacted with mono- and diglycerides of fatty acids	no		no		no	**no**
No		Food additives *	E 1103 - Invertase	no		no		no	**no**
No		Food additives *	E 1410 - Monostarch phosphate	no		no		no	**no**
No		Food additives *	E 1412 - Distarch phosphate	no		no		no	**no**
No		Food additives *	E 1413 - Phosphated distarch phosphate	no		no		no	**no**
No		Food additives *	E 1414 - Acetylated distarch phosphate	no		no		no	**no**
No		Food additives *	E 1420 - Acetylated starch	no		no		no	**no**
No		Food additives *	E 475 - Polyglycerol esters of fatty acids	no		no		no	**no**
No		Food additives *	E 634 - Calcium 5'-ribonucleotides	no		no		no	**no**
No		Food additives *	E 635 - Disodium 5'-ribonucleotides	no		no		no	**no**
No		Food additives *	E 477 - Propane-1,2-diol esters of fatty acids	no		no		no	**no**
No		Food additives *	E 442 - Ammonium phosphatides	no		no		no	**no**
No		Food additives *	E 452 - Polyphosphates	no		no		no	**no**
No		Food additives *	E 474 - Sucroglycerides	no		no		no	**no**
No		Food additives *	E 960a - Steviol glycosides from Stevia	no		no		no	**no**
No		Food additives *	E 960c - Enzymatically produced steviol glycosides	no		no		no	**no**
No		Food additives *	E 960d - Glucosylated steviol glycosides	no		no		no	**no**
No		Food additives *	E 964 - Polyglycitol syrup	no		no		no	**no**
No		Food additives *	E 969 – Advantame	no		no		no	**no**
No		Food additives *	E 243 - Ethyl lauroyl arginate	no		no		no	**no**
No		Food additives *	E 246 – Glycolipids	no		no		no	**no**
No		Food additives *	E 267 - Buffered vinegar	no		no		no	**no**
No		Food additives *	E 322a - Oat lecithin	no		no		no	**no**
No		Food additives *	E 345(i) - Trimagnesium dicitrate	no		yes	B-MAG	no	**yes**

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Food additives *	E 423 - Octenyl succinic acid modified gum arabic	no		no		no	**no**
No		Food additives *	E 456 - Potassium polyaspartate	no		no		no	**no**
No		Food additives *	E 463a - Low-substituted hydroxypropyl cellulose (L-HPC)	no		no		no	**no**
No		Food additives *	E 499 - Stigmasterol-rich plant sterols	no		no		no	**no**
No		Food additives *	E 534 - Iron tartrate	no		no		no	**no**
No		Food additives *	E 1206 - Neutral methacrylate copolymer	no		no		no	**no**
No		Food additives *	E 1207 - Anionic methacrylate copolymer	no		no		no	**no**
No		Food additives *	E 1208 - Polyvinylpyrrolidone-vinyl acetate copolymer	no		no		no	**no**
No		Food additives *	E 1209 - Polyvinyl alcohol-polyethylene glycol-graft-co-polymer	no		no		no	**no**
No		Food additives *	E 1210 - Carbomer	no		yes	AQUAREST 0,2 %, gel opthalmique en récipient unidose	no	**yes**
Yes	CMDv list	Formaldehyde	Formaldehyde	no		yes	FORMALDEHYD SMARTPRACTICE EUROPE	no	**yes**
No		Formic acid	Formic acid	yes	Formicpro 68,2g Лента за пчелен кошер за медоносни пчели	yes	SPIRYTUS MRÓWCZANY	no	**yes**
No		Frangulae cortex, stan- dardised extracts and preparations thereof	Frangulae cortex, stan-dardised extracts and preparations thereof	yes	PURGARUMINA TIPO FORTE	yes	FAVILAX	no	**yes**

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No		Furosemide	Furosemide	yes	Dimazon 50 mg/ml Injektionslösung	yes	CO-AMILOFRUSE	no	**yes**
No		Gamithromycin	Gamithromycin	yes	Zactran 150 mg/ml - Solution for injection (cattle, pigs)	no		no	**yes**
Yes	AEMPS	Gentamicin	Gentamicin	yes	Emdogent 100 mg/ml Oplossing voor injectie	yes	BEDICORT G	no	**yes**
No		Gentianae radix, stan- dardised extracts and preparations thereof	Gentianae radix, stan-dardised extracts and preparations thereof	yes	PURGARUMINA TIPO FORTE	yes	Sinupret acute	no	**yes**
No		Ginkgo biloba	Ginkgo biloba	no		yes	CEFAVORA	no	**yes**
No		Ginseng	Ginseng	yes	Ginseng-logoplex injekció	yes	Ginseng Compositum N	no	**yes**
No		Ginseng, stan-dardised extracts and preparations thereof	Ginseng, standardised extracts and preparations thereof	no		yes	Gerivit Dragees	no	**yes**
No		Glutamic acid	Glutamic acid	yes	ENERGHEPA	yes	AMINOMEL	no	**yes**
No		Glutamine	Glutamine	no		yes	RELAVIT FÓSFORO	no	**yes**
No		Glutaraldehyde	Glutaraldehyde	no		yes	GLUTARALDEHYD SMARTPRACTICE EUROPE	no	**yes**
No		Glycerol formal	Glycerol formal	no		no		no	**no**
No		Glycine	Glycine	yes	Metabolase	yes	ACTIVAL JUNIOR	no	**yes**
Yes	FMP survey	Gonadotrophin releasing hormone	GONADORELIN	yes	Fertagyl	yes	GONADORELIN INTRAPHARM LABORATORIES	no	**yes**
No		Guaiacol	Guaiacol	no		yes	ALGINA	no	**yes**

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No		Guanosine and its 5'-mono-, 5'- di- and 5'-triphosphates	Guanosine	no		no		no	**no**
No		Halofuginone	Halofuginone	yes	Stenorol Crypto 0,5 mg/ml orale oplossing voor kalveren	no		no	**yes**
No		Hamamelis virginiana	Hamamelis virginiana	yes	Trauma-logoplex forte injekció	yes	Hamamelis Virginiana	no	**yes**
No		Harpagophytum procumbens	Harpagophytum procumbens	no		yes	Harpagophytum Hevert Injekt	no	**yes**
No		Harunga madagascariensis	Harunga madagascariensis	no		yes	Metaharonga® Homöopathisches Arzneimittel Zur Anwendung Bei Jugendlichen Ab 12 Jahren Und Erwachsenen	no	**yes**
No		Heparin and its salts	Heparin sodium	yes	Compagel gel for horses	yes	AESCIN	no	**yes**
No		Heptaminol	Heptaminol	yes	Analeptol 50 mg/ml + 50 mg/ml oldatos injekció szarvasmarha, ló, sertés, kutya és macska részére	yes	CHLORHYDRATE D'HEPTAMINOL LIBERTY PHARMA	no	**yes**
No		Hesperidin	Hesperidin	no		yes	BIOFLEVIN	no	**yes**
No		Hesperidin methyl chalcone	Hesperidin methyl chalcone	no		yes	ACTILAM PER-OS	no	**yes**
No		Hexaflumuron	Hexaflumuron	no		no		no	**no**
No		Hexetidine	Hexetidine	no		yes	ABRASONE RECTAL	no	**yes**

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No		Hippocastani semen	Hippocastani semen	no		yes	SAPOVEN T	no	**yes**
No		Histidine	Histidine	yes	DUPHALYTE injekčný roztok	yes	AMINO-MEL NEPHRO	no	**yes**
No		Human meno-pausal urinary gonadotrophin	Human menopausal urinary gonadotrophin	no		yes	MENOGON	no	**yes**
Yes	CMDv list	Human chorionic gonadotropin (natural HCG and its synthetic analogues)	Human chorionic gonadotropin	yes	PG 600	yes	CHORAPUR	no	**yes**
No		Humic acids and their sodium salts	Humic acids	yes	Dysticum - Pulver für Tiere	no		no	**yes**
No		Hyaluronic acid	Hyaluronic acid	yes	Halevox 10 mg/ml roztwór do wstrzykiwań	yes	HYALART	no	**yes**
Out of scope	Excipient only	Hydrochloric acid	Hydrochloric acid	yes	DIGESTIA	no		no	**no**
No		Hydrochloro-thiazide	Hydrochlorothiazide	yes	Diurizone solução injetável para bovinos e equinos	yes	ACCURETIC	no	**yes**
No		Hydrocortisone	Hydrocortisone	yes	OXYTETRA spray	yes	ANGINOVAG	no	**yes**
No		Hydrocortisone aceponate	Hydrocortisone aceponate	no		yes	EFFICORT HYDROPHILE	no	**yes**
Yes	CMDv list	Hydrogen peroxide	Hydrogen peroxide	no		yes	AGUA OXIGENADA CUVE	no	**yes**
No		Hydroxyethylsa-licylate	Hydroxyethyl salicylate	yes	COMPAGEL GEL POUR CHEVAUX	yes	ALGIPAN BALSAM	no	**yes**
No		Hyperici oleum	Hyperici oleum	yes	Uierbalsem, emulsie voor uitwendig gebruik	no		no	**yes**

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No		Hypericum perforatum	Hypericum perforatum	yes	Suprarenales comp. PlantaVet	yes	Mexivol	no	**yes**
Yes	CMDv list	Imidacloprid	Imidacloprid	no		no		no	**no**
No		Imidocarb	Imidocarb	yes	IMIDOTYL 85 MG/ML SOLUTION INJECTABLE POUR BOVINS ET CHIENS	no		no	**yes**
No		Inosine and its 5'-mono-, 5'-di- and 5'-triphos- phates	Inosine	yes	TONARSYL SOLUTION	yes	DELIMMUN	no	**yes**
No		Inositol	Inositol	yes	BLAP HELP	yes	FARCOVIT B12	no	**yes**
No		Iodine and iodine inorganic compounds including: — Sodium and potassium- iodide — Sodium and potassium- iodate — Iodophors including polyvi-nylpyr- rolidone-iodine	Iodine	yes	Нозестат - разтвор	yes	ACTIVAL EXTRA	no	**yes**
No			Potassium iodide	yes	JODOPHARM-aerosolum spumiferum intrauterinicum	yes	ADDAMEL	no	**yes**
No			Povidone, iodinated	yes	ЙОДОУТЕР – разтвор за ветеринарномедицинска употреба	yes	BETADINE	no	**yes**

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No		Iodine organic compounds — Iodoform	Iodoform	yes	METROSEPT E	yes	TAMPONADE 2000	no	**yes**
No		Iron ammonium citrate	Iron ammonium citrate	no		no		no	**no**
No		Iron dextran	Iron dextran	yes	FERRIBION 100 mg/ml solution for injection	yes	FERRUM	no	**yes**
No		Iron dichloride	Iron dichloride	no		no		no	**no**
No		Iron fumarate	Iron fumarate	no		yes	Fumafer	no	**yes**
No		Iron glucoheptonate	Iron glucoheptonate	no		no		no	**no**
No		Iron sulphate	Iron sulphate	no		yes	Timoferol	no	**yes**
No		Isobutane	Isobutane	no		no		no	**no**
Yes	CMDv list	Isoeugenol	Isoeugenol	no		yes	EPITEST 36	no	**yes**
No		Isoflurane	Isoflurane	yes	ISOFLU-VET 1000 MG/G LIQUIDE POUR INHALATION PAR VAPEUR	yes	AERRANE	no	**yes**
No		Isoleucine	Isoleucine	yes	Duphalyte Solution for Injection	yes	AMINO-MEL NEPHRO	no	**yes**
No		Isopropanol	Isopropanol	no		yes	Timoferol	no	**yes**
No		Isoxsuprine	Isoxsuprine	no		no		no	**no**
Yes	AAC	Ivermectin	Ivermectin	yes	IVERTIN LA	yes	BALRITI	no	**yes**
No		Jecoris oleum	Jecoris oleum	no		no		no	**no**
No		Juniperi fructus	Juniperi fructus	no		yes	NIERENTONIKUM	no	**yes**
No		Kanamycin	Kanamycin	yes	KANAMICINA FP 25%	yes	KANAMICINA PANPHARMA	no	**yes**
No		Ketamine	Ketamine	yes	Ketexx 100 mg/ml soluzione iniettabile	yes	CETAMINA G.L. PHARMA	no	**yes**

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No		Ketanserin tartrate	Ketanserin tartrate	yes	Vulketan 2.5 mg/g gel for horses	no		no	**yes**
No		Ketoprofen	Ketoprofen	yes	Labiprofen 150 mg/ml solution for injection	yes	ALKET	no	**yes**
No		Lachnanthes tinctoria	Lachnanthes tinctoria	no		no		no	**no**
No		Lactic acid	Lactic acid	yes	4XLA Post-Milking Germicidal Teat Dip Solution	yes	ABE	no	**yes**
No		Lanolin	Lanolin	no		yes	ADEPS LANAE SMARTPRACTICE EUROPE	no	**yes**
No		Lasalocid	Lasalocid	no		no		no	**no**
No		Lauri folii aetheroleum	Lauri folii aetheroleum	yes	Uierbalsem, emulsie voor uitwendig gebruik	yes	GASTROFUNKTEN	no	**yes**
No		Lauri fructus	Lauri fructus	no		no		no	**no**
No		Lavandulae aetheroleum	Lavandulae aetheroleum	no		yes	Huile Essentielle De Lavande	no	**yes**
No		Lecirelin	Lecirelin	yes	Dalmarelin 25 µg/ml šķīdums injekcijām govīm, ķēvēm un trušu mātēm	no		no	**yes**
No		Lectin extracted from red kidney beans Phaseolus vulgaris	Lectin extracted from red kidney beans Phaseolus vulgaris	no		no		no	**no**
No		Lespedeza capitata	Lespedeza capitata	no		no		no	**no**
No		Leucine	Leucine	yes	AMINODIAN	yes	AMINO-MEL NEPHRO	no	**yes**
Yes	CMDv list for	Levamisole	Levamisole hydrochloride	yes	NAXOLOT, πόσιμο εναιώρημα για	yes	DECARIS	no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
	aquarium fish				βοοειδή και πρόβατα				
No		Levomethadone	Levomethadone	yes	Recudon 5 mg/ml + 0.25 mg/ml solution for injection for horses and dogs	yes	AGOVADIN	no	**yes**
No		Levothyroxine	Levothyroxine	no		yes	LEVAXIN	no	**yes**
No		Lidocaine	Lidocaine	yes	Lidor 20 mg/ml oplossing voor injectie voor paarden, honden en katten	yes	ACTILOGIC	no	**yes**
Yes	AAC	Lincomycin	Lincomycin	yes	LINCOSPECTIN® STERILE SOLUTION	yes	COMYCIN	no	**yes**
No		Linear alkyl benzene sulphonic acids with alkyl chain lengths ranging from C9 to C13, containing less than 2,5 % of chains longer than C13	Linear alkyl benzene sulphonic acids with alkyl chain lengths ranging from C9 to C13, containing less than 2,5 % of chains longer than C13	no		no		no	**no**
No		Lini oleum	Lini oleum	no		yes	LINOMAG	no	**yes**
No		Lobaria pulmonaria	Lobaria pulmonaria	yes	BRONCHORYL	yes	Anfokali	no	**yes**
No		Lobeline	Lobeline	yes	ZOOLOBELIN 1,8 mg/ml soluzione iniettabile per bovini, equini, suini, ovini, cani	no		no	**yes**
Out of scope	Excipient only	L-tartaric acid and its mono- and di-	Tartaric acid	no		yes	GEFFER	no	**no**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
		basic salt of sodium, potassium and calcium							
Yes	AEMPS	Lufenuron (RS-isomers)	LUFENURON	no		no		no	**no**
No		Luprostiol	Luprostiol	yes	PROSOLVIN	no		no	**yes**
No		Luteinising hormone (natural LH from all species and their synthetic analogues)	Luteinising hormone (natural LH from all species and their synthetic analogues)	yes	PLUSET vet 500 IU / 500 IU injektiokuiva-aine ja liuotin, liuosta varten	yes	Hmg-Lepori	no	**yes**
No		Lysine	Lysine	yes	IMULYZIN, Injekční suspenze	yes	AMINOACIDI ESSENZIALI GALENICA SENESE	no	**yes**
No		Magnesium	Magnesium	yes	BIOVEINE ELECTROLYTES	yes	ABECOL	no	**yes**
No		Magnesium acetate	Magnesium acetate	yes	ERGOGEN COMPLEX	yes	ELETTROLITICA BILANCIATA DI MANTENIMENTO CON GLUCOSIO I FRESENIUS KABI ITALIA	no	**yes**
No		Magnesium aluminium silicate	Aluminium magnesium silicate	yes	Dysticum - Pulver für Tiere	yes	GELUSIL LAC	no	**yes**
No		Magnesium aspartate	Magnesium aspartate	yes	MYOTROFIL	yes	ASMAG	no	**yes**
No		Magnesium carbonate	Magnesium carbonate	no		yes	Citrato Espresso Gabbiani	no	**yes**
No		Magnesium chloride	Magnesium chloride	yes	NEATOX, soluzione iniettabile per bovini, equini, suini, cani e gatti	yes	CLINOMEL N4 - 550	no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terres-trial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Magnesium citrate	Magnesium citrate	no		yes	B-MAG	no	**yes**
No		Magnesium gluconate	Magnesium gluconate	yes	Solução de cálcio Braun solução injetável	yes	ARPHOS	no	**yes**
No		Magnesium glutamate	Magnesium glutamate	no		no		no	**no**
No		Magnesium glycerop- hosphate	Magnesium glycerophosphate	no		yes	ACTILAM PER-OS	no	**yes**
No		Magnesium hydroxide	Magnesium hydroxide	yes	Diaproof K	yes	ACIDO-GIT MAALOX	no	**yes**
No		Magnesium hypophosphite	Magnesium hypophosphite	yes	MAGNOPHOS	no		no	**yes**
No		Magnesium orotate	Magnesium orotate	no		yes	MAGNEROT	no	**yes**
No		Magnesium oxide	Magnesium oxide	yes	Biopect, poeder voor gebruik in drinkwater/melk voor kalveren, lammeren en biggen	yes	ASPIMAG	no	**yes**
No		Magnesium phosphate	Magnesium phosphate	yes	GAMALC, (166+34+50+220)MG/ML ενέσιμο διάλυμα για πρόβατα	yes	BIOMAGNESIN	no	**yes**
No		Magnesium stearate	Magnesium stearate	no		no		no	**no**
Yes	EG	Magnesium sulphate	Magnesium sulfate	yes	Магнезиев сулфат	yes	CITORSAL	no	**yes**
No		Magnesium trisilicate	Magnesium trisilicate	no		yes	Magentabletten	no	**yes**
No		Majoranae herba	Majoranae herba	no		yes	MAŚĆ MAJERANKOWA	no	**yes**
Out of scope	Excipient only	Malic acid	Malic acid	yes	DERMAFLON Crema per cani,	yes	ACERBINE	no	**no**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
					gatti, cavalli, bovini e suini				
No		Manganese carbonate	Manganese carbonate	yes	Multimin Solution for Injection for Cattle	no		no	**yes**
No		Manganese chloride	Manganese chloride	no		yes	NUTRITRACE	no	**yes**
No		Manganese gluconate	Manganese gluconate	yes	Vitaminsol multi, poeder voor toediening via het drinkwater voor kalf, varken en pluimvee	yes	ADDEL JUNIOR	no	**yes**
No		Manganese glycerop- sphate	Manganese glycerophosphate	no		yes	IRONORM	no	**yes**
No		Manganese oxide	Manganese monoxide	no		no		no	**no**
No		Manganese pidolate	Manganese pidolate	no		no		no	**no**
No		Manganese ribonucleate	Manganese ribonucleate	no		no		no	**no**
No		Manganese sulphate	Manganese sulfate	yes	Vitacon extra W.O., poeder voor oraal gebruik	yes	CALTRATE PLUS	no	**yes**
No		Mannitol	Mannitol	no		yes	ARDEAOSMOSOL MA	no	**yes**
No		Marbofloxacin	Marbofloxacin	yes	MARBOCYL 10%	no		no	**yes**
No		Matricaria recutita and preparations thereof	Matricaria recutita and preparations thereof	no		yes	AGUA DEL CARMEN	no	**yes**
No		Matricariae flos	Matricariae flos	no		yes	ABT STRABO MAGEN-DARMTEE	no	**yes**
Yes	AAC	Mebendazole	Mebendazole	yes	SUPAVERM	yes	ANTI-WORM MEBENDAZOL LEIDAPHARM	no	**yes**
No		Mecillinam	Mecillinam	no		yes	SELEXID	no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Medicago sativa extractum	Medicago sativa extractum	no		yes	ALUSTAL	no	**yes**
No		Medroxyproges-terone acetate	Medroxyprogesterone acetate	yes	SINCRO-GEST ESPONJAS MEDICAMENTOS AS	yes	DEPO PRODASONE	no	**yes**
No		Melatonin	Melatonin	yes	MELOVIN	yes	ADAFLEX	no	**yes**
No		Melissae aethe-roleum	Melissae aethe-roleum	no		yes	ARGOL ESSENZA BALSAMICA	no	**yes**
No		Melissae folium	Melissae folium	no		yes	ABT STRABO SCHLAF-NERVENTEE	no	**yes**
No		Meloxicam	Meloxicam	yes	Pyrocam 15 mg/ml oral suspension for pigs	yes	AGLAN	no	**yes**
No		Menadione	Menadione	yes	Agribon pó para administração na água de bebida	no		no	**yes**
No		Menbutone	Menbutone	yes	Menbuton WERFFT 100 mg/ml Roztwór do wstrzykiwań	no		no	**yes**
No		Menthae arvensis aethe- roleum	Menthae arvensis aethe-roleum	no		no		no	**no**
No		Menthae piperitae aethe- roleum	Menthae piperitae aetheroleum	yes	Ecostop impregnált csík mézelő méhek kezelésére A.U.V.	yes	Apercap	no	**yes**
No		Menthol	Menthol	yes	API LIFE VAR	yes	ABIOSTIL	no	**yes**
No		Mepivacaine	Mepivacaine	yes	MEPIDOR SOLUTION INJECTABLE POUR CHEVAUX	yes	BIOCAINE PLAIN	no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Mercaptamine hydrochloride	Mercaptamine hydrochloride	no		yes	CYSTADROPS	no	**yes**
No		Metamizole	Metamizole	yes	Spasmalgan compositum 500 mg/ml + 4 mg/ml Ενέσιμο διάλυμα για άλογα, βοοειδή, χοίρους και σκύλους	yes	METAMIZOL CINFA	no	**yes**
No		Methionine	Methionine	yes	DUPHALYTE, Injekční roztok	yes	ACIMETHIN	no	**yes**
No		Methyl nicotinate	Methyl nicotinate	no		yes	ALGIPAN BALSAM	no	**yes**
No		Methyl salicylate	Methyl salicylate	yes	Novaderma	yes	ALGINA	no	**yes**
No		Methylbenzoate	Methylbenzoate	no		no		no	**no**
No		Methylpredni-solone	Methylprednisolone	yes	Depo-Medrone V 40 40 mg/ml Zawiesina do wstrzykiwań	yes	DEPO-MEDRONE WITH LIDOCAINE	no	**yes**
No		Millefolii herba	Millefolii herba	no		yes	BITTERSTOFF TEE	no	**yes**
No		Mineral hydro-carbons, low to high viscosity including micor-cristalline waxes, approximately C10-C60, aliphatic, branched aliphatic and alicyclic compounds	Liquid paraffin	no		yes	Dermalo Bath Emollient	no	**yes**
Yes	AEMPS	Monensin	Monensin	yes	Kexxtone 32.4 g - Continuous-release	no		no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
					intraruminal device				
No		Monepantel	Monepantel	yes	Zolvix 25 mg/ml - Oral solution	no		no	**yes**
No		Monothiog- lycerol	Monothioglycerol	no		no		no	**no**
No		Montanide	Montanide	no		no		no	**no**
No		Morantel	Morantel	yes	MORANTEL TARTRATO 4% LIQUIDO, 40 mg/ml soluzione orale per bovini, ovini e caprini	no		no	**yes**
No		Moxidectin	Moxidectin	yes	Equest Pramox, Perorální gel	no		no	**yes**
No		Myglyol	Myglyol	no		no		no	**no**
No		Myristicae aetheroleum	Myristicae aetheroleum	no		yes	CARMOL	no	**yes**
No		Nafcillin	Nafcillin	yes	Nafpenzal T - Salbe zur intramammären Anwendung für Rinder	no		no	**yes**
No		Natamycin	Natamycin	no		yes	PIMAFUCIN	no	**yes**
No		n-Butane	n-Butane	no		no		no	**no**
Out of scope	Excipient only	n-Butanol	n-Butanol	no		no		no	**no**
Yes	AEMPS	Neomycin (including framycetin)	Neomycin	yes	Neopen 200000 IU/ml - 100 mg/ml Suspensie voor injectie	yes	ABIOSTIL	no	**yes**
No		Neostigmine	Neostigmine	yes	Neoskilab, 1,5 mg/ml süstelahus veistele, lammastele,	yes	COMBISTIG	no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
					kitsedele ja hobustele				
No		Netobimin	Netobimin	yes	Hapadex 50 mg/ml - Suspension zum Eingeben für Schafe	no		no	**yes**
No		Nickel sulphate	Nickel sulfate	no		yes	EPITEST 36	no	**yes**
No		Nickel gluconate	Nickel gluconate	no		yes	OLIGOSOL	no	**yes**
No		Nicoboxil	Nicoboxil	no		yes	FINALGON	no	**yes**
No		Nitroxinil	Nitroxinil	yes	Fascionix 34% Inj.	no		no	**yes**
No		Nonivamide	Nonivamide	no		yes	ABC LOKALE SCHMERZ-THERAPIE WÄRME-PFLASTER MIT SENSITIV-VLIES	no	**yes**
No		Norgestomet	Norgestomet	no		no		no	**no**
No		Novobiocin	Novobiocin	yes	Albadry Plus, 200mg/400mg, intramammaarsuspensioon veistele	no		no	**yes**
No		Octenidine dihydrochloride	Octenidine dihydrochloride	no		yes	DUOSEPTIC	no	**yes**
No		Okoubaka aubrevillei	Okoubaka aubrevillei	no		yes	DIGESTO HEVERT VERDAUUNGSTROPFEN	no	**yes**
No		Oleyloleate	Oleyloleate	no		no		no	**no**
No		Omeprazole	Omeprazole	yes	Omeproshield 370 mg/g oral paste for horses	yes	ACIDCARE	no	**yes**
No		Orgotein	Orgotein	no		no		no	**no**
No		Ornithine	Ornithine	yes	METABOLIK	yes	AMINOPLASMAL HEPA	no	**yes**
No		Orotic acid	Orotic acid	no		yes	FARCOVIT B12	no	**yes**

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terres-trial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Ovotransferrin	Ovotransferrin	no		no		no	**no**
No		Oxacillin	Oxacillin	yes	Stapenor retard	yes	ISTOPEN	no	**yes**
No		Oxalic acid	Oxalic acid	yes	API-Bioxal 886 mg/g powder for in-hive use	yes	SOLCO-DERMAN	no	**yes**
Yes	AAC	Oxfendazole	Oxfendazole	yes	Interzol 67,5 mg/g - Pulver zum Eingeben für Rinder, Schafe, Schweine	no		no	**yes**
No		Oxibendazole	Oxibendazole	yes	ROMOXIBENDAZOL 15%	no		no	**yes**
No		Oxidation products of Terebinthinae oleum	Oxidation products of Terebinthinae oleum	no		no		no	**no**
Yes	CMDv list	Oxolinic acid	Oxolinic acid	yes	INOXYL PATE ORALE	no		no	**yes**
No		Oxyclozanide	Oxyclozanide	yes	ПОЛИВЕРМИН - L болуси	no		no	**yes**
Yes	CMDv list	Oxytetracycline	Oxytetracycline	yes	Engemycine 10% LA 100 mg/ml Solution injectable	yes	ATECORTIN	no	**yes**
No		Oxytocin	Oxytocin	yes	OXITOVET 10 IU/ml solution for injection	yes	OFOST	no	**yes**
No		Pancreatin	Pancreatin	yes	PANA VEYXAL, tepalas	yes	CREON	no	**yes**
No		Papain	Papain	yes	ПАНА ВЕЙКСАЛ унгвент за кожа	yes	CARIDENT	no	**yes**
No		Papaverine	Papaverine	yes	ПАПАВЕРИН АТРОПИН разтвор за инжекции 10 ml	yes	Papaverin Oba	no	**yes**

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terres-trial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Paracetamol	Paracetamol	yes	Pracetam Vet. 20 % pulver til anvendelse i drikkevand	yes	Gopain	no	**yes**
No		Parconazole	Parconazole	yes	PARCONAZOLE 6 PINTADE	no		no	**yes**
No		Paromomycin	Paromomycin	yes	Parofor crypto 140 000 IU/ml oral solution for pre-ruminant cattle	yes	GABBRORAL	no	**yes**
No		Peforelin	Peforelin	yes	Maprelin 75 µg/ml solution for injection for pigs	no		no	**yes**
No		Pegylated bovine granulocyte colony stimulating factor	Pegylated bovine granulocyte colony stimulating factor	yes	Imrestor 5.5 mg/ml - Solution for injection in pre-filled syringe	no		no	**yes**
No		Penethamate	Penethamate	yes	PERMACYL Powder and solvent for suspension for injection for cattle	no		no	**yes**
No		Pepsin	Pepsin	yes	DIGESTIA	yes	PEPSIN WEIN	no	**yes**
Yes	FMP survey	Peracetic acid	Peracetic acid	no		no		no	**no**
No		Permethrin	Permethrin	yes	Auriplak	yes	INFECTOMITE	no	**yes**
No		Phenol	Phenol	yes	АФЛЕГМОН	yes	Bepantiseptic First Aid	no	**yes**
No		Phenoxymethyl-penicillin	Phenoxymethylpenicillin	yes	FENOVET 100 mg/g PREMEZCLA MEDICAMENTOS	yes	ACIPEN-V	no	**yes**

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
					A PARA PORCINO				
No		Phenylalanine	Phenylalanine	yes	Duphalyte - Roztwór do wstrzykiwań	yes	AMINO-MEL NEPHRO	no	**yes**
No		Phloroglucinol	Phloroglucinol	no		yes	PHLOROGLUCINOL ARROW	no	**yes**
No		Phoxim	Phoxim	yes	SEBACIL, διάλυμα εξωτερικής χρήσης, για χοίρους	no		no	**yes**
No		Phytolacca americana	Phytolacca americana	yes	Lactovetsan-N	yes	Mercurius S	no	**yes**
No		Phytomenadione	Phytomenadione	yes	Vitamin K1 10 mg/ml Solution for Injection	yes	ACTIVAL EXTRA	no	**yes**
No		Piceae turiones recentes extractum	Piceae turiones recentes extractum	yes	Stullmisan 30,56 mg/g - Pulver zum Eingeben für Tiere	no		no	**yes**
No		Piperazine	Piperazine	yes	PIPERACINA SYVA 1000 mg/g POLVO ORAL PARA PORCINO, POLLOS DE ENGORDE Y CABALLOS NO DESTINADOS AL CONSUMO HUMANO	yes	PIPERMEL	no	**yes**
No		Piperazine dihydrochloride	Piperazine dihydrochloride	no		no		no	**no**

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Piperonyl butoxide	Piperonyl butoxide	yes	ACA CERULEN R, Spray auricolare per conigli	yes	SPREGAL	no	**yes**
No		Pirlimycin	Pirlimycin	yes	Pirsue 5 mg/ml - Intramammary solution	no		no	**yes**
No		Policresulen	Policresulen	yes	LOTAGEN, 360mg/g, Koncentrát pro vaginální/kožní roztok	yes	ALBOTHYL	no	**yes**
No		Poloxalene	Poloxalene	no		no		no	**no**
No		Poloxamer	Poloxamer	no		yes	CO-DANTHRAMER	no	**yes**
Out of scope	Excipient only	Polyethylene glycol 15 hydroxystearate	Polyethylene glycol 15 hydroxystearate	no		no		no	**no**
No		Polyethylene glycol 7 glyceryl cocoate	Polyethylene glycol 7 glyceryl cocoate	no		no		no	**no**
Out of scope	Excipient only	Polyethylene glycol stearates with 8-40 oxyethylene units	Polyethylene glycol stearates with 8-40 oxyethylene units	no		no		no	**no**
No		Polyethylene glycols (molecular weight ranging from 200 to 10 000)	Polyethylene glycols (molecular weight ranging from 200 to 10 000)	no		no		no	**no**
No		Polyoxyethylene sorbitan mono-oleate and trioleate	Polyoxyethylene sorbitan mono-oleate and trioleate	no		no		no	**no**
Out of scope	Excipient only	Polyoxyl castor oil with 30 to 40 oxyethylene units	Polyoxyl 35 castor oil	no		no		no	**no**

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
Out of scope	Excipient only	Polyoxyl hydrogenated castor oil with 40 to 60 oxyethylene units	Polyoxyl hydrogenated castor oil with 40 to 60 oxyethylene units	no		no		no	**no**
No		Polysorbate 80	Polysorbate 80	no		yes	PRORHINEL RHUME	no	**yes**
No		Polysulphated glycosaminoglycan	Polysulfated glycosaminoglycan	yes	Adequanin vet. 250 mg/ml Injektionsvätska, lösning	yes	HIRUDOID	no	**yes**
No		Porcine prolactin	Prolactin, porcine	no		no		no	**no**
No		Potassium DL-aspartate	Potassium DL-aspartate	yes	MYOTROFIL	yes	Aspavim	no	**yes**
No		Potassium glucuronate	Potassium glucuronate	no		no		no	**no**
No		Potassium glycerophosphate	Potassium glycerophosphate	no		yes	Potassium Liberty Pharma	no	**yes**
No		Potassium nitrate	Potassium nitrate	no		yes	SILBERNITRAT - KALIUMNITRAT RÖSCH	no	**yes**
No		Potassium selenate	Potassium selenate	no		no		no	**no**
Yes	Norway list	Praziquantel	Praziquantel	yes	Equest Pramox, Perorální gel	yes	BERMOXEL	no	**yes**
No		Prednisolone	Prednisolone	yes	Synulox Lactating Cow Intramammary suspension.	yes	ABIRASOLON-MCRPC KOMBIPACKUNG	no	**yes**
No		Pregnant mare serum gonadotrophin	Pregnant mare serum gonadotrophin (chorionic gonadotropin: Gonadotropin, equine, serum)	yes	Folligon 1000 RÜ, süstelahuse pulber ja lahusti	no		no	**yes**
No		Prethcamide (crotethamide and cropro- pamide)	Prethcamide (crotethamide and cropro-pamide)	no		no		no	**no**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Procaine	Procaine	yes	Procasel 2%	yes	PROKAIN HIDROKLORID TEVA	no	**yes**
No		Progesterone	Progesterone	yes	Dib 1,0 g dispositivo intravaginal para bovinos	yes	AGOLUTIN	no	**yes**
No		Proline	Proline	no		yes	AMINO-MEL NEPHRO	no	**yes**
No		Propane	Propane	no		no		no	**no**
Out of scope	Preservative only (then excipient only)	Propyl 4- hydroxy-benzoate and its sodium salt	Propyl 4-hydroxy-benzoate and its sodium salt	no		no		no	**no**
No		Propylene glycol	Propylene glycol	yes	Chanatol Oral Solution	yes	DECODERM	no	**yes**
No		Prunus laur-ocerasus	Prunus laurocerasus	no		yes	Ho-Len-Complex Pulmo-Cyl	no	**yes**
No		Purified semi-solid extract from Humulus lupulus L. containing approximately 48 % of beta acids (as potassium salts)	Purified semi-solid extract from Humulus lupulus L. containing approximately 48 % of beta acids (as potassium salts)	no		no		no	**no**
No		Pyrantel embonate	Pyrantel embonate	yes	STRIKE pasta orale 38 g/100 g per equini	yes	COMBANTRIN	no	**yes**
No		Pyrethrum extract	Pyrethrum extract	yes	ACA CERULEN R, Spray auricolare per conigli	yes	GOLDGEIST FORTE	no	**yes**
Out of scope	Preservative only (then	Quatresin	Quatresin	no		no		no	**no**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
	excipient only)								
No		Quercus cortex	Quercus cortex	no		yes	EICHENRINDE BOMBASTUS-WERKE	no	**yes**
No		Quillaia saponins	Quillaia saponins	no		yes	QUILLA SIMPLEX	no	**yes**
No		Rafoxanide	Rafoxanide	yes	Orafluke 5 % w/v Oral Suspension	no		no	**yes**
No		R-Cloprostenol	R-Cloprostenol	yes	GESTAVET-PROST, 75 mg/ml d-Cloprostenol, solution for injection for cattle and pig	no		no	**yes**
No		Rhei radix, standardised extracts and preparations thereof	Rhei radix, standardised extracts and preparations thereof	yes	PURGARUMINA TIPO FORTE	yes	EPAREMA	no	**yes**
Out of scope	Excipient only	Ricini oleum	Ricini oleum	no		yes	ACEITE DE RICINO ORRAVAN	no	**no**
No		Rifaximin	Rifaximin	yes	FATROXIMIN, ενδομαστική αλοιφή	yes	COLIDIMIN	no	**yes**
No		Romifidine	Romifidine	yes	SEDIVET	no		no	**yes**
No		Rosmarini aetheroleum	Rosmarini aetheroleum	yes	Uierbalsem, emulsie voor uitwendig gebruik	yes	Rowiren	no	**yes**
No		Rosmarini folium	Rosmarini folium	no		yes	BOLDOFLORINE	no	**yes**
No		Ruscus aculeatus	Ruscus aculeatus	no		yes	ARKOGELULES FRAGON	no	**yes**
No		Ruta graveolens	Ruta graveolens	no		no		no	**no**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Salicylic acid	Salicylic acid	yes	Dophacyl, 1000 mg/g pulber joogivees/piimas manustamiseks veistele ja sigadele	yes	2 - DROP	no	**yes**
No		Salviae folium	Salviae folium	yes	Kamilloplant - Konzentrat zur Herstellung einer Lösung zur Anwendung auf der Haut für Tiere	yes	ABT STRABO HALS- UND RACHENTEE	no	**yes**
No		Sambuci flos	Sambuci flos	no		yes	BIO KINDER-ERKÄLTUNGSTEE	no	**yes**
No		Sarafloxacin	Sarafloxacin	no		no		no	**no**
No		Selenicereus grandiflorus	Selenicereus grandiflorus	no		yes	Naranocor Hm	no	**yes**
No		Serenoa repens	Serenoa repens	no		yes	Sabal Serrulata	no	**yes**
No		Serine	Serine	no		yes	AKTIFERRIN	no	**yes**
No		Serotonin	Serotonin	no		no		no	**no**
No		Silybum marianum	Silybum marianum	yes	Hepar comp. PlantaVet	yes	HEPAR HEVERT INJEKT	no	**yes**
No		Sinapis nigrae semen	Sinapis nigrae semen	no		no		no	**no**
No		Sisapronil	Sisapronil	no		no		no	**no**
No		Sodium 2- methyl-2- phenoxy-propanoate	Sodium 2-methyl-2-phenoxy-propanoate	no		no		no	**no**
No		Sodium acetyl-salicylate	Sodium acetylsalicylate	no		no		no	**no**
No		Sodium benzyl 4-hydroxy- benzoate	Sodium benzyl 4-hydroxy-benzoate	no		no		no	**no**
No		Sodium boro-formiate	Sodium boroformiate	no		no		no	**no**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Sodium butyl 4-hydroxy- benzoate	Sodium butyl 4- hydroxybenzoate	no		no		no	**no**
No		Sodium cetostearyl sulphate	Sodium cetostearyl sulphate	no		no		no	**no**
Yes	EG	Sodium chloride	Sodium chloride	yes	Neatox solução injectável para bovinos, equinos, suínos, cães e gatos	yes	ACCUSOL 35	no	**yes**
No		Sodium chlorite	Sodium chlorite	yes	4XLA Post-Milking Germicidal Teat Dip Solution	no		no	**yes**
No		Sodium dichloroisocyanurate	Sodium dichloroisocyanurate	yes	Agrisept MC Tabs 2.5 g effervescent tablet for teat dip/spray solution	no		no	**yes**
No		Sodium dioctylsulphosuccinate	Sodium dioctilsulfosuccinate	no		no		no	**no**
No		Sodium formaldehydesulphoxylate	Sodium formal-dehydesulphoxylate	no		no		no	**no**
No		Sodium glycerophosphate	Sodium glycerophosphate	yes	Kaltetan, 250 mg/ml + 80 mg/ml + 10 mg/ml solution for infusion for horses, cattle and pigs	yes	AMINOMIX 4	no	**yes**
No		Sodium hypophosphite	Sodium hypophosphite	yes	CALCIOVET S	yes	ERIGON	no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Sodium lauryl sulphate	Sodium lauryl sulphate	no		no		no	**no**
No		Sodium nitrite	Sodium nitrite	no		yes	NATRIUMNITRIET HOPE	no	**yes**
No		Sodium pyro-sulphite	Sodium pyrosulfite	no		no		no	**no**
No		Sodium selenate	Sodium selenate	yes	Cosecure Cattle Bolus Continuous Release Intraruminal Device	no		no	**yes**
No		Sodium selenite	Sodium selenite	yes	Vitamin E + Selenium šķīdums injekcijām liellopiem, zirgiem, cūkām, aitām, kazām, suņiem un kaķiem	yes	ADDAVEN	no	**yes**
No		Sodium stearate	Sodium stearate	no		no		no	**no**
No		Sodium thio-sulphate	Sodium thiosulfate	no		yes	CARBOTOX	no	**yes**
No		Sodium cromoglycate	Sodium cromoglycate	no		yes	Chromoprol	no	**yes**
No		Sodium propionate	Sodium propionate	yes	Lactolyte Poudre pour solution buvable	no		no	**yes**
No		Sodium salicylate	Sodium salicylate	yes	Dophacyl SB, 1000 mg/g, prašak za primjenu u vodi za pića/mlijeku,	yes	BRULEX	no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terres-trial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
					za goveda i svinje				
No		Solidago virgaurea	Solidago virgaurea	yes	DRAINOSYL	yes	AKUTUR	no	**yes**
No		Solvent naphtha, light aromatic, with cumene concentration not exceeding 2,5 %, and benzene concen- tration not exceeding 0,0002 %	Solvent naphtha, light aromatic, with cumene concentration not exceeding 2,5 %, and benzene concentration not exceeding 0,0002 %	no		no		no	**no**
No		Somatosalm	Somatosalm	no		no		no	**no**
No		Sorbitan sesquioleate	Sorbitan sesquioleate	no		yes	REMEDERM	no	**yes**
No		Sorbitan trioleate	Sorbitan trioleate	no		no		no	**no**
Yes	EG	Spectinomycin	Spectinomycin	yes	PNEUMOSPECTIN	yes	KIRIN	no	**yes**
No		Spiramycin	Spiramycin	yes	SPIRAMICINA 2% + FURALTADONE 2% FORMEVET	yes	BI MISSILOR	no	**yes**
No		Streptomycin	Streptomycin	yes	STREPTOFTAL perorálny prášok	yes	STREPTOMYCIN PAN	no	**yes**
No		Strychni semen	Strychni semen	no		no		no	**no**
No		Strychnine	Strychnine	no		no		no	**no**
No		Substances used in homeopathic veterinary medicines	Substances used in homeopathic veterinary medicines	yes	CERVICYL	-	-	no	**yes**
No		Sulfogaiacol	Sulfogaiacol	no		yes	APIPULMOL	no	**yes**
Yes	CMDv list (in combinati on with	Sulfonamides (all substances belonging to the sulfonamide group)	Sulfadiazine	yes	HYDROTRIM 500 MG/G + 100 MG/G POUDRE POUR ADMINISTRATIO	yes	ADIAZINE	no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terres-trial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
	trimethoprim)				N DANS L'EAU DE BOISSON OU LE LAIT POUR BOVINS, OVINS, PORCS ET POULETS				
Yes	CMDv list (in combination with trimethoprim)	Sulfonamides (all substances belonging to the sulfonamide group)	Sulfadoxine	yes	Dofatrim-Ject 40 mg - 200 mg Injektionslösung	yes	FALCISTAT	no	**yes**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfaisodimidine	no		no		no	**no**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfamethizole	no		yes	LUCOSIL	no	**yes**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfadimidine	yes	SULPHADIMIDINE 30.47G/100ML ΕΝΕΣΙΜΟ ΔΙΑΛΥΜΑ	yes	SEPTOSYL	no	**yes**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfapyridine	yes	IZOPIRIDINA	no		no	**yes**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfafurazole	no		yes	SULFAFURAZOL ARENA	no	**yes**
No		Sulfonamides (all substances	Sulfanilamide	yes	IZOASPERSORIO	yes	AZOL	no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
		belonging to the sulfonamide group)							
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfathiazole	yes	Polisulfamid (50 mg + 40 mg + 30 mg) /1 ml Roztwór do wstrzykiwań	yes	NORSULFAZOL KUPRO	no	**yes**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfathiourea	no		no		no	**no**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfamethoxazole	yes	HEMOSUL- P прах за перорално приложение	yes	BACTRIM	no	**yes**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfamoxole	no		no		no	**no**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfadimethoxine	yes	PRIDIMET, 200 mg/ml + 40 mg/ml soluzione iniettabile per bovini e suini	no		no	**yes**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfalene	no		no		no	**no**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfametomidine	no		no		no	**no**
No		Sulfonamides (all substances	Sulfanetoxydiazine	no		no		no	**no**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010 Original extracted name	2nd step: cleaned substance names SMS[3] Substance name (cleaned)	3rd step: analysis result VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	AM[1] reserved for human use y/n	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		belonging to the sulfonamide group)							
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfamethoxypyridazine	yes	CHLORIDAZINE S	no		no	**yes**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfaperin	no		no		no	**no**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfamerazine	yes	Duotrim S (100 mg + 20 mg)/g Proszek do sporządzania roztworu doustnego	no		no	**yes**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfaphenazole	no		no		no	**no**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfamazone	no		no		no	**no**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfapyrazole	no		no		no	**no**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfamethizole	no		yes	LUCOSIL	no	**yes**
No		Sulfonamides (all substances	Sulfachlorpyridazine	yes	Cosumix Plus 100 mg/g Pulver zum	no		no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
		belonging to the sulfonamide group)			Eingeben über das Trinkwasser				
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfatroxazol	no		no		no	**no**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfaquinoxaline	yes	Sulfaquinoxalin Na neu	no		no	**yes**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfamerazine	yes	Duotrim S (100 mg + 20 mg)/g Proszek do sporządzania roztworu doustnego	no		no	**yes**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfamonomethoxine	yes	ENDOSPRAY, gimdos putos	no		no	**yes**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfalene	no		no		no	**no**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfacetamide	yes	Polisulfamid (50 mg + 40 mg + 30 mg) /1 ml Roztwór do wstrzykiwań	yes	ANTISETTICO ASTRINGENTE SEDATIVO	no	**yes**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Formosulfathiazole	yes	Socatyl SFD	no		no	**yes**
No		Sulfonamides (all substances	Phthalylsulfathiazole	yes	STREPTONAMID, Perorální prášek	no		no	**yes**

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
		belonging to the sulfonamide group)							
No		Sulfonamides (all substances belonging to the sulfonamide group)	Sulfaguanidine	yes	DIAR STOP FORTE powder for oral use for calves, swine, pigs, dogs and cats	no		no	**yes**
No		Sulfonamides (all substances belonging to the sulfonamide group)	Succinylsulfathiazole	no		no		no	**no**
No		Sulphur	Sulphur	no		yes	COCOIS	no	**yes**
No		Symphyti radix	Symphyti radix	no		yes	FLEXAGILE	no	**yes**
No		Syzygium cumini	Syzygium cumini	no		yes	Diabene	no	**yes**
No		Tanninum	Tanninum albuminatum	yes	Electrolytenmix, poeder voor toediening via drinkwater voor kalveren en biggen	yes	BOLUS ADSTRINGENS	no	**yes**
No		Tau fluvalinate	Tau fluvalinate	yes	APISTAN, avilio juostelės	no		no	**yes**
Yes	CMDv list	Teflubenzuron	Teflubenzuron	no		no		no	**no**
No		Terebinthinae aetheroleum rectificatum	Terebinthinae aetheroleum rectificatum	no		yes	ABSZESS-ILON	no	**yes**
No		Terebinthinae laricina	Terebinthinae laricina	no		yes	ABSZESS-ILON	no	**yes**
No		Terpin hydrate	Terpin hydrate	no		yes	COLDREX	no	**yes**
No		Tetracaine	Tetracaine	yes	T 61	yes	AMETOP	no	**yes**
No		Tetracycline	Tetracycline	yes	Utertab 2000 mg intrauterine tablet for cattle	yes	ALFATEX	no	**yes**

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No		Theobromine	Theobromine	no		no		no	**no**
No		Theophylline	Theophylline	yes	Tabernil antiasmático, solução oral para canários, pombos e aves ornamentais	yes	AFONILUM SR	no	**yes**
No		Thiabendazole	Thiabendazole	yes	THIABENDAZOLE /PROVET 2000MG/TAB ΔΙΣΚΙΟ	no		no	**yes**
Yes	AAC	Thiamphenicol	Thiamphenicol	yes	URFAMUCOL INTRAUTERINO liofilizzato e solvente per irrigazioni intrauterine in bovine	yes	THIOPHENICOL	no	**yes**
No		Thiamylal	Thiamylal	no		no		no	**no**
No		Thioctic acid	Thioctic acid	yes	METABOLASE, injekcinis tirpalas	yes	ACID TIOCTIC ROMPHARM	no	**yes**
Out of scope	Preservative only (then excipient only)	Thiomersal	Thiomersal	no		yes	EPITEST 36	no	**yes**
No		Thiopental sodium	Thiopental sodium	yes	PENTOTHAL SODIUM 0,5 g/20 ml polvere e solvente per soluzione iniettabile per cani, gatti, equini, bovini, ovini e suini	yes	PENTOCUR	no	**yes**

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		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Threonine	Threonine	yes	Duphalyte Solution for Injection	yes	AMINO-MEL NEPHRO	no	**yes**
No		Thuja occidentalis	Thuja occidentalis	yes	FICOSYL	yes	Echtrosept	no	**yes**
No		Thymi aetheroleum	Thymi aetheroleum	no		yes	Baby Luuf Ätherische Öle	no	**yes**
No		Thymidine	Thymidine	no		no		no	**no**
No		Thymol	Thymol	yes	APIGUARD GEL (25% THYMOL) FOR BEEHIVE USE	yes	AFRONIS	no	**yes**
No		Tiamulin	Tiamulin	yes	KARIMULINA 101,2 MG/ML SOLUTION POUR ADMINISTRATION DANS L'EAU DE BOISSON POUR POULETS DINDES ET PORCINS	no		no	**yes**
No		Tiaprost	Tiaprost	no		no		no	**no**
No		Tildipirosin	Tildipirosin	yes	Zuprevo 180 mg/ml - Solution for injection	no		no	**yes**
No		Tiliae flos	Tiliae flos	no		yes	BAD HEILBRUNNER BIO HUSTEN-BRONCHIAL TEE FÜR KINDER	no	**yes**
No		Tilmicosin	Tilmicosin	yes	Pulmotil 100 Vet Premix 100 mg/g Premix voor gemedicineerd voer	no		no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Tiludronic acid (in the form of disodium salt)	Tiludronic acid disodium salt hemihydrate	yes	TILDREN	no		no	**yes**
Out of scope	Preservative only (then excipient only)	Timerfonate	Timerfonate	no		no		no	**no**
No		Toldimfos	Toldimfos	yes	TONIPHOS	no		no	**yes**
No		Tolfenamic acid	Tolfenamic acid	yes	TOLFINE 80 mg/ml SOLUCION INYECTABLE PARA BOVINO	yes	CLOTAM	no	**yes**
Yes	AAC	Toltrazuril	Toltrazuril	yes	DOZURIL 50 MG/ML ORAL SUSPENSION FOR PIGS	no		no	**yes**
Yes	FMP survey	Tosylchloramide sodium	Tosylchloramide sodium	yes		no	CLONAZONE	no	**yes**
No		Tragacanth	Tragacanth	no		no		no	**no**
Yes	CMDv list	Tricaine mesilate	Tricaine mesilate	no		no		no	**no**
No		Trichlorme-thiazide	Trichlormethiazide	yes	Naquadem 200 mg / 5 mg, Granulat zum Eingeben oder zur Herstellung einer Suspension für Rinder und Pferde	no		no	**yes**
No		Triclabendazole	Triclabendazole	yes	Endex 8,75%, orale suspensie voor schapen	yes	EGATEN	no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terres-trial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
Yes	CMDv list (in combination with sulfonamide)	Trimethoprim	Trimethoprim	yes	Norodine Vet. 288,3 + 58 mg/g oral pasta	yes	BACTRIM	no	**yes**
No		Trimethylphlo-roglucinol	Trimethylphloroglucinol	no		yes	PHLOROGLUCINOL / TRIMETHYLPHLOROGLUCINOL ACINO	no	**yes**
No		Triptorelin acetate	Triptorelin acetate	yes	OvuGel 0.1 mg/ml - Vaginal gel	yes	DECAPEPTYL	no	**yes**
No		Trypsin	Trypsin	yes	МАМИКУР	yes	ANGINOVA	no	**yes**
No		Tryptophan	Tryptophan	yes	Duphalyte - Roztwór do wstrzykiwań	yes	AMINO-MEL NEPHRO	no	**yes**
No		Tulathromycin	Tulathromycin	yes	LABIXXIN 100MG/ML SOLUTION FOR INJECTION FOR CATTLE, PIGS AND SHEEP	no		no	**yes**
No		Turnera diffusa	Turnera diffusa	no		yes	Lonvect	no	**yes**
Yes	FMP survey	Tylosin	Tylosin	yes	PHARMASIN 100.000 UI/g PREMEZCLA MEDICAMENTOSA PARA PORCINO POLLOS DE ENGORDE Y POLLITAS	no		no	**yes**
No		Tylvalosin	Tylvalosin	yes	Aivlosin Surrendered: 8.5 mg/g - Premix	no		no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
					for medicated feeding stuff				
No		Tyrosine	Tyrosine	no		yes	AMINO-MEL NEPHRO	no	**yes**
No		Urea	Urea	no		yes	AMYCOR ONYCHOSET	no	**yes**
No		Urginea maritima	Urginea maritima	no		yes	Presselin Hk Mischung	no	**yes**
No		Uridine and its 5'-mono-5'-di- and 5'-triphos- phates	Uridine	no		yes	CENTRUM	no	**yes**
No		Urticae herba	Urticae herba	no		yes	PULMORAN	no	**yes**
No		Valine	Valine	yes	Duphalyte - Roztwór do wstrzykiwań	yes	AMINO-MEL NEPHRO	no	**yes**
No		Valnemulin	Valnemulin	yes	BIOTILINA 10% premix for medicated feed for pigs and rabbits	no		no	**yes**
No		Vedaprofen	Vedaprofen	yes	Quadrisol Surrendered - 50 mg / ml - Solution for injection	no		no	**yes**
No		Vetrabutine hydrochloride	Vetrabutine hydrochloride	yes	Monzal 100 mg/ml solução injetável para suínos e cães	no		no	**yes**
No		Vincamine	Vincamine	yes	CANDILAT VEAUX	yes	ANACERVIX	no	**yes**
No		Virginiamycin	Virginiamycin	no		no		no	**no**
No		Virola sebifera	Virola sebifera	yes	ABCEDYL GA	yes	Sulfur Pentarkan H	no	**yes**
No		Viscum album	Viscum album	yes	Renes/Viscum comp. PlantaVet	yes	Homviotensin	no	**yes**
No		Vitamin A	Vitamin A	yes	LABIASOL AD3E-500,	yes	Actival Extra	no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
					(500+75+50)IU/ ML ενέσιμο εναιώρημα για ιπποειδή, βοοειδή, πρόβατα, αίγες και χοίρους				
Yes	EG	Vitamin B1	Vitamin B1	yes	MULTIVIT– MINERAL, injekcinis tirpalas	yes	ACTIVAL EXTRA	no	**yes**
No		Vitamin B12	Vitamin B12	yes	Duphalyte solução injetável para bovinos, equinos, suínos, cães e gatos	yes	VITAMIN B12 WÖRWAG PHARMA	no	**yes**
No		Vitamin B2	Vitamin B2	yes	ОКСИТЕТРАВИТ	yes	ABIDEC MULTIVITAMIN	no	**yes**
No		Vitamin B3	Niacin	yes	BECO-JECT, injekcinis tirpalas	yes	ABIDEC MULTIVITAMIN	no	**yes**
No		Vitamin B5	Pantothenate	yes	VITAMIN B KOMPLEX, injekcinis tirpalas arkliams, galvijams, kiaulėms, šunims, katėms, audinėms ir lapėms	yes	APOVIT B-COMBIN STÆRK	no	**yes**
No		Vitamin B6	Vitamin B6	yes	VITAMIVEN COMPLEJO SOLUCION INYECTABLE	yes	BECOZYME, ASSOCIAÇÃO	no	**yes**
No		Vitamin D	Vitamin D	yes	TRIAVIT injekčný roztok	yes	ACARA TRIO	no	**yes**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Vitamin E	Vitamin E	yes	Selepherol, emulsão injetável para equinos, bovinos, ovinos e suínos	yes	ACTIVAL EXTRA	no	**yes**
No		Wool alcohols	Wool alcohols	no		yes	WOLLWACHSALKOHOLSALBE SMARTPRACTICE EUROPE	no	**yes**
No		Xylazine hydro-chloride	Xylazine hydrochloride	yes	Xylamidor 20 mg/ml raztopina za injiciranje za govedo, konje, pse in mačke	no		no	**yes**
No		Zinc acetate	Zinc acetate	no		yes	ACNERYZ-CURE	no	**yes**
No		Zinc aspartate	Zinc aspartate	no		yes	VITION	no	**yes**
No		Zinc chloride	Zinc chloride	no		yes	ADDAMEL	no	**yes**
No		Zinc gluconate	Zinc gluconate	yes	Vitaminsol multi, poeder voor toediening via het drinkwater voor kalf, varken en pluimvee	yes	ADDEL JUNIOR	no	**yes**
No		Zinc oleate	Zinc oleate	no		no		no	**no**
No		Zinc oxide	Zinc oxide	yes	MULTIMIN, otopina za injekciju, za goveda	yes	AKNEDERM	no	**yes**
No		Zinc stearate	Zinc stearate	no		no		no	**no**
No		Zinc sulphate	Zinc sulphate	yes	MULTIVIT–MINERAL, injekcinis tirpalas	yes	AFTAGEL	no	**yes**
No		1-Methyl-2-pyrrolidone	1-Methyl-2-pyrrolidone	no		no		no	**no**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terrestrial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		2-Aminoethanol	2-Aminoethanol	no		yes	Monoethanolamin Smartpractice Europe	no	**yes**
No		2-Aminoethanol glucuronate	2-Aminoethanol glucuronate	no		no		no	**no**
No		2-Aminoethyl dihydro-genphosphate	2-Aminoethyl dihydrogenphosphate	no		no		no	**no**
No		2-Pyrrolidone	2-Pyrrolidone	no		no		no	**no**
No		3,5-Diiodo-L-thyrosine	3,5-Diiodo-L-thyrosine	no		no		no	**no**
No		8-Hydroxyqui-noline	8-Hydroxyqui-noline	no		yes	LEIODERM P	no	**yes**
No		Bovine casein hydrolysate (bCNH), produced from sodium caseinate hydrolysed with trypsin, heat treated, for intramammary use in cows	Bovine casein hydrolysate (bCNH), produced from sodium caseinate hydrolysed with trypsin, heat treated, for intramammary use in cows	no		no		no	**no**
No		Probiotic components including bacteria and yeasts	Probiotic components including bacteria and yeasts	yes	Protect Oral Suspension for New Born Calves	yes	Carbolevure	no	**yes**
No		Recombinant bovine IL-8 (His-tag) for intrauterine use in cattle at a dose of up to 1,000 µg per animal	Recombinant bovine IL-8 (His-tag) for intrauterine use in cattle at a dose of up to 1,000 µg per animal	no		no		no	**no**

Important or out of scope substance (y/n/out of scope)	Reason for important or for out of scope	1st step: substances in Table 1 of Regulation 37/2010	2nd step: cleaned substance names	3rd step: analysis result				AM[1] reserved for human use	Substance eligible for assessment (= in overlap[2] and not out of scope) y/n
		Original extracted name	SMS[3] Substance name (cleaned)	VMP FP terres-trial[4] (y/n)	VMP name example	HMP[5] (y/n)	HMP name example	y/n	
No		Stem cells	Chondrogenic induced equine allogeneic peripheral blood-derived mesenchymal stem cells - alisvetcel	yes	Arti-Cell Forte	no		no	**yes**
No		Stem cells	Equine umbilical cord-derived mesenchymal stem cells	yes	Horstem	no		no	**yes**
No		Stem cells	Tenogenic primed equine allogeneic peripheral blood-derived mesenchymal stem cells - tesrivetcel	yes	RenuTend	no		no	**yes**
No		Varroa destructor calmodulin gene-specific double-stranded interfering RNA EP15 (naked unmodified dsRNA)	Varroa destructor calmodulin gene-specific double-stranded interfering RNA EP15 (naked unmodified dsRNA)	no		no		no	**no**

* Complete original extracted name for food additives: Food additives (substances with a valid E number approved as additives in foodstuffs for human consumption)

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Annex 5.2.1: Assessment of substances identified by aquaculture sector as important for the treatment of food-producing aquatic species

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Albendazole

Albendazole is a broad-spectrum anthelmintic and antiprotozoal agent of the benzimidazole type used for the treatment of different intestinal parasite infections, including ascariasis, trichuriasis, strongyloidiasis, taeniasis, clonorchiasis, opisthorchiasis, cutaneous larva migrans, giardiasis, and gnathostomiasis.

ATCVet code: QP52AC11.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS? Yes, albendazole is authorised in several VMP for food terrestrial animals, for example:

   - Albex 2,5 % and 10% as oral solution is a broad-spectrum multi-purpose anthelmintic for sheep and cattle (Albex 2.5 % Oral Suspension | UPD, Albex 10 % Oral Suspension | UPD https://medicines.health.europa.eu/veterinary/en/600000064569, https://medicines.health.europa.eu/veterinary/en/600000064570).

   - Albex Gold 200 mg/ml oral suspension for cattle (https://medicines.health.europa.eu/veterinary/en/600000048594).

In addition, albendazole is also authorised in medicinal products for human use, for example:

   - Albendazole (Elbazole) tablets 400 mg for human use.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

SPC:

The following information is available in the SPC of the VMP for food-producing terrestrial species Albex Gold 200 mg/ml oral suspension for cattle (https://medicines.health.europa.eu/veterinary/en/600000048594).

"Special precautions for the protection of the environment: Albendazole is toxic to dung fauna and aquatic organisms. Due to the risk to dung organisms, the product should not be used more than once per year. Treated animals (cattle) should not have access to surface water for 7 days after treatment to avoid adverse effects on aquatic organisms."

"Environmental properties: Faeces containing albendazole excreted onto pasture by treated cattle reduce the abundance of dung fauna feeding organisms which may impact on dung degradation. Albendazole is toxic to aquatic organisms from direct exposure and from drainage and/or run-off of

albendazole from the soil. The main metabolite of albendazole, albendazole sulfoxide have been shown to be very persistent."

To avoid the risk of albendazole leaching from feed into the aquatic environment during fish medication via the oral route, a specific procedure for drug incorporation in the feed (coating feed pellets) must be applied.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

No PBT (not listed in the PBT database of ECHA (https://echa.europa.eu/pbt)), vPvB, or ED (not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/) properties. Nevertheless, as indicated above the main metabolite of albendazole, albendazole sulfoxide has been shown to be very persistent (https://medicines.health.europa.eu/veterinary/en/600000048594).

Classified in CLP list:

H400 – Very toxic to aquatic life.

H410 – Very toxic to aquatic life with long lasting effects.

Water Framework Directive (WFD)

Albendazole is not in the Annex X list of priority substances in the field of water policy of the Water Framework Directive.

Conclusion

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No. Albendazole is an antiparasitic substance.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes: an environmental risk cannot be excluded. Article 107(6) is not applicable as albendazole is an antiparasitic substance.

2. Is there an alternative substance (with lower risk for the environment)?

Other substances authorised for food-producing terrestrial animals may be used against endoparasites in food-producing aquatic animals. However, there are not sufficient information available to conclude that those would represent a lower environmental risk (see also point 3 below).

3. Is/Are the alternative substance/s enough to cover availability and avoid development of resistances (eg. for antiparasitics – AMR resistance is not considered)?

No. There is a lack of authorised VMPs for use against endoparasites in aquatic species. To avoid/reduce resistance several antiparasitics with different modes of action should be available. Albendazole is considered a useful tool that should be available for use in food-producing aquatic species.

Conclusion

Albendazole is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when albendazole is used according to Article 114 of Regulation (EU) 2019/6:

Albendazole is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.

Ammonium lauryl sulfate (ammonium dodecyl sulfate)

Ammonium lauryl sulfate, also known as ammonium dodecyl sulfate, is a surfactant used in veterinary medicine as an antiseptic/disinfectant. The substance is also used as a biocide.

ATCvet code: QD08AX**.**

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Yes, Helodip 3.1 % w/v Teat Dip Concentrate is available as concentrated solution for disinfection of ruminant tits (in cattle).

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

There is no environmental risk at the concentration used in VMP.

The most likely use of this substance as a veterinary medical product would be as a topical disinfectant. Currently there is no published study or indication that Ammonium dodecyl sulfate substance is/can/will be used as treatment on food-producing fish. There are some examples of off-label use of quaternary ammonium compounds for treatment of amoebic gill disease (Ark-Klens' and NT Labs 'Gill Wash' in the UK), however, these QACs are not structurally related to ammonium dodecyl sulfate. Therefore, it may be possible that use of the substance in accordance with to Article 114 of Regulation (EU) 2019/6 as a topical treatment will be relevant in the future, possibly through bath application with currently unknown concentration.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

PBT – no: Results of PBT and vPvB assessment. This substance is not considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB). The substance is not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

ED – no: The substance is not considered to have endocrine disrupting properties according to REACH Article 57(f) or Commission Delegated regulation (EU) 2017/2100 or Commission Regulation (EU) 2018/605. The substance is not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

CLP - According to the classification provided by companies to ECHA in CLP notifications this substance has not been classified with any statements relating to aquatic toxicity.

In concentrations used in available veterinary medical products, there are no environmental concerns. However, with use of concentrated substance (e.g. from Sigma) and in quantities that are highly unlikely to be applied on fish as treatment, there are toxicity concerns:

https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/29244

The substance is not included in Annex X (Priority substances) of the Water Framework Directive (Directive 2000/60/EC establishing a framework for Community action in the field of water policy).

Conclusion on the environmental risks

The information available does not allow to reach a definitive conclusion on the environmental risks of the substance. The substance has no hazard classifications, and there is no other information that would indicate a risk to the environment when the substance is used as a veterinary medicine in aquatic species. Due to the inherent properties of the substance, it is not expected that the use of ammonium lauryl sulfate will pose an unacceptable risk for the environment.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

No.

2. Is there an alternative substance (with lower risk for the environment)?

There are no current known alternatives (See introduction).

Conclusion:

Ammonium dodecyl sulfate is recommended to go on the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

Risk mitigation measures are not considered necessary.

Amoxicillin

Amoxicillin is a beta-lactam antibiotic.

ATCvet code QJ01CA04.

It is placed in category D (Prudence) in the AMEG categorisation system for antibiotics. Categorisation of antibiotics for use in animals (europa.eu).

In the AMEG document, the following advice is given for category D substances:

- should be used as first line treatments, whenever possible.
- as always, should be used prudently, only when medically needed.

General questions related to the substance

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Amoxicillin is licensed for fish in Italy. The authorised product is a premix for medicated feed with the strength 100 mg/g, Gammamix 10g/100g (Amoxicillin trihydrate). The authorisation date is before 2005.

Amoxicillin is used against bacterial infections in fish.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

There are many authorised products containing amoxicillin for food-producing terrestrial animals in the EU. Many of them are premixes for medicated feed, some with the same concentration of active substance as Gammamix, and could be used in accordance with the approved SPCs for the premix authorised for fish. One example is Decamox 100 mg/g, premix for medicated feed for pigs.

The substance is also used in human medicine.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

Yes. In Italy as a premix for fish. No environmental information is included in the SPC. As the authorisation was made before 2005 the assessment might not be in accordance with today's regulations.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

No environmental information could be found in SPCs for products authorised in terrestrial species. It should be noted that the environmental assessment of amoxicillin for use in food-producing terrestrial animals (chickens, ducks, turkeys) was carried out on penicilloic acid of amoxicillin (APA), the primary degradation product of amoxicillin.

In the ECHA database and the EPA database it has the hazard statement codes H400 and H410.

No information found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt)No information found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (Priority substances) of the Water Framework Directive (Directive 2000/60/EC establishing a framework for Community action in the field of water policy).

Daphnia toxicity (Norman database) LC50_48_hr_µg/L: 603624.6.

Aquatic toxicity endpoints:

Cyanobacteria: Anabaena flos-aquae NOEC = 8.8 µg/L

(research project: https://www.umweltbundesamt.de/en/publikationen/joint-effects-of-pharmaceuticals-chemicals)

Anabaena flos-aquae NOEC = 3 µg/L (unpublished study report)

A high percentage is excreted unmetabolized via urine and faeces. Experimentally no adverse effects have been observed in soil bacteria involved in the nitrogene cycle, earthworms or plants from concentrations close to the ones found in natural conditions (Litskas, V.D., Karamanlis, X.N., Prousali, S.P. et al. Effects of the Antibiotic Amoxicillin on Key Species of the Terrestrial Environment Bull Environ Contam Toxicol **100**, 509–515 (2018)).

High concentrations (50-100 mg/l) can cause inhibition of catalase activity in the brain of Zebra fish, Danio rerio (Grossi Botelho R, Monteiro SH, Tornisielo VL. Emerging Pollutants in the Environment - Current and Further Implications. IntechOpen; 2012. Chapter 5-Veterinary antibiotics in the environment; pp. 135–152.).

Amoxicillin is among the least toxic antibiotics to Vibrio fischeri, Daphnia magna, Moina macrocopa, and Oryzias latipes (Park, S., Choi, K. Hazard assessment of commonly used agricultural antibiotics on aquatic ecosystems. Ecotoxicology **17**, 526–538 (2008)). Less toxic than for example trimethoprim, sulfamethoxazole and oxytetracycline.

Amoxicillin is toxic to Spirodela polyrhiza in microgram concentrations (LC50 0.089 µg/ L) (Vineet Singh, Bhawna Pandey, Surindra Suthar, Phytotoxicity of amoxicillin to the duckweed Spirodela polyrhiza: Growth, oxidative stress, biochemical traits and antibiotic degradation, Chemosphere, Volume 201, 2018, Pages 492-502).

The cyanobacteria Synechococcus leopoliensis is highly sensitive to Amoxicillin with a NOEC of 0,78 µg/L (Roberto Andreozzi, Vincenzo Caprio, Claudia Ciniglia, Marcella de Champdoré, Roberto Lo Giudice, Raffaele Marotta, and Ettore Zuccato Environmental Science & Technology **2004** 38 (24), 6832-6838).

Conclusion on the environmental risks

The CLP classification statements (H400 and H410) imply that an environmental risk cannot be excluded due to the intrinsic properties of the substance. The only product authorised for aquatic species were approved before 2005 and therefore the environmental risk assessment is not made according to today's regulations. There is evidence that the substance is toxic to some single cell organisms but less so than many other antimicrobial substances used in aquaculture. To reduce environmental risk, proper use is essential. Before treatment the prescribing veterinarian should obtain all necessary information related to the intended use and perform a benefit risk assessment to ensure a responsible use of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No, except in combination with a beta-lactamase inhibitor such as clavulanic acid.

If the substance cannot be used in combination with a beta-lactamase inhibitor, the impact on animal and public health is considered negligible.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes.

1. Is there an alternative substance (with lower risk for the environment)?

Yes, but a spectrum of substances for treating bacterial infections are needed to be able to choose substance according to situation. The alternative antibiotics does not necessarily pose a lesser risk to the environment.

2. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

No.

Conclusion

Amoxicillin is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when amoxicillin is used according to Article 114 of Regulation (EU) 2019/6:

Amoxicillin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[2] is required before discharge in the environment.

The substance is not recommended to be used in combination with beta-lactamase inhibitors.

Amprolium

Amprolium is a coccidiostat used in poultry. It is used to prevent and treat intestinal coccidiosis by blocking the thiamine transporter of coccidia, which results in disruption of cell metabolism.

ATC vet code: QP51AX09.

[2] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

General questions related to the substance

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes. The substance is included in food-producing terrestrial animals VMPs. Some examples are:

- Amprolium 20% oral (amprolium 20% oral | upd (europa.eu)) authorised 17/05/2016.
- Amproline 400 mg/ml solution for use in drinking water for chickens and turkeys (amproline 400 mg/ml solution for use in drinking water for chickens and turkeys | upd (europa.eu)) authorised 17/05/2016.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

The substance is included in food-producing terrestrial animals VMPs across EU for which a complete environmental risk assessment according to the current guidelines have been performed (only ERA carried out after 2005 could be considered as meeting the current ERA standards, considering the date of effect of guideline VICH GL38 Environmental impact assessments for veterinary medicinal products – Phase II).

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

PBT properties

The following information has been obtained from the available terrestrial animals VMPs PuAR.

AMPROLINE 400 mg/mL. Solution for use in drinking water for chickens and turkeys.

The applicant provided a phase I and a phase II environmental risk assessment in compliance with the relevant guidelines. The assessment concluded that amprolium is a persistent molecule in soils, is neither bioaccumulative nor toxic. Warnings and precautions as listed in the product literature are adequate to ensure safety to the environment when the product is used as directed.

SURRICOXX 400 MG/ML (https://www.ircp.anmv.anses.fr/pdf/RPE621.pdf). Solution for use in drinking water for chickens, turkeys, ducks, and guinea fowls.

The risk characterisation resulted in risk quotients (RQs) below 1 for the surface water, groundwater and soil compartments indicating that the product will not pose a risk to those compartments when used as recommended (when applied to soil through manure).

PBT assessment

PBT-assessment			
Parameter	**Result relevant for conclusion**		**Conclusion**
Bioaccumulation	BCF	log Kow <0	not B
Persistence	$DT_{50,\ compartment,\ 12\ °C}$	716 d	(v)P
Toxicity	NOEC	>0.1 mg/L	Not T
PBT-statement :	The compound is considered as vP		

Amprolium is classified as very persistent in soil. No toxic for aquatic organisms.

ED properties.

No information found. Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

CLP classification

No aquatic hazard statement included (C&L Inventory).

Water Framework Directive

The substance is not included in Annex X (Priority substances) of the Water Framework Directive (Directive 2000/60/EC establishing a framework for Community action in the field of water policy).

Conclusion

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species.

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes. While no standard risk assessment about the risks for the environment due to the exposure through the aquatic branch is available, a potential environmental risk cannot be excluded due to the

persistence of the substance in soil. In addition, there is no standard information available about the persistence of the substance in sediment.

2. Is there an alternative substance (with lower risk)?

No. There is no authorised VMPs for aquatic organisms for the same indication.

Conclusion

Amprolium is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when amprolium is used according to Article 114 of Regulation (EU) 2019/6:

Amprolium is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[3] is required before discharge in the environment.

Bambermycin

Bambermycin (flavophospholipol) is an antibacterial consisting of several components.

ATCvet code: QA10AB01.

It is used in poultry, rabbit and aquarium fish.

Bambermycin had been used as a growth-promoting antibacterial in animal feeds till its ban in 2006.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

National authorisation (Bulgaria) for poultry, rabbit, and aquarium fish.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes.

[3] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Indicated for the treatment and metaphylaxis of necrotizing enteritis caused by *Clostridium perfringens* in broilers and laying chickens. National authorisation (Bulgaria). FLAVOMYCIN 80 | UPD

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

There is no information on environmental properties for bambermycin obtainable from the only SPC of VMP for terrestrial species (Bulgarian. deepl.com translation).

There is no assessment report publicly available in any EU MS.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

There is a hazard classification from ECHA: GHS Classification GHS Hazard Statements: H413: May cause long lasting harmful effects to aquatic life [Hazardous to the aquatic environment, long-term hazard].

However, there is some useful additional information on the substance available from the European public MRL assessment report (EPMAR) from 2022:

"Bambermycin is used worldwide as a growth-promoting antibacterial in animal feeds. From 2006, the use of bambermycin in feedstuffs for rabbits, laying hens, chickens for fattening, turkeys, piglets, pigs, calves and cattle for fattening has been banned in the EU (Regulation (EC) 1831/2003). The in vivo effect of bambermycin occurs mainly by contributing to the gastro-intestinal microbiota equilibrium by reducing colonization of pathogens, such as *Salmonella enterica, Clostridium perfringens* and *Fusobacterium* spp. While availability of an authorised VMP containing bambermycin increases the possibility of its misuse, this is expected to be adequately mitigated by clear product information as well as existing restrictions and controls on the use of antimicrobial veterinary medicinal products in the EU. Concerns over the use of bambermycin outside the EU were noted and acknowledged. However, due to its molecular weight (>1500 g/mol), bambermycin is not expected to be absorbed from the gastro-intestinal tract to any significant extent."

Hence, excretion to the environment is expected to be high.

"Resistance to bambermycin seems to develop slowly amongst bacterial populations through mutations in the bacterial chromosome and is non-transferable."

PBT classification

No standard public information available on the PBT properties of the substance. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

ED

Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

CLP classification

H413 – May cause long lasting harmful effects to aquatic life (https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/106408).

Water Framework Directive

The substance is not included in Annex X (Priority substances) of the Water Framework Directive (Directive 2000/60/EC establishing a framework for Community action in the field of water policy).

Conclusion:

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

Not applicable. This antimicrobial substance is not in the list.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes.

2. Is there an alternative substance (with lower risk for the environment)?

Yes.

3. Is/Are the alternative substance/s enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

Yes.

The EPMAR elaborates on the availability of other substances.

Availability of alternative medicines

Alternative veterinary medicines for the treatment of necrotic enteritis are available in the EU. For example, several authorised veterinary medicinal products containing the active substances lincomycin, or tylosin have this indication on the SPC.

Options to treat infections with *Clostridium perfringens* include amoxicillin, penicillin G or tetracyclines.

Furthermore, efficacy of bambermycin against many infections with gram+ pathogens is limited due to widespread natural resistance among many bacterial species.

Conclusion

Bambermycin is not recommended to be included in the list.

The substance is currently authorised for in-feed use for rabbits, poultry and aquarium fish, but not food-producing aquatic species. The usability for the treatment of gram+ infections is limited to few gram+ bacterial species. The potential risks to the environment cannot be assessed, however according to its classification, bambermycin may cause long lasting harmful effects to aquatic life.

Due to the hazardous properties of bambermycin for aquatic organisms, and the presence of alternatives, bambermycin is not included in the list.

Benzocaine

Benzocaine (4-aminobenzoic acid ethyl ester) is a local anaesthetic of the ester type with a poor solubility in water. It is used in bath for the anaesthesia and sedation of fish.

ATCvet code: QN01AX92.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Yes.

Spain. Aquacen Benzocaine: AQUACEN BENZOCAINE 200 mg/ml Concentrate for dip solution | UPD.

Norway. Benzoak Vet: Benzoak vet 200 mg/ml konsentrat til bad, oppløsning | UPD

Optomease Vet 200mg/ml Concentrate for Solution for Fish Treatment: Optomease 200mg/ml concentrate for solution for fish treatment | UPD

2. Is the substance included in a food-producing terrestrial animals or in a medicinal product for human use in EU MS?

Yes.

Mainly for topic use.

Sheep and cattle oral drench (e.g. Gardal 10%, Albex 2,5 % and 10%, Tramazole 10% oral solution, Ascacid 10%).

AUREOZASYP 2% powder (Benzocaine 1%):

Dog, Cat, Pig, Cattle, Sheep, Horse AUREOZÁSYP 20 mg/g dermálny zásyp | UPD

Many medicinal products containing benzocaine authorised for human use.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

Yes.

Widely used in fish for many years.

Many scientific papers endorse its use ("benzocaine fish anaesthesia").

- Google Scholar: 4240 results.
- Pubmed: 28 results.

Benzocaine is licensed for fish in Portugal, Greece, Spain, Norway, Denmark. The authorisation dates for most products are after 2005. The environmental warnings from the SPC of Optomease (authorised in 2020) are stated below.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties.

PBT properties: No information was found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

ED properties: No information was found indicating that the substance is an endocrine disruptor. Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

CLP classification: The substance is notified H413 Aquatic chronic toxicity 4 'May cause long lasting harmful effects to aquatic life' (link). This CLP category applies to cases when data do not allow classification under the other categories submitted to numerical threshold values, but when there are some grounds for concern.

Water framework directive: benzocaine is not included as environmental hazard in the Annex X list of priority substances in the field of water policy of the Water Framework Directive.

Conclusion on the environmental risk

The CLP classification statement (H413) implies that an environmental risk cannot be excluded due to the intrinsic properties of the substance. However, medicinal products for aquatic species were authorised after 2005 and their environmental risk assessment has been considered in the overall benefit/risk assessment.

From Optomease SPC:

"Section 4.5iii: In order to protect the environment, used solution must be transferred to a holding tank filled with water with subsequent controlled release for dilution in the effluent to be discharged from the facility."

"Section 6.6: This product is dangerous to fish and other aquatic organisms in the concentrated form. Do not contaminate ponds, streams, lochs or inlets with product or used packaging. Used solution must be transferred to a holding tank filled with water with subsequent controlled release for dilution in the effluent to be discharged from the facility. The use of the product is limited to facilities equipped with suitable technology to guarantee safe discharges as indicated below. Transfer of used solution to a holding tank filled with water and controlled release for dilution in effluent will ensure that the concentration of spent benzocaine in discharge water does not exceed 1 µg/L. Dilution in effluent must ensure that the concentration of spent benzocaine in discharge water does not exceed the trigger of 1

µg/L safeguarding environmentally good water quality. When releasing the solution from the holding tank, flow rates are calculated based on the following equation:

$$\text{Discharge (L/hr)} = \frac{\text{Farm flow rate (L/min)} \times 0.90 \text{ (safety factor)}}{\text{Holding tank concentration (mg/L)} \times 1000} \times 60$$

Eg. Holding tank concentration (mg/L)	Farm flow rate (L/min)	Discharge flow from holding tank (L/h)
5	10,000 / 20,000 / 30,000	108 / 216 / 324
10	10,000 / 20,000 / 30,000	54 / 108 / 162
20	10,000 / 20,000 / 30,000	27 / 54 / 81
40	10,000 / 20,000 / 30,000	14 / 27 / 41

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements."

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes, risk for the environment.

2. Is there an alternative substance (with lower risk for the environment)?

There are other anaesthetic agents authorised for fish: isoeugenol and tricaine mesilate. But benzocaine is considered a very important anaesthetic agent for fish and cannot fully be replaced by the other anaesthetics.

3. Are the alternative substances enough to cover availability and avoid development of resistances?

Not applicable.

Conclusion

Benzocaine is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when benzocaine is used according to Article 114 of Regulation (EU) 2019/6:

Benzocaine is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[4] is required before discharge in the environment.

Bronopol

Bronopol (2-bromo-2-nitropropane-1,3-diol) is an antimicrobial active against bacteria and fungi. It is used as an antifungal in fish and fish eggs.

ATCvet code: QD01AE91.

General questions related to the substance

1) Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Yes, PYCEZE 500 mg/ ml Concentrate for solution for fish treatment in France, Norway and Spain, authorised 31/10/2008, 15/06/2010, and 31/10/2008, respectively.

2) Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Bronopol is not approved for food-producing terrestrial animals; the entry in the annex of EU 37/2010 is limited to use in fish.

Bronopol is active substance of medicines for human use (e.g. BRONOPOL SMARTPRACTICE EUROPE).

Main assessment regarding the mandate criteria

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals? **Yes.**

- VMP PYCEZE 500 mg/ml Concentrate for solution for fish treatment in France, Norway and Spain, authorised 31/10/2008, 15/06/2010, and 31/10/2008, respectively.

As the substance is already authorised for food-producing aquatic organisms the risks for the environment through aquatic exposure has been already assessed:

From the SPC of PYCEZE 500 mg/ml,

"Other Precautions:

This product is designed for use following dilution and waterborne administration. Without any dilution the product is harmful to other aquatic life.

A discharge consent may be required for release of this product into the aquatic environment. This must be obtained, prior to use of the product, from the relevant authority. Otherwise the product should only be used if the flow rate of untreated waters allows for a minimum dilution of the volume of

[4] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

treated water. For fish treatment the product should only be used if the flow rate of untreated water allows a dilution of 1:2000 times the volume of treated water. For egg treatment the product should only be used if the flow rate of untreated water allows a dilution of 1:5000 times the volume of treated water. Where the appropriate dilution of treated water cannot be achieved, the farm must have a discharge process to limit the release of product into the environment to within the parameters described. This can be achieved by the use of holding tanks and ponds, discharge lagoons and biofilters to clean treated water. Where this applies, the user must monitor the discharge concentration to ensure the parameters are not exceeded."

It is noted that the above dilution factors, applied to treatment concentrations of 20 mg/L for fish treatment and 50 mg/L for egg treatment as indicated in the SPC, lead to a discharge concentration of 10 µg/L.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

PBT properties

Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

ED properties

As of February 2023, Bronopol is under assessment as endocrine disrupting substance by ECHA but no outcome has been published at the time or writing (https://echa.europa.eu/ed-assessment/-/dislist/details/0b0236e1889cbb46).

Other environmental hazards: CLP

Classification	
Hazard Class and Category Code(s)	Hazard Statement Code(s)
Aquatic Acute 1	H400

https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discli/details/117530

Compliance with current ERA standards

First authorisation in 2008, compliant with current ERA standards.

Water Framework Directive (WFD)

The substance is not included in Annex X (Priority substances) of the Water Framework Directive (Directive 2000/60/EC establishing a framework for Community action in the field of water policy).

Any other available information

Bronopol rapidly hydrolyzes in natural waters, producing the more stable 2-bromo-2-nitroethanol (BNE) and bromonitromethane (BNM)

According to Cui et al. 2011 "Judging from toxicity assays and the relative pesticide toxicity index, these degradation products (i.e., BNE and BNM), more persistent and higher toxic than the parent, probably accumulated in natural waters and resulted in higher or prolonging adverse impacts".

Magara et al. 2021 published a theoretical environmental risk assessment for bronopol and its degradation product BNE, based on data from the freshwater bivalve *Sinanodonta woodiana* and available literature. The authors conclude through the theoretical model some environmental risk in aquaculture facilities with small basins in particular. See table below:

Table 3
risk quotient (RQ) of (A) 2-bromo-2-nitroethanol as Bronopol (2.5 and 50 mg/L) *by-product* and H_2O_2 as Detarox® AP *by-product* (1.11 and 22.26 mg/L) (B) released once-a-week for one year in three basins (1500, 65,000 and 200,000 km^2) by small, medium and large-size aquaculture facilities (25, 50 and 100 tonnage of production).

A) RQ of 2-bromo-2-nitroethanol as Bronopol *by-product*

	Bronopol 2.5 mg/L			Bronopol 50 mg/L		
	25 t	50 t	150 t	25 t	50 t	150 t
SB	37.9960	75.9919	2.27×10^2	7.6×10^2	1.5×10^3	4.5×10^4
MB	0.2505	0.5010	1.5031	5.0104	10.0209	30.0627
LB	0.02850	0.0570	0.1710	0.5699	1.1399	3.4196

Conclusion on the environmental risks

The substance poses an environmental risk if treated water is discharged without dilution, according to the SPC of the authorised product.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

Bronopol is authorised for use in aquatic animals to prevent fungal infections (Saprolegnia spp.). Not identified considering Article 107(6).

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

If instructions in SPC are followed, there are no clearly established known environmental risks or restrictions of concern at the time of writing.

2. Is there an alternative substance (with lower risk for the environment)?

No. There are no other antifungal substances currently authorised for food-producing aquaculture.

Conclusion

Bronopol is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when bronopol is used according to Article 114 of Regulation (EU) 2019/6:

Bronopol is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1µg/L[5] is required before discharge in the environment.

Buserelin

Buserelin is a synthetic analog of hypothalamic gonadotropin releasing hormone (GnRH, LHRH). It is used to induce ovulation in terrestrial animals and to facilitate stripping in fish.

ATCvet code: QH01CA90.

General questions related to the substance:

1) Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Yes. Licenced for use in trout and carp.

Receptal 0.004mg/ml Solution for injection

2) Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes. Licenced widely across the EU as hormone for injection (0.004mg/ml as Buserelin acetate) for cattle, horses, pigs and rabbit.

Receptal 0.004mg/ml Solution for injection.

The substance is also authorised in medicinal products for human use.

[5] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

Yes (see above).

Product is licenced for food-producing aquatic animals. Date of first Authorisation 1999, date of last renewal 28th August 2009. Special precautions are needed for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products.

The substance is included in food-producing terrestrial animals VMPs across EU for which a complete environmental risk assessment according to the current guidelines have been performed.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties.

CLP Classification

No aquatic hazard statements noted.

PBT properties:

Not classified as a P, B or T substance. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

Endocrine Disruption (ED) properties:

Buserelin has recognized endocrine disruption properties due to its hormonal actions. Its method of administration must be restricted to injection route to ensure potential effect on environment is limited during this period.

Water Framework Directive:

The substance is not included in Annex X (Priority substances) of the Water Framework Directive (Directive 2000/60/EC establishing a framework for Community action in the field of water policy).

Conclusion on the environmental risks:

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

Given the method of administration (injection), the rapid metabolism, the nature of the product (a natural hormone), and the small scale of use (broodstock), it is considered that the exposure to the environment is very limited and that therefore a significant risk to the environment is unlikely.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6).

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No (not an antimicrobial).

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

Buserelin is commonly used as a specific treatment required for a specific indication. There is no suitable alternative available and it is availability is deemed necessary to ensure welfare and management of aquatic species.

Conclusion:

Even though buserelin is an endocrine disruptor, its intramuscular use is unlikely to cause harm to the environment, due to its fast metabolism. The substance is deemed necessary for animal welfare and management. Buserelin is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures are recommended when buserelin is used according to Article 114 of Regulation (EU) 2019/6:

Buserelin shall be administered by injection only.

Caryophylli aetheroleum (clove oil)

Clove oil (*Caryophylli aetheroleum*) is an essential oil obtained from the dried flower buds, leaves, or stems of the clove tree (*Syzygium aromaticum*). It has properties as antimicrobial, analgesic (pain-relieving; often used for dental and topical pain relief), anti-inflammatory, antioxidant, and anaesthetic.

The primary active components of clove oil include:

- Eugenol (70–90%): Responsible for its analgesic, antimicrobial, and anti-inflammatory properties.
- Eugenyl acetate: Contributes to its pleasant aroma and therapeutic effects.
- Beta-caryophyllene: A terpene with anti-inflammatory and analgesic properties.

Uses in veterinary medicine:

- Anaesthetic for fish: Clove oil is widely used as a sedative or anaesthetic for fish during handling, transport, or minor procedures.
- Topical antimicrobial: Applied to minor wounds or infections in animals.
- Pain and inflammation relief: Used in diluted forms for animals to manage localized pain or swelling.
- Insect repellent: Used as a natural remedy to repel parasites like ticks and fleas.

ATCvet code: none.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Clove oil is not authorised in a VMP as a single active ingredient. However, clove oil is included in mixtures of various active substances, and no VMPs containing clove oil alone have been found.

- Melissengeist ademspray, neusspray voor herkauwers, paarden en varkens. Nasal use. Active substances: CINNAMON OIL, NUTMEG OIL, FENNEL OIL, CARAWAY OIL, CITRONELLA OIL, LEMON OIL, Lidocaine hydrochloride, **CLOVE OIL.** Authorised: 09/01/1992. https://medicines.health.europa.eu/veterinary/en/600000067687.
- Uierbalsem, emulsie voor uitwendig gebruik. Teat use. Active substances: LAUREL LEAF OIL, ROSEMARY OIL, **CLOVE OIL**, ARNICA TINCTURE, EUCALYPTUS OIL, Camphor, racemic, HYPERICI OLEUM. Authorised: 16/01/1992. https://medicines.health.europa.eu/veterinary/en/600000067660.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

Sources of information:

PuAR from the use of the substance in any authorised product in food-producing animals: https://medicines.health.europa.eu/veterinary/en

ECHA C&L inventory (the search is not intuitive, try different ways to include the name of the substance): https://echa.europa.eu/information-on-chemicals/cl-inventory-database (or substance search from https://echa.europa.eu/information-on-chemicals and then click C&L inventory)

ECHA chemTOX: https://chem.echa.europa.eu/

ECHA PBT: https://echa.europa.eu/pbt

PBT UBA list: List of putative PBT substances_UBA.xls

EFSA: EFSA | Science, safe food, sustainability (europa.eu)

EPA: CompTox Chemicals Dashboard (epa.gov)

NORMAN database: https://www.norman-network.com/nds/susdat/

PUbmed: https://pubmed.ncbi.nlm.nih.gov/

PBT properties

The substance is not listed as a PBT/vPvB in ECHA. The following information is included in ECHA in this respect: The registered substance is a natural complex substance, which consists of one major constituent (Eugenol, present at 75-95%) and up to three minor constituents (Caryophyllene 2 -20%, Eugenyl acetate 0-15% and Humulene 0-5%). Each constituent has been taken into account in the PBT assessment:

Although Caryophyllene and humulene are screened as potentially B based on log kow, they are neither P or T. Eugenol and Eugenyl Acetate are neither P, B or T. Therefore none of the constituents in the registered substance are PBT/vPvB (Complex substance of 4,11,11-trimethyl-8-methylenebicyclo[7.2.0]undec-4-ene and 4-allyl-2-methoxyphenol and 4-allyl-2-methoxyphenyl acetate 100.142.398 | 197be8d0-9f2b-46f2-9f1e-befdb972b68e - ECHA CHEM).

ED properties

No information is found indicating that the substance is an endocrine disruptor (ED).

Other environmental hazards: CLP

In the absence of test data on the registered mixture, the substance has been classified using the "summation of classified components" approach. For each constituent, it was checked if a harmonised classification exists for acute and chronic toxicity hazards in Annex VI of the CLP regulation. No harmonised classification exists. Therefore, on the basis of the gathered information presented in this REACH dossier each constituent was assessed for their short-term (acute) and long-term (chronic) environmental hazards as shown below:

Eugenol, concentration range 75 to 95%, lowest EC/LC50 = 1.9 mg/L (daphnia, measured value), readily biodegradable, log Kow 2.0.

- the component **is not classified for acute hazard or for long-term hazard** in categories Chronic 1, 2 or 3.

Caryophyllene, concentration range 2 to 20%, no acute toxicity up to solubility limit, readily biodegradable, log Kow 6.3.

- the component **is not classified for acute hazard or for long-term hazard** in categories Chronic 1, 2 or 3.

Eugenyl Acetate, concentration range 0 to 15%, EC/LC50 = 4.4 mg/L (algae, QSAR), readily biodegradable, log Kow 2.3.

- the component **is not classified for acute hazard or for long-term** hazard in categories Chronic 1, 2 or 3.

Humulene, concentration range 0 to 5%, no acute toxicity up to solubility limit, inherently biodegradable (achieved > 60% within 28 days but failed 10d window criterion), log Kow 6.9.

- the component **is not classified for acute hazard** but based on the fact that the substance is not rapidly degradable and has a log Kow > 4 the "safety net classification" of Category Chronic 4 has been applied.

Humulene is the only component that is classified. However, it is present at < 25% in the registered biocide product. As a consequence, there is no need to classify the whole substance.

Complex substance of 4,11,11-trimethyl-8-methylenebicyclo[7.2.0]undec-4-ene and 4-allyl-2-methoxyphenol and 4-allyl-2-methoxyphenyl acetate 100.142.398 | 197be8d0-9f2b-46f2-9f1e-befdb972b68e - ECHA CHEM.

Water Framework Directive (WFD)

If a substance is not the Annex X (Priority substances) of the Water framework directive (Directive 2000/60/EC establishing a framework for Community action in the field of water policy).

Conclusion on the environmental risks

The available information does not provide enough evidence to draw a definitive conclusion regarding the environmental risks of the substance. While the substance has no hazard classifications, and there is no other information that would indicate a risk to the environment when the substance is used as a veterinary medicine in aquatic species, it should be noted that the potential environmental risks arising from exposure to the substance have not been assessed. Nevertheless, considering the assessment performed according to section 3.1.2, no unacceptable risk for the environment can be expected from the use of the substance according to Article 114.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

No. As it is a natural substance and considering the intrinsic properties of the substance no unacceptable risk for the environment is anticipated. Furthermore, its use is not restricted under Article 107(6).

2. Is there an alternative substance (with lower risk for the environment)?

Not applicable due to the low environmental risks of the substance.

3. Is/Are the alternative substance/s enough to cover availability and avoid development of resistances (e.g. for antiparasitics - AMR resistance is not considered)?

There may be alternative antimicrobials, anaesthetics, or anti-inflammatory agents available. However, given that clove oil is a natural substance with a low anticipated environmental risk, it is proposed to include it in the list as an alternative treatment option.

Conclusion

Clove oil is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

Risk mitigation measures are not considered necessary.

Chlortetracycline

Chlortetracycline is a broad-spectrum antimicrobial agent in the tetracycline group.

ATCvet code: QJ01 AA03.

Chlortetracycline is used against bacterial infections in fish.

It is placed in category D (Prudence) in the AMEG categorisation system for antibiotics. Categorisation of antibiotics for use in animals (europa.eu).

In the AMEG document, the following advice is given for category D substances:

- should be used as first line treatments, whenever possible.
- as always, should be used prudently, only when medically needed.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Chlortetracycline is the active substance in VMPs authorised for fish in Italy. The authorised products are premixes for medicated feed, with the strength 200 mg/g, e.g Clorobiotic 200 premix for medicated feed and Clortetra 200 premix for medicated feed.

However, the information in the UPD indicates that none of the marketing authorisations for aquatic animals are issued after October 2005.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Chlortetracycline-containing products are authorised in EU MS for food-producing terrestrial animals. The pharmaceutical forms approved include premix for medicated feed, oral powder and cutaneous spray. The premixes are usually either 100 mg/g or 200 mg/g, and they could therefore be used in accordance with the approved SPCs for the premixes authorised for fish in case of shortages of the fish products.

Some examples are Chlorosol 50% powder for oral solution for chicken and pig, Chlortetraciclin 40%-BG oral powder for pig and chicken and Clortetradem 10% premix for medicated feed for pig and chicken. Some of the MAs for food-producing terrestrial animals are issued after October 2005. It is therefore assumed that the benefit risk assessment performed by the Competent Authorities covers environmental risks when chlortetracyclin is used for terrestrial animals (pig and chicken).

The substance is also used in human medicine.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

Yes. In the Italian SPC for two different premixes for fish no precautionary measures related to environmental effects could be found. However, as the chlortetracycline products authorised for fish received their MA before October 2005, it cannot be assumed that the submitted documentation on environmental properties and the ERA assessment performed by the Competent Authority are in full accordance with current regulatory requirements.

Chlortetracycline has been assessed and approved for fish in an EU MS. However, the MAs were issued before October 2005.

No information on environmental effects is included in the SPC for the products authorised for fish.

However, some of the MAs for terrestrial animals are issued after October 2005. It is therefore assumed that the submitted documentation and the assessment performed by the Competent Authorities are in accordance with current requirements regarding environmental effects relevant for terrestrial use.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

No information is found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information is found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

In the ECHA database the substance has not been classified with any statements relating to aquatic toxicity according to the CLP regulation.

Other information

Norman: Lowest PNEC 0.29994 µg/L Daphnia magna.

DT50 (predicted) 147.943 days.

BCF (predicted) 1.61309.

Not B, not M, potentially T.

EPA, environmental fate:

Property	Experimental average	Predicted average	Experimental median	Predicted median	Experimental range	Predicted range	Unit
Biodeg. Half-Life		148 (1)		148	-	148	days
Bioconcentration Factor		1.62 (2)		1.62	-	1.37 to 1.86	L/kg
Atmos. Hydroxylation Rate		8.32e-11 (1)		8.32e-11	-	8.32e-11	cm3/molecule*sec
Fish Biotrans. Half-Life (Km)		0.398 (1)		0.398	-	0.398	days
ReadyBiodeg		0.00 (1)		0.00	-	0.00	Binary 0/1
Soil Adsorp. Coeff (Koc)		1.51e+3 (1)		1.51e+3	-	1.51e+3	L/kg

Conclusion on the environmental risk

The information available indicates that an environmental risk cannot be excluded.

However, the environmental risks derived from the exposure of the environment to the substance following its use in aquaculture have not been assessed.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

No environmental RMMs are included in the SPCs of authorised fish products. The substance has not been classified for aquatic toxicity according to the CLP regulation. Nevertheless, the reported PNEC based on studies in Daphnia indicate that a risk for the aquatic environment cannot be excluded at concentrations above 0.3 u/L.

There are no restrictions according to article 107(6).

2. Is there an alternative substance (with lower risk for the environment)?

Other antimicrobials are authorised in EU MS for use in fish, e.g. oxytetracycline, florfenicol, flumequine and oxolinic acid. However, limited information related to environmental effects is publicly available for the antimicrobials authorised for fish, and generally no environmental RMMs are included in the SPCs. It is therefore difficult to draw firm conclusions on whether the alternatives have a lower risk for the environment.

The general RMM relating to the responsibility of the veterinarian for all treatments under Article 114(1) should apply.

3. Are the alternative substances enough to cover availability and avoid development of resistances?

No. As chlortetracycline is categorised as a first line treatment in the AMEG categorisation system, and as it is suitable for treatment of some bacterial infections in fish, it is considered important that the substance is available for use in fish.

Prudent use of chlortetracycline is important to reduce the risk for the environment as well as the risk for development of resistance. Important measures to reduce the need for treatment with antibacterials are good management practices/hygiene and vaccination.

Conclusion

Chlortetracycline is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6. Whereas a risk for the aquatic environment cannot be fully excluded, it is considered necessary to maintain the availability of a range of category D antibiotics for animal health and welfare reasons.

The following risk mitigation measures should be considered when chlortetracycline is used according to Article 114 of Regulation (EU) 2019/6:

Chlortetracycline is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[6] is required before discharge in the environment.

Clavulanic acid

Clavulanic acid is a β-lactam that has no antibiotic effect in itself, but functions as a β-lactamase inhibitor. It is used in combination with penicillins and has no ACTvet code of its own.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS??

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes in combination with amoxicillin (e.g. VMP Synulox, HMP Augmentin). The impact on animal and public health if the food-producing aquatic species affected cannot receive treatment with the substance.

[6] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No. No environmental information could be found in SPCs for products authorised in terrestrial species.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications….

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties.

Clavulanic acid has no relevant hazard statement codes under CLP.

No information found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water Framework Directive.

Conclusion on the environmental risks

The environmental risks from the use of clavulanic acid following its use in aquatic species have not been assessed in the context of a marketing authorisation application. The information available does not allow to reach a conclusion on the environmental risks of the substance. Specific hazards for the aquatic environment have not been identified, and there is no other information that suggests that clavulanic acid is harmful for the environment.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

Yes. It is specified that the substance in combination with aminopenicillins should not be used in food-producing aquatic animals. All approved medicines with clavulanic acid are combined with amoxicillin (an aminopenicillin). There is no use for clavulanic acid if it is not combined with a penicillin, therefore all practical use of the substance is recommended to be prohibited in the scientific advice.

If the substance cannot be used in combination with an aminopenicillin, the impact on animal and public health is considered negligible.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

In the scientific advice mentioned above it is recommended to be prohibited for use in combination with aminopenicillins.

2. Is there an alternative substance (with lower risk for the environment)?

There is a spectrum of antibiotics that can be used without being combined with clavulanic acid.

3. Is the alternative substance enough to cover availability and avoid development of resistances (e.g. for antiparasitics)?

Yes.

Conclusion

Clavulanic acid is not recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6 due to the following reasons: The combination of beta-lactamase inhibitors and aminopenicillins is not recommended in aquatic food-producing species according to scientific advice under Article 107(6), and there are sufficient alternatives.

Copper sulfate

Copper sulfate is used as a fungicide, algaecide, root killer, and herbicide in both agriculture and non-agricultural settings. It is also used as an antimicrobial and molluscicide. Also used in aquaculture against pathogenic algae, protozoan ectoparasites and dinoflagellates in marine fish.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes. In the Netherlands as Copper-sol 50 mg/ml (Reg NL 8285) for poultry and swine.

in Lituania as MULTIVIT-MINERAL (injectable solution with many vitamins/minerals and 0.02 mg/ml copper sulphate) and also as Aqua Cuprozincica (zinc 25.5 mg/ml + copper sulphate 7.65 mg/ml).

In Italy as DESSAMOR for dip solution in ornamental fish against parasites (Acriflavinium chloride, Methylthioninium chloride, Ethacridine lactate and COPPER SULFATE).

It was also used in human medicine in the past as an emetic and antidote in cases of fluoride poisoning. Copper gluconate approved as dietary supplement.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No (only for ornamental fish and without veterinarian prescription).

SPC of VMP for ornamental fish: "Lower animals such as invertebrates, mussels, shrimps (Caridine) and snails do not tolerate treatment with copper sulfate) and must therefore be removed from the aquarium and kept in a separate tank for the entire duration of the treatment. Aquatic plants with very fine, particularly delicate leaves, such as Ceratophyllum, *Cabomba aquatica* or Myriophyllum, can suffer temporary damage such as falling or yellowing of the leaves."

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties.

No PBT or EDT properties. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

Other environmental hazards: CLP

H400 – Very toxic to aquatic life.

H410 – Very toxic to aquatic life with long lasting effects.

Not included in the Annex X list of priority substances in the field of water policy of the Water Framework Directive,

Conclusion on the environmental risks

The CLP classification statements (H400 and H410) imply that an environmental risk cannot be excluded due to the intrinsic properties of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Copper sulfate is very toxic to aquatic organisms of the environment. Copper sulfate is not an antimicrobial: Article 107(6) does not apply.

2. Is there an alternative substance (with lower risk for the environment)?

No.

3. Is/Are the alternative substance/s enough to cover availability and avoid development of resistances (eg. for antiparasitics – AMR resistance is not considered)?

No, there is a real lack of antiparasitic VMPs and substances against algae causing health problems and suffering in aquaculture.

Conclusions

While copper sulfate might pose a risk to aquatic environment, its use is deemed necessary for some indications (such as algae causing health problems and suffering in fish) where there is a lack of alternative. Copper sulfate is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when copper sulfate is used according to Article 114 of Regulation (EU) 2019/6:

Copper sulfate is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[7] is required before discharge in the environment.

Decoquinate

Decoquinate is a quinolone coccidiostat used in calves and lambs.

ATCvet code QP51AX14.

[7] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes, as a coccidiostat in calves and lambs (and previously for poultry) under the name Decoxx.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

No environmental information could be found in SPCs for products authorised in terrestrial species.

Additional threshold to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

No information found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water Framework Directive.

Hazard statement code H413 – May cause long lasting harmful effects to aquatic life.

Daphnia toxicity (Norman database) LC50 48 hr µg/L: 7204.70.

Algae toxicity (Norman database) EC50 72 hr µg/L: 24.86.

There are VMPs authorised after 2005.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes. It is only to be administered orally.

2. Is there an alternative substance (with lower risk for the environment)?

Yes: amprolium. However, it does not have evidently lower environmental risk.

3. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

No.

Conclusion

Decoquinate is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

There is a lack of information regarding the impact on aquatic species and it is marked with hazard statement code H413. Some restrictions are advised.

The following risk mitigation measures should be considered when it is used according to Article 114 of Regulation (EU) 2019/6:

Decoquinate shall be administered in feed only.

Decoquinate is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[8] is required before discharge in the environment.

Deltamethrin

Deltamethrin is a synthetic pyrethroid ectoparasiticide used in ruminants and fish.

ATCvet code QP53AC11.

[8] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Yes**:**

- Alpha Max 10 mg/ml Concentrate for solution for fish treatment (Alpha Max 10 mg/ml Concentrate for solution for fish treatment | UPD (europa.eu)). Authorised 12/07/2006.
- VMP AMX 10 mg/ml Concentrate for solution for fish treatment (AMX 10 mg/ml Concentrate for Solution for Fish Treatment | UPD (europa.eu)). Authorised 17/12/2008.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes, it is included in several food-producing terrestrial animals VMPs, for example:

- Butox 7,5 mg/mL pour on, poliv, suspezija, za goveda i ovce (https://medicines.health.europa.eu/veterinary/en/600000074060).
- DELTAVETo – 5 (https://medicines.health.europa.eu/veterinary/en/600000090430).

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

Yes:

- VMP AMX 10 mg/ml Concentrate for solution for fish treatment (AMX 10 mg/ml Concentrate for Solution for Fish Treatment | UPD (europa.eu)). Authorised 17/12/2008.

As the substance is already authorised for food-producing aquatic organisms the risks for the environment through aquatic exposure has been already assessed. The following precautions should be considered when the substance is used under Article 114(1) (information included in the SPC of the VMP AMX 10 mg/ml Concentrate for solution for fish treatment):

"Deltamethrin is toxic to aquatic and sediment living species and may cause adverse effects in the vicinity of treated sea cages. Also at distances of up to 4 kms downstream short-term effects after treatment can be seen in sensitive organisms. Deltamethrin demonstrates high affinity to organic matter and particles in the water column and in sediments. Deltamethrin is very stable and slowly degradable when bound to sediments, both at aerobic and anaerobic conditions. The environmental risk assessment of deltamethrin, is based on the theoretical use of only a single (annual) application in a single cage at one site. More frequent use and/or use on a larger scale may pose an increased risk to the environment. In order to ensure safe use (including large scale and multiple treatments) of deltamethrin under a combination of different environmental conditions (e.g. low water current speeds, shallow waters, short distance to the shore etc.) local environmental regulations governing discharges, where applicable, must be adhered to. If there is any doubt about safe use, relevant competent authorities should be consulted or professional advice sought accordingly."

"Other precautions:

The substance is toxic to crustaceans and should not be used in sea farms where crabs or lobsters are kept in the close vicinity of the treated sea-cages (<200 m), or when local water-currents increase the

likelihood of exposure. To prevent toxic effects on local aquatic organisms and to prevent toxic waste of deltamethrin to be washed into the littoral zone, bath treatment should be performed at outgoing tide or during periods with a local outgoing current."

Additional threshold to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications….

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

PBT properties

No information is found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt). Nevertheless, although not PBT, the following is indicated in the SPC of the VMP Deltadot 10 mg/ml Pour-on Solution Deltamethrin for Cattle and Sheep (Deltadot 10 mg/ml Pour-on Solution for Cattle and Sheep | UPD (europa.eu): *Deltamethrin is very toxic to dung fauna, aquatic organisms and honey bees, is persistent in soils and may accumulate in sediments*.

ED properties

No relevant information found. Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

CLP classification

H400 – Very toxic to aquatic life.

H410 – Very toxic to aquatic life with long lasting effects.

Water Framework Directive

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

Conclusion:

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No. Deltamethrin is an antiparasitic.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes. A risk for the environment might be expected according to the public information available.

2. Is there an alternative substance (with lower risk)?

Yes. Deltamethrin is intended for treatment of adult and preadult sea lice *(Lepeophtheirus salmonis*) in different fish species.

According to the CMDv list of VMPs authorised for fish (July 2023), the following substances are available for the treatment of sea lice:

- Emamectin benzoate.
- Hydrogen peroxide.
- Azamethiphos.
- Imidacloprid (not eligible substance to be included in the Article 114 of Regulation (EU) 2019/6 list).

According to the VICH GL 6 (Guideline on environmental impact assessment (EIAs) for veterinary medicinal products – Phase I), the ecotoxicological potential of ecto/endoparasitics need to be assessed more in deep (phase II). Therefore, it cannot be anticipated that the available alternatives to deltamethrin suppose less risk for the environment without an in-depth environmental assessment according to the current guidelines in force.

3. Are the alternative substances enough to cover availability and avoid development of resistances?

No. Even assuming that the alternatives would suppose lower risk for the environment, the Fish diseases lacking document (FishMedPlus Coalition, 2017) identified the sea lice as one of the main priority diseases that need treatment alternatives (due to problems with increasing levels of resistance to medicines, combined with off label use, e.g. increased doses/holding times and ineffective combination treatments, which is leading to rising mortality to treatments).

Conclusions

Deltamethrin is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when deltamethrin is used according to Article 114 of Regulation (EU) 2019/6:

Deltamethrin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L is required before discharge in the environment.

Deltamethrin is toxic to aquatic and sediment living species and may cause adverse effects in the vicinity of treated sea cages. Also at distances of up to 4 kms downstream short-term effects after treatment can be seen in sensitive organisms. Deltamethrin demonstrates high affinity to organic matter and particles in the water column and in sediments. Deltamethrin is very stable and slowly degradable when bound to sediments, both at aerobic and anaerobic conditions. The environmental risk assessment of deltamethrin, is based on the theoretical use of only a single (annual) application in a single cage at one site. More frequent use and/or use on a larger scale may pose an increased risk to the environment. In order to ensure safe use (including large scale and multiple treatments) of deltamethrin under a combination of different environmental conditions (e.g. low water current speeds, shallow waters, short distance to the shore etc.) local environmental regulations governing discharges, where applicable, must be adhered to. If there is any doubt about safe use, relevant competent authorities should be consulted or professional advice sought accordingly.

Other precautions:

The substance is toxic to crustaceans and should not be used in sea farms where crabs or lobsters are kept in the close vicinity of the treated sea-cages (<200 m), or when local water-currents increase the likelihood of exposure. To prevent toxic effects on local aquatic organisms and to prevent toxic waste of deltamethrin to be washed into the littoral zone, bath treatment should be performed at outgoing tide or during periods with a local outgoing current.

Doxycycline

Doxycycline is a broad-spectrum semisynthetic tetracycline derivative used in terrestrial food-producing species and in humans.

ATCvet code: QJ01AA02

In the AMEG categorisation system doxycycline is assigned to category D ("Prudence") as doxycycline should be used as first line treatment for some type of infections.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes. Many products such as Doxylin, Doxyvet, Altidox for chicken, turkey, cattle, pigs.

Several authorised products for human use.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

Risk characterisation indicated that no relevant risk is expected for aquatic non-target organisms when doxycycline is used with the maximum recommended dosage for intensively reared terrestrial food-producing animals.

Aquatic toxicity endpoints (literature):

Algae, *Raphidocelis subcapitata*: NOEC growth 6.95 µg/L endpoint, PuAR.

Daphnia magna: NOEC immobilisation ≥ 100 mg/L endpoint, PuAR.

Fish, *Oncorhynchus mykiss*: NOEC 42.8 mg/L endpoint, PuAR.

Doxycycline is toxic to algae, cyanobacteria, and terrestrial plants.

Additional threshold to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

No information found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance has no CLP hazard statement codes relevant to aquatic species.

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No, doxycycline as a tetracycline derivative is not listed to be excepted from this use.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes, due to the inherent properties of the substances, a risk to the environment cannot be excluded. However, no restrictions for use or mitigation measures are included in SPCs or PuARs.

2. Is there an alternative substance (with lower risk for the environment)?

No

3. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

No. As these substances are effective for treatment of certain bacterial infections in fish and are categorised as a first line treatment in the AMEG categorisation system, it is considered important that the substance is available for use in fish.

However, prudent use of these substances is important both to protect the environment and to reduce the risk for development of resistance. Important measures to reduce the need for treatment with antibacterials are good management practices/hygiene and vaccination.

Conclusion

Doxycycline is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

Doxycycline is toxic to algae, cyanobacteria, and terrestrial plants.

The following risk mitigation measure should be considered when doxycycline is used according to Article 114 of Regulation (EU) 2019/6:

Doxycyline is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[9] is required before discharge in the environment.

Enrofloxacin

Enrofloxacin is a fluoroquinolone antibiotic.

ATCvet code QJ01MA90.

[9] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

It is placed in category B (Restrict) in the AMEG categorisation system for antibiotics. Categorisation of antibiotics for use in animals (europa.eu).

In the AMEG document, the following advice is given for category B substances:

- antibiotics in this category are critically important in human medicine and use in animals should be restricted to mitigate the risk to public health.
- should be considered only when there are no antibiotics in Categories C or D that could be clinically effective.
- use should be based on antimicrobial susceptibility testing, wherever possible.

General questions related to the substance

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Enrofloxacin is licensed for fish in Romania. The authorised product is a premix for medicated feed with the strength 500 mg/g, Enrodem 50 (Enrofloxacin hydrochloride). The authorisation date is after 2005 (2006 and changed in 2016).

Enrofloxacin is used against bacterial infections in fish.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

There are many authorised products containing enrofloxacin for food-producing terrestrial animals in the EU, most of them for parenteral use, but also for oral use. One example is ENROFLOXACINA FP, premix for medicated feed for pigs, chickens and turkeys.

The main metabolite of the substance, ciprofloxacin, is also used in human medicine.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

Yes. In Romania as a premix for fish.

The SPC specifies the following text:

"For environmental protection, the product must not be disposed of in wastewater or household waste but in designated collection points. Any unused veterinary pharmaceutical product or waste derived from such products must be disposed of in accordance with local regulations. Treated animals must be kept in shelters for the entire duration of the treatment, and collected excreta must not be used for soil fertilization."

As the authorisation was made after 2005 the assessment might be in accordance with today's regulations.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

No environmental information could be found in SPCs for products authorised in terrestrial species.

In the ECHA database and the EPA database it has the following hazard statement codes:

- GHS08 (serious health hazard).
- GHS07 (health hazard).
- GSH09 (hazardous to the environment).

According to the classification provided by companies to ECHA in **CLP notifications** this substance this substance is:

- H400 – Very toxic to aquatic life.
- H410 – Very toxic to aquatic life with long lasting effects.

No information was found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information was found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

Daphnia toxicity (Norman database) LC50_48_hr_µg/L: 38929.99.

Aquatic toxicity endpoints (literature):

Cyanobacteria: *Anabaena flos-aquae* (Ebert et al. 2011, Environmental Toxicology and Chemistry, Vol. 30, No. 12, pp. 2786–2792, 2011) NOEC = 19 µg/L.

Aquatic Plants: *Lemna minor* (Ebert et al. 2011, Environmental Toxicology and Chemistry, Vol. 30, No. 12, pp. 2786–2792, 2011) NOEC = 30 µg/L.

The main metabolite of enrofloxacin is ciprofloxacin.

Ciprofloxacin aquatic toxicity:

Cyanobacteria: *Anabaena flos-aquae* (Ebert et al. 2011, Environmental Toxicology and Chemistry, Vol. 30, No. 12, pp. 2786–2792, 2011) E_rC10 = 4.5 µg/L.

Aquatic Plants: *Lemna minor* (Ebert et al. 2011, Environmental Toxicology and Chemistry, Vol. 30, No. 12, pp. 2786–2792, 2011) NOEC = 10 µg/L.

Conclusion on the environmental risks

The CLP classification statements (H400 and H410) imply that an environmental risk cannot be excluded due to the intrinsic properties of the substance. The only product authorised for aquatic

species was approved after 2005 (2006 and changed in 2016) and therefore the environmental risk assessment was made according to today's regulations.

To reduce environmental risk, proper use is essential. Before treatment the prescribing veterinarian should obtain all necessary information related to the intended use and perform a benefit risk assessment to ensure a responsible use of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

Yes, in some cases. The scientific advice under Article 107(6) states for quinolones and fluoroquinolones:

- 'When the proposed route of administration is outside of the terms of the SPC or when using an extemporaneous formulation, the product should be administered in individual animals only.
- Human medicinal products should be administered to individual animals only.'

If the substance cannot be used in animals other than individual animals, the impact on animal health is considered high. Furthermore, it is noted that the recommendation from the scientific advice under Article 107(6) restricting the use to individual animals would apply only in some cases (when the proposed route is outside of terms of the SPC, or when the medicinal product is a human medicinal product).

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes, there is a risk to the environment.

2. Is there an alternative substance (with lower risk for the environment)?

Yes. Other antibacterials are authorised for use in food-producing aquatic species. However, the alternative antibiotics do not necessarily pose a lesser risk to the environment. Enrofloxacin has a history of well-established use in food-producing aquatic species as a last resort.

3. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

No. A spectrum of substances for treating bacterial infections are needed to be able to choose substance according to situation.

Conclusion

Enrofloxacin is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when enrofloxacin is used according to Article 114 of Regulation (EU) 2019/6:

Enrofloxacin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[10] is required before discharge in the environment.

Erythromycin

Erythromycin is a macrolide antibiotic. It is used to treat a broad range of bacterial infections in fish.

It is placed in category C (Caution) in the AMEG categorization system for antibiotics. Categorization of antibiotics for use in animals (europa.eu).

In the AMEG document, the following advice is given for category C substances:

- For antibiotics in this category there are alternatives in human medicine.
- For some veterinary indications, there are no alternatives belonging to Category D.
- Should be considered only when there are no antibiotics in Category D that could be clinically effective.

ATCvet code: QJ01FA01

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes. There are many authorised products containing erythromycin for food-producing terrestrial animals in the EU. One example is *Eritromicina 15% Chemifarma 150 mg/g, polvere orale per uso in acqua da bere, per polli da carne, tacchini e galline ovaiole.*

Erythromycin is also used in human medicine.

[10] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

PBT properties

Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

ED properties

Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties.

No environmental information could be found in SPCs for products authorised in terrestrial species.

In the ECHA database and the EPA database erythromycin has the hazard statement codes H400 and H410:

H400: Very toxic to aquatic life.

H410: Very toxic to aquatic life with long lasting effects.

No information found indicating that the substance is a PBT or a vPvB.

No information found indicating that the substance is an endocrine disruptor (ED).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

SCHEER (2022) proposed environmental quality standards (EQS) for chronic exposure to algae and cyanobacteria, expressed as maximum allowable concentration (MAC-EQS):

- $MAC\text{-}EQS_{freshwater}$ 1 mg/L.
- $MAC\text{-}EQS_{marin}$ 0.1 mg/L.

Daphnia_toxicity (Norman database) LC50_48_hr_µg/L: 38372.87.

Minski et al. (2020) Report delayed hatching and decreased survival of zebrafish at 0.1 ug/L. All tested environmentally relevant concentrations (0.001, 0.01, 0.1 and 1 ug/L) increased heart rate. (Minski, V. T., Garbinato, C., Thiel, N., & Siebel, A. M. (2020). Erythromycin in the aquatic environment: deleterious effects on the initial development of zebrafish. *Journal of Toxicology and Environmental Health, Part A*, *84*(2), 56–66. https://doi.org/10.1080/15287394.2020.1834477).

Ji et al. (2012) assessed the environmental risks of various veterinary pharmaceuticals in freshwater bodies of water testing two freshwater invertebrates (*Daphnia magna* and *Moina macrocopa*) and a fish

(*Oryzias latipes*). The authors also summarize various other sources of published work on other aquatic species. The ranges of No Observed Effect Concentrations (NOEC) per taxonomic group are listed below:

- Algae 0.0031 - 12.5 mg/L.
- Invertebrae 11.1 – 50 mg/L.
- Fish 100-1000 mg/L.

For more detailed information please refer to the published paper.

Ji, K., Kim, S., Han, S. et al. Risk assessment of chlortetracycline, oxytetracycline, sulfamethazine, sulfathiazole, and erythromycin in aquatic environment: are the current environmental concentrations safe?. Ecotoxicology 21, 2031–2050 (2012). https://doi.org/10.1007/s10646-012-0956-6).

Conclusion on the environmental risks

The CLP classification statements (H400 and H410) imply that an environmental risk cannot be excluded due to the intrinsic properties of the substance.

Due to its usage in human medicine, erythromycin is frequently detected in bodies of water near populated areas (Ji et al. 2012). In surface water samples within Europe, erythromycin is detected within ranges of 0.000004 mg/L (France, Seine river in 2011) up to 0.00062 mg/L (Germany, Lutter river in 1998).

To reduce environmental risk, proper use is essential. Before treatment the prescribing veterinarian should obtain all necessary information related to the intended use and perform a benefit risk assessment to ensure a responsible use of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

Not listed.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes, there is a risk for the environment.

2. Is there an alternative substance (with lower risk for the environment)?

Yes, but other options against (e.g.) lactococcosis or *Flavobacterium* spp. such as florfenicol, oxytetracycline or amoxicillin also carry a risk to the aquatic environment.

3. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

As resistance against tetracyclines and florfenicol is encountered frequently by experts in the aquaculture industry, the availability of a macrolide antibiotic seems necessary to safeguard animal health and welfare in case of disease outbreaks with bacteria not susceptible to the other options.

Conclusion

Erythromycin is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when erythromycin is used according to Article 114 of Regulation (EU) 2019/6:

Erythromycin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L11 is required before discharge in the environment.

Fenbendazole

Fenbendazole is a member of the class of benzimidazoles that is 1H-benzimidazole which is substituted at positions 2 and 5 by (methoxycarbonyl)amino and phenylsulfanediyl groups, respectively. A broad-spectrum anthelmintic used, particularly in veterinary medicine, for the treatment of nematodal infections. In fish the substance is used against tapeworms in cases of praziquantel resistance.

ATCvet code: QP52AC13.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for food-producing aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes approved for multiple food-producing and non-food-producing species.

Eg. Arrest Oral Suspension for sheep in Ireland.

Curofen 50 mg/g oral powder for pigs | UPD was authorised in 2015, i.e. after 2005.

[11] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Main assessment regarding the mandate criteria

a) risks to the environment if the food-producing aquatic species are treated with those substances:

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

The substance is included in food-producing terrestrial animals VMPs across EU for which a complete environmental risk assessment according to the current guidelines has been performed.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

CLP classification:

Hazard Statement Codes Include the following:

H400 Aquatic Acute1.

H410 Aquatic Chronic 1.

H412 Aquatic Chronic 3.

PBT properties:

PBT Assessment:			
Parameter	**Result relevant for conclusion**		**Conclusion:**
Bioaccumulation	BCF 14.1	Log Kow 3.45	No
Persistence	Biodegradable half life	5.25 days	No
Toxicity	LD50	1.00e+4 mg/kg	No
PBT-statement:	Fenbendazole is not considered a PBT substance		

Fenbendazole has a relatively high affinity to water and to soil. Corresponding K d value of 14 C - fenbendazole were 63 ± 7 l/kg resulting in Soil Adsorption Coefficient (K OC) > 1500 l/kg. Special attention should be paid to the high values of octanol-water partition coefficients of FBZ (3.93) which can influence their bioavailability and bioaccumulation.

Endocrine disruption (ED) properties

No information found. It is not thought that this compound has endocrine disrupting properties. Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

Water Framework Directive

The substance is not included in the Annex X List of Priority Substances in the Field of Water Policy of the Water Framework Directive.

Conclusion on the environmental risks

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No. Antiparasitic substances are not under the scope of the Article 107(6).

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes, there is a risk to the environment.

2. Is there an alternative substance (with lower risk for the environment)?

Yes, but the alternative antiparasitics do not necessarily pose a lesser risk to the environment.

3. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

No. There are few products authorised to treat parasitic diseases in aquatic species. There is a need for several antiparasitics with different modes of action to avoid the development of resistance.

Many countries report widespread specific need in relation to a potential treatment option for tapeworm infestation. Praziquantel is a potential alternative but resistance is reported.

Given the use in many countries for tapeworm infestation and risk of antiparasitic resistance there is a genuine need for this substance's availability.

Conclusion:

Even though fenbendazole is somewhat toxic to environment, its use is deemed necessary for some indications. Fenbendazole is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when fenbendazole is used according to Article 114 of Regulation (EU) 2019/6:

Fenbendazole is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L12 is required before discharge in the environment.

Florfenicol

Florfenicol is a fluorinated amphenicol. This is a wide spectrum synthetic antibacterial used in terrestrial animals and fish. ATC-vet-code QJ01 BA90.

Florfenicol is used against bacterial infections in fish.

Florfenicol is placed in category C (Caution) in the AMEG categorisation system for antibiotics. Categorisation of antibiotics for use in animals (europa.eu).

In the AMEG document, the following advice is given for category C substances:

- for antibiotics in this category there are alternatives in human medicine.
- for some veterinary indications, there are no alternatives belonging to Category D.
- should be considered only when there are no antibiotics in Category D that could be clinically effective.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Yes. Available e.g. as Aquaflor 500 mg/g premix for medicated feed for fish in several MS (authorised through a common EU procedure) and in Norway (National MA). The Spanish MA was first issued in 2013, and the MA was changed in 2018.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes. Many florfenicol-containing products are authorised in the EU MS for food-producing terrestrial animals. Several pharmaceutical forms are approved, including premix for medicated feed in different strengths, suspension for use in drinking water and granules for use in drinking water. Some examples are Alphaflorovet 20 mg/g premix for medicated feed for pigs, Florfenidem 50 500 mg/g premix for chicken, fish and pig and Amphen 200 mg/g granules for use in drinking water for pigs.

The premixes approved for terrestrial food-producing animals could be used in accordance with the SPCs for the fish products in situations where fish products are not available.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

[12] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Yes. MA has been issues in several MSs after October 2005. The submitted ERA documentation and the assessment performed by Competent Authorities are therefore considered to be in accordance with current requirements.

The authorised SPCs for florfenicol premix for fish do not contain any information on environmental properties of the substance, nor do they contain any risk mitigation measures (RMM).

As several MS have issued MA after October 2005, it is considered that sufficient documentation has been submitted to perform a benefit risk assessment, including environmental risk. There is also some information publicly available.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

No information is found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information is found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

However, in the ECHA database, the substance has been classified with the following statements according to the CLP regulation:

- H400: Very toxic to aquatic life.
- H410: Very toxic to aquatic life with long lasting effects.
- H411: Toxic to aquatic life with long lasting effects.
- H412: Harmful to aquatic life with long lasting effects.

Other information:

Data from: 'Environmental Assessment for AQUAFLOR (Florfenicol) 50% Type A Medicated Article Fed at a Dose up to 15 mg florfenicol/kg body weight/day for Control of Mortality Associated with Bacterial Diseases in Freshwater-Reared Finfish in Recirculating Aquaculture System (US FDA)':

Table 4. Degradation of florfenicol in three different sediment-water systems

Source	Type of Site	Sediment Type*	% Organic Carbon	Degradation Rates for Sediment/Water Systems(days)		K_d	K_{oc}
				DT_{50}**	DT_{90}		
Duxbury Marine (DM)	Marine	Loam	3.2	13.0	43.1	0.293	9.1
Goose River (GR)	Freshwater	Loam	2.4	8.4	27.8	0.434	18.1
Weweantic River (WR)	Freshwater	Sand	0.76	19.4	64.5	0.250	32.9

Reference: Gledhill (2005)

* USDA textural type; ** DT in this table stands for degradation time.

Table 11. Chronic toxicity of florfenicol to invertebrates

Species, Reference, and Toxicity Endpoint	Toxicity Value, mg/L	Guideline
Daphnia magna (Gallagher et al., 2008b) Survival, NOEC Reproduction, NOEC Growth (length), NOEC Growth (weight), NOEC	 3.0 1.5 3.0 3.0	OECD 211
Brachionus calyciflorus (Sayers, 2009b) Reproduction (intrinsic rate of increase), NOEC	0.76	Snell and Moffat (1992); ASTM E 1440-91
Chironomus riparius (Bradley, 2009) Percent emergence, NOEC Development rate, NOEC	 25 25	OECD 219

Table 12. Acute toxicity of florfenicol and major metabolites to freshwater fish

	Florfenicol	Principal Metabolites		
		Amine	Alcohol	Oxamic Acid
SPAH Code No.	**SCH 25298**	**SCH 40458**	**SCH 45705**	**SCH 48057**
Oncorhynchus mykiss				
LC_{50} (mg/L)	>780	>19	>15	>23
NOEC (mg/L)	780	19	15	23
Reference	LeLievre (1991e)	LeLievre (1991g)	LeLievre (1991h)	LeLievre (1991i)
Lepomis macrochirus				
LC_{50} (mg/L)	>830	>20	>15	>25
NOEC (mg/L)	830	20	15	25
Reference	LeLievre (1991f)	LeLievre (1991j)	LeLievre (1991k)	LeLievre (1991l)

Toxicity to algae/aquatic plants:

Various values available, e.g.

NOEC (Skeletonema costatum (marine diatom)): 0.00423 mg/l.

Exposure time: 72 h.

Method: ISO 10253.

Safety data sheet: Florfenicol Solid Formulation_AH_US_EN.pdf

Conclusion US EPA:

'Based on the data, assumptions, and calculations presented in this EA, the use of Aquaflor® in recirculating aquaculture systems for freshwater finfish does not present any significant risk to the environment,'

EPA, environmental fate:

Property	Experimental average	Predicted average	Experimental median	Predicted median	Experimental range	Predicted range	Unit
Bioconcentration Factor		2.33 (2)		2.33	-	1.78 to 2.88	L/kg
Biodeg. Half-Life		3.55 (1)		3.55	-	3.55	days
Atmos. Hydroxylation Rate		1.95e-11 (1)		1.95e-11	-	1.95e-11	cm3/molecule*sec
Fish Biotrans. Half-Life (Km)		0.589 (1)		0.589	-	0.589	days
Soil Adsorp. Coeff. (Koc)		50.1 (1)		50.1	-	50.1	L/kg
ReadyBiodeg		0.00 (1)		0.00	-	0.00	Binary 0/1

Public literature:

At higher concentrations (> 1µg/L), florfenicol could significantly inhibit the chlorophyll content in M. flos-aquae.

Meixian Wang, Yuxuan Zhang, Peiyong Guo, Effect of florfenicol and thiamphenicol exposure on the photosynthesis and antioxidant system of Microcystis flos-aquae, Aquatic Toxicology, Volume 186, 2017, Pages 67-76.

Conclusion on environmental risk

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

However, as MAs have been issued after 2005, and Competent Authorities therefore have performed a benefit risk assessment in accordance with current requirements, including environmental risk, it is considered that when florfenicol is used in accordance with the approved SPC the benefits outweigh the risk to the environment. To reduce environmental risk, proper use is essential. Before treatment the prescribing veterinarian should obtain all necessary information related to the intended use and perform a benefit risk assessment to ensure a responsible use of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No, florfenicol is not listed in accordance with Article 107(6). Florfenicol is placed in AMEG category C and products are already authorised for fish – hence authorised information on correct use (positive benefit-risk) in fish is available.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

No environmental RMMs are included in the SPC for the authorised fish products. The benefits are therefore considered to outweigh the risk for the environment provided the substance is used in line with the SPCs of the authorised fish VMPs. If the substance is used in any other way, the prescribing veterinarian is responsible for ensuring prudent use and should obtain all necessary information related to the intended use and perform a benefit risk assessment.

There are no restrictions according to Article 107(6).

2. Is there an alternative substance (with lower risk for the environment)?

Other antimicrobials are authorised in EU MS for use in fish, e.g. chlortetracycline, oxytetracycline and oxolinic acid. However, limited information related to environmental effects is publicly available for the antimicrobials authorised for fish, and generally no environmental RMMs are included in the SPCs. It is therefore difficult to draw firm conclusions on this issue. However, florfenicol has been assessed and approved for fish by several EU MS Competent Authorities.

The general RMM relating to the responsibility of the veterinarian for all treatments under Article 114(1) should apply.

3. Is the alternative substance enough to cover availability and avoid development of resistances (e.g. for antiparasitics)?

No. The other antimicrobials which are authorised in EU MS for use in fish are not sufficient. As florfenicol is the antimicrobial of choice for some bacterial infections in fish, and it is not in category A or B of the AMEG categorisation system, it is considered important that the substance is available for use in fish. However, prudent use of florfenicol is important both to protect the environment and to reduce the risk for development of resistance. Important measures to reduce the need for treatment with antibacterials are good management practices/hygiene and vaccination.

Conclusion

An environmental risk cannot be excluded due to the intrinsic properties of the substance. However, as MAs have been issued after 2005, and Competent Authorities therefore have performed a benefit risk assessment in accordance with current requirements, including environmental risk, it is considered that when used in accordance with the approved SPC the benefits outweigh the risk to the environment.

As

- the other antimicrobials which are authorised in EU MS for use in fish are not sufficient,
- florfenicol is the antimicrobial of choice for some bacterial infections in fish,

it is considered important that the substance is available for use in fish.

Florfenicol is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when florfenicol is used according to Article 114 of Regulation (EU) 2019/6:

Florfenicol is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[13] is required before discharge in the environment.

Flubendazole

Flubendazole is an anthelmintic, tape worms included, used both in humans and for veterinarian purposes (mainly chicken and pigs into drinking water).

ATCVet code: QP52AC12.

General questions related to the substance:

3. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

4. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes, for terrestrial: Fludosol 200 mg/ml and Fluvermal 20% for pigs and poultry, Flubendazole 1% (for chicken in NL).

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

SPC: no information available about environmental risk.

[13] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

No ED (not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/)), vPvB or PBT properties (not listed in the PBT database of ECHA (https://echa.europa.eu/pbt), not included as environmental hazard according to CLP classification or in the Annex X list of priority substances in the field of water policy of the Water Framework Directive.

Flubendazole is likely to pose hazard to aquatic and sediment dwelling invertebrates like *Tubifex tubifex* (also called the sludge worm or sewage worm, is a species of segmented worm that inhabits the sediments of lakes and rivers and sold as feed for ornamental fish) and *Dugesia gonocephala* (flat worm) The dose used to kill hydra (aquarium pest) is also toxic to snails.

Conclusion on the environmental risks

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

Not applicable as flubendazole is an antiparasitic medicine.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Flubendazole is somewhat toxic to aquatic organisms of the environment. Restrictions for use according to Article 107(6) is not applicable as flubendazole is an antiparasitic medicine.

2. Is there an alternative substance (with lower risk for the environment)?

Yes, but the alternative antiparasitics do not necessarily pose a lesser risk to the environment.

3. Is/Are the alternative substance/s enough to cover availability and avoid development of resistances (eg. for antiparasiticsAMR resistance is not considered)?

No. There are limited number of VMPs authorised to treat parasitic diseases in aquatic species. There is a need for several antiparasitics with different modes of action to avoid the development of resistances.

Conclusion

Even though flubendazole is somewhat toxic to environment, its use is deemed necessary for some indications. Flubendazole is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when flubendazole is used according to Article 114 of Regulation (EU) 2019/6:

Florfenicol is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[14] is required before discharge in the environment.

Flumequine

Flumequine, belonging to the fluoroquinolones group, is a first-generation fluoroquinolone antibiotic that was used in both human and veterinary medicine to treat different intestinal tract infections. active mainly against Gram-negative microorganisms.

ATCVet code: QJ01MB07.

AMEG: Category B – Restrict.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Yes (VMPs): FLUMEKVIN 10 % powder for oral use in treatment of acute hemorrhagic septicemia condition (furunculosis, yersiniosis, vibriosis,) chronicle and latent infections, caused by bacteria sensitive to flumequine, metaphylaxia and treatment of secondary infections caused by stress conditions and viruses. FLUMIQUIL 50 % for the treatment of diseases caused by microorganisms sensitive to flumequine. COLIFARM 200 (for fish and pigs). Others, total of 6 (https://medicines.health.europa.eu/veterinary/en/search-medicines?f%5B0%5D=product_status%3Aauthorised&f%5B1%5D=target_species%3A10119&keys=flumequine).

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes (VMPs): ENTERFLUME (cattle, pigs, chicken/poultry 500 mg), FLUMESOL (cattle, pigs, poultry, calves, lambs, oral 200 mg/g), others total of 44

[14] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

(https://medicines.health.europa.eu/veterinary/en/search-medicines?f%5B0%5D=product_status%3Aauthorised&keys=flumequine).

No (HMP): Suspended MAs since 2019 (https://www.ema.europa.eu/en/medicines/human/referrals/quinolone-fluoroquinolone-containing-medicinal-products).

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

Yes.

SPC:

Flumequine should not be discharged into waterways as it may be hazardous to fish and other aquatic organisms.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties.

European Chemicals Agency (ECHA):

H411 Toxic to aquatic life with long lasting effects

Not included in PBT or vPvB (not listed in the PBT database of ECHA (https://echa.europa.eu/pbt), ED list of ECHA (https://echa.europa.eu/ed-assessment/) or in the Annex X List of Priority Substances in the Field of Water Policy of the Water Framework Directive.

Conclusion on the environmental risks

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

Yes, in some cases.

The scientific advice under Article 107(6) states for quinolones and fluoroquinolones:

- When the proposed route of administration is outside of the terms of the SPC or when using an extemporaneous formulation, the product should be administered in individual animals only.
- Human medicinal products should be administered to individual animals only.'

If the substance cannot be used in animals other than individual animals, the impact on animal health is considered high. Furthermore, it is noted that the recommendation from the scientific advice under Article 107(6) restricting the use to individual animals would apply only in some cases (when the proposed route is outside of terms of the SPC, or when the medicinal product is a human medicinal product).

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Flumequine is somewhat toxic to aquatic organisms of the environment (https://www.echemi.com/products/pd1805145366-flumequine.html#col202205111004, section "toxicity/ecotoxicity excerpts"). H411. There are some 107(6) restrictions (see above).

2. Is there an alternative substance (with lower risk for the environment)?

No. VMPs with other antibacterial substances are authorised for fish. However, there is not sufficient information available to conclude that those would represent a lower environmental risk.

3. Is/Are the alternative substance/s enough to cover availability and avoid development of resistances (e.g. for antiparasitics – AMR resistance is not considered)?

No. There is a need for several antibacterial substances with different modes of action. Fluoroquinolones (flumequine) are needed for use in cases of bacterial infections in food-producing aquatic organisms.

Conclusion

Even though flumequine is somewhat toxic to the environment, its use is deemed necessary for some indications. Flumequine is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when flumequine is used according to Article 114 of Regulation (EU) 2019/6:

Flumequine is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[15] is required before discharge in the environment.

Formaldehyde

Formaldehyde is an antiparasitic and antifungal substance used for bath treatments in fish.

ATCvet code QP53AX19.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Yes. In Spain, Portugal and Greece under the name Aquacen formaldehyde 380 mg/ml. The indication for use is to treat external parasites.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes: Formaldehyd Smartpractice Europe.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

Yes. As a concentrate for dip solution.

The authorisation was made after 2005 and the SPC includes the following information:

"5.3 Environmental properties

The average life of formaldehyde in air (city air on a sunny day) is 1-2 hours. Formaldehyde in water is biodegraded to low levels in a few days, the half-life in water is 36 hours. The effects of formaldehyde on soil are unknown and there is no evidence of bioaccumulation. Formaldehyde in a 35% aqueous solution undergoes biodegradation of 97.5% in 5 days."

Additional thresholds to be consider

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

No information found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

[15] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

The substance has no hazard statement codes relevant to aquatic species.

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

According to ECHA only one long-term study is available for formaldehyde. In a long-term study on the reproduction of Daphnia magna a NOEC of 1.04 mg/L (based on age of first reproduction) was determined." 59c9d260-a4a7-0b0e-dbd6-972470a84066 (europa.eu).

Daphnia toxicity (Norman database) LC50 48 hr ug/L: 21106.72.

Algae toxicity (Norman database) EC50 72 hr ug/L: 107899.00.

Conclusion on the environmental risks

There is an environmental assessment made for the VMP. It is authorised after 2005.

There are no reasons for concern after going through the relevant databases.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

No.

2. Is there an alternative substance (with lower risk for the environment)?

No. There is a risk for the animal health if the product would not be allowed for use in aquatic animals and there is no fully satisfying alternative.

3. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

No.

Conclusion

It is noted that formaldehyde is classified as carcinogenic category 1B and mutagen category 2, in accordance with Regulation (EC) No 1272/2008. However, this is not considered to fall within the criteria specified in Article 114(3) since the CMR properties are not factored in the classification categories for substances hazardous to the aquatic environment by Regulation (EC) No 1272/2008.

Formaldehyde is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measure should be considered when formaldehyde is used according to Article 114 of Regulation (EU) 2019/6:

Formaldehyde is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[16] is required before discharge in the environment.

Gentamicin

Gentamicin is an aminoglycoside antibiotic indicated for the treatment of a variety of bacterial infections. It is normally used as the sulphate salt. In veterinary medicine gentamicin is used mainly as a solution for injection for pigs, cattle and horses and as an oral solution for poultry (EMA/106359/2015).

ATCvet code: QJ01GB03.

A need for gentamicin in the aquaculture sector has been identified by Committee on availability of the Spanish Authority. In particular, oral pharmaceutical forms and/or bath treatment are required. (https://www.aemps.gob.es/la-aemps/informe-del-comite-de-disponibilidad-de-medicamentos-veterinarios-codi-vet-sobre-vacios-terapeuticos-y-otras-necesidades-prioritarias-2/).

It is classified as category C (Caution) in the EMA Categorisation of antibiotics for use in animals for prudent and responsible use (AMEG). For this category, the following is indicated:

- there are alternatives in human medicine,
- for some veterinary indications, there are no alternatives belonging to Category D, and
- should be considered only when there are no antibiotics in Category D that could be clinically effective.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes. The substance is authorised in food-producing terrestrial animals VMPs e.g.:

[16] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

- Sintage 80 mg/g + 20 mg/g pré-mistura medicamentosa para alimento medicamentoso para suínos (Link). Authorised 14/04/2020.
- GANABEN PREMIX, gentamicina, premiscela per alimenti medicamentosi per suini (Link). Authorised 01/06/2013.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals? No.

There is no standard risk assessment available about the risks for the environment due to the exposure through the aquatic branch.

Gentamicin is included in some food-producing terrestrial VMPs authorised after October 2005. When, this is the case it is expected that an environmental risk assessment according to the current guidelines have been performed for food-producing terrestrial animals (only ERA carried out after 2005 could be considered as meeting the current ERA standards, considering the date of effect of guideline VICH GL38 Environmental impact assessments for veterinary medicinal products - Phase II).

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

PBT properties

Gentamicin has not been classified as PBT in any of the available VMPs PuARs. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

ED properties

No information available in this sense. Gentamicin is neither included in the EPA's Endocrine Disruptor Screening Program (EDSP) that evaluates chemicals for potential endocrine disruption (CompTox Chemicals Dashboard (epa.gov)).

CLP classification

Gentamicin is classified by ECHA (Link) as:

Aquatic acute 1 (H400): Very toxic to aquatic life, and,

Aquatic chronic 1 (H401): Very toxic to aquatic life with long lasting effects.

Water Framework Directive

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

Conclusion:

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No. The active substance gentamicin is not included in the scientific advice under Article 107(6) of Regulation (EU) 2019/6 for the establishment of a list of antimicrobials which shall not be used in accordance with Articles 112, 113 and 114 of the same Regulation or which shall only be used in accordance with these articles subject to certain conditions.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes. Based on the scarce available information a potential risk for the environment cannot be excluded. There is no standard risk assessment available about the risks for the environment due to the exposure through the aquatic branch.

2. Is there an alternative substance (with lower risk for the environment)?

Availability of several antimicrobials with different mode of action is essential. In addition, a need for gentamicin in the aquaculture sector has been identified.

Therefore, it is considered that the alternatives available are not enough to cover availability.

Conclusion

Gentamicin is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when gentamicin is used according to Article 114 of Regulation (EU) 2019/6:

Gentamicin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[17] is required before discharge in the environment.

Gonadorelin

Gonadorelin is a synthetic analogue of the natural gonadotropin-releasing hormone (GnRH).

ATCvet code: QH01CA01.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS? *Yes*

Decentralised authorisations for VMPs for cattle, e.g. Gonadovet.

Several authorisations for HMPs.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties.

No aquatic hazard statements are noted under CLP classification.

No information is found indicating that the substance is PBT or vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

Gonadorelin is a hormone that promotes the production of sex hormones in the hypophysis, indicating that the substance is an endocrine disruptor (ED).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

The active substance is a synthetic gonadorelin, physiologically and chemically identical to the natural gonadorelin released by the hypothalamus in mammalian species and is no different from endogenous

[17] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

gonadotropin releasing hormone which is excreted by e.g. all female cattle of breeding age in normal circumstances.

Given the method of administration (injection), the rapid metabolism, the nature of the product (a natural hormone), and the small scale of use (broodstock), this substance carries acceptable risk to the environment due to a very limited exposure.

Therefore, gonadorelin will be unlikely to have an adverse impact on the environment. The active substance is a natural substance, the use of which will not alter the concentration or distribution of the substance in the environment given its limited applications (broodstock).

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No. Gonadorelin is a hypothalamus hormone.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Gonadorelin will be unlikely to have an adverse impact on the environment, when administered by injection in broodstock. Article 107(6) is not applicable.

2. Is there an alternative substance (with lower risk for the environment)?

Not applicable.

3. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

Not applicable.

Conclusion

Even though gonadorelin is an endocrine disruptor, its use is deemed necessary for improved animal welfare and management. Gonadorelin is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures are recommended when gonadorelin is used according to Article 114 of Regulation (EU) 2019/6:

Gonadorelin shall be administered by injection only.

Human Chorionic Gonadotropin

Human Chorionic Gonadotropin hormone primarily produced during pregnancy by the placenta. It plays a crucial role in supporting pregnancy by maintaining the production of progesterone. Is widely used in animal reproduction, including fish.

ATCvet code QG03GA01.

General questions related to the substance

3. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Yes. E.g. Chorulon 10 000 IU | UPD authorised in 2008, changed in 2014

4. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

VMP authorised for swine reproduction, Gestavet HGC 200 / PMSG 400 authorised in several EU countries. Authorised, at least, in 2009.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

Yes.

No environmental information is included in the SPC.

As the authorisation was made after 2005 the assessment might be in accordance with today's regulations.

No environmental information could be found in SPCs for products authorised in terrestrial species.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

In the ECHA database and the EPA database it has the following hazard statement codes:

- GHS08 (serious health hazard)
- GHS07 (health hazard)
- GSH09 (hazardous to the environment).

According to the classification provided by companies to ECHA in CLP notifications this substance is not toxic for aquatic organisms.

No information found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

Human Chorionic Gonadotropin is a hormone that plays a crucial role in supporting pregnancy by maintaining the production of progesterone. Consequently, the substance is considered an endocrine disruptor (ED).

No information found regarding Daphnia toxicity (Norman database).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water Framework Directive.

Conclusion on the environmental risks

Human Chorionic Gonadotropin is a natural substance, the use of which will not alter the concentration or distribution of the substance in the environment given its limited applications (broodstock).

To reduce environmental risk, proper use is essential. Before treatment the prescribing veterinarian should obtain all necessary information related to the intended use and perform a benefit risk assessment to ensure a responsible use of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No. Human Chorionic Gonadotropin is not an antimicrobial: Article 107(6) does not apply.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes.

2. Is there an alternative substance (with lower risk for the environment)?

Yes, but this substance is critical for fish reproduction, been impossible to substitute it by another substance in many aquatic species.

3. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

No.

Conclusion

Human Chorionic Gonadotropin is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when Human Chorionic Gonadotropin is used according to Article 114 of Regulation (EU) 2019/6:

Human chorionic gonadotropin shall be administered by injection only.

Hydrogen peroxide

Hydrogen peroxide is an antiparasitic- and antiprotozoal substance used for bath treatments in fish.

ATCvet code: QD08AX01.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Yes: Paramove 49.5 % w/w Hydrogen Peroxide Concentrate for Solution for Fish Treatment Paramove, 49.5% w/w Hydrogen Peroxide concentrate for solution for fish treatment | UPD

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

No VMP for food-producing terrestrial animals were found. For human use, hydrogen peroxide is authorised in for example France:

- DOSOXYGENEE 10 VOLUMES, solution pour application cutanée en récipient unidose (link).
- EAU OXYGENEE 10 VOLUMES COOPER, solution pour application cutanée (link).

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

Yes. See above.

From the SPC of Paramove:

"Other precautions:

Depending on regional requirements, the user may need to apply for and obtain consent for discharge. Check with the relevant regional legislative body.

The most important mechanisms for removal of hydrogen peroxide in coastal waters is dilution and degradation which are increased by water movements including the flushing effects in sea lochs. Do not use at times of slack water as poor dilution and dissociation of residuals may occur.

After treatment care should be taken to provide sufficient water through the net to dilute residual hydrogen peroxide. The water from a boat's propeller may be used to increase water exchange in cases where low water exchange rates cannot be avoided."

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

In the ECHA database and the EPA database hydrogen peroxide has the hazard statement codes:

- H411 Toxic to aquatic life with long lasting effects.
- H412 Harmful to aquatic life with long lasting effects.

No information found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

Daphnia_toxicity (Norman database) LC50_48_hr_µg/L: 38372.87.

Conclusion on the environmental risks

The CLP classification statements (H411 and H412) imply that an environmental risk cannot be excluded due to the intrinsic properties of the substance.

Special instructions for disposal of treatment water are present in the SPC of (at least) one of the authorised aquatic VMPs.

To reduce environmental risk, proper use is essential. Please refer to risk management measure in the conclusion.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes. Based on the scarce available information a potential risk for the environment cannot be excluded.

There is no standard risk assessment available about the risks for the environment due to the exposure through the aquatic branch.

2. Is there an alternative substance (with lower risk for the environment)?

There are other substances that may be used against sealice (e.g. deltamethrin, azamethiphos, emamectin, teflubenzuron, diflubenzuron), however unlikely with a lower risk to the environment.

3. Is the alternative substance enough to cover availability and avoid development of resistances (e.g. for antiparasitics)?

To avoid/reduce resistance there is a need for several anti-sealice VMPs with different modes of action. Hydrogen peroxide is a valuable tool in sealice treatment. Furthermore, hydrogen peroxide is necessary for some off label treatments.

Conclusion

Hydrogen peroxide is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when hydrogen peroxide is used according to Article 114 of Regulation (EU) 2019/6:

Hydrogen peroxide is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[18] is required before discharge in the environment.

Isoeugenol

Isoeugenol is an anaesthetic agent.

ATCvet code: QN01 AX94

It is especially suitable for sedation, and in Norway it is widely used to reduce stress in connection with transportation and moving of fish.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Yes. The substance is authorised in Norway and Iceland as Aqui-S, 540 mg/ml concentrate for treatment solution for Atlantic salmon and rainbow trout. The approved indication is "For sedation and anaesthesia of Atlantic salmon and rainbow trout in connection with handling procedures (sorting, moving, transportation, sea lice counting, stripping of broodfish) and for vaccination."

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

No product authorised for food-producing terrestrial animals could be found in the Union Product Database. However, according to the substance overview provided by EMA isoeugenol is included in the human medicinal product Epitest 36 in EU MS.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

Yes. The substance is authorised in Norway and Iceland. The Norwegian MA was issued in 2013, and the Icelandic MA was issued in 2016. Relevant ERA-documentation has been provided by the MA holder

[18] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

and an assessment has been performed by the Norwegian and Icelandic Competent Authorities and are therefore considered to be in accordance with current requirements.

Information on environmental properties is included in the SPC.

Environmental properties (from SPC):

"Isoeugenol may be harmful for organisms living in water. If concentrated solutions are released into water bodies, sufficient dilution in the recipient must be ensured. To ensure dilution and spreading of large volumes, a significant water current must be present. Isoeugenol is considered easily degradable in water. Relevant data indicate low or no bioaccumulation in the food chain."

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

No information is found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information is found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

In the ECHA database the substance has not been classified with any statements relating to aquatic toxicity according to the CLP regulation.

Other information.

US EPA Environmental fate:

Property	Experimental average	Predicted average	Experimental median	Predicted median	Experimental range	Predicted range	Unit
Bioconcentration Factor		15.9 (2)		15.9	-	10.7 to 21.1	L/kg
Biodeg. Half-Life		3.31 (1)		3.31	-	3.31	days
Atmos. Hydroxylation Rate		3.39e-11 (1)		3.39e-11	-	3.39e-11	cm3/molecule*sec
Fish Biotrans. Half-Life (Km)		0.195 (1)		0.195	-	0.195	days
Soil Adsorp. Coeff. (Koc)		1.86e+3 (1)		1.86e+3	-	1.86e+3	L/kg
ReadyBiodeg		1.00 (1)		1.00	-	1.00	Binary 0/1

Conclusion on the environmental risk:

The main environmental risk is considered to be short-term local harmful effects on water-living organisms if large volumes of concentrated solution is released.

The environmental risk is considered to be low and acceptable when sufficient dilution of released treatment solution is ensured, in accordance with the SPC of the authorised VMP.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No. Isoeugenol is not an antimicrobial.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

The risk for the environment is considered low and acceptable provided that the RMM related to discharge of used treatment solution is respected. Article 107(6) is not relevant for the substance.

2. Is there an alternative substance (with lower risk for the environment)?

No. Other anaesthetic agents authorised for fish are available: benzocaine and tricaine mesilate. However, as the environmental risk for isoeugenol is considered to be low and acceptable when sufficient dilution of released treatment solution is ensured, the environmental risk is probably not lower for the available alternative anaesthetic agents.

The following RMM (from the SPC) should however be included for isoeugenol:

"If concentrated solutions are released into water bodies, sufficient dilution in the recipient must be ensured. To ensure dilution and spreading of large volumes, a significant water current must be present."

3. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

No. The other anaesthetic agents authorised for fish, benzocaine and tricaine mesylate, are not equally suitable for all established uses of isoeugenol. The availability of isoeugenol is therefore considered important for animal welfare reasons.

Development of resistance is not relevant.

Conclusion

It is noted that isoeugenol is classified as possibly carcinogenic category 2B in accordance with Regulation (EC) No 1272/2008. However, this is not considered to fall within the criteria specified in Article 114(3) of Regulation (EU) 2019/6 since the CMR properties are not factored in the Classification categories for substances hazardous to the aquatic environment by Regulation (EC) No 1272/2008.

The main environmental risk is considered to be short-term local harmful effects on water-living organisms if large volumes of concentrated solution is released.

The environmental risk is considered to be low and acceptable when sufficient dilution of released treatment solution is ensured, in accordance with the approved SPC.

The other anaesthetic agents authorised for fish, benzocaine and tricaine mesylate, are not equally suitable for all established uses of isoeugenol. The availability of isoeugenol is therefore considered important for animal welfare reasons.

Isoeugenol is recommended to be included in the list of active substances that may be used in food-producing aquatic animal species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when isoeugenol is used according to Article 114 of Regulation (EU) 2019/6:

Isoeugenol is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[19] is required before discharge in the environment.

Ivermectin

Ivermectin is an avermectin (macrolide) antiparasitic drug.

ATCvet code: QP54AA01.

General questions related to the substance

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

There are many authorised products containing ivermectin for food-producing terrestrial animals in the EU. Some of these are authorised as premix for different food-producing species. One example is IVOMEC premix, premix for medicated feed for pigs in several EU countries.

The substance is also used in human medicine.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

[19] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

No.

The SPC of the products authorised for terrestrial animals indicates the following:

"Extremely dangerous to fish and aquatic life. Do not contaminate surface waters or ditches with the product or used container.

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements."

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

In the ECHA database and the EPA database it has the following hazard statement codes:

- GHS08 (serious health hazard).
- GSH09 (hazardous to the environment).

CLP Notification:

- H400 – Very toxic to aquatic life.
- H410– Very toxic to aquatic life with long-lasting effects.

No information found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water Framework Directive.

Daphnia toxicity (Norman database) LC50_48_hr_µg/L: 2975881.17.

Aquatic toxicity endpoints (literature):

Algae: NOEC 391 µg/L *Raphidocelis subcapitata*, Garric, J. et al., 2007.

doi:10 016/jelemosphere 2007.05.070.

Daphnia: NOEC 0.0003 ng/L *Daphnia. magna*, Garric, J. et al., 2007.

doi:10 016/jelemosphere 2007.05.070.

Sediment: NOEC6.3 µg/kg d.w. *Chironomus riparius*, Egeler P. et al. 2010.

Dwelling J Soils Sediments (2010) 10:368-376.

The margin of safety is narrow for fish, as shown in some studies:

Høy, T.; Horsberg, T.E.; Nafstad, I. The disposition of ivermectin in Atlantic salmon (*Salmo salar*). Pharmacol. Toxicol., 1990, 67(4), 307-312.

Katharios, P.; Pavlidis, M.; Iliopoulou-Georgudaki, J. Accumulation of ivermectin in the brain of sea bream, Sparus aurata after intraperitoneal administration. Environ. Toxicol. Pharm., 2004, 17(1), 9-12.

Conclusion on the environmental risks

The CLP classification statements (H400 and H410) and available scientific information (e.g. NOEC in *Daphnia magna*) indicate a high environmental risk if the substance is used in accordance with Article 114(1).

The SPC of the products authorised for terrestrial animals stress the effect on the environment of this product.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes, there is a high risk to the environment.

2. Is there an alternative substance (with lower risk for the environment)?

Yes. There are products authorised to treat parasitic diseases in aquatic species. Alternative substances are also recommended for inclusion in the list referred to in Article 114(3).

3. Is the alternative substance enough to cover availability and avoid development of resistances (e.g. for antiparasitics)?

Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the serious environmental concerns identified under criterion a), the substance cannot be included in the list.

Conclusion

Due to the high risk to the environment, ivermectin is not recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

Levamisole

Levamisole belongs to imidazothiazolids and is broad spectrum anthelmintic for use in the treatment and control of nematode infections (in its hydrochloride form). It is indicated for use in cases of

parasitic gastro-enteritis and lungworm diseases caused by mature and developing immature forms of those organisms sensitive to treatment.

ATCVet code: QP52AE01.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Yes (VMPs) but only for ornamental fish: SH-Levapet (280 mg/mL as Levamisole hydrochloride, spot-on treatment) for Guinea pig, Snake, Lizard, Turtle, Fish (fresh water, ornamental fish only). Levorom 200 mg/g Levamisole hydrochloride powder for use in drinking water for homing pigeons and ornamental fish.

https://medicines.health.europa.eu/veterinary/en/search-medicines?f%5B0%5D=active_substance%3A600805&f%5B1%5D=product_status%3Aauthorised&f%5B2%5D=target_species%3A10123&f%5B3%5D=target_species%3A10124&keys=Levamisole.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes (VMPs): Multiple, at least 114 different authorised VMPs for different species and application routes https://medicines.health.europa.eu/veterinary/en/search-medicines?f%5B0%5D=active_substance%3A600805&f%5B1%5D=product_status%3Aauthorised&keys=Levamisole.

No (HMP): Levamisole/hydrochloride is no longer approved for use in Human Medicine Products in the EU.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

SPC: "Special precautions for environmental protection: Avoid release to the environment. Prevent further leakage or spillage if safe to do so. Prevent spreading over a wide area (e.g. by containment or oil barriers). Retain and dispose of contaminated wash water. Local authorities should be advised if significant spillages cannot be contained."

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties.

Toxicity to fish: LC50 (*Oryzias latipes* (Japanese medaka)): 37.3 mg/l (Exposure time 96 h). OECD Test Guideline 203. Toxicity to daphnia and other aquatic invertebrates: EC50 for *Daphnia magna* (Water flea) is 64 mg/l, with exposure time of 48 h. OECD Test Guideline 202.

European Chemicals Agency (ECHA)

H412 Harmful to aquatic life with long lasting effects (as levamisole hydrochloride, not as Levamisole).

Not included in PBT (https://echa.europa.eu/pbt) or vPvB, ED (https://echa.europa.eu/ed-assessment) list or in the Annex X List of Priority Substances in the Field of Water Policy of the Water Framework Directive.

Conclusion on the environmental risks

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No. It is an antiparasitic substance.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Levamisole as hydrochloride is somewhat toxic to aquatic organisms of the environment.

2. Is there an alternative substance (with lower risk for the environment)?

No.

3. Is/Are the alternative substance/s enough to cover availability and avoid development of resistances (e.g., for antiparasiticsAMR resistance is not considered)?

No. There is a need for several antiparasitic substances with different modes of action.

Conclusion

Even though levamisole (as hydrochloride) is somewhat toxic to environment, its use is deemed necessary for some indications. Levamisole is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures (RMM) are recommended when levamisole is used according to Article 114 of Regulation (EU) 2019/6:

Levamisole is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[20] is required before discharge in the environment.

Lincomycin

Lincomycin is a lincosamide antibiotic which is produced by Streptomyces lincolnensis.

ATCvet code: QJ01FF02.

In the AMEG document, the following advice is given for category C substances:

- for antibiotics in this category there are alternatives in human medicine.
- for some veterinary indications, there are no alternatives belonging to Category D.
- should be considered only when there are no antibiotics in Category D that could be clinically effective.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes, in different VMPs, for example Lincoral 400 mg/g powder for use in drinking water for pigs and chickens. It is also approved in combination with other substances, for example in Albiotic (neomycin) and Lismay (spectinomycin).

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

No environmental information could be found in SPCs for products authorised in terrestrial species. There are VMPs authorised after 2005. Lincomycin may pose a risk to terrestrial plants and algae, especially when used in combination with spectinomycin.

[20] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

No information found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

In the ECHA database it has hazard classifications:

- Hazardous to the aquatic environment – Chronic Hazard H410.
- Harmful for aquatic life with long lasting effects – Chronic Hazard H412.

According to the Council of Europe safety data sheet it is marked with:

- Hazardous to the aquatic environment – Acute Hazard H400.
- Hazardous to the aquatic environment – Chronic Hazard H410.

No information found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water Framework Directive.

Aquatic toxicity endpoints:

Cyanobacteria: *Anabaena flos-aquae* NOEC = 6.1 µg/L (unpublished study report).

Conclusion on the environmental risks

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

There might be a risk for microalgae among other species.

2. Is there an alternative substance (with lower risk for the environment)?

Yes.

3. Is the alternative substance enough to cover availability and avoid development of resistances (e.g. for antiparasitics)?

No. A spectrum of antibiotics is needed to be able to choose according to antimicrobial resistance.

Conclusion

Lincomycin is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6. The substance might pose a risk for microalgae and there are no good sources for half-life in water and soil.

The following risk mitigation measures should be considered when lincomycin is used according to Article 114 of Regulation (EU) 2019/6:

Lincomycin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[21] is required before discharge in the environment.

Magnesium sulfate

Magnesium sulfate is an inorganic compound indicated for the treatment of hypomagnesaemia terrestrial species. In addition, it can be used for constipation: to enhance motility and secretion in the digestive tract (including in cases of hypotonia and atony of the fore stomachs in ruminants); to improve appetite (in low doses): as a carrier for administering drugs into the abomasum (true stomach) of ruminants; in inflammations of organs in closed cavities (meningoencephalitis, pododermatitis, pleuritis, pericarditis, etc.) and in liver diseases, purulent wounds, and fistulas (locally as a hypertonic solution).

ATC code: A06AD04.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes. The substance is authorised in food-producing terrestrial animals VMPs e.g.:

[21] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

- Magnesii sulfas: oral powder to be used in cattle, sheep, goat, horse, pig, dog, cat and chicken. Authorised 31/10/1999.
- Duphalyte - Roztwór do wstrzykiwań: Solution for injection in cattle, horse, cat, chicken, pig and dog. Authorised: 28/02/1995.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as VMP for food-producing aquatic animals?

No. There is no standard risk assessment available that address the risks for the environment due to the exposure through the aquatic branch. The potential risks to the environment as a consequence of the use of the substance under Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications, number of treatments…. Therefore, the environmental risk assessment under this mandate will be focused on the potential risks of the substance due to its available inherent properties (hazards).

Magnesium sulfate is included in some food-producing terrestrial VMPs authorised before October 2005. It is not expected that the environmental risk assessment performed in the authorised product was made according to the current guidelines. Only ERA carried out after 2005 could be considered as meeting the current ERA standards, considering the date of effect of guideline VICH GL38 Environmental impact assessments for veterinary medicinal products - Phase II). However, Magnesium sulfate is an inorganic substance which is naturally present in the environment in seawater, mineral springs and in minerals such as kieserite and epsomite (https://www.fao.org/fileadmin/templates/agns/pdf/jecfa/cta/68/Magnesium_Sulfate.pdf). Therefore, its use as VMP is not expected to increase the natural abundance of the substance.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

PBT properties

According to ECHA (Magnesium sulphate 100.028.453 | 37a73f74-d019-45ab-8881-ec469afdaee3 - ECHA CHEM) PBT assessment does not apply as according to Annex XIII of Regulation (EC) No 1907/2006, no PBT and vPvB assessment has been conducted since magnesium sulphate is inorganic.

ED properties

Not Applicable as it is an inorganic substance.

Water Framework Directive

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water Framework Directive.

Other environmental hazards: CLP

Not classified.

Conclusion on the environmental risks

The information available does not allow to reach a definitive conclusion on the environmental risks of the substance. The substance has no hazard classifications, and there is no other information that would indicate a risk to the environment when the substance is used as a veterinary medicine in aquatic species. Due to the inherent properties of the substance it is not expected that the use of magnesium sulfate will pose an unacceptable risk for the environment.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

Not applicable.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

No.

2. Is there an alternative substance (with lower risk for the environment)?

No.

3. Is/Are the alternative substance/s enough to cover availability and avoid development of resistances (eg. for antiparasitics – AMR resistance is not considered)?

Not applicable.

Conclusion

Magnesium sulfate is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

Risk mitigation measures are not considered necessary.

Mebendazole

Mebendazole, belonging to the benzimidazole group like albendazole and flubendazole, is an anthelmintic used in both human and veterinary medicine to treat different parasitic worm infestations (ascariasis, pinworm infection, hookworm infections, and giardia too).

ATCVet code: QP52AC09

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes (VMPs): LEN (mebendazole 150 mg for cat and dogs), Mebenver 600 mg bolus - Seponver plus (Mebendazole 75 mg + Closantel 50 mg), Rafendazol premix (Rafoxanide 10mg + Mebendazole 8 mg).

Yes (HMP): Vermox 100 mg tablets, Ovex suspension 150 mg.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

SPC: no information included in dog/cat products (a veterinary prescription is not compulsory)

Premix for sheep, beef, etc: Special precautions for environmental protection: during the treatment period and for the following 7 days the animals must be confined, away from streams, lakes or ponds.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

European Chemicals Agency (ECHA)

According to the classification provided by companies to ECHA in CLP notifications this substance is very toxic to aquatic life and is very toxic to aquatic life with long lasting effects.

H400 – Very toxic to aquatic life.

H410 – Very toxic to aquatic life with long lasting effects.

Not included in PBT (https://echa.europa.eu/pbt) or vPvB, ED list (https://echa.europa.eu/ed-assessment) or in the Annex X list of priority substances in the field of water policy of the Water Framework Directive.

Conclusion on the environmental risks

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

Not applicable, mebendazole is not an antimicrobial.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Mebendazole is somewhat toxic to aquatic organisms of the environment. Restrictions for use according to Article 107(6) is not applicable, mebendazole is not an antimicrobial.

2. Is there an alternative substance (with lower risk for the environment)?

Yes, but the alternative antiparasitics do not necessarily pose a lesser risk to the environment.

3. Is/Are the alternative substance/s enough to cover availability and avoid development of resistances (eg. for antiparasitics – AMR resistance is not considered)?

No. There are limited number of VMPs authorised to treat parasitic diseases in aquatic species. There is a need for several antiparasitics with different modes of action to avoid the development of resistances.

Conclusion

Even though mebendazole is somewhat toxic to environment, its use is deemed necessary for some indications. Mebendazole is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when mebendazole is used according to Article 114 of Regulation (EU) 2019/6:

Mebendazole is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[22] is required before discharge in the environment.

[22] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Monensin

Monensin is an ionophore antibiotic.

ATCvet code: QP51AH01.

No information found about the AMEG classification for monensin.

General questions related to the substance

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. 2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

There is only one product authorised for food-producing animals, but in several countries. Kexxtone 32.4 g - Continuous-release intraruminal device. The authorisation is currently suspended due to quality problems.

The substance is not used in human medicine.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

No environmental information could be found in SPCs for product authorised in terrestrial species.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

No hazard statements in the ECHA database and the EPA databases.

No information found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (Priority substances) of the Water Framework Directive (Directive 2000/60/EC establishing a framework for Community action in the field of water policy).

Daphnia toxicity (Norman database) LC50_48_hr_µg/L: 522791.73.

Based on EFSA opinion on the feed additive consisting of monensin sodium (Coxidin®) a risk for aquatic compartment cannot be excluded when the substance is used as a coccidiostat for chickens for fattening. Reference: Safety and efficacy of a feed additive consisting of monensin sodium (Coxidin®) for chickens for fattening, chickens reared for laying, turkeys for fattening and turkeys reared for breeding (Huvepharma N.V.) | EFSA https://www.efsa.europa.eu/en/efsajournal/pub/8628 .

Conclusion on the environmental risks

Considering the information above, a risk for the environment cannot be excluded.

To reduce environmental risk, proper use is essential. Before treatment the prescribing veterinarian should obtain all necessary information related to the intended use and perform a benefit risk assessment to ensure a responsible use of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

An environmental risk cannot be excluded.

2. Is there an alternative substance (with lower risk for the environment)?

No. Monensin has shown effects against some internal parasites (e.g. coccidia). At this moment, there is not authorised VMPs for this indication.

Molnár, K. and Ostoros, G. (2007). Efficacy of some anticoccidial drugs for treating coccidial enteritis of the common carp caused by goussia carpelli (apicomplexa: eimeriidae). Acta Veterinaria Hungarica, 55(1), 67-76. https://doi.org/10.1556/avet.55.2007.1.7

Speare, D., Daley, J., Dick, P., Novilla, M., & Poe, S. (2000). Ionophore-mediated inhibition of xenoma-expression in trout challenged with loma salmonae (microspora). Journal of Fish Diseases, 23(3), 231-233. https://doi.org/10.1046/j.1365-2761.2000.00226.x

3. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

No.

Conclusion

Monensin is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when monensin is used according to Article 114 of Regulation (EU) 2019/6:

Monensin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[23] is required before discharge in the environment.

Neomycin

Neomycin is an aminoglycoside antibiotic with bactericidal activity, typically used against Gram-negative aerobic bacteria.

It is placed in category C (Caution) in the AMEG categorization system for antibiotics. Categorization of antibiotics for use in animals (europa.eu)

In the AMEG document, the following advice is given for category C substances:

- For antibiotics in this category there are alternatives in human medicine
- For some veterinary indications, there are no alternatives belonging to Category D
- Should be considered only when there are no antibiotics in Category D that could be clinically effective

ATCvet code: QA07AA01

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes. There are many authorised products containing neomycin for food-producing terrestrial animals in the EU. One example is NEOMYCINE 50 COOPHAVET (link EMA website).

Neomycin is also used in human medicine.

[23] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

No environmental information could be found in SPCs for products authorised in terrestrial species.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

PBT properties

Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

However, neomycin is persistent in the environment (soil): https://medicines.health.europa.eu/veterinary/en/600000044257.

ED properties

Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

In the ECHA database neomycin has the hazard statement codes H400, H410, H411 and H412 for neomycin sulphate, but for other neomycin substances these are not reported.

No information found indicating that the substance is a PBT or a vPvB.

No information found indicating that the substance is an endocrine disruptor (ED).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

An ecological risk assessment has been performed by Lee *et al.* (2021) on multiple antibiotics including neomycin. The authors conclude that after a 21-day exposure to neomycin, no observed effect concentration (NOEC) for the reproduction of *Daphnia magna* was detected at 0.15 mg/L. For the survival of juvenile *Oryzias latipes* following the 40-d exposure, NOEC was found at 0.87 mg/L. Based on the results of the chronic toxicity tests and those reported in the literature, predicted no-effect concentrations (PNECs) were determined at 3.0 ug/L. Compared to the other antibiotics evaluated (amoxicillin and enrofloxacin) these values are relatively low. (Lee S, Kim C, Liu X, Lee S, Kho Y, Kim W-K, Kim P, Choi K. Ecological Risk Assessment of Amoxicillin, Enrofloxacin, and Neomycin: Are Their Current Levels in the Freshwater Environment Safe? *Toxics*. 2021; 9(8):196. https://doi.org/10.3390/toxics9080196).

Conclusion on the environmental risks

The CLP classification statements imply that environmental risk cannot be excluded due to the intrinsic properties of the substance.

To reduce environmental risk, proper use is essential. Please refer to the conclusion below.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

Not listed.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes. Based on the scarce available information a potential risk for the environment cannot be excluded. There is no standard risk assessment available about the risks for the environment.

2. Is there an alternative substance (with lower risk for the environment)?

Other aminoglycoside antibiotics are used in aquatic species: spectinomycin (AMEG D categorization) and gentamicin (AMEG C categorization). Studies comparing these substances toward risks to the environment are not available.

3. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

Availability of several antimicrobials with different mode of action is essential. In addition, a need for neomycin in the aquaculture sector has been identified.

Conclusion

Neomycin is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measure should be considered when neomycin is used according to Article 114 of Regulation (EU) 2019/6:

Neomycin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[24] is required before discharge in the environment.

Oxfendazole

Oxfendazole is the sulfoxide metabolite of fenbendazole. It is a broad-spectrum anthelmintic, it is used, particularly in veterinary medicine, for the treatment of roundworm, strongyles, pinworms and tapeworms.

ATCvet code: QP52AC02

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for food-producing aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes, it is authorised for food-producing animals in the EU- namely cattle and sheep.

Bovex 2.265% | UPD (europa.eu).

Main criteria from the mandate

a) risks to the environment if the food-producing aquatic species are treated with those substances:

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

There is limited published data available on the environmental effects of oxfendazole. It is known that the related substance fenbendazole, can negatively affect the environment, especially the aquatic environment and given its chemical properties similar risk is expected. Fenbendazole has a negative effect on crustaceans (*Daphnia Magna*) and less effect on duckweed (*L. minor*) and green algae (*S. vacuolatus*). Mechanism of the effect is not fully understood.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications….

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

CLP Classification:

Hazard statement codes include the following:

H400 Very toxic to aquatic life [Warning Hazardous to the aquatic environment, acute hazard].

[24] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

H410 Very toxic to aquatic life with long lasting effects [Warning Hazardous to the aquatic environment, long-term hazard].

PBT properties

Property	Unit	Predicted average
Fish Biotrans. Half-Life (Km)	Days	1.05 (1)
ReadyBiodeg	Binary	0.00 (1)
Soil Adsorp. Coeff. (Koc)	L/kg	457 (1)
Biodeg. Half-Life	Days	3.55 (1)
Bioconcentration Factor	L/kg	4.19 (2)
Atmos. Hydroxylation Rate	Cm3/molecule*sec	1.38e-11 (1)
PBT-statement:	Oxfendazole is not considered a PBT substance	

It was noted in the assessment for fenbendazole that it had a high value of octanol-water partition coefficient of fenbendazole (3.93) which influenced its bioavailability and bioaccumulation. Oxfendazole on the other had has a lower octanol water coefficient of 1.61

Endocrine disruption (ED) properties

No information found. Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/). It is not thought that this compound has endocrine disrupting properties.

Water Safety Framework:

It is not included as environmental hazard in the Annex X List of Priority Substances in the Field of Water Policy of the Water Framework Directive.

Conclusion on the environmental risks

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to article 107(6)?

Yes, there is a risk to the environment.

2. Is there an alternative substance (with lower risk for the environment)?

Yes, but the alternative antiparasitics do not necessarily pose a lesser risk to the environment.

Use would be similar to that of fenbendazole i.e.treatment of roundworms, pinworms and tapeworms. Potential alternatives include emamectin and praziquantel dependant on indication.

3. Is the alternative substance enough to cover availability and avoid development of resistances (e.g. for antiparasitics)?

No. There are few products authorised to treat parasitic diseases in aquatic species. There is a need for several antiparasitics with different modes of action to avoid the development of resistance.

Given the risk of antiparasitic resistance it is necessary to include oxfendazole on the list to ensure health and welfare of aquatic species.

Conclusion:

Oxfendazole is listed as a metabolite of febantel and fenbendazole and also as an active substance in table 1 of EU Regulation 37/2010 for all food-producing species except fin fish. The concern here is environmental protection.

Even though oxfendazole is somewhat toxic to environment, its use is deemed necessary for some indications. Oxfendazole is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when oxfendazole is used according to Article 114 of Regulation (EU) 2019/6:

Oxfendazole is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[25] is required before discharge in the environment.

Oxolinic acid

Oxolinic acid is a bactericidal belonging to the quinolone family effective in the treatment of acute and chronic infections in fish.

AMEG classification: category B (restrict) as WHO-CIAs (Critically Important Antimicrobials) list so its use should be limited and only after an Antimicrobial Susceptility Test has been performed.

ATCVet code: QJ01MB05.

[25] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Yes: Branzil Vet (Denmark), Inoxyl Acide Oxolinique 240 Salmonides (France), Linacivet 50 % premix for medicated feed (Greece).

Some products authorised again in 2023.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes (VMPs): Inoxil 11,5 % (Greece, chicken and cattle), Inoxil 20 mg (pigs Netherland).

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

Yes, a new marketing authorisation was issued in 2023.

No additional Risk Mitigation Measures to prevent environmental hazards.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

Oxolinic acid hasn't any PBT (not listed in the PBT database of ECHA (https://echa.europa.eu/pbt), vPvB, ED properties (Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/) and it's not included in the Annex X list of priority substances in the field of water policy of the Water Framework Directive.

It's classified according to CLP regulation as:

H411 – Toxic to aquatic life with long lasting effects (link)

Conclusion on the environmental risks

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

Yes, in some cases.

The scientific advice under article 107(6) states for quinolones and fluoroquinolones:

- 'When the proposed route of administration is outside of the terms of the SPC or when using an extemporaneous formulation, the product should be administered in individual animals only.
- Human medicinal products should be administered to individual animals only.'

If the substance cannot be used in animals other than individual animals, the impact on animal health is considered high. Furthermore, it is noted that the recommendation from the scientific advice under Article 107(6) restricting the use to individual animals would apply only in some cases (when the proposed route is outside of terms of the SPC, or when the medicinal product is a human medicinal product).

Oxolinic acid is considered WHO-CIAs (Critically Important Antimicrobials) so its use should be limited and only after an Antimicrobial Susceptility Test has been performed.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes, a potential risk to environment cannot be excluded.

2. Is there an alternative substance (with lower risk for the environment)?

Yes.

3. Is/Are the alternative substance/s enough to cover availability and avoid development of resistances (eg. for antiparasitics - AMR resistance is not considered)?

Yes, but there is a lack of antimicrobials available for AM therapy in aquatic animals.

Conclusion

Oxolinic acid is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measure should be considered when oxolinic acid is used according to Article 114 of Regulation (EU) 2019/6:

Oxolinic acid is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[26] is required before discharge in the environment.

[26] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Oxytetracycline

Oxytetracycline is a broad-spectrum antimicrobial agent in the tetracycline group.

ATCvet code: QJ01 AA06.

The substance is used against bacterial infections in fish.

It is placed in category D (Prudence) in the AMEG categorisation system for antibiotics. Categorisation of antibiotics for use in animals (europa.eu)

In the AMEG document, the following advice is given for category D substances:

- should be used as first line treatments, whenever possible.
- as always, should be used prudently, only when medically needed.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Yes. The substance is licensed for fish in most EU MS with an aquaculture industry. There are several authorised products, most of which are premixes for medicated feed, with strengths varying from 5% to 100%. Some oral powders are also authorised. Some examples are Anprociclina 200, 200 g/kg premix, Orimycin vet 200 mg/g oral powder and Oxidem 50 powder for oral solution.

The MA for Oxidem was issued in 2006 in Romania. For MAs issued after October 2005 it is considered that the documentation provided by the MA holder and the ERA assessment of the MS Regulatory Authority are in accordance with current regulatory requirements.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Many oxytetracycline-containing products are authorised in the EU MS for food-producing terrestrial animals, both mammals and birds. Several pharmaceutical forms are approved, including premix for medicated feed, oral powder for use in drinking water and solution for injection. Some examples are: Tetravet 50% premix for medicated feed and Oxyvet 10% solution for injection. The premixes and oral powders for terrestrial animals could be used in accordance with the approved SPCs for the premixes and oral powders authorised for fish, in case of a shortage for the fish products. Some of the MA-holding products hold MA for both fish and food-producing terrestrial animals.

According to the substance overview provided by EMA the substance is also found in human medicinal products, e.g. in the product Atecortin.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

Yes. Furthermore, at least one of the oxytetracycline products authorised for fish (Oxidem oral powder) has received the MA after October 2005. It is therefore considered that the documentation provided by the MA holder and the ERA assessment of the MS Regulatory Authority are in accordance with current regulatory requirements.

In the Italian and Irish SPCs for two different premixes for fish no precautionary measures related to environmental effects could be found.

Oxytetracycline has been assessed and approved for fish in several MS, and at least one of the MAs was issued after 2005. No environmental information/RMMs could be found in SPCs.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

No information is found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt). The substance is considered as P.

No information is found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

However, in the ECHA database *oxytetracycline* is classified with the following statements according to the CLP regulation:

- H400: Very toxic to aquatic life.
- H410: Very toxic to aquatic life with long lasting effects.

and *oxytetracycline HCl* is classified with the following statements:

- H400: Very toxic to aquatic life.
- H410: Very toxic to aquatic life with long lasting effects.
- H411: Toxic to aquatic life with long lasting effects.

Other information

Data from PuAR OXTRA DD 100 mg/ml solution for injection, for cattle, sheep, pigs, horses, dogs and cats:

Effect studies			
Study type	**Endpoint**	**Result**	**Unit**
Algae growth inhibition test/ *Anabaena flos-aquae*	EC_{50}	0.261	mg/l
Daphnia sp. immobilisation	EC_{50}	0.17	mg/l
Fish, acute toxicity/ *Oncorhynchus mykiss*	LC_{50}	100	mg/l

Data from 'An Environmental Assessment of the Proposed Use of Oxytetracycline-Medicated Feed in Freshwater Aquaculture from the US EPA:'

Oxytetracycline n-octanol/water partition coefficient: 0.0035- 9.078 (pH 2.1 and 3.9 respectively).

Half-life of oxytetracycline in marine sediment: 9 – 419 days (bottom exposed to currents and bottom stagnant respectively).

Lowest freshwater toxicity endpoint: Activated sludge bacteria growth inhibition – EC50 0.08. mg/L.

Lowest brackish toxicity endpoint: whiteleg shrimp immobilisation: EC50 61.1 mg/L.

Cyanobacteria: Anabaena flos-aquae NOErC = 0.0062 mg/L (unpublished study report).

Conclusion from the US EPA

'The algal, invertebrate, fish, and bacterial acute and chronic toxicity data for OTC solubilized in water suggest that there is little if any potential risk to populations of aquatic organisms from total-dissolved OTC discharged from intensive aquaculture facilities, nor is it likely to be a potential threat to public health or safety. Discharge of OTC sorbed to solids, associated with DOM, or chelated by divalent cations is also unlikely to result in risk of concern towaterborne organisms because of the poor biological availability of OTC under these circumstances.'

US EPA, environmental fate:

Oxytetracycline

Property	Experimental average	Predicted average	Experimental median	Predicted median	Experimental range	Predicted range	Unit
Bioconcentration Factor	0.403 (3)	3.34 (4)	0.340	2.29	0.240 to 0.630	0.895 to 7.87	L/kg
Atmos. Hydroxylation Rate		7.24e-11 (1)		7.24e-11	-	7.24e-11	cm3/molecule*sec
Biodeg. Half-Life		148 (1)		148	-	148	days
Bioaccumulation Factor		0.895 (1)		0.895	-	0.895	L/kg
ReadyBiodeg		0.00 (1)		0.00	-	0.00	Binary 0/1
Soil Adsorp. Coeff. (Koc)		269 (2)		269	-	1.24 to 537	L/kg
Fish Biotrans. Half-Life (Km)		0.407 (1)		0.407	-	0.407	days

Oxytetracycline HCl

Property	Experimental average	Predicted average	Experimental median	Predicted median	Experimental range	Predicted range	Unit
Bioconcentration Factor	1.00e+3 (3)	3.34 (4)	1.00e+3	2.29	0.390 to 2.00e+3	0.895 to 7.87	L/kg
Fish Biotrans. Half-Life (Km)		0.407 (1)		0.407	-	0.407	days
Soil Adsorp. Coeff. (Koc)		269 (2)		269	-	1.24 to 537	L/kg
ReadyBiodeg		0.00 (1)		0.00	-	0.00	Binary 0/1
Bioaccumulation Factor		0.895 (1)		0.895	-	0.895	L/kg
Biodeg. Half-Life		148 (1)		148	-	148	days
Atmos. Hydroxylation Rate		7.24e-11 (1)		7.24e-11	-	7.24e-11	cm3/molecule*sec

Norman database; *Daphnia magna* PNEC 0.42944 µg/L.

DT50 148 days.

BCF 0.4 – 3.34.

Conclusion on the environmental risks

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

However, as at least one MA has been issued after 2005, and a Competent Authority therefore has performed a benefit risk assessment in accordance with current requirements, it is considered that use in accordance with the approved SPC represents an acceptable risk to the environment. To reduce environmental risk, proper use is essential. Before treatment the prescribing veterinarian should obtain all necessary information related to the intended use and consider both benefits and risks of the intended treatment to ensure a responsible use of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No. Oxytetracycline is placed in AMEG category D and products are already authorised for several fish species – hence authorised information on correct use (positive benefit-risk) in several fish species is available.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

No environmental RMMs are included in the SPC for the authorised fish products. The risk for the environment is therefore considered acceptable provided the substance is used in line with the SPCs of the authorised fish VMPs. Please refer to the conclusion below.

There are no restrictions according to Article 107(6).

2. Is there an alternative substance (with lower risk for the environment)?

Other antimicrobials are authorised in EU MS for use in fish, e.g. chlortetracycline, florfenicol and oxolinic acid. However, limited information related to environmental effects is publicly available for the antimicrobials authorised for fish, and generally no environmental RMMs are included in the SPCs. It is therefore difficult to draw firm conclusions on this issue. Furthermore, oxytetracycline has been assessed and approved for use in fish by several EU MS Competent Authorities.

The general RMM relating to the responsibility of the veterinarian for all treatments under Article 114(1) should apply.

3. Are the alternative substances enough to cover availability and avoid development of resistances?

No. As oxytetracycline is effective for treatment of certain bacterial infections in fish, and it is categorised as a first line treatment in the AMEG categorisation system, it is considered important that the substance is available for use in fish.

However, prudent use of oxytetracycline is important both to protect the environment and to reduce the risk for development of resistance. Important measures to reduce the need for treatment with antibacterials are good management practices/hygiene and vaccination.

Conclusion

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

However, as at least one MA has been issued after 2005, a Competent Authority therefore has performed a benefit risk assessment in accordance with current requirements, it is considered that use in accordance with the approved SPC represents an acceptable risk to the environment.

As

- the alternative substances are not sufficient to cover availability,

- oxytetracycline is effective for treatment of certain bacterial infections in fish,

it is considered important that the substance is available for use in fish.

Oxytetracycline is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measure should be considered when oxytetracycline is used according to Article 114 of Regulation (EU) 2019/6:

Oxytetracycline is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[27] is required before discharge in the environment.

Praziquantel

Praziquantel is a pyrazino-isoquinolein derivative from the thioxantonic group used as a broad anthelmintic. Specifically, it is known as a treatment of trematodes and cestodes infections such as schistosomiasis, taeniasis, and cysticercosis.

ATCVet code: QP52AA01.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No (VMPs)

2. Is the substance authorised as a VMP in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes (VMPs): Multiple, at the time of substance evaluation (February 2025) over 2000 different authorised VMPs for different species and application routes are registered: https://medicines.health.europa.eu/veterinary/en/search-medicines?f%5B0%5D=product_status%3Aauthorised&keys=praziquantel.

Yes (HMP): Praziquantel is on the WHO essential medicine list for control of schistosomiasis.

[27] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance approved for food-producing aquatic animals?

No.

SPC: no special precautions listed in authorised VMPs regarding environmental concerns due to disposal of unused products or waste.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

European Chemicals Agency (ECHA):

H412 Harmful to aquatic life with long lasting effects.

Not included in PBT (https://echa.europa.eu/pbt) or vPvB, ED list (https://echa.europa.eu/ed-assessment/) or in the Annex X list of priority substances in the field of water policy of the Water Framework Directive.

Aquatic toxicity endpoint:

Algae: NOErC 9700 µg/L *Raphidocelis subcapitata.*

Conclusion on the environmental risks

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No. It is an antiparasitic substance.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Praziquantel is somewhat toxic to aquatic organisms of the environment at high concentrations.

2. Is there an alternative substance (with lower risk for the environment)?

No. Some other substances, e.g. fenbendazole, can be used against tapeworm in fish. However, there is no information available that alternatives represent a lower risk for the environment.

3. Is/Are the alternative substance/s enough to cover availability and avoid development of resistances (e.g., for antiparasitics - AMR resistance is not considered)?

No. There is a need for several antiparasitic substances with different modes of action.

Conclusion

Even though praziquantel is somewhat toxic to environment, its use is deemed necessary for some indications. Praziquantel is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following Risk Mitigation Measures (RMM) should be considered when praziquantel is used according to Article 114 of Regulation (EU) 2019/6:

Praziquantel is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[28] is required before discharge in the environment.

Sodium chloride

Sodium chloride is an ionic compound with many applications. In veterinary medicine it can for instance be used to control electrolyte balance and to treat ectoparasites in fish.

ATCvet code: QB05BB01.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes, in many different VMPs. In most cases to adjust electrolyte balance in blood, for example AQUPHARM SODIUM CHLORIDE 9 MG/ML SOLUTION FOR INJECTION/INFUSION in cattle sheep dog and more species.

[28] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

There is environmental information in the PUAR that concludes that no further risk assessment was needed after the first phase assessment.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

In the ECHA database and the EPA database no relevant hazard statements could be found.

No information found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water Framework Directive.

Any other available information

According to the European Medicines Agency guideline on environmental risk assessments of medicinal products for human use (EMA/CHMP/SWP/4447/00) vitamins, electrolytes, amino acids, peptides and several other groups, are unlikely to result in significant risk to the environment. There are no reasons that it would be different in animal use.

33-day NOEC value of 252 mg/L for sodium chloride was determined in a continuous flow-through exposure system with early life stage fathead minnows (*Pimephales promelas*) (ECHA) [Kl. Score = 2].

A 21-day NOEC (reproduction, *Daphnia pulex*) was determined to be 314 mg/L (ECHA) [Kl. Score = 2]

Conclusion on the environmental risks

The information available does not allow to reach a definitive conclusion on the environmental risks of the substance. The substance has no hazard classifications, and there is no other information that would indicate a risk to the environment when the substance is used as a veterinary medicine in aquatic species. Due to the inherent properties of the substance, it is not expected that the use of sodium chloride will pose an unacceptable risk for the environment.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

No.

Conclusion

Sodium chloride is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

Risk mitigation measures are not considered necessary.

Spectinomycin

Spectinomycin is a broad-spectrum aminoglycoside antibiotic primarily indicated for the treatment of respiratory and gastrointestinal infections mostly related with *Pasteurella*, *Mycoplasma* and *E. Coli*.

ATCvet code: QJ01XX04.

In the AMEG categorisation system spectinomycin is assigned to category D ("Prudence").

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes. In most cases, it is used in combination with Lincomycin.

Lincoral-S 222 mg/g + 444.7 mg/g powder for use in drinking wáter (https://medicines.health.europa.eu/veterinary/en/600000991047). Authorised 27/12/2023.

ESPECTINOMICINA 300 mg/g GANADEXIL POLVO PARA ADMINISTRACIÓN EN AGUA DE BEBIDA (https://medicines.health.europa.eu/veterinary/en/600000054768). Authorised 17/07/1992.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance approved as a VMP for food-producing aquatic animals?

No.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

PBT properties

No information is found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

Spectinomycin is classified as vP in the environment (section 4.3 of the SPC of Lincoral-S 222 mg/g + 444.7 mg/g powder for use in drinking water (https://medicines.health.europa.eu/veterinary/en/600000991047).

Aquatic toxicity endpoint

Cyanobacteria: Anabaena flos-aquae **ErC10 = 0.056 mg/L** (unpublished study report).

ED properties

No information is found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

Other environmental hazards: CLP

No relevant CLP classification found in the ECHA webpage.

Water Framework Directive (WFD)

Spectinomycin is not included in Annex X (Priority substances) of the Water framework directive (Directive 2000/60/EC establishing a framework for Community action in the field of water policy).

Conclusion on the environmental risks

An environmental risk cannot be excluded due to the intrinsic properties of the substance (i.e. vP in the environment).

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes. A risk for the environment cannot be excluded due to (at least) the persistence of the substance.

2. Is there an alternative substance (with lower risk for the environment)?

Other antimicrobials are authorised in EU MS for use in fish, e.g. chlortetracycline, oxytetracycline and oxolinic acid. However, limited information related to environmental effects is publicly available for the antimicrobials authorised for fish, and generally no environmental RMMs are included in the SPCs. It is therefore difficult to draw firm conclusions on this issue.

3. Is/Are the alternative substance/s enough to cover availability and avoid development of resistances (eg. for antiparasitics – AMR resistance is not considered)?

No. The other antimicrobials which are authorised in EU MS for use in fish are not sufficient. As spectinomycin is not in category A or B of the AMEG categorisation system, it is considered important that the substance is available for use in fish. However, prudent use of spectinomycin is important both to protect the environment and to reduce the risk for development of resistance.

Conclusion

Spectinomycin is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when spectinomycin is used according to Article 114 of Regulation (EU) 2019/6:

Spectinomycin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[29] is required before discharge in the environment.

Sulfadiazine and Sulfadoxine

Sulfadiazine and sulfadoxine are sulfonamide antibiotics. They are assessed together since they have similar properties and were both identified by aquaculture sector as important for treatment of aquatic food-producing species. They are broad-spectrum antimicrobial agents against a variety of gram-positive and gram-negative bacteria.

ATCvet code: QJ01EQ.

Sulfadiazine has an antiparasitic and bacteriostatic effect. Sulfadoxine had been used for malaria prevention in human medicine, but to-date is only used in veterinary medicine. Both are placed in category D (Prudence) in the AMEG categorisation system for antibiotics.

In the AMEG document, the following advice is given for category D substances:

- should be used as first line treatments, whenever possible.
- as always, should be used prudently, only when medically needed.

Both are usually used in combination with trimethoprim and has been used for treatment in aquaculture.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Yes, Neopridimet Orale (Italy), authorised in 2006, Doxatrim (Italy), authorised in 1996.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes:

- veterinary: Norodine 24 injectable solution (Bulgaria), Bimotrim Co Injection (Ireland), Borgal Lösung 24% (Germany).
- human: Flammazine (Germany).

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

Yes, Sulfadoxine (Borgal Lösung 24%), Sulfadiazine (Neopridimet Orale).

No environmental information is included in the SPC.

[29] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

Sulfadoxine and Sulfadiazine are classified as Aquatic acute 1 (H400) and Aquatic chronic 1 (H410) by ECHA (Database of C&L inventory (europa.eu)). Sulfadiazine is also classified as Aquatic chronic 2 (H411). Sulfonamides are toxic to plants.

No information is found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information is found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

Sulfadiazine: Aquatic toxicity endpoint.

Cyanobacteria: Anabaena flos-aquae NOErC = 0.0025 mg/L (unpublished study report).

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes: due to the inherent properties of the substances, a risk to the environment cannot be excluded. However, no restrictions for use or mitigation measures are included in SPCs or PuARs.

2. Is there an alternative substance (with lower risk for the environment)?

There are several antibiotic substances belonging to sulfonamides. Following ASTAG (Australian Strategic and Technical Advisory Group on Antimicrobial Resistance) grouping (for human use), there are a reasonable number of alternative antibacterials in different classes available.

3. Is/Are the alternative substance/s enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

No. As these substances are effective for treatment of certain bacterial infections in fish, and are categorised as a first line treatment in the AMEG categorisation system, it is considered important that the substance is available for use in fish.

However, prudent use of these substances is important both to protect the environment and to reduce the risk for development of resistance. Important measures to reduce the need for treatment with antibacterials are good management practices/hygiene and vaccination.

Conclusion

Sulfadoxine and Sulfadiazine are recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when sulfonamides are used according to Article 114 of Regulation (EU) 2019/6:

Sulfadiazine and sulfadoxine are expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[30] is required before discharge in the environment.

Thiamphenicol

Thiamphenicol belongs to the amphenicols and is a semisynthetic derivative of chloramphenicol with a broad spectrum of antibacterial activity. It is used in veterinary medicine against bacterial infections. ATC-vet-code QJ01 BA02.

Thiamphenicol is suitable for treatment of e.g. vibriosis and pasteurellosis in fin fish.

Thiamphenicol is placed in category C (Caution) in the AMEG categorisation system for antibiotics. Categorisation of antibiotics for use in animals (europa.eu)

- In the AMEG document, the following advice is given for category C substances:
  - for antibiotics in this category there are alternatives in human medicine.
- for some veterinary indications, there are no alternatives belonging to Category D.
- should be considered only when there are no antibiotics in Category D that could be clinically effective.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

[30] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes. Several products are authorised, for different animal species and in different pharmaceutical forms. E.g. Thiamphenicol 20 % solution for injection for cattle and chicken and Thiamphenicole 20 % oral powder for pigs.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

The substance is found in several VMPs for terrestrial food-producing animals even though it is not approved for aquatic species. Environmental risk assessments have therefore been performed by competent authorities for use in terrestrial animals. Some environmental information is publicly available.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

No information is found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information is found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

In the ECHA database, the substance has not been classified with statements related to aquatic toxicity according to the CLP regulation.

ECHA (old database, the new database has no environmental information on thiamphenicol):

EC50 72h (*Pseudokirchneriella subcapitata*) = 8.86 (8.27 -9.50) mg/l.

EC50 72h (*Chlorella vulgaris*) = 522 (489 -580) mg/l.

NOEC 72h (*Chlorella vulgaris*) = 198 mg/l.

NOEC 72h (*Pseudokirchneriella subcapitata*) = 4.06 mg/l.

Aquatic toxicity endpoint:

Cyanobacteria: Anabaena flos-aquae NOErC = 0.0578 mg/L (unpublished study report).

US EPA, environmental fate:

Property	Experimental average	Predicted average	Experimental median	Predicted median	Experimental range	Predicted range	Unit
Atmos. Hydroxylation Rate		1.95e-11 (1)		1.95e-11	-	1.95e-11	cm3/molecule*sec
Biodeg. Half-Life		2.95 (1)		2.95	-	2.95	days
Bioconcentration Factor		1.16 (2)		1.16	-	0.873 to 1.45	L/kg
ReadyBiodeg		0.00 (1)		0.00	-	0.00	Binary 0/1
Soil Adsorp. Coeff (Koc)		141 (1)		141	-	141	L/kg
Fish Biotrans. Half-Life (Km)		0.135 (1)		0.135	-	0.135	days

European EPAR on TAF spray 28.5 mg/g thiamphenicol for horses, cattle, goats, sheep, pigs, mink, rabbits:

The applicant has provided a first phase environmental risk assessment in compliance with the relevant guideline which showed that no further assessment is required.

Public literature:

DT50 in swine compost (manure + rice husk): 1.6 days.

Wenjin Ma, Lei Wang, Xiangyue Xu, Meixia Huo, Kaixiang Zhou, Kun Mi, Xiaoyuan Tian, Guyue Cheng, Lingli Huang, Fate and exposure risk of florfenicol, thiamphenicol and antibiotic resistance genes during composting of swine manure, Science of The Total Environment, Volume 839, 2022.

At higher concentrations (> 1µg/L), thiamphenicol could significantly inhibit the chlorophyll content in M. flos-aquae.

Meixian Wang, Yuxuan Zhang, Peiyong Guo, Effect of florfenicol and thiamphenicol exposure on the photosynthesis and antioxidant system of Microcystis flos-aquae, Aquatic Toxicology, Volume 186, 2017, Pages 67-76.

Thiamphenicol belongs to the same group of antimicrobials as florfenicol (amphenicols). As florfenicol is authorised for fish in the EU, thiamphenicol should only be used when an antimicrobial from this group is considered the best treatment option and florfenicol is not available or not suitable. The environmental risk from thiamphenicol used for food-producing aquatic species is therefore probably relatively low due to limited exposure.

Conclusion on the environmental risk

The information available does not allow to reach a firm conclusion on the environmental risk of the substance. The intrinsic properties of the substance seem to indicate an acceptable risk for the environment. However, the environmental risks derived from the exposure of the environment to the substance have not been assessed.

The substance has not been classified with statements related to aquatic toxicity according to the CLP regulation. Furthermore, SPCs for veterinary medicinal products authorised for terrestrial animals generally do not include RMMs related to the aquatic environment. Additionally, as a substance from the same group (florfenicol) is authorised for food-producing fish, use of thiamphenicol for food-producing fish is expected to be relatively low, leading to limited exposure.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No, thiamphenicol is not listed in accordance with Article 107(6). Thiamphenicol is placed in AMEG category C and as such can be considered when no antimicrobials in category D is considered suitable/sufficiently efficacious and when florfenicol is not available/suitable.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

A risk for the environment cannot be excluded. There are no restrictions according to Article 107(6).

2. Is there an alternative substance (with lower risk for the environment)?

Other antimicrobials are authorised in EU MS for use in fish, e.g. chlortetracycline, oxytetracycline, florfenicol, flumequine and oxolinic acid. Therefore, these substances are considered first-choice for treatment of bacterial infections in fish. Use of thiamphenicol is therefore expected to be relatively low, as it should only be used when no authorised fish-antimicrobial is suitable or when they are expected not to be efficacious. Hence, use of thiamphenicol is considered to represent a relatively low environmental risk.

However, limited information related to environmental effects is publicly available for the antimicrobials used for fish, and generally no environmental RMMs are included in the SPCs for antimicrobials which are approved for use in fish. It is therefore difficult to draw firm conclusions on the relative environmental risk of the antibacterials used for treatment of fish. Thiamphenicol has not been classified with statements related to aquatic toxicity according to the CLP regulation.

3. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

No. The antimicrobials which are authorised in EU MS for use in fish are not sufficient. Several antimicrobials with different mode of actions should be available for use in fish. As thiamphenicol can be useful for some bacterial infections in fish, and it is not in category A or B of the AMEG categorisation system, it is considered important that the substance is available for use in fish when authorised fish antimicrobials are not suitable or when they are not expected to be efficacious.

The general RMM relating to the responsibility of the veterinarian for all treatments under Article 114(1) should apply.

Before treatment the prescribing veterinarian should obtain all necessary information related to the intended use and perform a benefit risk assessment to ensure a responsible use of the substance.

Conclusion

The information available does not allow to reach a firm conclusion on the environmental risk of the substance. The intrinsic properties of the substance seem to indicate an acceptable risk for the

environment. However, the environmental risks derived from the exposure of the environment to the substance have not been assessed.

The substance has not been classified with statements related to aquatic toxicity according to the CLP regulation. Furthermore, SPCs for terrestrial animals generally do not include RMMs related to aquatic environment. Additionally, as a substance from the same group (florfenicol) is authorised for food-producing fish, use of thiamphenicol for food-producing fish is expected to be relatively low, leading to limited exposure.

As

- thiamphenicol can be useful for some bacterial infections in fish,
- the selection of antimicrobials which are authorised in EU MS for use in fish are not sufficient,

it is considered important that the substance is available for use in fish when authorised fish antimicrobials are not suitable or when they are not expected to be efficacious.

Thiamphenicol is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when thiamphenicol is used according to Article 114 of Regulation (EU) 2019/6:

Thiamphenicol is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[31] is required before discharge in the environment.

Toltrazuril

Toltrazuril is a triazinetrione derivative administered orally in the drinking water for the treatment of coccidiosis in chickens and turkeys and as an oral suspension for several mammalian species. It may be used for the treatment of certain protozoal infestations of aquatic species.

ATCvet Code: QP51AJ01.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for food-producing aquatic animal use anywhere in the EU MS?

No.

[31] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

It is broadly licenced across Europe as a coccidiostat for use in cattle, pigs, sheep, goats, chickens, turkeys and dogs. Example: Baycox.

https://medicines.health.europa.eu/veterinary/en/600000015164

Main criteria from the mandate

a) risks to the environment if the food-producing aquatic species are treated with those substances:

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

Environmental properties

The major metabolite of toltrazuril, toltrazuril sulfone (ponazuril), has been shown to be both very persistent (half-life ca. 1 year) and mobile in soil and to be toxic to plants including crop species. For the mentioned environmental reasons, the following restrictions on the use apply:

Manure from treated animals is recommended to be applied to the same piece of land every year to minimise area affected.

Cattle and Sheep: The metabolite of toltrazuril, toltrazuril sulfone (ponazuril) is a very persistent (half-life ca. 1 year) and mobile compound and has adverse effects on both the growth and emergence of plants. Given the persistent properties of ponazuril repeated spreading of manure from treated animals may lead to an accumulation in the soil and consequently a risk to plants. The accumulation of ponazuril in soil together with its mobility also leads to a risk of leaching to groundwater.

The substance is included in food-producing terrestrial animals VMPs across EU for which a complete environmental risk assessment according to the current guidelines have been performed.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

CLP Classification:

Hazard Statement Codes include the following:

H400 Very toxic to aquatic life [Warning Hazardous to the aquatic environment, acute hazard].

H410 Very toxic to aquatic life with long lasting effects [Warning Hazardous to the aquatic environment, long-term hazard].

PBT properties:

Property	Predicted average (units)
Fish Biotrans. Half-Life (Km)	2.63 (days)
Soil Adsorp. Coeff. (Koc)	1.17e+4 (L/kg)
ReadyBiodeg	0.00 (Binary)
Bioconcentration Factor	20.7 (L/kg)
Biodeg. Half-Life	3.55 (days)
Atmos. Hydroxylation Rate	1.38e-11 (cm3/molecule*sec)

Toltrazuril is classified as a PT substance. There is a data gap in the assessment in its bioaccumulation data.

Endocrine disruption (ED) properties:

Toltrazuril is not recognised as having any endocrine disrupting effects/properties. Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

Water Safety Framework:

It is not included as environmental hazard in the Annex X List of Priority Substances in the Field of Water Policy of the Water Framework Directive.

Conclusion on environmental risk:

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

It is a PT substance with known concern to the aquatic environment.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

Toltrazuril is one of a very limited range of compounds used for treatment/prevention of protozoal infections in fish. It is deemed very important to have it available as a treatment option to maintain aquatic animal health and welfare.

R.M. Jaafar, K. Buchmann; 2011 doi: 10.3750/AIP2011.41.1.09 Toltrazuril (Baycox® vet.) in feed can reduce Ichthyophthirius multifiliis invasion of rainbow trout (Salmonidae) (pensoft.net).

Conclusion:

While toltrazuril might pose a risk to aquatic environment, it is useful for the treatment/prevention of protozoal infections in fish, where there is a lack of alternatives. Toltrazuril is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when toltrazuril is used according to Article 114 of Regulation (EU) 2019/6:

Toltrazuril is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[32] is required before discharge in the environment.

Tosylchloramide sodium

Tosylchloramide sodium, also known as Chloramine T, is a disinfectant and antiseptic agent utilized in various applications.

ATCvet code: QD08AX04.

It is placed as "Other antiseptics and disinfectants".

General questions related to the substance

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No products containing tosylchloramide sodium are authorised to treat aquatic animals.

Widely used as disinfectant in aquaculture to treat some important diseases, as Amoebic Gill Disease or Bacterial Gill Disease.

Harris, J., Powell, M., Attard, M., & Green, T. (2004). Efficacy of chloramine-t as a treatment for amoebic gill disease (agd) in marine atlantic salmon (salmo salar l.). Aquaculture Research, 35(15), 1448-1456. https://doi.org/10.1111/j.1365-2109.2004.01170.x.

Bowker, J., Carty, D., Telles, L., David, B., & Oviedo, D. (2008). Efficacy of chloramine-t to control mortality in freshwater-reared salmonids diagnosed with bacterial gill disease. North American Journal of Aquaculture, 70(1), 20-26. https://doi.org/10.1577/a06-042.1.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

[32] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

No products containing tosylchloramide sodium are authorised to treat terrestrial animals.

There are some medicinal products for human use: Clonazone (in Belgium), Euclorina (in Italy).

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

According to the classification provided by companies to ECHA in CLP notifications this substance is classified H411 'toxic for aquatic life with long-lasting effects'.

No information found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (Priority substances) of the Water Framework Directive (Directive 2000/60/EC establishing a framework for Community action in the field of water policy).

Daphnia toxicity (Norman database) LC50_48_hr_µg/L: 62210.9549886594.

Other references to the toxicity for aquatic animals:

https://chemicalsafety.ilo.org/dyn/icsc/showcard.display?p_card_id=0413 The substance is toxic to aquatic organisms. The substance may cause long-term effects in the aquatic environment.

https://animaldrugsatfda.fda.gov/adafda/app/search/public/document/downloadFonsi/81#:~:text=ENVIRONMENTAL%20WARNING,product%20directly%20into%20natural%20waterways Chloramine-T may be hazardous to aquatic life, including invertebrates and algae. Do not release the undiluted product directly into natural waterways.

Conclusion on the environmental risks

An environmental risk cannot be excluded due to the intrinsic properties of the substance.

To reduce environmental risk, proper use is essential. Before treatment the prescribing veterinarian should obtain all necessary information related to the intended use and perform a benefit risk assessment to ensure a responsible use of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes – a potential risk to environment cannot be excluded.

2. Is there an alternative substance (with lower risk for the environment)?

No.

3. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

Not relevant as alternatives are not available. It is also noted that tosylchloramide sodium can help to reduce the use of antibiotics in aquatic animals production.

Conclusion

Tosylchloramide sodium is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measure should be considered when tosylchloramide sodium is used according to Article 114 of Regulation (EU) 2019/6:

Tosylchloramide is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[33] is required before discharge in the environment.

[33] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Trimethoprim

Trimethoprim is a bacteriostatic antibiotic, belongs to the diaminopyrimidines and has a broad-spectrum usage in human and veterinary medicine.

ATCvet code: QJ01EA.

It is used exclusively in combination with sulphonamides. Trimethoprim is on the WHO's List of Essential Medicines.

It is placed in category D (Prudence) in the AMEG categorisation system for antibiotics.

In the AMEG document, the following advice is given for category D substances:

- should be used as first line treatments, whenever possible.
- as always, should be used prudently, only when medically needed.

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

Yes: Borgal Lösung 24% (Germany, first authorisation 2003), Trimethoprim & Sulfadiazine/Vethellas 50% (Greece, 2007), Neopridimet orale (Italy, 2006) – all in combination with sulfadiazine.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes: see above for fish or salmonid. Also, e.g. used for chicken, cattle, etc.:

Bisulvet (Bulgaria), Doxatrim (Lithuania), Alfatrim (Ireland). There are also several medicinal products for human use containing Trimethoprim.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

Yes: See above. No risk mitigation measures mentioned in SPCs.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

Trimethoprim is classified as Aquatic chronic 3 (H412) by ECHA (Database of C&L inventory (europa.eu)). Trimethoprim is persistent in soil. No information is found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information is found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

Aquatic toxicity endpoint:

Cyanobacteria: Anabaena flos-aquae NOErC = 1 mg/L (unpublished study report).

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes: due to the inherent properties of the substances, a risk to the environment cannot be excluded. However, there are no restrictions for use or mitigation measures included in SPCs or PuARs.

2. Is there an alternative substance (with lower risk for the environment)?

No.

3. Is/Are the alternative substance/s enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

No. As trimethoprim is effective for treatment of certain bacterial infections in fish, and it is categorised as a first line treatment in the AMEG categorisation system, it is considered important that the substance is available for use in fish.

However, prudent use of trimethoprim is important both to protect the environment and to reduce the risk for development of resistance. Important measures to reduce the need for treatment with antibacterials are good management practices/hygiene and vaccination.

Conclusion

Trimethoprim is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when trimethoprim is used according to Article 114 of Regulation (EU) 2019/6:

Trimethoprim is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[34] is required before discharge in the environment.

Tylosin

Tylosin is a macrolide active mainly against Gram positive bacteria.

ATCvet code: QJ01FA90.

It is placed in category C (Caution) in the AMEG categorisation system for antibiotics. Categorisation of antibiotics for use in animals (europa.eu).

In the AMEG document, the following advice is given for category C substances:

should be considered only when there are no antibiotics in Category D that could be clinically effective.

General questions related to the substance

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No.

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

There are many authorised products containing tylosin for food-producing terrestrial animals in the EU. Many of them are premixes for medicated feed (e.g. TYLOVET 22% premix for medicated feeding stuff; https://medicines.health.europa.eu/veterinary/es/600000042856), some oral powder (Tylovet e.g. TYLOVET pulvis water soluble powder for chickens, turkeys, pigs and calves; https://medicines.health.europa.eu/veterinary/es/600000093243), some others as solution for injection (Tylan, Pharmasin 50 e.g. Pharmasin 50 solution for injection; https://medicines.health.europa.eu/veterinary/es/600000094030)).

The substance is not used in human medicine.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

The SPC of the VMP tilolab tartrato 800.000 ui/g polvo para administracion en agua de bebida o en leche (https://medicines.health.europa.eu/veterinary/es/600000097460) indicates the following:

[34] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

"Special precautions for the protection of the Environment: Tylosin is toxic for terrestrial plants and cyanobacteria.

Environmental properties: Tylosin is persistent in soil. "

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

In addition, according to the classification provided by companies to ECHA in CLP notifications this substance is very toxic to aquatic life H400, is very toxic to aquatic life with long lasting effects (H410).

No information found indicating that the substance is a PBT or a vPvB. Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt).

No information found indicating that the substance is an endocrine disruptor (ED). Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

The substance is not included in Annex X (Priority substances) of the Water Framework Directive (Directive 2000/60/EC establishing a framework for Community action in the field of water policy).

Daphnia toxicity (Norman database) LC50_48_hr_µg/L: 603624.6

Aquatic toxicity endpoints (literature):

Cyanobacteria, Anabaena flos-aquae: NOEC growth 3.65 µg/L endpoint, PuAR

Daphnia sp.: EC10 immobilisation45000 µg/L Wollenberger et al. (2000), Chemosphere 40: 723-730

Fish, *Oncorhynchus mykiss*: LC50 18400 µg/L endpoint, PuAR.

Conclusion on the environmental risks

The information included in the SPC of some products and the CLP classification statements (H400 and H410) imply that an environmental risk cannot be excluded due to the intrinsic properties of the substance. To reduce environmental risk, proper use is essential. Before treatment the prescribing veterinarian should obtain all necessary information related to the intended use and perform a benefit risk assessment to ensure a responsible use of the substance.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

Yes, a risk for the environment cannot be excluded.

2. Is there an alternative substance (with lower risk for the environment)?

There are alternative substances, but a spectrum of substances for treating bacterial infections are needed to be able to choose substance according to situation. The alternative antibiotics does not necessarily pose a lesser risk to the environment.

3. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

No.

Conclusion

Tylosin is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

The following risk mitigation measures should be considered when Tylosin is used according to Article 114 of Regulation (EU) 2019/6:

Tylosin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.

When possible, any treatment shall take place in a closed system with:

a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment.

b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system.

c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[35] is required before discharge in the environment.

Thiamine (Vitamin B1)

ATCvet code: QA11DA01

Thiamine is an essential micronutrient for humans and animals. It is also known as Vitamin B1. Thiamine may be supplemented in case of thiamine deficiency in fish and invertebrates. The substance is usually used in the form of thiamine hydrochloride or thiamine mononitrate.

[35] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

General questions related to the substance:

1. Is the substance authorised as a veterinary medicinal product (VMP) for aquatic animal use anywhere in the EU MS?

No

2. Is the substance included in a food-producing terrestrial animals VMP or in a medicinal product for human use in any EU MS?

Yes; There are many authorised products containing thiamine authorised for use in livestock animals. For example Vitasol Multi (REG NL 4147) or MULTIVIT–MINERAL, injekcinis tirpalas (link EMA).

Thiamine is also used in human medicine to treat thiamine deficiency.

Main assessment regarding the mandate criteria:

a) risks to the environment if the food-producing aquatic species are treated with those substances

Is the substance authorised as a VMP for food-producing aquatic animals?

No.

No environmental information could be found in SPCs for products authorised in terrestrial species.

Additional thresholds to be considered

The potential **risks** to the environment as a consequence of the exposure of the environment to the use of the substance according to Article 114(1) cannot be addressed as there are several gaps that cannot be covered i.e. dose, target species, indications.

Therefore, the environmental risk assessment under this mandate will be focused on the potential **hazards** of the substance due to its inherent properties**.**

PBT properties

Not listed in the PBT database of ECHA (https://echa.europa.eu/pbt)

The substance has been shown to be readily biodegradable in a study conducted in accordance with the standardised guidelines OECD 301B, EU Method C.4-C and EPA OCSPP 835.3110, under GLP conditions. The study was awarded a reliability score of 1 in accordance with the criteria set forth by Klimisch et al. (1997). As such the substance does not fulfil the "P" criterion.

Whilst the substance has been shown to be an eye irritant no other toxicological or ecotoxicological properties were determined as a results of the test conducted on the substance and therefore the substance does not meet the "T" criterion.

No bioaccumulation data are available on the substance, however the substance's log Pow was determined to be -3.04 and, as such, it is not considered to meet the "B" criterion.

ED properties

Not listed in the ED database of ECHA (https://echa.europa.eu/ed-assessment/).

CLP classification

In the ECHA database thiamine(hydrochloride) has no relevant hazard statement codes.

Water Framework Directive

The substance is not included in Annex X (list of priority substances in the field of water policy) of the Water framework directive.

Some short-term exposure ecological toxicity assessments are publicly available and may be found in the ECHA Chemicals Database. The outcomes suggest no environmental risks, although in this database no data is reported on potential long-term effects of the aquatic environment.

An EFSA Scientific Opinion published in 2011 (link) on thiamine mononitrate concluded no foreseeable risk for the environment.

Conclusion on the environmental risks

The information available does not allow to reach a definitive conclusion on the environmental risks of the substance. The substance has no hazard classifications, and there is no other information that would indicate a risk to the environment when the substance is used as a veterinary medicine in aquatic species. Due to the inherent properties of the substance, it is not expected that the use of the substance will pose an unacceptable risk for the environment.

b) impact on animal and public health if the food-producing aquatic species affected cannot receive an antimicrobial listed in accordance with Article 107(6)

Is the substance an antimicrobial not recommended for use under Article 114 of Regulation (EU) 2019/6 in the scientific advice under Article 107(6)? Or is the substance an antimicrobial recommended for use under Article 114 in individual animals only, in that scientific advice?

No. Not listed.

c) availability or lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species

1. Is there a risk for the environment and/or any restriction for use according to Article 107(6)?

No.

2. Is there an alternative substance (with lower risk for the environment)?

No.

3. Is the alternative substance enough to cover availability and avoid development of resistances (eg. for antiparasitics)?

Not applicable.

Conclusion

Thiamine (-hydrochloride and -mononitrate), also known as Vitamin B1, is recommended to be included in the list of active substances that may be used in food-producing aquatic species in accordance with Article 114 of Regulation (EU) 2019/6.

Risk mitigation measures are not considered necessary.

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Annex 5.2.2: Assessment of substances not identified by aquaculture sector as important for the treatment of food-producing aquatic species, other than antiparasitic, antibacterial, antifungal and homeopathic substances

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1. Introduction

Other non-immunological substances are eligible substances not identified by aquaculture sector as important for the treatment of fish.

According to the mandate provided by the Commission, the overall objective of Regulation (EU) 2019/6 is to increase the availability of veterinary medicinal products, while ensuring the highest standards of public and animal health and environmental protection. When considering the criteria laid down in Article 114(3), any risks to the environment from the treatment of food-producing aquatic species (criterion (a)) is a key consideration for the assessment of eligible substances that have no identified important use in aquaculture. Criterion (b) as laid down in Article 114(3) becomes not applicable since no substance in this sub-group is an antimicrobial. With regards criterion (c), it is considered by default that for this sub-group of substances, there is not a lack of availability of other medicinal products, treatments or measures for prevention or treatment of diseases or certain indications in food-producing aquatic species; therefore, criterion (c) was not considered further for these substances. This general approach with regards criterion (c), was considered not entirely applicable for hormonal substances identified within this sub-group as well as for the substances isoflurane and ketamine, as these substances might be potentially relevant to the aquaculture sector with regards criterion (c) (see further details below).

Therefore, the overall key element for the assessment of these substances was the risk to the environment (criterion (a)). It is recognised that the potential risks to the environment as a consequence of the exposure of the environment due to the use of these substances in accordance with Article 114(1) cannot be addressed, as there are several data gaps that cannot be covered, e.g. dose and target species. Therefore, it was agreed that the environmental risk assessment would focus on the potential hazards of these substances due to their inherent properties. In the general case where criterion (c) was not considered further, only those substances for which an environmental risk is not identified based on the identification of hazard endpoints are recommended for inclusion in the list.

2. Methodology

The detailed methodology for each criterion laid down in Article 114(3) is as follows:

Criterion (a) risk to environment

As already indicated, the methodological approach for assessing these substances pertains to the environmental hazard identification. In doing so, each substance was searched for in the databases of ECHA (European Chemicals Agency), US EPA (Environmental Protection Agency), and in safety data sheets (SDS), to determine whether it had been classified under any of the following statements according to CLP regulation:

H400 – Very toxic to aquatic life.

H410 – Very toxic to aquatic life with long lasting effects.

H411 – Toxic to aquatic life with long lasting effects.

H412 – Harmful to aquatic life with long lasting effects.

H413 – May cause long lasting harmful effects to aquatic life.

The following statements specific to GHS were also considered:

H401 – Toxic to aquatic life.

H402 – Harmful to aquatic life.

PubChem was used to find synonyms for the substances.

When the search in the above-mentioned databases did not retrieve a hazard endpoint, an additional (final) step for hazard identification involved searching the published literature with a view to identify any indication of potential risk of the substance to the aquatic environment.

As part of the environmental assessment, consideration was given to whether the substance is recognised as PBT or ED; indication of PBT properties would exclude the substance from the list; indication of ED properties for a substance not used as a hormone would exclude the substance from the list. For hormonal substances, ED properties can be assumed. However, in order to not discard hormonal substances of potential interest for aquaculture these substances were assessed against criterion (c) as below.

The above-mentioned search process stopped at the first indication of any environmental hazard.

Criterion (b) related to antimicrobials listed in accordance with Article 107(6)

As already indicated, this criterion does not apply since none of these substances are antimicrobials.

Criterion (c) related to availability of alternatives

With the exception of hormonal substances, and of ketamine and isoflurane, it was considered that these substances are not considered relevant for treating or preventing a disease or certain indication for which there is lack of availability of other treatments or measures since none of these substances had been identified as being immediately useful for the treatment of food-producing aquatic species. Consequently, when an issue related to criterion (a) was identified [i.e. a hazard to environment was identified], the conclusion would be negative [i.e. recommendation to not include in the list]. For hormonal substances, ketamine and isoflurane, consideration was given to whether the substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.

Conclusion

With the exception of hormonal substances and of the substances isoflurane and ketamine, when an environmental hazard was declared/identified, the conclusion was as follows: "an environmental risk cannot be excluded", and the substance was recommended not to be included in the list. When no environmental hazard was declared/identified, the conclusion was as follows: "from the available information, a risk to the environment was not identified", and the substance was recommended for inclusion in the list.

For hormonal substances and for isoflurane and ketamine, a case-by-case decision was taken based on whether any of these would constitute an alternative treatment. Only in cases when the substance was deemed needed to treat or prevent a disease or certain indication for which there is lack of availability of other treatments or measures, the result would be positive [i.e. substance would be recommended for inclusion in the list]. For these substances, when it was concluded to recommend the inclusion in the list, risk management measures were considered.

Further clarifications

Limited data or no data available

Given the high-level nature of this evaluation and the attention paid to the availability of medicinal products, in the absence of information or absence of evidence of aquatic hazard, the approach was to recommend the substance for inclusion in the list. In the following cases, it was considered that no hazard is declared/identified for the substance and the substance was proposed for inclusion in the list:

- Substance appears in ECHA, EPA, SDS database(s) with no hazard for aquatic environment but with other CLP/GHS notifications and literature search did not identify any aquatic hazard.
- Substance appears in ECHA, EPA database(s) but with no CLP, GHS notification information (i.e. substance with no hyperlink in the below table) and SDS database and literature search did not identify any aquatic hazard.
- Substance does not appear at ECHA, EPA, SDS databases and literature search did not identify any aquatic hazard.

Hazard indication from literature

For a small number of substances (7 in total) no hazard was declared in ECHA, EPA, SDS databases but the literature search suggested a hazard for the aquatic environment. For these substances, the concentrations used in the studies, when those were available, were compared to the thresholds for classifying substances as hazardous to the aquatic environment as per the CLP regulation. The nature of the effects was also considered, i.e. whether they fall under the criteria for aquatic toxicity in the CLP regulation. The outstanding cases (ketamine, isoflurane) underwent an ad-hoc assessment factoring the usefulness of the substance for food-producing aquatic species for treating or preventing a disease or certain indication for which there is lack of availability of other treatments or measures.

Herbal substances

The herbal substances eligible for assessment may include various parts of the plant, such as leaves, flowers, whole herbs, essential oils, fruits, roots, bark, seeds, and extracts. In cases where no ECHA, EPA, or SDS database entry was available for the specific part of the plant indicated by its name, the substance was linked to the closest available entry in the database, whether it pertains to the whole plant or another specific part, or extracts derived from them.

Harmonised and notified classifications

Harmonised classification under the CLP Regulation is an official, EU-wide system for classifying hazardous substances. It ensures consistent safety standards across all EU member states and is mandatory for manufacturers, importers, or users of these substances. These classifications are listed in Annex VI of the CLP Regulation. On the other hand, notified classifications are provided by manufacturers, importers, or users through C&L notifications or registration dossiers. While these classifications are not mandatory, they are shared with ECHA for reference and can be updated by the notifier. ECHA maintains the C&L Inventory but does not verify the accuracy of the information.

For substances listed in the C&L Inventory with both harmonised and notified classifications, both are included in the assessments, with hyperlinks provided for each classification type ('harmonised' and 'notified').

Assessment template

The above-mentioned steps are summarised in the table below, which represents the assessment template:

Substance	Data available on toxicity	Conclusion	Include in list
<Substance> [general case]	Brief introduction:<text> - Hazard from ECHA - Hazard from EPA - Hazard from SDS - Hazard from published literature - Consider PBT or ED	<From the available information, a risk to the environment was not identified> OR < An environmental risk cannot be excluded >	<Yes> OR <No>
<Substance> [case of hormones, isoflurane and ketamine]	Brief introduction:<text> - Hazard from ECHA - Hazard from EPA - Hazard from SDS - Hazard from published literature - Consider PBT or ED Ad-hoc assessment in relation to criterion c)	<Despite the potential risk(s) due to XX identified under criterion a), the substance is needed with regards criterion c).> OR <Potential risk(s) due to XX are identified under criterion a), and the substance is not needed with regards criterion c).>	<Yes and add RMM if needed> OR <No>

3. Assessment

The tables below follow the assessment template as shown in section 1.2.

A

Substance	Data available on toxicity	Conclusion	Include in list
***Absinthium* extract**	Extract of *Artemisia absinthium*, or common wormwood. ECHA: notified H411, H412.	An environmental risk cannot be excluded.	No
Acetyl cysteine	Derivative of amino acid L-cysteine. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Acetylmethionine	Amino acid. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Acetylsalicylic acid	NSAID. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: hazard H402.	An environmental risk cannot be excluded.	No
Acetylsalicylic acid DL-lysine	As for acetylsalicylic acid.	An environmental risk cannot be excluded.	No
Adenosine and its 5'-mono-, 5'-di-and 5'-triphosphates	Ribonucleoside. ECHA: notified (& mono-, di-, tri-, tri-, tri-, tri-, tri-) no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Alanine	Aminoacid. ECHA: notified DL-Alanine and L-Alanine no hazard declared. EPA: GHS data DL-Alanine and L-Alanine no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Alarelin	Synthetic nonapeptide analogue of luteinizing-hormone releasing hormone (LHRH), also known as gonadotropin-releasing hormone (GnRH). ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Alarelin has been studied for its effects on fish reproduction, particularly in species such as the sterlet (Acipenser ruthenus), Zebra fish (Danio rerio). Research indicates that alarelin can significantly influence reproductive processes,	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.

Substance	Data available on toxicity	Conclusion	Include in list
	including spermiation and follicular development, by modulating hormonal pathways in fish. The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Alfacalcidol	Member of the class of D3 vitamins that is calciol in which the hydrogen at the 1alpha position is replaced by a hydroxy group. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Alfaprostol	Fatty acid methyl ester. Analog of prostaglandin F2α. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Alfaprostol is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.	Potential risk(s) due to ED properties are identified under criterion a), and the substance is not needed with regards criterion c).	No
Allantoin	Endogenous substance to the human body and also found as a normal component of human diets. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Aloe vera* gel and whole leaf extract of *Aloe vera	Gel and extract from a succulent plant species of the genus *Aloe*. ECHA: notified gel and extract no hazard declared. EPA: no hazard declared.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
Aloes, Barbados and Capae, their standardised dry extract and preparations thereof	As for *Aloe vera*.	From the available information, a risk to the environment was not identified.	Yes
Altrenogest	Steroidal progestin. ECHA: notified H400, H410. PBT or ED: hormone–like activity. Ad-hoc assessment in relation to criterion c): Altrenogest is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.	Potential risk(s) due to ED properties are identified under criterion a), and the substance is not needed with regards criterion c).	No
Aluminium distearate	Chemical compound of aluminium. ECHA: notified H410, H411.	An environmental risk cannot be excluded.	No
Aluminium hydroxide	Chemical compound of aluminium. ECHA: notified H400, H410.	An environmental risk cannot be excluded.	No
Aluminium phosphate	Chemical compound of aluminium. ECHA: notified no hazard declared. EPA: GSH data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Aluminium salicylate, basic	Chemical compound of aluminium. ECHA: not found. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Ammonium chloride	Inorganic chloride compound having ammonium as the counterion. ECHA: notified H400, H410, H411.	An environmental risk cannot be excluded.	No
Angelicae radix aetheroleum	Volatile oil obtained by steam distillation from toots of *Angelica archangelica* L. ECHA: notified H411.	An environmental risk cannot be excluded.	No
Anisi aetheroleum	Essential oil derived from *Pimpinella anisum*.	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
	ECHA: notified H411, H412.		
***Anisi stellati fructus*, standardised extracts and preparations thereof**	The fruit of *Illicium verum* Hook F. (Chinese star anise). ECHA: notified no hazard declared. EPA: not found. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Arginine	Amino acid. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
***Arnica montana* (*arnicae flos* and *arnicae planta tota*)**	European flowering plant in the daisy family *Asteraceae* that has a large yellow flower head. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: not found. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Asparagine	Amino acid. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Aspartic acid	Amino acid. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Atropine	An anticholinergic and cholinergic muscarinic antagonist. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Azaperone	A pyridinylpiperazine and butyrophenone agent that is capable of eliciting neuroleptic sedative and antiemetic effects. ECHA: notified no hazard declared. EPA: GHS data no hazard declared.	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
	SDS: hazard H402.		

B

Substance	Data available on toxicity	Conclusion	Include in list
Balsamum peruvianum	Herbal non-homeopatic. Naturally derived from a tree (*Myroxylon balsamum* var. *pereirae*). ECHA: notified H411, H400, H412, H402.	An environmental risk cannot be excluded.	No
Beclomethasone dipropionate	Synthetic glucocorticoid. ECHA: notified H410. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Beclomethasone dipropionate is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.	Potential risk(s) due to ED properties are identified under criterion a), and the substance is not needed with regards criterion c).	No
Benzyl benzoate	Organic compound, ester of benzyl alcohol and benzoic acid. ECHA: harmonised H411 and notified H400, H410, H412.	An environmental risk cannot be excluded.	No
Benzyl p-hydroxy-benzoate	As for benzyl benzoate.	An environmental risk cannot be excluded.	No
Betaine	Normal component of human food; naturally derived from choline (by oxidation). ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Betamethasone	Synthetic corticosteroid. ECHA: notified H410. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Betamethasone is not needed to treat or prevent a disease or certain	Potential risk(s) due to ED properties are identified under criterion a), and the substance is not needed with regards criterion c).	No

Substance	Data available on toxicity	Conclusion	Include in list
	indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.		
Biotin	Organic heterobicyclic compound (Vitamin B7). ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Bismuth subsalicylate	Salt of bismuth; non-essential trace element that is a normal component of the human diet. ECHA: notified H400, H410.	An environmental risk cannot be excluded.	No
Bismuth subgallate	As for bismuth subsalicylate.	An environmental risk cannot be excluded.	No
Bismuth subnitrate	As for bismuth subsalicylate.	An environmental risk cannot be excluded.	No
Bituminosulfonate, ammonium and sodium salts	Bituminosulfonates (ammonium and sodium salts of dark or light bituminosulfonate), AKA[1] ichthammol, are topical therapeutic agents derived from shale oil. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Boldo folium	Leaves of the tall shrub *Peumus boldus*. ECHA: notified H411.	An environmental risk cannot be excluded.	No
Boric acid and borates	$B(OH)_3$, a weak acid often used as an antiseptic, insecticide, flame retardant, neutron absorber, or precursor to other boron compounds. ECHA: notified no hazard declared. EPA: GHS data H402.	An environmental risk cannot be excluded.	No
Bromelain	Enzyme extract derived from the stems of pineapples. ECHA: notified stem and juice no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Bromhexine	Mucolytic drug used in the treatment of respiratory disorders associated with viscid or excessive mucus.	An environmental risk cannot be excluded.	No

[1] AKA: Also known as

Substance	Data available on toxicity	Conclusion	Include in list
	ECHA: notified H400, H410.		
Bromide, potassium salt	Salt widely used as an anticonvulsant and a sedative. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Bromide, sodium salt	Inorganic compound; widely used source of the bromide ion. ECHA: notified H400, H410.	An environmental risk cannot be excluded.	No
Brotizolam	Benzodiazepine analogue. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Bupivacaine	An amino-amide local anaesthetic. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Butafosfan	Organic phosphorus compound used as a phosphorus source. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Butorphanole tartrate	A synthetic morphinan analgesic with narcotic antagonist action. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Butyl 4-hydroxybenzoate	Organic compound used as preservative. ECHA: notified H412, H413 PBT or ED: endocrine disrupting.	An environmental risk cannot be excluded.	No
Butylscopolaminium bromide	Organic bromide salt of butylscopolamine; quaternary ammonium salt. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

C

Substance	Data available on toxicity	Conclusion	Include in list
Cabergoline	Ergoline derivative with dopaminergic activity. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: hormone-like activity. In its evaluation of Velactis CVMP indicated that cabergoline is considered a substance with potential endocrine disrupting properties and that potentially harmful effects to aquatic species could not be ruled out. Ad-hoc assessment in relation to criterion c): Cabergoline is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.	Potential risk(s) due to ED properties are identified under criterion a), and the substance is not needed with regards criterion c).	No
Caffeine	Methylxanthine alkaloid and psychoactive stimulant. ECHA: notified no hazard declared. EPA: GHS Data H402, H412.	An environmental risk cannot be excluded.	No
Calcium acetate	Calcium salt of acetic acid used to treat hyperphosphataemia. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: hazard H401, H411.	An environmental risk cannot be excluded.	No
Calcium borogluconate	Calcium gluconate combined with boric acid; currently used for the treatment of hypocalcaemia. ECHA: notified no hazard declared. EPA: not found. SDS: no hazard declared. Literature: toxic to fish, water fleas, and algae (Kim et al., 2023). Genotoxic effects (Gülsoy et al. 2015). Toxicity data are for boron under the form of boric acid, sodium tetraborate, and sodium pentaborate	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	pentahydrate. No information was found for calcium borogluconate.		
Calcium citrate	Calcium salt of citric acid; used for the treatment of hypocalcaemia and as a food additive. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Calcium glucheptonate	Calcium salt of D-gluco-heptonic acid; used for the treatment of hypocalcaemia. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Calcium glycerophosphate	Calcium salt of glycerophosphoric acid; used for the treatment of hypocalcaemia, hypophosphatemia and in dental products. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Calcium hypophosphite	Used in polymers; industrial use. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Calcium oxide	Otherwise known as quicklime; used in oxygen steelmaking, production of concrete blocks and glass. Food additive to the FAO: E529. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: hazard H402.	An environmental risk cannot be excluded.	No
Calcium panthotenate	Dietary supplement used for the treatment of Vitamin B5 deficiency. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Calcium carbonate	Inorganic compound commonly found in rocks, eggshells and gastropod shells. Therapeutically used for calcium supplementation and as an antacid. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: hazard H402.	An environmental risk cannot be excluded.	No
Calcium chloride	Inorganic compound; used therapeutically for the prevention of hypocalcaemia. ECHA: notified no hazard declared. EPA: not found. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Calcium gluconate	The calcium salt of gluconic acid; used therapeutically for the treatment of hypocalcaemia, hyperkalaemia and magnesium toxicity. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Calcium glucono glucoheptonate	A mixed salt combining calcium gluconate and calcium glucoheptonate. ECHA: not found. EPA: not found. SDS: not found. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Calcium hydroxide	Inorganic compound; used as a fungicide in orchard crops and as a dressing in endodontics. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: hazard H402.	An environmental risk cannot be excluded.	No
Calcium phosphate	Calcium salt of phosphoric acid; used as antacid, in dental products and as a feed additive. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Calcium propionate	Inorganic compound; used to prevent milk fever in cows and as a feed additive. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Calcium sulphate	Food additive; used in dental products. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Calendulae flos	Herbal non-homeopathic; used as an analgesic, anti-diabetic, anti-ulcer, anti-inflammatory and for gastrointestinal tract, gynaecological, ocular and dermal disorders and as an anti-tumour agent. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Camphor	A terpenoid and cyclic ketone derived from the wood of the camphor laurel tree; also produced from the oil of turpentine. ECHA: notified H400, H410.	An environmental risk cannot be excluded.	No
Capsici fructus acer	Herbal non-homeopathic; physiological effects via histamine release and cell-mediated immunity. A food additive (FDA). ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Carazolol	A β-adrenergic receptor agonist or beta blocker; used to treat hypertension. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Carbasalate calcium	As for acetylsalicylic acid.	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
Carbetocin	A synthetic analogue of oxytocin; it causes uterine contraction and is used to control post-partum haemorrhage and to decrease blood loss during hysteroscopic myomectomy. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Carbetocin is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.	Potential risk(s) due to ED properties are identified under criterion a), and the substance is not needed with regards criterion c).	No
Cardamon extract	Non-homeopathic herbal with antibacterial and anti-inflammatory properties. A food additive (FDA). ECHA: notified H411.	An environmental risk cannot be excluded.	No
Carlinae radix	Non-homeopathic herbal with reported antibacterial properties. ECHA: not found. EPA: not found. SDS: not found. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Carnitine	A quaternary ammonium compound involved in metabolism in most mammals, fish and plants; concentrated in skeletal and cardiac muscle that use fatty acids as an energy source. Naturally present in many foods and available as a food supplement. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Carprofen	NSAID; used in cats, dogs, cattle and horses. ECHA: notified no hazard declared.	From the available information, a risk to	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	the environment was not identified.	
Carvi aetheroleum	Non-homeopathic herbal, AKA caraway oil; used for relief of digestive system problems. ECHA: notified H400, H410, H412.	An environmental risk cannot be excluded.	No
Centellae asiaticae extractum	Herbal non-homeopathic; consumed as a vegetable and used in traditional medicine for minor wounds. ECHA: no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Cetostearyl alcohol	A fatty alcohol used as an emusion stabiliiser, opacifying agent and foam-boosting surfactant. Used in hair-products. ECHA: notified H412, H413.	An environmental risk cannot be excluded.	No
Cetrimide	Quaternary ammonia compound; used as antiseptic in wounds, cuts, burns. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: hazard H401, H412.	An environmental risk cannot be excluded.	No
Chlorhexidine	A bisbiguanide compound with broad-spectrum antimicrobial properties; used as an antiseptic and disinfectant in mouthwashes for oral infections, as a surgical scrub and surgical instrument disinfectant. ECHA: notified H400, H410, H411.	An environmental risk cannot be excluded.	No
Chlormadinone	A progestin and antiandrogen medication used for birth control. ECHA notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: Antiandrogenic and antiglucocorticoid activity in fish; transcriptional changes in exposed zebrafish eleutheroembryos (Siegenthaler et al. Jan 2017). Exposure of adult zebrafish to chlormadinone led to a significant but weak reduction in egg production and	Potential risk(s) due to ED properties are identified under criterion a), and the substance is not needed with regards criterion c).	No

Substance	Data available on toxicity	Conclusion	Include in list
	several significant changes in gene expression in brains, livers and gonads of adult zebrafish (Siegenthaler et al. April 2017). PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Chlormadinone is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.		
Chlorocresol	Potent disinfectant and antiseptic; used as an anti-microbial preservative and as a preservative in paints. Chlorocresol-based products are considered biocides. ECHA: harmonised and notified H400, H412	An environmental risk cannot be excluded.	No
Chlorphenamine	H1-receptor antagonist (antihistamine) used for allergic reactions, hay fever, rhinitis, urticaria and asthma. ECHA: notified H411.	An environmental risk cannot be excluded.	No
Choline	An essential nutrient (formally considered a B vitamin (Vit B4)) found in eggs, meat, wheat germ. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Chymotrypsin	A digestive (proteolytic) enzyme produced by the pancreas. ECHA: notified H400.	An environmental risk cannot be excluded.	No
Ciclesonide	A corticosteroid used to treat asthma and allergic rhinitis in humans and horses. ECHA: notified H413. PBT or ED: hormone–like activity. Ad-hoc assessment in relation to criterion c): Ciclesonide is not needed to treat or prevent a disease or certain	Potential risk(s) due to ED properties are identified under criterion a), and the substance is not needed with regards criterion c).	No

Substance	Data available on toxicity	Conclusion	Include in list
	indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.		
Cimicifugae racemosae rhizoma	Herbal non-homeopathic, AKA black cohosh; used for menopausal symptoms such as hot flushes and excessive sweating. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
***Cinchonae cortex*, standardised extracts and preparations thereof**	Herbal non-homeopathic. Derived from the *Rubiaceae* flowering plants, the bark of which yields quinine and other alkaloids. Previously used for the treatment of malaria. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: Bark of cinchona reduced the feeding rate, growth and reproduction of tilapia fish (Saha and Kaviraj, 1996). The relevance of these effects in relation to the CLP thresholds is unclear. In particular, these effects were only seen at high doses (0.3 mg/l and above of spent bark (SB) tannic acid, the dose of bark or of standardised extract being higher and unknown. No other reference has been identified.	From the available information, a risk to the environment was not identified.	Yes
Cinnamomi cassiae aetheroleum	Herbal non-homeopathic, AKA cinnamon oil. Used for the treatment of digestive problems and as a feed additive. ECHA: notified H411, H412.	An environmental risk cannot be excluded.	No
***Cinnamomi cassiae cortex*, standardised extracts and preparations thereof**	Herbal non-homeopathic, AKA cinnamon bark; reported anti-inflammatory and antioxidant properties. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Cinnamomi ceylanici aetheroleum	As for *Cinnamomi cassiae aetheroleum*.	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
Citri aetheroleum	Herbal non-homeopathic, AKA lemon oil; used for skin conditions and anxiety ECHA: notified H400, H410, H411.	An environmental risk cannot be excluded.	No
Citronellae aetheroleum	Herbal non-homeopathic, AKA lemongrass oil; used to treat digestive disorders and high blood pressure. ECHA: notified H411, H412.	An environmental risk cannot be excluded.	No
Citrulline	A non-essential amino acid made in the body and also found in foodstuffs such as watermelon. It has a role as a nitric oxide synthase inhibitor, a protective agent, a nutraceutical and micronutrients and a human, *E. coli*, *S. cerevisiae* and mouse metabolite. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Clodronic acid	A bisphosphonate used for the prevention and treatment of osteoporosis in post-menopausal women and in men, hyperparathyrodisim, hypercalcaemia of malignancy and myeloma in humans; used in horses for the treatment of bone resorption associated with navicular syndrome. ECHA: no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Cloprostenol	A synthetic analogue of PGF2α. A luteolytic agent; it is used to induce oestrous and abortion in cattle, horses and pigs. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c):	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.

Substance	Data available on toxicity	Conclusion	Include in list
	Cloprostenol has been increasingly recognised for its role in reproductive management in various animal species, including fish. In fish, cloprostenol has been shown to influence reproductive parameters significantly. For instance, Sato et al. investigated the effects of cloprostenol in the South American fish species *Piaractus mesopotamicus*, demonstrating that the administration of this prostaglandin analogue during hypophysation (a common method for inducing ovulation) resulted in a notable resumption and progression of meiosis, alongside altered circulating steroid levels (Sato et al. 2020). This suggests that cloprostenol not only facilitates ovulation but also plays a crucial role in the maturation of oocytes, which is essential for successful breeding programs in aquaculture. The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Cobalt dichloride	A cobalt salt used as an indicator for water in desiccants. Also, an allergen, a calcium channel blocker and a sensitiser. ECHA: harmonised H400, H410 notified H400, H411, H410.	An environmental risk cannot be excluded.	No
Cobalt gluconate	An organometallic compound used in electroplating, water treatment, mouthwashes and skincare. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
***Condurango cortex*, standardised extracts**	Herbal non-homeopathic; used for indigestion. ECHA: no hazard declared.	From the available information, a risk to	Yes

Substance	Data available on toxicity	Conclusion	Include in list
and preparations thereof	EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	the environment was not identified.	
Copper chloride	AKA cupric chloride. Used in petroleum, textile and metal industries. Also used in agricultural products, as a feed additive and in total parenteral nutrition. ECHA: harmonised H400, H410 notified H400, H410, H411.	An environmental risk cannot be excluded.	No
Copper gluconate	Copper salt of D-gluconic acid, orally bioavailable and used as a dietary supplement and feed additive. ECHA: notified H400, H410, H411.	An environmental risk cannot be excluded.	No
Copper methionate	Used in conjunction with vitamin B12 for the treatment of hypocuprosis in cattle and sheep, anaemia in piglets and fungal and bacterial diseases in fish. ECHA: not found. EPA: not found. SDS: no hazard declared. Literature: no hazard identified. PBR or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Coriandri aetheroleum	Herbal non-homeopathic. Oil from the seeds of coriander plant. Reported antimicrobial effects. ECHA: notified H411.	An environmental risk cannot be excluded.	No
Cysteine	A non-essential amino acid. Administered in total parenteral nutrition formulations and also in the treatment of acetaminophen overdosing. ECHA: notified no hazard declared. SDS: hazard H402.	An environmental risk cannot be excluded.	No
Cytidine and its 5'-mono-, 5'-di- and 5'-triphosphates	A pyrimidine nucleoside which is a human, *E. coli*, *S. cerevisiae* and mouse metabolite. ECHA: notified cytidine and 5'-triphosphate no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

D

Substance	Data available on toxicity	Conclusion	Include in list
Dembrexine	Mucolytic agent. ECHA: not found. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Denaverine hydrochloride	Spasmolytic agent, benzyl acid derivative. ECHA: notified no hazard declared. EPA: GSH data no hazard declared. SDS: not found. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Detomidine	Sedative agent, imidazole derivative and α2-adrenergic agonist. ECHA: not found. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Dexamethasone	Synthetic Glucocorticoid. ECHA: notified H410. PBT or ED: hormone–like activity. Ad-hoc assessment in relation to criterion c): Dexamethasone has been studied for its therapeutic potential in fish, particularly in stress management and immune response modulation. Research on species like Siberian sturgeon (*Acipenser baerii*) suggests that intraperitoneal injections of dexamethasone can alter phsyiological stress responses, indicating its potential benefit in aquaculture settings where stress is prevalent due to overcrowding or environmental changes (Falahatkar et al. 2022). Research on the freshwater fish *Hoplias malabaricus* suggests that dexamethasone can modulate immune function in fish (Ribas et al. 2015; Sayed et al. 2022). Additionally, dexamethasone has	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.

Substance	Data available on toxicity	Conclusion	Include in list
	demonstrated anti-inflammatory properties, influencing inflammatory mediator production in fish infected with nodavirus, indicating potential applications in enhancing fish health and reducing infection-related morality rates (Montes et al. 2010; Desgens-Martin and Keller, 2021). The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Dexpanthenol	Alcoholic analogue of D-pantothenic acid (vit B5). ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Diclofenac	NSAID. ECHA: notified H411, H412.	An environmental risk cannot be excluded.	No
Dimethicone	Silicone polymer. Included in list of substances generally recognised as safe for the consumer. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Dimethyl phthalate	Ester derived from o-phthalic acid and methanol, used as plasticizer and insect repellent. ECHA: notified H402, H412.	An environmental risk cannot be excluded.	No
Dimethyl sulphoxide	Organosulphur compound. Included in list of substances generally recognised as safe for the consumer. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Dinoprost tromethamine	Analogue prostaglandin F2 alpha. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: hormone-like activity.	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.

Substance	Data available on toxicity	Conclusion	Include in list
	Ad-hoc assessment in relation to criterion c): Prostaglandins play an important role in fish reproduction. There are studies confirming the effectiveness of dinoprost tromethamine in fish reproduction (Cole and Stacey, 1984). The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Dinoprostone	Analogue of prostaglandin E2. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Prostaglandins play an important role in fish reproduction. There are studies about the use of dinoprostone in Senegalese sole (*Solea senegalensis*), Medaka (*Oryzias latipes*), catfish (*Heteropneustes fossilis*) (Norambuena et al. 2012; Joy and Singh, 2013; Fujimori et al. 2012). The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.
Diprophylline	N-substituted theophylline derivative, used as bronchodilator. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Doxapram	Respiratory stimulant. ECHA: no hazard declared. EPA: no hazard declared. SDS: no hazard declared.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	Literature: no hazard identified. PBT or ED: no.		
D-Phenylalanine (6)-luteinizing-hormone-releasing hormone	Common name is LH-RH. It is an analogue of GnRH. ECHA: not found. EPA: not found. SDS: not found. Literature: no hazard identified. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): GnRH and its analogs are widely used in fish reproduction. LH-RH is an analog of GnRH that has also been studied for many years in fish reproduction with good results, such in Coho salmon (*Oncorhynchus kisutch*) or Rainbow trout (*Oncorhynchus mykiss*) (Van der Kraak et al. 1984; Chang et al. 1995; Pan et al. 1981; Uehara et al. 2024; Kennedy et al. 2015). The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.

E

Substance	Data available on toxicity	Conclusion	Include in list
Echinacea purpurea	Herbal non-homeopathic, for topical administration on wounds. Naturally derived from a flowering plant (*Asteraceae*). ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Epinephrine	Adrenaline; hormone, neurotransmitter. ECHA: notified H412. PBT or ED: hormone–like activity.	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed	Yes The substance shall be

Substance	Data available on toxicity	Conclusion	Include in list
	Ad-hoc assessment in relation to criterion c): Epinephrine is gaining attention in aquaculture for its potential role in stress management and disease control. Stress can lead to immunosuppression in fish, increasing susceptibility to disease, while epinephrine influences metabolic processes that help fish cope with adverse conditions (Leung and Bates, 2012; Sidoruk and Cymes, 2018). Its administration may also enhance immune responses during disease outbreaks, potentially reducing infection severity and improving survival rates, which is particularly relevant amid concerns about antimicrobial resistance (Watts et al. 2017). Additionally, epinephrine's effects on feeding behavior and nutrient absorption suggest it could support growth and feed conversion efficiency, contributing to improved aquaculture productivity (Rosidah and Mulyani, 2022). The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.	with regards criterion c)	administered by injection only.
Ergometrine maleate	Naturally occurring alkaloid found in ergot (*Claviceps purpurea*), for use in parturient animals only. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Ethamsylate	Antihaemorragic and vasoprotective agent. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Ethylenediamine -tetraacetic acid (EDTA) and salts	Aminopolycarboxylic acid, chelator agent Included in list of substances generally recognised as safe for the consumer. ECHA: notified H411, H412.	An environmental risk cannot be excluded.	No
Etiproston tromethamine	Analogue of prostaglandin PGF 2 alpha. ECHA: not found. EPA: not found. SDS: not found. Literature: no hazard identified. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Etiproston tromethamine is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.	Potential risk(s) are identified due to ED properties under criterion a), and the substance is not needed with regards criterion c).	No
Eucalypti aetheroleum	Herbal non-homeopathic. Antibacterial and antifungal activity. Approved as a spice. ECHA: notified H410, H411.	An environmental risk cannot be excluded.	No
Eucalyptol	Monoterpenoid. Included in list of substances generally recognised as safe for the consumer. Derived from different plants such as *Eucalyptus spp.* or *Artemisia spp*. ECHA: notified H411, H412.	An environmental risk cannot be excluded.	No

F

Substance	Data available on toxicity	Conclusion	Include in list
Fenpipramide hydrochloride	Parasympatholytic agent; combined with levomethadone to counteract the vagus effect of levomethadone. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Firocoxib	NSAID COX-2 selective. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Flugestone acetate	Synthetic progesterone. ECHA: notified H410. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Flugestone is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.	Potential risk(s) due to ED properties are identified under criterion a), and the substance is not needed with regards criterion c).	No
Flunixin	NSAID and non-narcotic analgesic with antipyretic activities. ECHA: notified H411, H412.	An environmental risk cannot be excluded.	No
Foeniculi aetheroleum	The oil obtained from the ripe fruits of *Foeniculum vulgare Miller var. vulgare* (fennel oil). ECHA: notified H400, H410.	An environmental risk cannot be excluded.	No
Folic acid	Member of the B vitamins group. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: hazard may cause long-term adverse effects in the aquatic environment.	An environmental risk cannot be excluded.	No
Follicle stimulating hormone (natural FSH from all species and their synthetic analogues)	Hormone produced by the anterior pituitary in response to gonadotropin-releasing hormone (GnRH) from the hypothalamus. ECHA: not found. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Literature indicates potential use of FSH and its analogues in fish reproduction, mainly to induce spermatogenesis (Zohar et al. 2010; Schulz et al. 2010; Muñoz-Cueto et al. 2020). The substance is needed to treat or prevent a disease or certain indication, for which there is lack of	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.

Substance	Data available on toxicity	Conclusion	Include in list
	availability of other treatments or measures in food-producing aquatic species.		
Food additive E 470a - Sodium, potassium and calcium salts of fatty acids	Salts of fatty acids; the basic components of larger lipid compounds. Serve as substrates for bioactive molecules. ECHA: notified H412, H411.	An environmental risk cannot be excluded.	No
Food additive E 466 - Sodium carboxy methyl cellulose, Cellulose gum	A cellulose derivative which is a beta-(1,4)-D-glucopyranose polymer: sodium salt of a partly O-carboxymethylated cellulose. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Food additive E 1202 - Polyvinylpolypyrrolidone	A highly cross-linked modification of polyvinylpyrrolidone (PVP). Can be used as a drug, taken as a tablet or suspension to absorb compounds (endotoxins) that cause diarrhoea. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 290 - Carbon dioxide	Greenhouse gas. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no	From the available information, a risk to the environment was not identified.	Yes
Food additive E 320 - Butylated hydroxyanisole (BHA)	A synthetic food antioxidant used to prevent oils, fats and shortenings from oxidative deterioration and rancidity. BHA is a mixture of 3-tert-butyl-4-hydroxyanisole and 2-tert-butyl-4-hydroxyanisole. ECHA: notified H411, H410.	An environmental risk cannot be excluded.	No
Food additive E 321 - Butylated hydroxytoluene (BHT)	Synthetic antioxidant. ECHA: notified H410, H400, H413.	An environmental risk cannot be excluded.	No
Food additive E 520 - Aluminium sulphate	Water soluble salt. It belongs to a group of medicines called styptics which act to stop bleeding and can also soothe. ECHA: notified H400, H410, H411, H412.	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
Food additive E 905 - Microcrystalline wax	A type of wax produced by de-oiling petrolatum, as part of the petroleum refining process. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: According to Annex II of the MARPOL convention, petroleum waxes are classified as "high viscosity, solidifying, and persistent floating products," whose discharge at sea of tank-washing residues is strictly regulated, but currently permitted within certain limits. Once at sea or on the shoreline these substances can interact with marine fauna, with most of the studies concerning ingestion by seabirds. There is record of wax ingestion by marine organisms in 2015, when a piece was found in the GI tract of loggerhead turtle found lifeless on a beach. Most studies, however, are lacking chemical identification of the ingested material and realistic levels of exposure for marine populations are not known. Pollution events by paraffins and other petroleum waxes are posing a significant problem across Europe with new incidents being reported on a regular basis (Suaria et al., 2018)	An environmental risk cannot be excluded.	No
Food additive E 967 - Xylitol	A colourless or white crystalline solid that is freely soluble in water; a polyalcohol and a sugar alcohol, specifically an alditol. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Food additive E 322 - Lecithins	The term "lecithin" refers to a fatty mixture rather than a single compound. Lecithins can be obtained from either plant or animal origin. They are mixtures of glycerophospholipids. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 522 - Aluminium potassium sulphate	A metal sulfate composed of potassium, aluminium and sulfate ions. It has a role as a flame retardant, a mordant and an astringent ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 200 - Sorbic acid	Unsaturated, six carbon fatty acid. ECHA: notified H411, H400, H410.	An environmental risk cannot be excluded.	No
Food additive E 512 - Stannous chloride	A white crystalline solid with the formula SnCl2. Widely used as a reducing agent (in acid solution), and in electrolytic baths for tinplating. ECHA: notified H412, H400, H410.	An environmental risk cannot be excluded.	No
Food additive E 586 - 4-Hexylresorcinol	An antioxidant with the molecular formula C12H18O2. ECHA: notified H411.	An environmental risk cannot be excluded.	No
Food additive E 514 - Sodium sulphates	Inorganic sodium salt with formula Na2SO4, as well as several related hydrates. ECHA: notified H412, H411.	An environmental risk cannot be excluded.	No
Food additive E 175 - Gold	Used in human medicine for reducing inflammation and to slow disease progression in patients with rheumatoid arthritis. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: hazard H401, H412.	An environmental risk cannot be excluded.	No
Food additive E 1203 - Polyvinyl alcohol (PVA)	A water-soluble synthetic polymer. ECHA: notified no hazard declared. EPA: no hazard declared.	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
	SDS: hazard may cause long-term adverse effects in the aquatic environment.		
Food additive E 127 - Erythrosine	An iodine-containing colour used in foods, drugs and cosmetics. ECHA: notified H411, H413, H412.	An environmental risk cannot be excluded.	No
Food additive E 432 - Polyoxyethylene sorbitan monolaurate (polysorbate 20)	Nonionic surfactant. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Food additive E 132 - Indigotine, Indigo carmine	Indigo dye is an organic compound with a distinctive blue colour. Indigo carmine, or 5,5′-indigodisulfonic acid sodium salt, is an organic salt derived from indigo by aromatic sulfonation. ECHA: notified H411.	An environmental risk cannot be excluded.	No
Food additive E 363 - Succinic acid	A C4-bicarboxylic acid synthesized as a vital intermediate of tricarboxylic acid (TCA) cycle. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Food additive E 553b - Talc	A clay mineral composed of hydrated magnesium silicate, with the chemical formula Mg3Si4O10(OH)2. ECHA: notified H413.	An environmental risk cannot be excluded.	No
Food additive E 941 - Nitrogen	Colorless gas, liquid or solid. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no	From the available information, a risk to the environment was not identified.	Yes
Food additive E 434 - Polyoxyethylene sorbitan monopalmitate (polysorbate 40)	Emulsifier. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 501 - Potassium carbonates	Inorganic salt with the formula K2CO3, soluble in water. ECHA: notified no hazard declared. EPA: GHS Data H402, H412.	An environmental risk cannot be excluded.	No
Food additive E 577 - Potassium gluconate	The potassium salt of the conjugate base of gluconic acid. ECHA: notified no hazard declared. EPA: not found.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	SDS: no hazard declared. Literature: no hazard identified. PBS or ED: no.		
Food additive E 500 - Sodium carbonates	Inorganic compound with the formula Na2CO3 and its various hydrates, AKA washing soda, soda ash and soda crystals. ECHA: notified no hazard declared. EPA: not found. SDS: no hazard declared. Literature: Washing soda caused alteration of phagocytic and cytotoxic responses in freshwater sponge, indicative to an undesirable shift in their immune system. Sponge cell generated a high degree of phenoloxidase activity under the experimental exposure of 2, 4, 8, 16 mg/l of sodium carbonate for 96 and 192 h. Significant decrease in phagocytic response of sponge cells under 4, 8, 16 mg/l of the toxin for 96h (Mukherjee et al., 2015). However, these effects do not fall under the toxicity criteria in the CLP regulation.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 223 - Sodium metabisulphite	Inorganic compound of chemical formula Na2S2O5 (synonym: disodium disulfite). ECHA: notified H412. EPA: GHS Data H401, H412.	An environmental risk cannot be excluded.	No
Food additive E 440 - Pectins	A class of heterogeneous polysaccharides found in plant cell walls. Has been used to control diarrhoea. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: hazard may cause long-term adverse effects in the aquatic environment.	An environmental risk cannot be excluded.	No
Food additive E 435 - Polyoxyethylene sorbitan monostearate (polysorbate 60)	A surface-active substance, used as an emulsifier and wetting agent, for example in food and pharmaceuticals. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	Literature: no hazard identified. PBT or ED: no.		
Food additive E 412 - Guar gum	A galactomannan polysaccharide extracted from guar beans that has thickening and stabilizing properties useful in food, feed, and industrial applications. It acts as a bulk-forming laxative. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Food additive E 262 - Sodium acetates	The sodium salt of acetic acid. Wide range of uses. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: hazard Harmful to aquatic life with long lasting effects; Harmful to aquatic life.	An environmental risk cannot be excluded.	No
Food additive E 340 - Potassium phosphates	Salts of potassium and phosphate ions including Monopotassium phosphate, Dipotassium phosphate, Tripotassium phosphate. ECHA: notified monopotassium, dipotassium, tripotassium no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 461 - Methyl cellulose	A methyl ester of cellulose. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: hazard may cause long-term adverse effects in the aquatic environment.	An environmental risk cannot be excluded.	No
Food additive E 300 - Ascorbic acid	Water soluble vitamin (Vitamin-C). ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 336 - Potassium tartrates	The potassium salt of tartaric acid. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Food additive E 339 - Sodium phosphates	A generic variety of salts of sodium (Na^+) and phosphate ($PO4^{3-}$). ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 464 - Hydroxypropyl methyl cellulose	A semisynthetic, inert, viscoelastic polymer. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 621 – Monosodium glutamate	A sodium salt of glutamic acid. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: Monosodium glutamate was toxic to fish and caused significant changes in the vital organs as the exposure period was extended. (Perumalsamy et al., 2024). However, the toxic effects were seen at concentrations higher (1500 mg/L and 150 mg/L) than thresholds for classifying substances as hazardous to aquatic environment as per CLP regulation (highest is 100 mg/L).	From the available information, a risk to the environment was not identified.	Yes
Food additive E 211 - Sodium benzoate	The sodium salt of benzoic acid ECHA: notified no hazard declared. EPA: no hazard declared. SDS: hazard H402.	An environmental risk cannot be excluded.	No
Food additive E 160d - Lycopene	An organic compound classified as a tetraterpene and a carotene. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 161b - Lutein	A xanthophyll and one of the naturally occurring carotenoids. ECHA: notified H413.	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
Food additive E 939 - Helium	Noble gas. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 218 - Methyl p-hydroxybenzoate	AKA methylparaben. The methyl ester of p-hydroxybenzoic acid. ECHA: notified H411, H412.	An environmental risk cannot be excluded.	No
Food additive E 260 - Acetic acid	The second simplest carboxylic acid. An important chemical reagent and industrial chemical across various fields. ECHA: notified H412. EPA: GHS Data H400, H410.	An environmental risk cannot be excluded.	No
Food additive E 515 - Potassium sulphates	The inorganic compound with formula K2SO4, a white water-soluble solid. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: hazard H411.	An environmental risk cannot be excluded.	No
Food additive E 261 - Potassium acetate	The potassium salt of acetic acid. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 325 - Sodium lactate	The sodium salt of lactic acid. ECHA: notified H413.	An environmental risk cannot be excluded.	No
Food additive E 400 - Alginic acid	A naturally occurring, edible polysaccharide found in brown algae. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 401 - Sodium alginate	The sodium salt of alginic acid. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: hazard may cause long-term adverse effects in the aquatic environment.	An environmental risk cannot be excluded.	No
Food additive E 524 - Sodium hydroxide	Inorganic compound with the formula NaOH. ECHA: notified H412, H402. EPA: GHS Data H402.	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
Food additive E 210 - Benzoic acid	Organic compound with the formula C6H5COOH, whose structure consists of a benzene ring with a carboxyl substituent. ECHA: notified H412, H400. EPA: GHS Data H402.	An environmental risk cannot be excluded.	No
Food additive E 948 - Oxygen	Gas. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 302 - Calcium ascorbate	The calcium salt of ascorbic acid, one of the mineral ascorbates. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 579 - Ferrous gluconate	The iron (II) salt of gluconic acid. Used as iron supplement. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 301 - Sodium ascorbate	Sodium salt of ascorbic acid. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: hazard H402.	An environmental risk cannot be excluded.	No
Food additive E 551 - Silicon dioxide	AKA silica, an oxide of silicon with the chemical formula SiO2. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Food additive E 576 - Sodium gluconate	The sodium salt of gluconic acid, produced by fermentation of glucose. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 966 - Lactitol	A disaccharide sugar alcohol produced from lactose. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Food additive E 332 - Potassium citrates	Potassium salt of citric acid. Effective in reducing the pain and frequency of urination when these are caused by highly acidic urine. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 508 - Potassium chloride	A metal halide salt composed of potassium and chlorine. ECHA: notified H412, H411.	An environmental risk cannot be excluded.	No
Food additive E 160a - Carotenes	The term carotene is used for many related unsaturated hydrocarbon substances having the formula C40Hx. (example of beta-carotene): ECHA: notified H412, H413.	An environmental risk cannot be excluded.	No
Food additive E 525 - Potassium hydroxide	An inorganic compound with the formula KOH, AKA caustic potash. ECHA: notified H412. EPA: GHS Data H402.	An environmental risk cannot be excluded.	No
Food additive E 331 - Sodium citrates	Sodium salts of citric acid. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 407 - Carrageenan	A family of natural linear sulfated polysaccharides that are extracted from red edible seaweeds. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 420 - Sorbitols	A sugar alcohol with a sweet taste which the human body metabolizes slowly. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Food additive E 327 - Calcium lactate	A salt that consists of two lactate anions for each calcium cation (Ca2+). ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 942 - Nitrous oxide	An oxide of nitrogen with the formula N2O. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 171 - Titanium dioxide	The inorganic compound derived from titanium with the chemical formula TiO2. ECHA: notified H411, H413.	An environmental risk cannot be excluded.	No
Food additive E 1201 - Polyvinylpyrrolidone	Commonly called polyvidone or povidone; a water-soluble polymer made from the monomer N-vinylpyrrolidone. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Food additive E 173 - Aluminium	A post-transition metal in the boron group. ECHA: notified H413, H400. EPA: GHS Data H413.	An environmental risk cannot be excluded.	No
Food additive E 422 - Glycerol	A triol obtained from animal fats and oils or by the fermentation of glucose. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 214 - Ethyl-p-hydroxybenzoate	Ethylparaben. The ethyl ester of p-hydroxybenzoic acid. ECHA: notified no hazard declared. EPA: GHS Data H401.	An environmental risk cannot be excluded.	No
Food additive E 330 - Citric acid	A weak acid found in citrus fruit, mostly in lemons and limes. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Food additive E 100 - Curcumin	A bright yellow chemical produced by plants of the Curcuma longa species. ECHA: notified no hazard declared. EPA: no hazard declared.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
Food additive E 1521 - Polyethylene glycol	A polyether compound derived from petroleum. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: Short-term exposure (72h) of tadpoles belonging to the species Physalaemus cuvieri to PEG induced oxidative stress and neurotoxicity (Nascimento et al., 2021). Exposure of fish and frog embryos to PEG caused hatching delay in Danio rerio, malformations in D. rerio and X. laevis (oedema, body malformations, changes in pigmentation and deformations of spine and tail), and changes in the heartbeat rate in both species. (Zicarelli et al., 2024). Mortality was seen at 0.5 mg/l which meets the criteria for acute 1 toxicity as per the CLP regulation.	An environmental risk cannot be excluded.	No
Food additive E 131 - Patent Blue V	A sky blue synthetic triphenylmethane dye. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 351 - Potassium malate	The potassium salt of malic acid. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 513 - Sulphuric acid	A mineral acid with the molecular formula H2SO4. ECHA: notified H412. EPA: GHS Data H402.	An environmental risk cannot be excluded.	No
Food additive E 172 - Iron oxides and hydroxides	Chemical compounds composed of iron, oxygen and hydrogen: yellow iron oxide (FeO(OH)·H2O), red iron	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
	oxide (Fe2O3) and black iron oxide (FeO·Fe2O3). ECHA: notified H411, H400, H410.		
Food additive E 416 - Karaya gum	An acid polysaccharide composed of the sugar galactose, rhamnose and galacturonic acid. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Food additive E 914 - Oxidised polyethylene wax	Polyethylene wax is an ultra-low molecular weight polyethylene consisting of ethylene monomer chains. The oxidized polyethylene wax is produced by oxidizing polyethylene wax. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: Due to its colour and smell, floating polyethylene often attracts aquatic animals; it may cause entanglement or be eaten by marine animals, which can trigger organ damage, apoptosis, genotoxicity, and death (Yao et al., 2022).	An environmental risk cannot be excluded.	No
Food additive E 392 - Extracts of rosemary	Extracted from leaves of *Rosmarinus officinalis*; contains a minimum of 5% Carnosic Acid, the active component and antioxidant of this material. ECHA: notified H411, H400, H410.	An environmental risk cannot be excluded.	No
Food additive E 319 - Tertiary-butyl hydroquinone (TBHQ)	A synthetic aromatic organic compound. A derivative of hydroquinone, substituted with a tert-butyl group. ECHA: notified H400, H410.	An environmental risk cannot be excluded.	No
Food additive E 345(i) – Trimagnesium dicitrate	A magnesium salt of citric acid in the anhydrous form. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Food additive E 1210 - Carbomer	Homopolymer of acrylic acid, cross-linked by allyl pentaerythritol. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Formic acid	The simplest carboxylic acid, with the chemical formula HCOOH. ECHA: notified H412. EPA: GHS Data H402.	An environmental risk cannot be excluded.	No
***Frangulae cortex*, standardised extracts and preparations thereof**	The dried, whole or fragmented bark of the stems and branches of *Rhamnus frangula L.* (*Frangula alnus Miller*). ECHA: notified no hazard declared. EPA: no hazard declared. SDS: not found. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Furosemide	A loop diuretic. ECHA: notified H412.	An environmental risk cannot be excluded.	No

G

Substance	Data available on toxicity	Conclusion	Include in list
***Gentianae radix*, standardised extracts and preparations thereof**	Herbal non-homeopathic. Dried root of *Gentiana lutea* (yellow gentian). Administered in veterinary medicine to treat gastric complaints in cattle, swine, sheep and horses. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: No.	From the available information, a risk to the environment was not identified.	Yes
***Ginseng*, standardised extracts and preparations thereof**	Herbal non-homeopathic, prepared from ginseng roots (*Panax ginseng*). Administered to treat tiredness/weakness. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Glutamic acid	Amino acid. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Glutamine	Amino acid. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Glutaraldehyde	Antiseptic and disinfectant agent. Included in list of substances generally recognised as safe for the consumer. ECHA: harmonised and notified H400, H411.	An environmental risk cannot be excluded.	No
Glycine	Amino acid. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Guaiacol	2-methoxyphenol, used as an expectorant, antiseptic, and local anesthetic. Included in list of substances generally recognised as safe for the consumer. ECHA: notified no hazard declared. EPA: GHS Data H402, H412.	An environmental risk cannot be excluded.	No

H

Substance	Data available on toxicity	Conclusion	Include in list
Hamamelis virginiana	Herbal non-homeopathic, commonly known as witch hazel. Administered orally for diarrhoea, vomiting, colds, fevers and cancer. Topical application for inflammatory skin conditions and insect bites. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	Literature: no hazard identified. PBT or ED: no.		
Heparin and its salts	Anticoagulant. Included in list of substances generally recognised as safe for the consumer. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Heptaminol	Amine derivative, cardiotonic and vasodilator in veterinary medicine. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Hesperidin	Bioflavonoid, treatment of vascular diseases. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Hesperidin methyl chalcone	Flavonoid for treatment of chronic venous diseases. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Hexetidine	Cationic antiseptic. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Hippocastani semen	Herbal non-homeopathic AKA horse-chestnut seed; used topically as a skin antiseptic. Other veterinary uses reported include treatment of emphysema and phlebitis in horses. ECHA: notified H411.	An environmental risk cannot be excluded.	No
Histidine	Amino acid. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Human menopausal urinary gonadotropin (hMG)	Naturally occurring gonadotrophin; combination of FSH and LH in a 1:1 ratio that is extracted from urine obtained from postmenopausal women; AKA menotropin. ECHA: not found. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Human menopausal urinary gonadotropin is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.	Potential risk(s) are identified due to ED properties under criterion a), and the substance is not needed with regards criterion c).	No
Humic acids and their sodium salts	Treatment of diarrhoea, dyspepsia and acute intoxications. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Hyaluronic acid	Naturally occurring mucopolysaccharide. Intra-	A risk cannot be disregarded.	No

Substance	Data available on toxicity	Conclusion	Include in list
	articular use for osteoarthritis, used cosmetically as a filler and applied topically for skin conditions. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: Adverse effects on the blood and spleen morphology, with signs of immune system disruption were seen in fish at 0.5 mg/l which meets the criteria for acute 1 toxicity as per the CLP regulation (Hamed et al., 2024).		
Hydrochlorothiazide	Benzothiadiazide derivative with diuretic and antihypertensive properties. ECHA: notified H410.	An environmental risk cannot be excluded.	No
Hydrocortisone	Corticosteroid, for topical use only in veterinary medicine. ECHA: notified H412. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Similar to other glucocorticoids, hydrocortisone can modulate immune function in fish and demonstrate anti-inflammatory properties, indicating potential applications in enhancing fish health and reducing infection-related mortality rates. The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.
Hydrocortisone aceponate	Synthetic corticosteroid applied topically in veterinary medicine for skin disorders. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared.	Potential risk(s) are identified due to ED properties under criterion a), and the substance is not needed with	No

Substance	Data available on toxicity	Conclusion	Include in list
	Literature: Synthetic glucocorticosteroid exposure in fish has shown to affect glucose metabolism, causes immunosuppression, increased heart rate and muscle atrophy (Hamilton et al., 2022). PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Hydrocortisone aceponate is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.	regards criterion c).	
Hydroxyethylsalicylate	NSAID. ECHA: notified H411.	An environmental risk cannot be excluded.	No
Hyperici oleum	Herbal non-homeopathic, oily extract of the flower of *Hypericum perforatum;* anti-inflammatory action. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

I

Substance	Data available on toxicity	Conclusion	Include in list
Inosine	A pyrimidine nucleoside which is a human, *E. coli*, *S. cerevisiae* and mouse metabolite. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Inositol	An osmolyte, a nutrient, and a human, *Daphnia magna*,	From the available information, a risk to	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	Saccharomyces cerevisiae, *E. coli* and mouse metabolite. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	the environment was not identified.	
Iodine	Naturally found in sea water, certain rocks and sediments. Used as a disinfectant, in soaps and bandages, for purifying water and added to some table salt. ECHA: harmonised H400 notified H400, H410.	An environmental risk cannot be excluded.	No
Potassium iodide	An oral antithyroid agent for the prevention of radioactive iodine uptake into the thyroid gland during a nuclear radiation emergency, as an adjunct in the treatment of hyperthyroidism and thyrotoxicosis and preoperatively to induce thyroid involution. Also, an expectorant. ECHA: notified H410, H411.	An environmental risk cannot be excluded.	No
Povidone, iodinated	A topical antiseptic for surgical purposes and for skin and mucous membrane infections. ECHA: no hazard declared. EPA: no hazard declared. SDS: hazard H411, H401.	An environmental risk cannot be excluded.	No
Iodoform	An organoiodine compound used as a healing and antiseptic dressing for wound sand sores, included in some disinfectants, dental paste and root canal filling materials ECHA: notified H411.	An environmental risk cannot be excluded.	No
Iron dextran	A complex of ferric oxyhydroxide and dextran. Presented as a parenteral preparation and used for the treatment of anaemia. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Iron fumarate	The fumarate salt form of iron which is used as a dietary supplement and to prevent iron deficiency syndromes.	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
	ECHA: no hazard declared. EPA: GHS Data H412.		
Iron sulphate	A compound of iron and sulphate used for the prevention and treatment of iron deficiency anaemia in humans and in textile and leather dyeing, fertilisers, pesticides, food supplements. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Isoflurane	An organofluorine compound used as an inhalational anaesthetic. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: High mortality rates in zebrafish (Chereen et al., 2014). Ad-hoc assessment in relation to criterion c): The substance is not needed as a potential additional anaesthetic, when there is lack of availability of other anaesthetics in food-producing aquatic species.	An environmental risk cannot be excluded. Additionally, even when there is a lack of availability of other anaesthetics in food-producing aquatic species, the substance is not needed in these species.	No
Isoleucine	An aspartate family amino acid and a proteinogenic amino acid. It is a *Saccharomyces cerevisiae*, *E. coli*, plant, human, algal and a mouse metabolite. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Isopropanol	A secondary alcohol used in cosmetics, perfumes, lacquers, window cleaner and as a rubbing alcohol. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

J

Substance	Data available on toxicity	Conclusion	Include in list
Juniperi fructus	Fruits from trees and shrubs of the genus *Juniperus*. ECHA: notified H400, H410, H411.	An environmental risk cannot be excluded.	No

K

Substance	Data available on toxicity	Conclusion	Include in list
Ketamine	Used as a general anaesthetic for short duration diagnostic and surgical procedures, however use is limited due to psychotropic effects. Also used as a recreational drug. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: Ketamine and norketamine presented high mortality for *D. magna* and growth inhibition for *T. thermophila* (Pérez-Pereira et al., 2020). Ketamine increased the mortality produced significant reproductive toxicity effects to *D. magna* (Li et al., 2017). Ad-hoc assessment in relation to criterion c): The substance is needed as a potential additional anaesthetic, when there is lack of availability of other anaesthetics in food-producing aquatic species.	An environmental risk cannot be excluded. However, when there is lack of availability of other anaesthetics, ketamine is considered useful as a potential additional anaesthetic. The substance shall be administered by injection only, in order to limit the exposure of the environment.	Yes, The substance shall be administered by injection only.
Ketanserin tartrate	A serotonin inhibitor used therapeutically to reduce blood pressure in hypertension. It also inhibits platelet aggregation. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Ketoprofen	A propionic acid derivative and a NSAID which is used to treat osteoarthritis and moderate pain.	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
	ECHA: notified H400, H410, H412, H413.		

L

Substance	Data available on toxicity	Conclusion	Include in list
Lactic acid	2-hydroxypropanoic acid; used therapeutically as a topical antimicrobial agent, as a source of bicarbonate for the correction of metabolic acidosis, as a caustic agent, and as an intestinal antiseptic and antiferment agent. ECHA: notified H400.	An environmental risk cannot be excluded.	No
Lanolin	A yellow fat obtained from sheep's wool. It is used as an emollient, cosmetic, and pharmaceutic aid. Included in list of substances generally recognised as safe for the consumer. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Lauri folii aetheroleum	Herbal non-homeopathic; ointment for topical administration to the udder or mammary glands. ECHA: notified H411, H412.	An environmental risk cannot be excluded.	No
Lavandulae aetheroleum	Herbal non-homeopathic; antiseptic and healing purposes. ECHA: notified H411, H412.	An environmental risk cannot be excluded.	No
Lecirelin	Synthetic hypothalamic gonadotropin releasing hormone (GnRH) analogue; intended for the induction of ovulation in cows, mares and rabbits, both for treatment of such conditions as ovarian cysts and for improvement of conception rates. ECHA: notified no hazard declared. EPA: not found. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: hormone-like activity.	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.

Substance	Data available on toxicity	Conclusion	Include in list
	Ad-hoc assessment in relation to criterion c): Literature indicates potential use of lecirelin in fish reproduction (Brzuska, 2006). The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Leucine	Amino acid. ECHA: notified L-leucine and DL-leucine no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Levomethadone	Opioid; the active enantiomer of methadone (R-(−)-methadone). ECHA notified H412.	An environmental risk cannot be excluded.	No
Levothyroxine	3,5,3´,5´-tetraiodo-L-thyronine, thyroxine, T4; chemically identical with the natural thyroxine hormone. Indicated for treatment of insufficient milk excretion, loss of weight, chronic indigestion and convalescence. ECHA: notified L-thyroxine and DL-thyroxine no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Levothyroxine is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.	Potential risk(s) are identified due to ED properties under criterion a), and the substance is not needed with regards criterion c).	No
Lidocaine	Anaesthetic, for local-regional anaesthesia only. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	PBT or ED: no.		
Lini oleum	Herbal non-homeopathic, a drying oil obtained by expression of linseeds. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Lobeline	Piperidine-like alkaloid from *Lobelia inflata.* Indicated for diagnostic purposes in food producing mammals during examination of the respiratory tract. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: hazard very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.	An environmental risk cannot be excluded.	No
Luprostiol	Synthetic prostaglandin F2 alpha analogue; for control of oestrus or induction of parturition in cattle, sheep, goat, horse, and pig. ECHA: not found. EPA: no hazard declared. SDS: not found. Literature: no hazard identified. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Luprostiol is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.	Potential risk(s) due to ED properties are identified under criterion a), and the substance is not needed with regards criterion c).	No
Luteinising hormone (natural LH from all species and their synthetic analogues)	Gonadotropic hormone secreted by the pituitary gland. Included in list of substances generally recognised as safe for the consumer. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: hormone-like activity.	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.

Substance	Data available on toxicity	Conclusion	Include in list
	Ad-hoc assessment in relation to criterion c): LH and its analogues are important for fish reproduction (Zohar et al. 2010; Schulz et al. 2010; Muñoz-Cueto et al. 2020). The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Lysine	Amino acid. ECHA: notified L-lysine & DL-lysine no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

M

Substance	Data available on toxicity	Conclusion	Include in list
Magnesium	An alkaline earth metal commonly found in natural foods. Administered therapeutically to treat magnesium deficiencies and indicated for the prevention of seizures in pre-eclampsia ECHA: notified H413. EPA: GHS Data H413.	An environmental risk cannot be excluded.	No
Magnesium acetate	An acetate salt form of magnesium used in cosmetics and as a source of magnesium or acetate ions in chemistry experiments. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Magnesium aluminium silicate	An emulsifying stabiliser, thickening agent and viscosity controller used in cosmetics and personal care products. ECHA: notified H411.	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
Magnesium aspartate	A magnesium salt of aspartic acid commonly used as a mineral supplement and in cosmetics. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Magnesium carbonate	Also known as magnesite, used for heartburn and upset stomach due to overproduction of acid. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Magnesium chloride	A magnesium chloride salt and used in medicine as a source of magnesium ions and as a cathartic. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Magnesium citrate	A magnesium citrate salt, used to relive constipation, prior to colonoscopy as a cathartic and in cosmetics. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Magnesium gluconate	A magnesium salt of gluconate, available as a dietary supplement, in antacids and laxatives. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Magnesium glycerophosphate	Used in cosmetics. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Magnesium hydroxide	Administered as an antacid or a laxative. Also used topically as a deodorant for canker sores. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Magnesium hypophosphite	Used in veterinary medicine to supplement magnesium and phosphorus deficiencies. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Magnesium orotate	Used as a mineral supplement to treat magnesium deficiency. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Magnesium oxide	Used as an antacid and mild laxative. ECHA: notified H400, H410, H411.	An environmental risk cannot be excluded.	No
Magnesium phosphate	Used as an antacid and as a food additive. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Magnesium trisilicate	Used as a food additive. ECHA: notified H413.	An environmental risk cannot be excluded.	No
Majoranae herba	A non-homeopathic herbal. Used for seasoning foods and medicinal uses include colds, coughs, cramps, depression, gastrointestinal problems, headaches, arthritis and muscle aches ECHA: notified H410.	An environmental risk cannot be excluded.	No
Manganese carbonate	Administered to cattle as manganese supplementation. ECHA: notified H411.	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
Manganese chloride	The dichloride salt of manganese, used as a nutraceutical and an MRI contrast agent. ECHA: notified H411.	An environmental risk cannot be excluded.	No
Manganese gluconate	Administered as a nutritional supplement, in food and cosmetics. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Manganese glycerophosphate	Administered as a nutritional supplement and in cosmetics. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Manganese sulphate	Used as a nutraceutical, in fertiliser and animal feeds. ECHA: notified H411.	An environmental risk cannot be excluded.	No
Mannitol	Used as an osmotic diuretic, a sweetening agent, an antiglaucoma drug and a food additive. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
***Matricaria recutita* and preparations thereof**	A non-homeopathic herbal, AKA chamomile. Used as a carminative and anti-inflammatory. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Matricariae flos	A non-homeopathic herbal. Chamomile. Used as a carminative and anti-inflammatory. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Medicago sativa extractum	A non-homeopathic herbal. Alfalfa, used in cattle feeds. Source of phytoestrogens. Used therapeutically for digestive disorders, diabetes, asthma, inflammation, gallstones and kidney disorders. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	PBT or ED: no.		
Medroxyprogesterone acetate	A progesterone derivative used to treat reproductive tract disorders, osteoporosis and is used in palliative care for endometrial and renal carcinoma. ECHA: notified H413. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Literature indicates potential application of medroxyprogesterone acetate in reproductive management and sex control in aquaculture (Mylonas et al. 2017; Zanuzzo et al. 2018; Budd et al. 2015; Levy and Sagi, 2020; Rotem-Dai et al. 2021). The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.
Melatonin	A hormone produced by the pineal gland, it is used for sleep disorders and benzodiazepine and nicotine withdrawal. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED hormone-like activity. Ad-hoc assessment in relation to criterion c): Melatonin is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.	Potential risk(s) are identified due to ED properties under criterion a), and the substance is not needed with regards criterion c).	No
Melissae aetheroleum	A non-homeopathic herbal. Lemon balm essential oil. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Melissae folium	A non-homeopathic herbal. Lemon balm leaves, used in veterinary for	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
	endometritis and unspecified sterility. Used in human medicine for nervous sleeping disorders and functional disorders of the gastrointestinal tract. ECHA: notified H412.		
Meloxicam	NSAID. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Menadione	A Vitamin K precursor and known as vitamin K_3. Used as a nutritional supplement in animal feed and for the treatment of hypoprothrombinemia. ECHA: notified H400, H410.	An environmental risk cannot be excluded.	No
Menbutone	A choleretic used to stimulate hepato-digestive activity in digestive disorders and hepatic insufficiency. ECHA: not found. EPA: no hazard declared. SDS: hazard slightly hazardous for water.	An environmental risk cannot be excluded.	No
Menthae piperitae aetheroleum	Peppermint oil. Administered orally for gastrointestinal disorders, applied topically for mild headaches and inhaled or sprayed into the mouth to relieve coughs and colds. ECHA: notified H411, H412.	An environmental risk cannot be excluded.	No
Menthol	Organic compound obtained from the oils of mints. ECHA: notified no hazard declared. SDS: hazard H402.	An environmental risk cannot be excluded.	No
Mepivacaine	Used as a local anaesthetic. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Mercaptamine hydrochloride	Used for the treatment of corneal cystine crystal deposits in cystinosis. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: notified toxic to aquatic life.	An environmental risk cannot be excluded.	No
Metamizole	A pyrazolone derivative used as an analgesic and antipyretic. ECHA: notified H412, H413.	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
Methionine	A nutraceutical, a micronutrient and an antidote to paracetamol poisoning. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Methyl nicotinate	Used as a rubefacient for muscle and joint pain and in veterinary medicine, to treat respiratory diseases, vascular disorders and rheumatoid arthritis. ECHA: notified no hazard declared. SDS: hazard H402.	An environmental risk cannot be excluded.	No
Methylprednisolone	A glucocorticoid, used for its anti-inflammatory and immunosuppressive effects. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Methylprednisolone is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.	Potential risk(s) are identified due to ED properties under criterion a), and the substance is not needed with regards criterion c).	No
Methyl salicylate	Used as a flavouring agent and as a rubefacient and analgesic for acute joint and muscular pain. ECHA: harmonised and notified H412.	An environmental risk cannot be excluded.	No
Millefolii herba	A non-homeopathic herbal. Yarrow Flower; reported antibacterial and anti-inflammatory effects. ECHA: notified H411.	An environmental risk cannot be excluded.	No
Mineral hydrocarbons, low to high viscosity including micro-crystalline waxes, approximately C10-C60, aliphatic, branched aliphatic and	Liquid paraffin. Used for constipation and in cosmetics. ECHA: notified H410, H411, H413.	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
alicyclic compounds			
Myristicae aetheroleum	Nutmeg oil. Used for pain and swelling, to improve sleep, digestion, heart health and for respiratory issues. ECHA: notified H400, H410.	An environmental risk cannot be excluded.	No

N

Substance	Data available on toxicity	Conclusion	Include in list
Neostigmine	Quaternary ammonium compound (carbamates), used for the treatment of gastrointestinal stasis, myasthenia gravis and as an antidote to curare in animals. Cholinesterase activity inhibitor. ECHA: notified H411.	An environmental risk cannot be excluded.	No
Nickel sulphate	Essential element; used in cases of nickel deficiency. ECHA: harmonised and notified H400, H410.	An environmental risk cannot be excluded.	No
Nickel gluconate	Essential element; used in cases of nickel deficiency. ECHA: harmonised and notified H400, H410.	An environmental risk cannot be excluded.	No
Nicoboxil	Ester of nicotinic acid (niacin) and 2-butoxyethanol. Used in combination with nonivamide as rubefacient in liniments. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Nonivamide	Synthetic analogue of capsaicin, for topical use only. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

o

Substance	Data available on toxicity	Conclusion	Include in list
Octenidine dihydrochloride	Antiseptic, used for skin and mucosal disinfection and short-term antiseptic wound treatment. ECHA: notified H400, H410, H412.	An environmental risk cannot be excluded.	No
Omeprazole	Benzimidazole, inhibitor of gastric secretion in animals and humans. For treatment of gastric ulcers in horses. ECHA: notified H412, H411.	An environmental risk cannot be excluded.	No
Ornithine	A non-proteinogenic α-amino acid that plays a role in the urea cycle. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Orotic acid	An intermediate in the de-novo synthetic pathway for pyrimidines. It used as a mineral carrier in some dietary supplements to increase their bioavailability. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Oxalic acid	An organic acid with the chemical formula (COOH)2. ECHA: notified no hazard declared. EPA: GHS Data H402, H412.	An environmental risk cannot be excluded.	No
Oxytocin	A peptide hormone and neuropeptide normally produced in the hypothalamus and released by the posterior pituitary. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: hazard H413. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Oxytocin plays an important role in reproduction of animal species, including fish. The substance can also be used to reduce aggressive behaviors in some species (Alvarenga	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.

Substance	Data available on toxicity	Conclusion	Include in list
	Oliveira et al. 2022; Mennigen et al. 2022). The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		

P

Substance	Data available on toxicity	Conclusion	Include in list
Pancreatin	Enzyme, used to treat malabsorption syndrome due to certain pancreatic problems. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Papain	Protease enzyme. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: while hazards H402, H412 are declared in one SDS it is not clear if due to papain component. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Papaverine	Benzylisoquinoline alkaloid that has a role as a vasodilator agent and an antispasmodic drug. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Paracetamol	Analgesic of the class of phenols. ECHA: notified H411, H412, H413.	An environmental risk cannot be excluded.	No
Peforelin	Gonadotropin-releasing hormone agonist (GnRH agonist). ECHA: notified no hazard declared. EPA: no hazard declared. SDS: not found. Literature: no hazard identified. PBT or ED: hormone-like activity.	Potential risk(s) due to ED properties are identified under criterion a), and the substance is not needed with regards criterion c).	No

Substance	Data available on toxicity	Conclusion	Include in list
	Ad-hoc assessment in relation to criterion c): Peforelin is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.		
Pegylated bovine granulocyte colony stimulating factor	Cytokine; stimulates the bone marrow to produce granulocytes and stem cells and release them into the bloodstream, which results in neutrophilia. ECHA: not found. EPA: not found. SDS: not found. Literature: no hazard identified. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Pegylated bovine granulocyte colony stimulating factor is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.	Potential risk(s) due to ED properties are identified under criterion a), and the substance is not needed with regards criterion c).	No
Pepsin	Enzyme; endopeptidase that breaks down proteins into smaller peptides and amino acids. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Phenol	Aromatic organic compound. ECHA: notified H400, H410, H411, H412.	An environmental risk cannot be excluded.	No
Phenylalanine	Essential aromatic amino acid. ECHA: notified L-phenylalanine and DL-phenylalanine no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Phloroglucinol	Organic compound used as antispasmodic. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Phytomenadione	Vitamin K1. ECHA: notified H413.	An environmental risk cannot be excluded.	No
Piceae turiones recentes extractum	Essential oil manufactured from *Picea abies*. ECHA: notified H410, H410.	An environmental risk cannot be excluded.	No
Piperonyl butoxide	Organic compound used as a component of pesticide formulations. ECHA: harmonised H400, H410 notified H400, H410, H411.	An environmental risk cannot be excluded.	No
Policresulen	Polycondensation product of meta-cresolsulfonic acid and phenol, used as a topical haemostatic and antiseptic. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: hazard toxic aquatic effects cannot be excluded.	An environmental risk cannot be excluded.	No
Poloxamer	Non-ionic triblock copolymer. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Polysorbate 80	Hydrophilic non-ionic surfactant. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Polysulphated glycosaminoglycan	Long, linear polysaccharides consisting of repeating disaccharide units. ECHA: not found. EPA: not found. SDS: not found Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Potassium DL-aspartate	Salt form of aspartic acid, an amino acid. ECHA: not found. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Potassium glycerophosphate	Salt formed from glycerophosphoric acid and potassium. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Potassium nitrate	Chemical compound consisting of potassium and nitrate ions. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Prednisolone	Glucocorticoid. ECHA: notified H411. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Prednisolone is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures of hormonal nature in food-producing aquatic species.	Potential risk(s) due to ED properties are identified under criterion a), and the substance is not needed with regards criterion c).	No
Pregnant mare serum gonadotrophin (PMSG)	Gonadotropic hormone produced in the chorion of pregnant mares. ECHA: not found. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard declared. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Pregnant mare serum gonadotrophin has been used in research and fish reproduction. There is proved effectiveness of inducing ovulation in frogs when added in the aquatic environment (Sakai et al. 1087; Ogawa et al. 2011; Mellisa et al. 2019; Hutagalung et al. 2015; Putra et al. 2017). The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.

Substance	Data available on toxicity	Conclusion	Include in list
Procaine	Benzoate ester, local anaesthetic. ECHA: notified no hazard declared. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Progesterone	An endogenous steroid and progestogen sex hormone. ECHA: notified H410. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Progesterone and its analogs are important for fish reproduction (Zohar et al. 2010; Schulz et al. 2010; Muñoz-Cueto et al. 2020). The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.
Proline	Amino acid. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Propylene glycol	Synthetic liquid substance that absorbs water. ECHA: not found. EPA: GHS data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
***Pyrethrum* extract**	Extracted from the dried flowers of *Chrysanthemum cinerariaefolium*. ECHA: notified H400, H410.	An environmental risk cannot be excluded.	No

Q

Substance	Data available on toxicity	Conclusion	Include in list
Quercus cortex	A non-homeopathic herbal. AKA Oak bark from the trees *Quercus robus*, *Quercus petraea* and *Quercus*	From the available information, a risk to	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	pubescens. Used for inflammatory conditions, diarrhoea and respiratory conditions. ECHA: Quercus robur and Quercus petraea no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	the environment was not identified.	
***Quillaia* saponins**	A natural aqueous extract obtained from the Chilean soapbark tree *Quillaja Saponaria.* ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no	From the available information, a risk to the environment was not identified.	Yes

R

Substance	Data available on toxicity	Conclusion	Include in list
R-Cloprostenol	As for cloprostenol. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): Cloprostenol has been increasingly recognised for its role in reproductive management in various animal species, including fish. In fish, cloprostenol has been shown to influence reproductive parameters significantly. For instance, Sato et al. investigated the effects of cloprostenol in the South American fish species *Piaractus mesopotamicus*, demonstrating that the administration of this prostaglandin analogue during hypophysation (a common method for inducing ovulation) resulted in a notable resumption and progression of meiosis, alongside altered	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.

Substance	Data available on toxicity	Conclusion	Include in list
	circulating steroid levels (Sato et al. 2020). This suggests that cloprostenol not only facilitates ovulation but also plays a crucial role in the maturation of oocytes, which is essential for successful breeding programs in aquaculture. The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
***Rhei radix*, standardised extracts and preparations thereof**	A non-homeopathic herbal. Common name Rhubarb root. Used for short term constipation relief. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Romifidine	A sedative used in veterinary medicine. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Rosmarini aetheroleum	A non-homeopathic herbal. Common name Rosemary oil. Used for hair growth, pain relief and as a parasite repellent. ECHA: notified H400, H410, H411.	An environmental risk cannot be excluded.	No
Rosmarini folium	A non-homeopathic herbal. Rosemary leaves. Used orally for gastrointestinal disorders and topically for muscle and join pain. Same as *Rosmarini aetheroleum*.	An environmental risk cannot be excluded.	No
Ruscus aculeatus	A non-homeopathic herbal. AKA Butcher's broom. Traditionally used as a diuretic, a laxative and to reduce swellings. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

S

Substance	Data available on toxicity	Conclusion	Include in list
Salicylic acid	Used as a food preservative, bactericide, as a treatment for warts, psoriasis and ringworm and in skincare products. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Salviae folium	A non-homeopathic herbal. Common name Sage leaf. Reported antioxidant activity, used for oral conditions such as cold sores and to reduce menopause symptoms. ECHA: notified H400, H410, H411, H412.	An environmental risk cannot be excluded.	No
Sambuci flos	A non-homeopathic herbal. Common name elder flower. Used to relieve constipation and sinusitis. ECHA: no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Serine	An amino acid. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Sodium chlorite	An oxidising agent, it is used to clean drinking water and in toothpastes and mouthwashes ECHA: notified H400, H410, H412.	An environmental risk cannot be excluded.	No
Sodium dichloroisocyanurate	Used as a cleaning agent and disinfectant. ECHA: harmonised and notified H400, H410.	An environmental risk cannot be excluded.	No
Sodium glycerophosphate	A source of phosphate in total parenteral nutrition. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Sodium hypophosphite	A feed additive; used in pharmaceutical manufacturing as an emulsifier or stabiliser. ECHA: notified no hazard declared.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
Sodium nitrite	Used as a food preservative and antidote to cyanide poisoning. ECHA: harmonised H400 notified H400, H412, H411.	An environmental risk cannot be excluded.	No
Sodium selenate	Administered to prevent exudative diathesis in chicks, white muscle disease in sheep and infertility in ewes ECHA: notified H400, H410.	An environmental risk cannot be excluded.	No
Sodium selenite	Administered to supplement selenium and for the treatment of selenium deficiency diseases, such as white muscle disease in cattle and pigs. ECHA: harmonised H411 notified H400, H411, H412.	An environmental risk cannot be excluded.	No
Sodium thiosulphate	Used as an antidote to cyanide poisoning, a nephroprotective agent and an antifungal. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Sodium cromoglycate	A mast cell stabilizer with anti-inflammatory activity. Administered as prophylactic treatment of allergic and exercise-induced asthma. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Sodium propionate	Used as an antifungal drug and a food preservative. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Sodium salicylate	NSAID. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared.	An environmental risk cannot be excluded.	No

Substance	Data available on toxicity	Conclusion	Include in list
	SDS: hazard H402.		
Sorbitan sesquioleate	A surfactant and emulsifier. ECHA: no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Sulfogaiacol	Used as an expectorant. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Sulphur	Used for dermatological conditions such as eczema, chronic atopic dermatitis and pruritus, and to relieve itching of ringworm and fungus infections of dogs and cats. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Symphyti radix	A non-homeopathic herbal. Common name comfrey root. Used to alleviate the symptoms of minor sprains and bruises. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

T

Substance	Data available on toxicity	Conclusion	Include in list
Tanninum albuminatum	Combination of tannins – tannic acid (tannin) and protein – albumin. Antidiarrheal. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Terebinthinae aetheroleum rectificatum	Common names: turpentine oil, pine oil. Produced by distillation from the turpentine (balsam) mainly from pines (Pinus spp.) and larch (Larix). ECHA: harmonised H411 and notified H410, H411.	An environmental risk cannot be excluded.	No
Terebinthinae laricina	An alcoholic extract of Larix decidua resin.	From the available information, a risk	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	ECHA: notified no hazard declared. EPA: not found. SDS: not found. Literature: no hazard identified. PBT or ED: no.	to the environment was not identified.	
Terpin hydrate	An expectorant, commonly used to loosen mucus and ease congestion in patients presenting with acute or chronic bronchitis, and related pulmonary conditions. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Tetracaine	An amino-ester class local anaesthetic. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Theophylline	Also known as 1,3-dimethylxanthine. It inhibits phosphodiesterase and blocks adenosine receptors. ECHA: notified no hazard declared. EPA: GHS Data H402.	An environmental risk cannot be excluded.	No
Thioctic acid	Also known as alpha-lipoic acid (ALA). An organosulfur compound derived from caprylic acid (octanoic acid). ECHA: notified H411, H412.	An environmental risk cannot be excluded.	No
Thiopental sodium	A rapid-onset short-acting barbiturate general anaesthetic. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Threonine	An amino acid that is used in the biosynthesis of proteins. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Thymi aetheroleum	Essential oil obtained by steam distillation from parts of the thyme plant. ECHA: notified H411.	An environmental risk cannot be excluded.	No
Thymol	A monoterpenoid phenol found naturally in oil extracted from *Thymus vulgaris L.*, commonly known as thyme, and many other plants. ECHA: harmonised H411.	An environmental risk cannot be excluded.	No
Tiliae flos	Commonly known as lime flower: whole dry flowers obtained from *Tilia platyphyllos Scop.*, *Tilia cordata Mill.*, *Tilia x vulgaris Hayne,* or their mixture. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: not found. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Tiludronic acid (in the form of disodium salt)	A first-generation bisphosphonate similar to etidronic acid and clodronic acid. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Toldimfos	An aromatic phosphorus compound which falls between phosphorous itself and phosphoric acid in the stages of oxidation. ECHA: notified [sodium salt] no hazard declared. EPA: not found.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
Tolfenamic acid	A member of the anthranilic acid derivatives (or fenamate) class of NSAID drugs. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Trichlormethiazide	A diuretic with properties similar to those of hydrochlorothiazide. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Trimethylphloroglucinol	Organic compound used as antispasmodic. ECHA: not found. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Triptorelin acetate	Agonist analogue of gonadotropin-releasing hormone (GnRH), repressing expression of luteinizing hormone (LH) and follicle-stimulating hormone (FSH). ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: hormone-like activity. Ad-hoc assessment in relation to criterion c): As a GnRH agonist, it is important for fish reproduction (Mylonas and Zohar, 2000; Nyuji	Despite the potential risk(s) due to ED properties identified under criterion a), the substance is needed with regards criterion c).	Yes The substance shall be administered by injection only.

Substance	Data available on toxicity	Conclusion	Include in list
	et al. 2019; Mylonas et al. 2020; Zepeda et al. 2020; Fakriadis et al. 2020). The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Trypsin	A serine protease found in the digestive system of many vertebrates, where it hydrolyzes proteins. ECHA: notified H400.	An environmental risk cannot be excluded.	No
Tryptophan	An α-amino acid and a precursor to the neurotransmitter serotonin, melatonin, and vitamin B3. ECHA: DL-tryptophan and L-tryptophan no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Tyrosine	Non-essential amino acid with a polar side group. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

U

Substance	Data available on toxicity	Conclusion	Include in list
Urea	Important role in the cellular metabolism of nitrogen-containing compounds by animals and is the main nitrogen-containing substance in the urine of mammals. ECHA: notified H413.	An environmental risk cannot be excluded.	No
Uridine and its 5'-mono-5'-di-	Uridine is a pyrimidine nucleoside, that consists of uracil and ribose. Uridine and its 5'-mono-5'-di- and 5'-	From the available information, a risk to	Yes

Substance	Data available on toxicity	Conclusion	Include in list
and 5'-triphosphates	triphos- phates are esters of pyrophosphoric acid with the nucleoside uridine. ECHA: notified uridine and 5'-diphosphate no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	the environment was not identified.	
Urticae herba	AKA nettle. A perennial flowering plant used for relief of minor articular pain and to increase the amount of urine to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints. Botanical name: *Urtica dioica L., Urtica urens L.* ECHA: notified Urtica dioica and Urtica urens no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

V

Substance	Data available on toxicity	Conclusion	Include in list
Valine	An amino acid. ECHA: notified L-Valine, D-Valine no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Vedaprofen	A NSAID used in veterinary medicine. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Vetrabutine hydrochloride	A spasmolytic agent which has been used in obstetrics. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	Literature: no hazard identified. PBT or ED: no.		
Vincamine	Used for the treatment of primary degenerative and vascular dementia. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Vitamin A	AKA retinol. Fat-soluble vitamin. ECHA: notified no hazard declared. EPA: GHS Data H413.	An environmental risk cannot be excluded.	No
Vitamin B12	AKA cobalamin. Water-soluble vitamin. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Vitamin B2	AKA Riboflavin. Water-soluble vitamin. ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Vitamin B3	AKA Niacin, Nicotinic acid, niacinamide. Water-soluble vitamin. ECHA: notified H412.	An environmental risk cannot be excluded.	No
Vitamin B5	AKA Pantothenic acid. Water-soluble vitamin. ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Vitamin B6	AKA Pyridoxine. Water-soluble vitamin. ECHA: notified [pyridoxine hydrochloride] H411.	An environmental risk cannot be excluded.	No
Vitamin D	AKA calciferol. A fat-soluble vitamin. ECHA: notified D3 H413, D2 no hazard declared.	An environmental risk cannot be excluded.	No
Vitamin E	AKA tocopherols. Fat-soluble vitamin. ECHA: notified H413.	An environmental risk cannot be excluded.	No

W

Substance	Data available on toxicity	Conclusion	Include in list
Wool alcohols	Lanolin. Used as a softener/conditioner in cosmetics and steroid creams. ECHA: notified H413.	An environmental risk cannot be excluded.	No

X

Substance	Data available on toxicity	Conclusion	Include in list
Xylazine hydrochloride	A clonidine analogue used as a non-opioid tranquilizer in veterinary medicine and as an emetic, especially in cats. ECHA: notified H412.	An environmental risk cannot be excluded.	No

Y

Substance	Data available on toxicity	Conclusion	Include in list
none			

Z

Substance	Data available on toxicity	Conclusion	Include in list
Zinc acetate	An acetate salt in which the cationic component is zinc(2+). ECHA: notified H411, H400, H410.	An environmental risk cannot be excluded.	No
Zinc aspartate	A salt of zinc with the amino acid aspartic acid. ECHA: notified H411.	An environmental risk cannot be excluded.	No
Zinc chloride	Inorganic chemical compound with the formula $ZnCl_2 \cdot nH_2O$. ECHA: harmonised and notified H400, H410.	An environmental risk cannot be excluded.	No
Zinc gluconate	The zinc salt of gluconic acid. ECHA: notified H400, H410.	An environmental risk cannot be excluded.	No
Zinc oxide	Inorganic compound with the formula ZnO. ECHA: harmonised and notified H400, H410.	An environmental risk cannot be excluded.	No
Zinc sulphate	Inorganic compound with the formula $ZnSO_4$ and historically known as "white vitriol". ECHA: notified H400, H410.	An environmental risk cannot be excluded.	No

Miscellaneous

Substance	Data available on toxicity	Conclusion	Include in list
2-Aminoethanol	A naturally occurring organic chemical compound. ECHA: notified H412.	An environmental risk cannot be excluded.	No
8-Hydroxyquinoline	An organic compound derived from the heterocycle quinoline. ECHA: harmonised H400, H410 notified H400, H410, H412.	An environmental risk cannot be excluded.	No
Probiotic components including bacteria and yeasts	Live microorganisms which when administered in adequate amounts confer a health benefit on the host. Assessment using the proposed methodology cannot be conducted due to the broad and non-specific nature of the entry 'probiotic components including bacteria and yeasts'. Conclusion is based solely on literature search. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Stem cells - Chondrogenic induced equine allogeneic peripheral blood-derived mesenchymal stem cells - alisvetcel	Stem cells derived from a donor horse and treated to promote cartilage-forming (chondrogenic) properties. These cells are used to reduce mild to moderate recurrent lameness associated with non-septic joint inflammation in horses. ECHA: not found. EPA: not found. SDS: not found. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes
Stem cells - Equine umbilical cord-derived mesenchymal stem cells	Stem cells derived from the umbilical cord of donor horses. These cells are used to reduce lameness associated with osteoarthritis in horses and dogs. ECHA: not found. EPA: not found. SDS: not found. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Substance	Data available on toxicity	Conclusion	Include in list
Stem cells - Tenogenic primed equine allogeneic peripheral blood-derived mesenchymal stem cells - tesrivetcel	Stem cells derived from a donor horse's peripheral blood that have been treated to promote tendon regeneration. They are used to improve healing of injuries of tendons and suspensory ligaments in horses. ECHA: not found. EPA: not found. SDS: not found. Literature: no hazard identified. PBT or ED: no.	From the available information, a risk to the environment was not identified.	Yes

Annex 5.2.3: Assessment of antibacterials, antiparasitics and antifungals not identified by aquaculture sector as important for the treatment of food-producing aquatic species

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1. Introduction

According to the mandate provided by EC, the overall objective of Regulation (EU) 2019/6 is to increase the availability of veterinary medicinal products, while guaranteeing the highest standards of public and animal health and environmental protection. When considering the criteria laid down in Article 114(3), any risks to the environment from the treatment of food-producing aquatic species (criterion (a)) is a key consideration for the assessment of eligible substances that have no identified important use in aquaculture. It is recognised that the potential risks to the environment as a consequence of the exposure of the environment due to the use of these substances according to Article 114(1) cannot be addressed, as there are several data gaps that cannot be covered (i.e. dose and target species). Therefore, it was agreed that the environmental risk assessment would be focused on the potential hazards of these substances due to their inherent properties. Criterion (b) as laid down in Article 114(3) is only applicable for the antibacterials in this sub-group of substances. With regards criterion (c), this sub-group of substances is deemed of relevance with regards providing for availability of medicinal products, treatments or measures, as even though recognised as not important for treatment of fish, their pharmacological activity indicates potential usefulness for such purpose.

The detailed methodology for each criterion laid down in Article 114(3) is as follows:

2. Methodology

Criterion (a) risk to environment

As already indicated, the methodological approach for assessing these substances pertains to the environmental hazard identification. In doing so, each substance was searched for in the databases of ECHA (European Chemicals Agency), EPA (Environmental Protection Agency), and in safety data sheets (SDS), to determine whether it has been classified under any of the following statements according to CLP regulation:

H400 – Very toxic to aquatic life.

H410 – Very toxic to aquatic life with long lasting effects.

H411 – Toxic to aquatic life with long lasting effects.

H412 – Harmful to aquatic life with long lasting effects.

H413 – May cause long lasting harmful effects to aquatic life.

The following statements specific to GHS were also considered:

H401 – Toxic to aquatic life.

H402 – Harmful to aquatic life.

PubChem was used to find synonyms for the substances.

When the search in the above-mentioned databases did not retrieve a hazard endpoint, an additional (final) step for hazard identification involved searching the published literature to identify any indication of potential risk of the substance to the aquatic environment. Parallel consideration was also given on whether the substance is recognised as PBT or ED; indication of such properties would exclude the substance from the list. The above-mentioned search process stopped at the first indication of any environmental hazard.

For the antiparasitics, it was agreed that there is no need to assess against thresholds, since a risk of these substances for the environment cannot be excluded due to the nature of the antiparasitic

activity. However, for information purposes only, the stepwise approach for hazard identification, as outlined above, was applied in the assessment of antiparasitics. It should be noted that the CLP statements on aquatic toxicity (H400, H410, H411, H412, H413, H401, H402) are based on toxicity observed in three types of organisms: fish, crustaceans and algae. They do not capture the toxicity of anthelmintics for worms.

Criterion (b) related to antimicrobials listed in accordance with Article 107(6)

Some antibacterials in this sub-group of substances are either not recommended for use under Article 114 in the scientific advice under Article 107(6) or are recommended for use under Article 114 for individual animals only, in this scientific advice. A 'Yes' in the relevant column of the assessment against criterion (b) means the antibacterial is subject to one of the two restrictions above. A 'No' means it is not.

Criterion (c) related to availability of alternatives

When an issue related to criterion (a) [i.e. hazard to environment is identified] and/or (b) [i.e. the substance is mentioned in the scientific advice related to Article 107(6)] was identified, the substance was assessed against criterion (c) [i.e. availability of alternatives]. Such assessment was conducted by ATCvet groups rather than by individual substances. With regards antiparasitics, as indicated above, the key element for the assessment of these substances was the availability of alternatives, as it is considered that for these substances an issue related to criterion (a) cannot be excluded, and criterion (b) is not applicable.

Conclusion

When there was no issue related to criteria (a) and (b), no further assessment with regards criterion (c) is warranted and the conclusion is proposed as follows: "From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6)", and the substance is recommended to be included in the list. When there was an issue with criteria (a) and/or (b), the substance was assessed against criterion (c). The conclusion is then as follows: "Despite the risk(s) identified under <criterion a)> <criterion b)> <criteria a) and b)>, the substance is needed with regards criterion c)", and the substance was recommended for inclusion in the list with risk mitigation measures (RMM) if needed, or "Risk(s) are identified under <criterion a)> <criterion b)> <criteria a) and b)>, and the substance is not needed with regards criterion c)", and the substance is recommended to not be included in the list.

Assessment template

The above-mentioned steps are summarised in the tables below, which represent the assessment templates:

Antibacterials

Substance	Assessment against mandate criteria		Conclusion	Include in list
<Substance>	<Brief introductory text>		If no issue with (a) nor (b), conclude: <From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6).> If issue with (a) or (b), conclude: <Despite the risk(s) identified under <criterion a)> <criterion b)> <criteria a) and b)>, the substance is needed with regards criterion c).> OR <Risk(s) are identified under <criterion a)> <criterion b)> <criteria a) and b)>, and the substance is not needed with regards criterion c).>	<Yes> OR Indicate: <Yes, and add RMM if needed > OR <No>
	<ATCvet>			
	<AMEG>			
	Criterion (a)	- Hazard from ECHA - Hazard from EPA - Hazard from SDS - Hazard from published literature - Consider PBT or ED.		
	Criterion (b)	<Yes> <No>		
	Criterion (c)	If issue with (a) or (b), assess against (c) per ATCVet group and consider the alternatives; otherwise, add 'N/A'.		

Antiparasitics

Substance	Assessment against mandate criteria		Conclusion	Include in list
<Substance>	<Brief introductory text>		Conclude: <Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).> OR <Risk(s) are identified under criterion a), and the substance is not needed with regards criterion c).>	Indicate: <Yes, and add RMM if needed > OR <No>
	<ATCvet>			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *- Hazard from ECHA* *- Hazard from EPA* *- Hazard from SDS* *- Hazard from published literature* *- Consider PBT or ED*		
	Criterion (b)	N/A		

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (c)	Since there is always issue with (a), assess against (c) per ATCVet group and mention the alternatives		

Antifungals

Substance	Assessment against mandate criteria		Conclusion	Include in list
<Substance>	<Brief introductory text>		If no issue with (a), conclude: <From the available information, a risk to the environment was not identified.> If issue with (a), Conclude: <Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).> OR <Risk(s) are identified under criterion a), and the substance is <u>not</u> needed with regards criterion c).>	Indicate: <Yes> OR Indicate: <Yes, and add RMM if needed > OR <No>
	<ATCvet>			
	Criterion (a)	- Hazard from ECHA - Hazard from EPA - Hazard from SDS - Hazard from published literature - Consider PBT or ED.		
	Criterion (b)	N/A		
	Criterion (c)	If issue with (a), assess against (c) per ATCVet group and mention the alternatives; otherwise, add 'N/A'.		

3. Assessment

Antibacterials

Substance	Assessment against mandate criteria		Conclusion	Include in list
Ampicillin	Extended spectrum aminopenicillin.		Despite the risk(s) identified under criteria a) and b), the substance is needed with regards to criterion c).	Yes Ampicillin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.
	QJ01CA Penicillins with extended spectrum			
	AMEG category D			
	Criterion (a)	ECHA: notified H400, H411.		
	Criterion (b)	Yes, if in combination with beta-lactamase inhibitor: "Not to be used in food-producing aquaculture". If the substance cannot be used in combination with a beta-		

Substance	Assessment against mandate criteria		Conclusion	Include in list
		lactamase inhibitor, the impact on animal and public health is considered negligible.		When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1µg/L[1] is required before discharge in the environment. Ampicillin shall not be used in combination with beta-lactamase inhibitors.
	Criterion (c)	Substance has some intrinsic properties which indicate a potential risk to the environment, however, there is not sufficient information available to conclude that other antimicrobial substances from this group would represent a lower environmental risk. There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Apramycin	Aminoglycoside antibiotic for veterinary use.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Apramycin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while
	QJ01G Aminoglycoside antibacterials			
	AMEG category C			
	Criterion (a)	ECHA: notified H410.		
	Criterion (b)	No		
	Criterion (c)	This substance would not be used as a first-choice antibiotic.		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1µg/L[1] is required before discharge in the environment.
Bacitracin	Polypeptide antibiotic; a mixture of related cyclic peptides produced by *Bacillus licheniformis* bacteria. It is used against gram-positive bacteria.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Bacitracin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or
	QJ01XX Other antibacterials			
	AMEG category D			
	Criterion (a)	ECHA: notified H411.		
	Criterion (b)	No		
	Criterion (c)	Substance has some intrinsic properties which indicate a potential risk to the environment, however, there is not sufficient information available to conclude that other		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		antimicrobial substances from this group would represent a lower environmental risk. There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. Although several groups of antibiotics are effective against gram-positive bacteria, availability of cyclic polypeptides, being a unique group of antibiotics, is valuable for the aquaculture sector. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1µg/L[1] is required before discharge in the environment.
Benzylpenicillin	AKA[2] Penicillin G. A natural penicillin used to treat infections caused by gram-positive bacteria.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Benzylpenicillin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.
	QJ01CE Beta-lactamase sensitive penicillins			
	AMEG category D			
	Criterion (a)	ECHA: notified H400, H412.		
	Criterion (b)	No		
	Criterion (c)	Substance has some intrinsic properties which indicate a		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

[2] AKA: Also known as

Substance	Assessment against mandate criteria		Conclusion	Include in list
		potential risk to the environment, however, there is not sufficient information available to conclude that other antimicrobial substances from this group would represent a lower environmental risk. There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1µg/L[1] is required before discharge in the environment.
Cefacetrile	Broad-spectrum first-generation cephalosporin against gram-positive and gram-negative bacteria.		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6). However, as per Regulation (EU) 2022/1255, the combination of cephalosporin with beta-lactamase inhibitors is reserved for treatment of certain infections in humans.	Yes Cefacetrile shall not be used in combination with beta-lactamase inhibitors.
	QJ01DB or QJ51DB First-generation cephalosporins			
	AMEG category C			
	Criterion (a)	ECHA: no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		
	Criterion (c)	N/A		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
Cefalexin	First-generation cephalosporin against gram-positive and gram-negative bacteria.		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6). However, as per Regulation (EU) 2022/1255, the combination of cephalosporin with beta-lactamase inhibitors is reserved for treatment of certain infections in humans.	Yes Cefalexin shall not be used in combination with beta-lactamase inhibitors.
	QJ01DB or QJ51DB First-generation cephalosporins			
	AMEG category C			
	Criterion (a)	ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		
	Criterion (c)	N/A		
Cefalonium	A first-generation cephalosporin used in veterinary medicine.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c). Also, as per Regulation (EU) 2022/1255, the combination of cephalosporin with beta-lactamase inhibitors is reserved for treatment of certain infections in humans.	Yes Cefalonium is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that
	QJ01DB or QJ51DB First-generation cephalosporins			
	AMEG category C			
	Criterion (a)	ECHA: notified H400, H411.		
	Criterion (b)	No		
	Criterion (c)	Substance has some intrinsic properties which indicate a potential risk to the environment, however, there is not sufficient information available to conclude that other antimicrobial substances from this group would represent a lower environmental risk. There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are		

Substance	Assessment against mandate criteria		Conclusion	Include in list
		unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		the substance is present at concentration levels lower than 1µg/L[1] is required before discharge in the environment. Cefalonium shall not be used in combination with beta-lactamase inhibitors.
Cefapirin	A broad-spectrum first-generation cephalosporin against gram-positive and gram-negative bacteria.		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6). However, as per Regulation (EU) 2022/1255, the combination of cephalosporin with beta-lactamase inhibitors is reserved for treatment of certain infections in humans.	Yes Cefapirin shall not be used in combination with beta-lactamase inhibitors.
	QJ01DB or QJ51DB First-generation cephalosporins			
	AMEG category C			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		
	Criterion (c)	N/A		
Cefazolin	Broad-spectrum cephalosporin mainly used for the treatment of skin bacterial infections and other moderate to severe bacterial infections in the lung, bone, joint, stomach, blood, heart valve, and urinary tract.		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6). However, as per Regulation (EU) 2022/1255, the combination of cephalosporin with beta-lactamase inhibitors is	Yes Cefazolin shall not be used in combination with beta-lactamase inhibitors.
	QJ01DB or QJ51DB First-generation cephalosporins			
	AMEG category C			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared.		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	reserved for treatment of certain infections in humans.	
	Criterion (b)	No		
	Criterion (c)	N/A		
Cefoperazone	Broad-spectrum cephalosporin used for the treatment of bacterial infections in various locations, including the respiratory tract, abdomen, skin, and female genital tracts.		Despite the risk(s) identified under criteria a) and b), the substance is needed with regards criterion c). Also, as per Regulation (EU) 2022/1255, the combination of cephalosporin with beta-lactamase inhibitors is reserved for treatment of certain infections in humans.	Yes Cefoperazone is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1µg/L[1] is required before discharge in the environment.
	QJ01DD Third-generation cephalosporins			
	AMEG category B			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: In comparison with the control group, the first laying and the first pregnancy of *Daphnia magna* were both delayed by amoxicillin, cefoperazone, and aztreonam and number of births per generation, number of generations, survival length and total birth number of *D. magna* were also decreased as affected by the three β-lactam antibiotics (Linjun et al., 2020).		
	Criterion (b)	Yes: "Not to be used in food-producing aquaculture"; "To be used in individual animals only". If the substance cannot be used the impact on animal health is considered high.		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (c)	Substance has some intrinsic properties which indicate a potential risk to the environment, however, there is not sufficient information available to conclude that other antimicrobial substances from this group would represent a lower environmental risk. There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. Specifically, cefoperazone is not to be used as first choice treatment and is to be used only in individual animals (e.g. broodstock or similar). The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		Cefoperazone shall be used in individual animals only. Cefoperazone shall not be used in combination with beta-lactamase inhibitors.
Cefquinome	Beta-lactamase resistant cephalosporin used in veterinary medicine.		Despite the risk(s) identified under criteria a) and b), the substance is needed with regards criterion c). Also, as per Regulation (EU) 2022/1255, the combination of cephalosporin with beta-lactamase inhibitors is reserved for treatment of certain infections in humans.	Yes Cefquinome is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.
	QJ01DE Fourth-generation cephalosporins			
	AMEG category B			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: hazard H400, H410.		
	Criterion (b)	Yes: "Not to be used in food-producing aquaculture"; "To be		

Substance	Assessment against mandate criteria		Conclusion	Include in list
		used in individual animals only". If the substance cannot be used the impact on animal health is considered high.		When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment. Cefquinome shall be used in individual animals only. Cefquinome shall not be used in combination with beta-lactamase inhibitors.
	Criterion (c)	Substance has some intrinsic properties which indicate a potential risk to the environment, however, there is not sufficient information available to conclude that other antimicrobial substances from this group would represent a lower environmental risk. There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. Specifically, cefquinome is not to be used as first choice treatment and is to be used only in individual animals (e.g. broodstock or similar). The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Ceftiofur	Beta-lactamase resistant cephalosporin used in veterinary medicine. QJ01DD Third-generation cephalosporins AMEG category B		Despite the risk(s) identified under criteria a) and b), the substance is needed with regards criterion c). Also, as	Yes Ceftiofur is expected to be harmful to the aquatic environment and must only

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (a)	ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: Ceftiofur and its presumable hydrolysis products induced deleterious effects in *Daphnia magna* (48 h EC50 139, LC50 179 in µM), which was not observed with Scenedesmus spec. (Ribeiro et al., 2018).	per Regulation (EU) 2022/1255, the combination of cephalosporin with beta-lactamase inhibitors is reserved for treatment of certain infections in humans.	be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment. Ceftiofur shall be used in individual animals only. Ceftiofur shall not be used in combination with beta-lactamase inhibitors.
	Criterion (b)	Yes: "Not to be used in food-producing aquaculture"; "To be used in individual animals only". If the substance cannot be used the impact on animal health is considered high.		
	Criterion (c)	Substance has some intrinsic properties which indicate a potential risk to the environment, however, there is not sufficient information available to conclude that other antimicrobial substances from this group would represent a lower environmental risk. There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. Specifically, ceftiofur is not to be used as first choice treatment and is to be used only in individual animals (e.g. broodstock or similar). The		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Cloxacillin	Semisynthetic penicillinase-resistant penicillin used primarily for the treatment of gram-positive aerobic cocci.		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6).	Yes
	QJ01CF Beta-lactamase resistant penicillins			
	AMEG category D			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		
	Criterion (c)	N/A		
Colistin	AKA polymyxin E; cyclic polypeptide antibiotic from *Bacillus colistinus*. It is used in treatment against gram-negative bacteria in many livestock species and humans.		Risk(s) are identified under criteria a) and b), and the substance is not needed with regards criterion c).	No
	QJ01XB Polymyxins			
	AMEG category B			
	Criterion (a)	ECHA: no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	Yes: "Not to be used in food-producing aquaculture"; "Human medicinal products should be administered to individual animals only". If the substance		

Substance	Assessment against mandate criteria		Conclusion	Include in list
		cannot be used, the impact on animal and public health is considered negligible.		
	Criterion (c)	Colistin has reportedly been used in aquaculture in Vietnam (Hedberg et al. 2018; Rico et al. 2013) but the rationale behind usage of colistin remains unclear. Considering the extremely low bioavailability of colistin, the indications allowing for successful use of colistin in aquaculture seem to be limited to gram-negative enteropathogenic bacteria. Evidence based literature supporting the usage of colistin to treat diseases in food-producing aquatic animals seems to be lacking, however. The substance is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Danofloxacin	Fluoroquinolone used in veterinary medicine.		Despite the risk(s) identified under criteria a) and b), the substance is needed with regards criterion c).	Yes Danofloxacin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.
	QJ01MA Fluoroquinolones			
	AMEG category B			
	Criterion (a)	ECHA: notified H412.		
	Criterion (b)	Yes: "When the proposed route of administration is outside the terms of the SPC, or when using an extemporaneous formulation, the product should be administered to individual animals only"; Human medicinal		

Substance	Assessment against mandate criteria		Conclusion	Include in list
		products should be administered to individual animals, only". If the substance cannot be used in animals other than individual animals, the impact on animal health is considered high.		When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Dicloxacillin	Narrow-spectrum penicillin used against gram-positive bacteria.		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6).	Yes
	QJ01CF Beta-lactamase resistant penicillins			
	AMEG category D			
	Criterion (a)	ECHA: no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		
	Criterion (c)	N/A		
Difloxacin	Second-generation, synthetic fluoroquinolone used in veterinary medicine.		Despite the risk(s) identified under criterion b), the	Yes
	QJ01MA Fluoroquinolones			

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
	AMEG category B		substance is needed with regards criterion c).	Difloxacin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	Criterion (a)	ECHA: no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	Yes: "When the proposed route of administration is outside the terms of the SPC, or when using an extemporaneous formulation, the product should be administered to individual animals only"; Human medicinal products should be administered to individual animals, only". If the substance cannot be used in animals other than individual animals, the impact on animal health is considered high.		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Dihydrostreptomycin	A derivative of streptomycin; an aminoglycoside antibiotic.		From the available information, a risk to the environment was not identified. Moreover, there is	Yes
	QJ01G Aminoglycoside antibacterials			
	AMEG category C			

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (a)	ECHA: no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	no restriction related to scientific advice under Article 107(6).	
	Criterion (b)	No		
	Criterion (c)	N/A		
Gamithromycin	Macrolide antibacterial used in veterinary medicine.		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6).	Yes
	QJ01FA Macrolides			
	AMEG category C			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		
	Criterion (c)	N/A		
Kanamycin	An aminoglycoside antibiotic produced by the fermentation of *Streptomyces kanamyceticus.*		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6).	Yes
	QJ01G Aminoglycoside antibacterials			
	AMEG category C			
	Criterion (a)	ECHA: no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		
	Criterion (c)	N/A		

Substance	Assessment against mandate criteria		Conclusion	Include in list
Marbofloxacin	A carboxylic acid derivative; third-generation fluoroquinolone antibiotic.		Despite the risk(s) identified under criteria a) and b), the substance is needed with regards criterion c).	Yes Marbofloxacin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	QJ01MA Fluoroquinolones			
	AMEG category B			
	Criterion (a)	ECHA: notified H412.		
	Criterion (b)	Yes: "When the proposed route of administration is outside the terms of the SPC, or when using an extemporaneous formulation, the product should be administered to individual animals only"; Human medicinal products should be administered to individual animals, only". If the substance cannot be used in animals other than individual animals, the impact on animal health is considered high.		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Mecillinam	Extended-spectrum penicillin antibiotic of the amidinopenicillin class.		Risk(s) are identified under criterion a), and the	No
	QJ01CA Penicillins with extended spectrum			

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
	AMEG category A		substance is not needed with regards criterion c).	
	Criterion (a)	ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: Mecillinam was highly toxic to the cyanobacterium *Microcystis aeruginosa* (EC50 5-60 microg/L) (Halling-Sørensen et al., 2000).		
	Criterion (b)	No		
	Criterion (c)	The substance is not needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Nafcillin	A narrow-spectrum penicillin, resistant to beta-lactamase.		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6).	Yes
	QJ01CF Beta-lactamase resistant penicillins			
	AMEG category D			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		
	Criterion (c)	N/A		
Natamycin	A polyene amphoteric macrolide antibiotic with antifungal properties.		From the available information, a risk to the environment was not identified. Moreover, there is	Yes
	N/A			
	N/A			

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (a)	ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.	no restriction related to scientific advice under Article 107(6).	
	Criterion (b)	No		
	Criterion (c)	N/A		
Novobiocin	AKA albamycin; an aminocoumarin antibiotic that is produced by the actinomycete *Streptomyces niveus.* It is considered a narrow-spectrum antibiotic, effective against mostly gram-positive bacteria.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Novobiocin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	QJ01XX Other antibacterials			
	N/A			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: environmental concentrations of novobiocin caused general stress and produced changes on biomarkers tested in *Corbicula fluminea* (Aguirre-Martínez et al., 2015). Novobiocin induced significant biomarker responses and DNA damage in crabs at environmentally relevant concentrations, indicating its potential aquatic toxicity (Aguirre-Martínez et al., 2013).		
	Criterion (b)	No		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. Studies on the efficacy of novobiocin in treatment of bacterial infections in food producing aquatic species seem to be absent in online-accessible sources. However, being such a unique group of antibiotics, having an aminocoumarin treatment option available seems to be of value for food-producing aquatic animals. In a recent study by Mehdi et al. (2020) novobiocin was found to be effective in vitro against multiple potentially pathogenic Vibrio isolates originating from black-lipped pearl oysters, while resistant against the more conventionally used antibiotics ampicillin, erythromycin, streptomycin, and oxacillin (Mehdi et al. 2020). The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Oxacillin	A second-generation penicillin, resistant to inactivation by penicillinases. QJ01CF Beta-lactamase resistant penicillins		From the available information, a risk to the environment was not	Yes

Substance	Assessment against mandate criteria		Conclusion	Include in list
	AMEG category D		identified. Moreover, there is no restriction related to scientific advice under Article 107(6).	
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		
	Criterion (c)	N/A		
Paromomycin	A broad-spectrum aminoglycoside antibiotic produced by *Streptomyces rimosus var. paromomycinus*.		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6).	Yes
	QJ01G Aminoglycoside antibacterials			
	AMEG category C			
	Criterion (a)	ECHA: no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		
	Criterion (c)	N/A		
Penethamate	An ester of benzylpenicillin (penicillin G).		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6).	Yes
	QJ01CE Beta-lactamase sensitive penicillins			
	AMEG category D			
	Criterion (a)	ECHA: not found. EPA: no hazard declared. SDS: not found. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (c)	N/A		
Phenoxymethylpenicillin	AKA penicillin V and penicillin VK, used mainly for treatment of strep throat, otitis media, and cellulitis.		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6).	Yes
	QJ01CE Beta-lactamase sensitive penicillins			
	AMEG category D			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		
	Criterion (c)	N/A		
Pirlimycin	A lincosamide antibiotic, used to treat mastitis in cattle.		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6).	Yes
	QJ51FF Lincosamides			
	AMEG category C			
	Criterion (a)	ECHA: notified [pirlimycin HCL] no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		
	Criterion (c)	N/A		
Rifaximin	A rifamycin-based non-systemic antibiotic used for the treatment of gastrointestinal bacterial infections.		Despite the risk(s) identified under criteria a) and b), the substance is needed with regards criterion c).	Yes Rifaximin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally
	N/A			
	AMEG category C			

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (a)	ECHA: notified H400, H410.		harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	Criterion (b)	Yes: "Conditions apply to use of human medicinal products, extemporaneous preparations and VMPs authorised in third countries, only. They do not apply to EU-authorised VMPs containing rifaximin; […] To be used in individual animals only". If the substance cannot be used in animals other than individual the impact on animal health is considered high.		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Spiramycin	Macrolide antibiotic used in veterinary and human medicine.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Spiramycin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that
	QJ01FA Macrolides			
	AMEG category C			
	Criterion (a)	ECHA: notified H411, H410.		
	Criterion (b)	No		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
Streptomycin	The first discovered aminoglycoside antibiotic, originally isolated from *Streptomyces griseus.*		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6).	Yes
	QJ01G Aminoglycoside antibacterials			
	AMEG category C			
	Criterion (a)	ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		
	Criterion (c)	N/A		
	Sulfonamide antibiotic.			Yes

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
Sulfonamides (all substances belonging to the sulfonamide group) - Sulfamethizole	QJ01E or QA07AB Sulfonamides and trimethoprim		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Sulfamethizole is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	AMEG category D			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: hazard H410. Literature: Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Sulfonamides (all substances belonging to the sulfonamide group) - Sulfadimidine	AKA sulfamethazine. A sulfonamide antibiotic.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Sulfadimidine is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental
	QJ01E or QA07AB Sulfonamides and trimethoprim			
	AMEG category D			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: hazard H402.		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		Literature: Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Sulfonamides (all substances belonging to the sulfonamide group) - Sulfapyridine	Sulfonamide antibiotic.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Sulfapyridine is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment
	QJ01E or QA07AB Sulfonamides and trimethoprim			
	AMEG category D			
	Criterion (a)	ECHA: notified H411. Literature: Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
Sulfonamides (all substances belonging to the sulfonamide group) - Sulfafurazole	AKA sulfisoxazole. A sulfonamide antibiotic.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Sulfafurazole is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at
	QJ01E or QA07AB Sulfonamides and trimethoprim			
	AMEG category D			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: Sulpha antibiotics can induce toxicity in aquatic animals. They can induce oxidative stress in fish by affecting antioxidant enzyme activity, potentially disrupting the cellular redox state. They can also accumulate in fish tissues, with high concentrations leading to teratogenic and lethal effects (Zhou et al. 2022). Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
Sulfonamides (all substances belonging to the sulfonamide group) - Sulfanilamide	Sulfonamide antibiotic. QJ01E or QA07AB Sulfonamides and trimethoprim AMEG category D		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Sulfanilamide is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: Sulpha antibiotics can induce toxicity in aquatic animals. They can induce oxidative stress in fish by affecting antioxidant enzyme activity, potentially disrupting the cellular redox state. They can also accumulate in fish tissues, with high concentrations leading to teratogenic and lethal effects (Zhou et al. 2022). Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (b)	No		the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Sulfonamides (all substances belonging to the sulfonamide group) - Sulfathiazole	Sulfonamide antibiotic.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Sulfathiazole is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a
	QJ01E or QA07AB Sulfonamides and trimethoprim			
	AMEG category D			
	Criterion (a)	ECHA: notified H412. Literature: Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		there is lack of availability of other treatments or measures in food-producing aquatic species.		recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
Sulfonamides (all substances belonging to the sulfonamide group) - Sulfamethoxazole	Sulfonamide antibiotic.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Sulfamethoxazole is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[2] is required before discharge in the environment.
	QJ01E or QA07AB Sulfonamides and trimethoprim			
	AMEG category D			
	Criterion (a)	ECHA: notified H400, H410, H411. Literature: Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38
[2] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
Sulfonamides (all substances belonging to the sulfonamide group) - Sulfadimethoxine	Sulfonamide antibiotic.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Sulfadimethoxine is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	QJ01E or QA07AB Sulfonamides and trimethoprim			
	AMEG category D			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: Sulpha antibiotics can induce toxicity in aquatic animals. They can induce oxidative stress in fish by affecting antioxidant enzyme activity, potentially disrupting the cellular redox state. They can also accumulate in fish tissues, with high concentrations leading to teratogenic and lethal effects (Zhou et al. 2022). Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		other treatments or measures in food-producing aquatic species.		
Sulfonamides (all substances belonging to the sulfonamide group) - Sulfamethoxypyridazine	Sulfonamide antibiotic.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Sulfamethoxypyridazine is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	QJ01E or QA07AB Sulfonamides and trimethoprim			
	AMEG category D			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: Sulpha antibiotics can induce toxicity in aquatic animals. They can induce oxidative stress in fish by affecting antioxidant enzyme activity, potentially disrupting the cellular redox state. They can also accumulate in fish tissues, with high concentrations leading to teratogenic and lethal effects (Zhou et al. 2022). Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		there is lack of availability of other treatments or measures in food-producing aquatic species.		
Sulfonamides (all substances belonging to the sulfonamide group) - Sulfamerazine	Sulfonamide antibiotic.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Sulfamerazine is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	QJ01E or QA07AB Sulfonamides and trimethoprim			
	AMEG category D			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: Sulpha antibiotics can induce toxicity in aquatic animals. They can induce oxidative stress in fish by affecting antioxidant enzyme activity, potentially disrupting the cellular redox state. They can also accumulate in fish tissues, with high concentrations leading to teratogenic and lethal effects (Zhou et al. 2022). Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Sulfonamides (all substances belonging to the sulfonamide group) - Sulfamethizole	Sulfonamide antibiotic.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Sulfamethizole is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	QJ01E or QA07AB Sulfonamides and trimethoprim			
	AMEG category D			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: hazard H410. Literature: Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Sulfonamides (all substances belonging to the sulfonamide group) - Sulfachlorpyridazine	Sulfonamide antibiotic.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Sulfachlorpyridazine is expected to be harmful to the aquatic environment
	QJ01E or QA07AB Sulfonamides and trimethoprim			
	AMEG category D			

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: Sulpha antibiotics can induce toxicity in aquatic animals. They can induce oxidative stress in fish by affecting antioxidant enzyme activity, potentially disrupting the cellular redox state. They can also accumulate in fish tissues, with high concentrations leading to teratogenic and lethal effects (Zhou et al. 2022). Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Sulfonamides (all substances belonging to	Sulfonamide antibiotic.		Despite the risk(s) identified under criterion a), the	Yes
	QJ01E or QA07AB Sulfonamides and trimethoprim			

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
the sulfonamide group) - Sulfaquinoxaline	AMEG category D		substance is needed with regards criterion c).	Sulfaquinoxaline is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: Sulpha antibiotics can induce toxicity in aquatic animals. They can induce oxidative stress in fish by affecting antioxidant enzyme activity, potentially disrupting the cellular redox state. They can also accumulate in fish tissues, with high concentrations leading to teratogenic and lethal effects (Zhou et al. 2022). Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
	Sulfonamide antibiotic.			Yes

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
Sulfonamides (all substances belonging to the sulfonamide group) - Sulfamerazine	QJ01E or QA07AB Sulfonamides and trimethoprim		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Sulfamerazine is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	AMEG category D			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: Sulpha antibiotics can induce toxicity in aquatic animals. They can induce oxidative stress in fish by affecting antioxidant enzyme activity, potentially disrupting the cellular redox state. They can also accumulate in fish tissues, with high concentrations leading to teratogenic and lethal effects (Zhou et al. 2022). Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
Sulfonamides (all substances belonging to the sulfonamide group) - Sulfamonomethoxine	Sulfonamide antibiotic.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Sulfamonomethoxine is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	QJ01E or QA07AB Sulfonamides and trimethoprim			
	AMEG category D			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: Sulpha antibiotics can induce toxicity in aquatic animals. They can induce oxidative stress in fish by affecting antioxidant enzyme activity, potentially disrupting the cellular redox state. They can also accumulate in fish tissues, with high concentrations leading to teratogenic and lethal effects (Zhou et al. 2022). Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		other treatments or measures in food-producing aquatic species.		
Sulfonamides (all substances belonging to the sulfonamide group) - Sulfacetamide	Sulfonamide antibiotic.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Sulfacetamide is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	QJ01E or QA07AB Sulfonamides and trimethoprim			
	AMEG category D			
	Criterion (a)	ECHA: notified no hazard declared. EPA: GHS Data no hazard declared. SDS: no hazard declared. Literature: Sulpha antibiotics can induce toxicity in aquatic animals. They can induce oxidative stress in fish by affecting antioxidant enzyme activity, potentially disrupting the cellular redox state. They can also accumulate in fish tissues, with high concentrations leading to teratogenic and lethal effects (Zhou et al. 2022). Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		there is lack of availability of other treatments or measures in food-producing aquatic species.		
Sulfonamides (all substances belonging to the sulfonamide group) - Formosulfathiazole	Sulfathiazole polymer with formaldehyde. Intrauterine use in cows.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Formosulfathiazole is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	QJ01E or QA07AB Sulfonamides and trimethoprim			
	AMEG category D			
	Criterion (a)	ECHA: not found EPA: not found SDS: not found Literature: Sulpha antibiotics can induce toxicity in aquatic animals. They can induce oxidative stress in fish by affecting antioxidant enzyme activity, potentially disrupting the cellular redox state. They can also accumulate in fish tissues, with high concentrations leading to teratogenic and lethal effects (Zhou et al. 2022). Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		there is lack of availability of other treatments or measures in food-producing aquatic species.		
Sulfonamides (all substances belonging to the sulfonamide group) - Phthalylsulfathiazole	Sulfonamide antibiotic.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Phthalylsulfathiazole is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	QJ01E or QA07AB Sulfonamides and trimethoprim			
	AMEG category D			
	Criterion (a)	ECHA: notified H412. Literature: Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Sulfonamides (all substances belongingto the sulfonamide group) - Sulfaguanidine	Sulfonamide antibiotic.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Sulfaguanidine is expected to be harmful to the aquatic environment
	QJ01E or QA07AB Sulfonamides and trimethoprim			
	AMEG category D			

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (a)	ECHA: notified H411. Literature: Sulfonamides are toxic to plants (Białk-Bielińska et al. 2011).		and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Tetracycline	Antibiotic in the tetracyclines family.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Tetracycline is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.
	QJ01AA Tetracyclines			
	AMEG category D			
	Criterion (a)	ECHA: notified H411.		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. Two substances in the tetracycline group are authorised for food producing fish in the EU: chlortetracycline (CTC) and oxytetracycline (OTC). For CTC no notifications are included in the ECHA database. For OTC the statements H400 and H410 are included, and for OTC hydrochloride H400, H410 and H411 are included. It can therefore be assumed that tetracycline is less – or at least not more – harmful for the environment than OTC, which is nevertheless authorised for food producing fish. It is furthermore considered that the range of antimicrobials to be available for use in food producing fish in accordance with Article 114 should be as broad as possible. The use of tetracycline would be limited, as CTC and OTC would be first choice when a substance in the tetracycline group is considered the best treatment option. It is nevertheless considered that tetracycline should be available for use in the few potential situations when the use of this substance is		When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		considered necessary and prudent. Overall, the potential environmental exposure from use of tetracycline in food producing fish is considered to be low. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Tiamulin	Pleuromutilin antibiotic used in veterinary medicine particularly for pigs and poultry.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Tiamulin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at
	QJ01XQ Pleuromutilins			
	AMEG category C			
	Criterion (a)	ECHA: notified H413.		
	Criterion (b)	No		
	Criterion (c)	This substance would not be used as a first-choice antibiotic. There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		

Substance	Assessment against mandate criteria		Conclusion	Include in list
				concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
Tildipirosin	A macrolide antibiotic used in pigs and cattle.		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6).	Yes
	QJ01FA Macrolides			
	AMEG category C			
	Criterion (a)	ECHA: notified no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		
	Criterion (c)	N/A		
Tilmicosin	A macrolide antibiotic used in veterinary medicine.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Tilmicosin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment
	QJ01FA Macrolides			
	AMEG category C			
	Criterion (a)	ECHA: notified H410, H400.		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		there is lack of availability of other treatments or measures in food-producing aquatic species.		b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
Tulathromycin	A macrolide antibiotic used in cattle, sheep and pigs.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Tulathromycin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[2]
	QJ01FA Macrolides			
	AMEG category C			
	Criterion (a)	ECHA: notified H412, H400, H410.		
	Criterion (b)	No		
	Criterion (c)	There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38
[2] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
				is required before discharge in the environment.
Tylvalosin	A macrolide antibiotic used in poultry and pigs.		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6).	Yes
	QJ01FA Macrolides			
	AMEG category C			
	Criterion (a)	ECHA: no hazard declared. EPA: no hazard declared. SDS: no hazard declared. Literature: no hazard identified. PBT or ED: no.		
	Criterion (b)	No		
	Criterion (c)	N/A		
Valnemulin	Pleuromutilin antibiotic used in pigs and rabbit.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Valnemulin is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system
	QJ01XQ Pleuromutilins			
	AMEG category C			
	Criterion (a)	ECHA: notified [valnemulin HCL] H400, H410.		
	Criterion (b)	No		
	Criterion (c)	This substance would not be used as a first-choice antibiotic. There is only limited number of antibacterials authorised in food-producing aquatic species. There is a need for several antibacterial substances in case the more commonly used substances are unavailable, and to be able to choose the substance according to situation. The substance is needed to treat or prevent infectious disease, for which there is lack of availability of		

Substance	Assessment against mandate criteria		Conclusion	Include in list
		other treatments or measures in food-producing aquatic species.		c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.

Antiparasitics

Substance	Assessment against mandate criteria		Conclusion	Include in list
Abamectin	A broad-spectrum parasiticide in the avermectins family used in veterinary medicine.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP54 Endectocides			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: harmonised and notified H400, H410.*		
	Criterion (b)	N/A		
	Criterion (c)	Abamectin could potentially be used against ecto- and endoparasites in fish. However, there seems to be no published information on therapeutic use in fish, and accordingly no established dosage regimen. On the other hand, there are many publications on risk for the aquatic environment, including fish toxicity. In SPCs of authorised products abamectin is characterised as extremely dangerous to fish and aquatic life.		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		There are limited alternatives available for use in food producing aquatic species. However, the substance emamectin from the same group is found in products authorised for food producing fish.		
Albendazole oxide	A broad-spectrum anthelmintic and antiprotozoal agent of the benzimidazole type.		Albendazole oxide is the pharmacologically active substance of albendazole. Albendazole was assessed as substance identified as important for the treatment of food-producing aquatic species and recommended to be included in the list. Despite the risk(s) identified under criterion a), the substance is recommended to be included in the list.	Yes Albendazole oxide is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	QP52 Anthelmintics			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified H400, H410.*		
	Criterion (b)	N/A		
	Criterion (c)	Albendazole oxide is the pharmacologically active substance of albendazole. Albendazole was assessed as substance identified as important for the treatment of food-producing aquatic species and recommended to be included in the list. The substance is needed to treat or prevent parasitic disease, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
	A broad-spectrum insecticide.			No

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
Alphacyper-methrin and cypermethrin	QP53 Ectoparasiticides, Insecticides and Repellents		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: harmonised and notified H400, H410.* *Cypermethrin, alpha-cypermethrin, beta-cypermethrin, theta-cypermethrin and zeta-cypermethrin is included in the list of priority substances of the Water Framework Directive (Directive 2000/60/EC).*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species. Another substance in the same group, deltamethrin, is included in a VMP authorised for fish. Cypermethrin is not expected to add significant benefits for treatment of fish parasites		
Amitraz	Non-systemic acaricide and insecticide.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP53 Ectoparasiticides, Insecticides and Repellents			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: harmonised and notified H400, H410.*		
	Criterion (b)	N/A		

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Clorsulon	Anthelmintic, used against the adult forms of parasitic flatworms in cattle.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	N/A			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified no hazard declared.* *EPA: GHS Data no hazard declared.* *SDS: no hazard declared.* *Literature: in combination with ivermectin, toxic to rainbow trout (Santamarina et al., 1991).* *PBT or ED: no.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Closantel	Halogenated salicylanilide with anti-parasitic activity.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP52 Anthelmintics			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified H410, H400.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		

Substance	Assessment against mandate criteria		Conclusion	Include in list
Coumafos	A non-volatile, fat-soluble phosphorothioate with ectoparasiticide properties.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP53 Ectoparasiticides, Insecticides and Repellents			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: harmonised and notified H400, H410.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Cyfluthrin	Pyrethroid insecticide and common household pesticide.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP53 Ectoparasiticides, Insecticides and Repellents			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: harmonised and notified H400, H410.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species		
Derquantel	A semi-synthetic paraherquamide analogue and nematocide.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion	No
	N/A			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity.		

Substance	Assessment against mandate criteria		Conclusion	Include in list
		For information: *ECHA: not found.* *EPA: not found.* *SDS: no hazard declared.* *Literature: ERMA New Zealand has classified derquantel as being harmful to aquatic environment (ERMA200037 E and R Report).*	a), the substance cannot be included in the list.	
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Diazinon	Non-systemic organophosphate insecticide.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP53 Ectoparasiticides, Insecticides and Repellents			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: harmonised and notified H400, H410.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Diclazuril	A coccidiostat, used in veterinary medicine for the control of coccidiosis.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP51 Antiprotozoals			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified H400, H410.*		

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Dicyclanil	Insecticide used for the prevention in blowfly strike in sheep.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP53 Ectoparasiticides, Insecticides and Repellents			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified H411, H412.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Doramectin	A broad-spectrum parasiticide in the avermectins family used in veterinary medicine.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP54 Endectocides			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified H400, H410.*		
	Criterion (b)	N/A		
	Criterion (c)	Doramectin is structurally closely related to ivermectin. It could potentially be used against endo- and ectoparasites in fish. There are some publications on use as an antiparasitic in some fish species, e.g. against *Lernaea cyprinacea* in carp and against Argulus. In SPCs of authorised		

Substance	Assessment against mandate criteria		Conclusion	Include in list
		products doramectin is characterised as "very toxic to aquatic organisms and may accumulate in sediments". There are limited alternatives available for use in food producing aquatic species. However, the substance emamectin from the same group is found in products authorised for food producing fish.		
Eprinomectin	A broad-spectrum antiparasitic of the avermectins family used in veterinary medicine.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP54 Endectocides			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. A serious risk for the environment is indicated in several authorized VMPs. ***For information:*** *ECHA: notified H400, H410.*		
	Criterion (b)	N/A		
	Criterion (c)	Eprinomectin is closely related to emamectin, an avermectin which is found in VMPs authorised for food producing fish. Like emamectin, eprinomectin is more water soluble than other avermectins, which leads to less passage over the blood-brain barrier in fish. There are several publications on adverse environmental effects, but no information seems to be available on therapeutic use in fish or appropriate dosage. In SPCs for authorised products emamectin is characterised as "very toxic to dung fauna and aquatic organisms, is persistent in soils and may accumulate in sediments."		

Substance	Assessment against mandate criteria		Conclusion	Include in list
		There are limited alternatives available for use in food producing aquatic species. However, the substance emamectin from the same group is found in products authorised for food producing fish.		
Febantel	An antiparasitic that interferes with carbohydrate metabolism in parasitic worms.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP52 Anthelmintics			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified H400, H410.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Flumethrin	A pyrethroid insecticide.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP53 Ectoparasiticides, Insecticides and Repellents			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified H410, H400.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Fluralaner	A systemic insecticide and acaricide that is administered orally or topically.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified	No
	QP53 Ectoparasiticides, Insecticides and Repellents			

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified H410, H400.*	need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Halofuginone	A coccidiostat used in cattle.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP51 Antiprotozoals			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified [lactate salt] H400, H410.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Imidocarb	Urea derivative used in veterinary medicine as an antiprotozoal agent.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Imidocarb is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected.
	QP51 Antiprotozoals			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified no hazard declared.* *EPA: GHS Data no hazard declared.* *SDS: no hazard declared.* *Literature: no hazard identified.* *PBT or ED: no.*		

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (b)	N/A		When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	Criterion (c)	Only 4 other antiprotozoals are proposed to be included in the list. The substance is needed to treat or prevent a disease or certain indication, for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Monepantel	An anthelmintic used in sheep and cattle to control gastrointestinal nematodes.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP52 Anthelmintics			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: not found.* *EPA: no hazard declared.* *SDS: no hazard declared.* *Literature: no hazard identified.* *PBT or ED: no.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Morantel	A broad-spectrum nematocide used in lactating cattle, goat and sheep.		Even though there are limited alternative antiparasitics available	No

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
	QP52 Anthelmintics		for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: no hazard declared.* *EPA: no hazard declared.* *SDS: no hazard declared.* *Literature: Morantel was baseline toxicant in the bioluminescence inhibition test with Vibrio fischeri and a test for inhibition of photosynthesis in green algae. (Escher et al., 2008).*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Moxidectin	A broad-spectrum parasiticide in the avermectins family used in veterinary medicine.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a) including PBT properties, the substance cannot be included in the list.	No
	QP54 Endectocides			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. *Moxidectin is a **PBT substance**, EMA* ***For information:*** *ECHA: notified H400, H410.*		
	Criterion (b)	N/A		
	Criterion (c)	Moxidectin could potentially be effective against fish parasites. Limited alternatives are available for use in food producing aquatic species. However, another avermectin (emamectin) is authorised for use in food producing fish. Moxidectin fulfils the criteria for a (very) persistent,		

Substance	Assessment against mandate criteria		Conclusion	Include in list
		bioaccumulative and toxic (PBT) substance; therefore, exposure of the environment to moxidectin must be limited to the extent possible. There are limited alternatives available for use in food producing aquatic species.		
Netobimin	A pro-benzimidazole anthelmintic used in cattle, sheep and goats.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP52 Anthelmintics			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified no hazard declared.* *EPA: GHS Data no hazard declared.* *SDS: no hazard declared.* *Literature: no hazard identified.* *PBT or ED: no.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Nitroxinil	An anthelmintic used in veterinary medicine against parasitic worms in sheep and cattle.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP52 Anthelmintics			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified H400, H412.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		

Substance	Assessment against mandate criteria		Conclusion	Include in list
Oxibendazole	A benzimidazole anthelminthic.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP52 Anthelmintics			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified no hazard declared.* *EPA: no hazard declared.* *SDS: no hazard declared.* *Literature: Oxibendazole was tested against infection of rainbow trout by Gyrodactylus, and was found toxic at dose levels (Tojo et al., 1992).*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Oxyclozanide	A salicylanilide anthelmintic.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP52 Anthelmintics			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified H400, H410, H413.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Permethrin	A synthetic pyrethroid.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion	No
	QP53 Ectoparasiticides, Insecticides and Repellents			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity.		

Substance	Assessment against mandate criteria		Conclusion	Include in list
		For information: *ECHA: harmonised and notified H400, H410.*	a), the substance cannot be included in the list.	
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Phoxim	An organophosphate insecticide.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP53 Ectoparasiticides, Insecticides and Repellents			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: harmonised and notified H400, H410.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Piperazine	An anthelminthic drug that selectively blocks the neuromuscular cholinergic receptors of worms.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP52 Anthelmintics			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified H410.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		

Substance	Assessment against mandate criteria		Conclusion	Include in list
Pyrantel embonate	An anthelminthic used to treat a number of parasitic worm infections e.g. ascariasis, hookworm infections, enterobiasis, trichinellosis.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP52 Anthelmintics			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified H412.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Rafoxanide	A salicylanilide anthelminthic.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP52 Anthelmintics			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified H413.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Tau fluvalinate	The (2R) diastereomers of fluvalinate, a synthetic pyrethroid insecticide.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP53 Ectoparasiticides, Insecticides and Repellents			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: harmonised and notified H400, H410.*		

Substance	Assessment against mandate criteria		Conclusion	Include in list
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Thiabendazole	A benzimidazole anthelmintic.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP52 Anthelmintics			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: harmonised and notified H400, H410.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		
Triclabendazole	An anthelmintic used to treat fascioliasis.		Even though there are limited alternative antiparasitics available for food-producing aquatic species, considering the lack of an identified need for the substance, and in view of the serious environmental concerns identified under criterion a), the substance cannot be included in the list.	No
	QP52 Anthelmintics			
	Criterion (a)	A risk for the environment cannot be excluded, due to the nature of antiparasitic activity. ***For information:*** *ECHA: notified H410, H413.*		
	Criterion (b)	N/A		
	Criterion (c)	There are limited alternatives available for use in food producing aquatic species.		

Antifungals

Substance	Assessment against mandate criteria		Conclusion	Include in list
Enilconazole	A fungicide widely used in agriculture, and in veterinary medicine as a topical antimycotic.		Despite the risk(s) identified under criterion a), the substance is needed with regards criterion c).	Yes Enilconazole is expected to be harmful to the aquatic environment and must only be used if other, less environmentally harmful treatment options are not available. If the substance can be used by multiple application methods, the method that will result in the lowest environmental exposure while achieving a satisfactory therapeutic effect must be selected. When possible, any treatment shall take place in a closed system with: a) removal or inactivation of the substance in used treatment water or solid waste before discharge into the environment b) if (a) is not possible, contaminated water should be released into a recognised wastewater treatment system c) if neither (a) nor (b) are possible, dilution of contaminated water so that the substance is present at concentration levels lower than 1 µg/L[1] is required before discharge in the environment.
	QD01AC Imidazole and triazole derivatives			
	Criterion (a)	ECHA: harmonised H410 notified H400, H410.		
	Criterion (b)	N/A		
	Criterion (c)	Substance has some intrinsic properties which indicate a potential risk to the environment, however, there is not sufficient information available to conclude that other antifungal substances from this group would represent a lower environmental risk. There is a need for several antifungal substances with different modes of action in cases of fungal infections in food producing aquatic organisms. Specifically, enilconazole is used in veterinary medicine as topical treatment for dermatophyte infections. It is not currently used in food producing aquatic animals, but its mode of action suggests potential effectiveness against aquatic pathogenic fungi. There is limited alternative available for use in food producing aquatic species. The substance is needed to treat or prevent fungal disease for which there is lack of availability of other treatments or measures in food-producing aquatic species.		
Parconazole	Broad-spectrum imidazole derivative with antifungal activity.		From the available information, a risk to the environment was not identified. Moreover, there is no restriction related to scientific advice under Article 107(6).	Yes
	QD01AC Imidazole and triazole derivatives			
	Criterion (a)	ECHA: no hazard declared. EPA: no hazard declared. SDS: not found. Literature: no hazard identified.		

[1] from Guideline on environmental impact assessment for VMPs in support of the VICH GL6 and GL38

Substance	Assessment against mandate criteria		Conclusion	Include in list
		PBT or ED: no.		
	Criterion (b)	N/A		
	Criterion (c)	N/A		

Annex 5.2.4: Assessment of homeopathic substances not identified by aquaculture sector as important for the treatment of food-producing aquatic species

1. Introduction

The homeopathic substances assessed in this report are the eligible homeopathic substances. They were not identified by aquaculture sector as important for the treatment of food-producing aquatic species. As indicated in the mandate provided by EC, the overall objective of the VMP regulation is to increase the availability of veterinary medicinal products, while ensuring the highest standards of public and animal health and environmental protection. The assessment of the environmental risk of homeopathic substances is based on the expected very low exposure, independently of their inherent properties i.e. hazards.

2. Methodology

- **Criterion (a) risk to environment**

Due to the high level of dilution of these substances in homeopathic veterinary medicinal products and in homeopathic medicinal product for human use, the concentrations of these substances in the environment - when used under Article 114 of Regulation (EU) 2019/6 for the treatment of food-producing aquatic species - are expected to be very low. Consequently, it is considered that there is negligible risk to the aquatic environment.

These substances shall be used under homeopathic conditions (specified in Table 1 of the Annex of Regulation (EU) No 37/2010) and consequently the exposure of the environment to these substances is very low. As a general principle, the 'Other provisions' of Table 1 of Regulation (EU) No 37/2010 also apply to the use under Article 114 of Regulation (EU) 2019/6. For homeopathic substances, these 'Other provisions' restrict the use to homeopathic veterinary medicinal products and sometimes to concentration limits.

- **Criterion (b) related to antimicrobials listed in accordance with Article 107(6) of Regulation (EU) 2019/6**

None of these substances is an antimicrobial recommended for restrictions in the Agency's scientific advice under Article 107(6) of Regulation (EU) 2019/6.

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- **Criterion (c) related to availability of alternatives**

Since there is no issue related to criterion (a) or (b) [i.e. negligible hazard to environment is expected, and there is no mention in the scientific advice related to Article 107(6)], there is no need to consider criterion (c) and the substances can be included in the list.

- **Conclusion**

The conclusion is as follows: the risk to the environment is considered negligible, and the substance is recommended for inclusion in the list.

The recommendation includes the following specific condition: The substance shall be used in line with the homeopathic conditions specified in Table 1 of the Annex of Regulation (EU) No 37/2010.

Note: this recommendation to include the substance in the list does not factor the usefulness for food-producing aquaculture.

- **Assessment template**

The above is summarised in this tabulated assessment template:

Substance	Data available on toxicity	Conclusion	Include in list
<Substance>	<Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use>	<The risk to the environment is considered negligible>	<Yes>

3. Assessment

The table below applies the assessment template of section 2.

Substance	Data available on toxicity	Conclusion	Include in list
Adonis vernalis	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Aesculus hippocastanum	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Agnus castus	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Ailanthus altissima	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal	The risk to the environment is	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	products and in homeopathic medicinal products for human use	considered negligible	
Allium cepa	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Apocynum cannabinum	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Artemisia abrotanum	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Atropa belladonna	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Bellis perennis	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Calendula officinalis	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Camphora	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Cardiospermum halicacabum	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Convallaria majalis	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal	The risk to the environment is considered negligible	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	products and in homeopathic medicinal products for human use		
Crataegus	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Echinacea	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Eucalyptus globulus	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Euphrasia officinalis	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Ginkgo biloba	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Ginseng	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Hamamelis virginiana[1]	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Harpagophytum procumbens	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Harunga madagascariensis	Not applicable, due to the high level of dilution of the substance in	The risk to the environment is	Yes

[1] *Hamamelis virginiana* is also eligible as herbal non-homeopathic substance (see the relevant assessment concluding also to inclusion in the list)

Substance	Data available on toxicity	Conclusion	Include in list
	homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	considered negligible	
Hypericum perforatum	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Lobaria pulmonaria	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Okoubaka aubrevillei	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Phytolacca americana	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Prunus laurocerasus	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Selenicereus grandiflorus	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Serenoa repens	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Silybum marianum	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Solidago virgaurea	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal	The risk to the environment is	Yes

Substance	Data available on toxicity	Conclusion	Include in list
	products and in homeopathic medicinal products for human use	considered negligible	
Substances used in homeopathic veterinary medicines	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Syzygium cumini	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Thuja occidentalis	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Turnera diffusa	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Urginea maritima	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Virola sebifera	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes
Viscum album	Not applicable, due to the high level of dilution of the substance in homeopathic veterinary medicinal products and in homeopathic medicinal products for human use	The risk to the environment is considered negligible	Yes

Condition applicable to all eligible homeopathic substances: The substance shall be used in homeopathic conditions specified in Table 1 of the Annex of Regulation (EU) 37/2010.