

Annex I

List of the names, pharmaceutical forms, strengths of the veterinary medicinal products, animal species, route of administration, applicant in the Member States

Member State EU/EEA	Applicant	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Austria	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml Pour-on Lösung zum Übergießen für Rinder und Schafe	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Belgium	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml Solution pour-on pour bovins et ovins	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Belgium	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 100 mg Solution spot-on pour bovins	Deltamethrin	10 mg/ml	Spot-on solution	Cattle	Topical use
Bulgaria	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Делтанил 10 мг/мл пурон разтвор, предназначен за говеда и овце.	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Cyprus	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml Διάλυμα για επίχυση για βοοειδή και πρόβατα	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Czech Republic	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml pour-on roztok pro aplikaci na kůži skotu a ovčí	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Denmark	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml Pour-on opløsning til kvæg og får	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use

Member State EU/EEA	Applicant	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Estonia	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil, 10 mg/ml, kriipsususpensioon veistele ja lammastele	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
France	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml Solution pour-on pour bovins et ovins	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
France	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 100 mg Solution spot-on pour bovins	Deltamethrin	10 mg/ml	Spot-on solution	Cattle	Topical use
Germany	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml Pour- on Lösung zum Übergießen für Rinder und Schafe	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Germany	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 100 mg Spot- on Lösung zum Auftropfen für Rinder	Deltamethrin	10 mg/ml	Spot-on solution	Cattle	Topical use
Greece	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml Διάλυμα για επίχυση για βοοειδή και πρόβατα	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Hungary	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml Pour- on szarvasmarha és juh részére	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use

Member State EU/EEA	Applicant	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
Iceland	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml áhella, lausn fyrir nautgripi og sauðfé	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Ireland	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml Pour- on Solution for cattle and sheep	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Italy	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml soluzione Pour-on per bovini ed ovini	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Latvia	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil, 10 mg/ml, šķīdums uzliešanai uz muguras liellopiem un aitām	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Lithuania	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil, 10 mg/ml, užpilamasis tirpalas galvijams ir avims	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Luxembourg	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml Solution pour-on pour bovins et ovins	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
The Netherlands	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml Pour- on Oplossing voor runderen en schapen	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use

Member State EU/EEA	Applicant	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
The Netherlands	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 100 mg Spot-on Oplissing voor runderen	Deltamethrin	10 mg/ml	Spot-on solution	Cattle	Topical use
Poland	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10mg/ml, roztwór do polewania dla bydła i owiec	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Portugal	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml solução Spot- on para bovinos e ovinos	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Romania	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml soluție pour-on pentru bovine și ovine	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Slovakia	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	DELTANIL 10 mg/ml Pour-on roztok pre hovädzí dobytok a ovce	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Slovenia	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml raztopina za kožni poliv za govedo in ovce	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
Spain	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml solución pour-on para bovino y ovino	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use

Member State EU/EEA	Applicant	Name	INN	Strength	Pharmaceutical form	Animal species	Route of administration
United Kingdom	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 10 mg/ml Pour- on Solution for cattle and sheep	Deltamethrin	10 mg/ml	Pour-on solution	Cattle and sheep	Topical use
United Kingdom	Virbac 1'ere Avenue, 2065m – LID 06516 Carros CEDEX FRANCE	Deltanil 100 mg Spot- on Solution for cattle	Deltamethrin	10 mg/ml	Spot-on solution	Cattle	Topical use

Annex II

Scientific conclusions and grounds for the granting of the marketing authorisation for Deltanil 10 mg/ml Pour-on Solution for cattle and sheep and Deltanil 100 mg Spot-on Solution for cattle

Overall summary of the scientific evaluation of Deltanil 10 mg/ml Pour-on Solution for cattle and sheep and Deltanil 100 mg Spot-on Solution for cattle

1. Introduction

Deltanil 10 mg/ml Pour-on Solution for cattle and sheep and Deltanil 100 mg Spot-on Solution for cattle contain deltamethrin, a synthetic pyrethroid. Deltamethrin is used topically (dip, spray or pour-on) for the control of ectoparasites in cattle and sheep. The active substance is well known and is included in veterinary medicinal products currently authorised in the EU.

The applications in question, submitted via the decentralised procedure, are generic applications according to Art. 13(3) of Directive 2001/82/EC, as amended, referring to the reference products Pfizer Pour On Insecticide 1% w/v Cutaneous Solution and Pfizer Spot On Insecticide 1% w/v Cutaneous Solution multidose authorised in the United Kingdom. The reference member state (RMS) is the United Kingdom for both products. For the pour-on product 24 concerned member states (CMS) are involved: Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, the Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia and Spain. For the spot-on product Belgium, France, Germany and the Netherlands are involved as CMS.

Potential serious risks were identified during the decentralised procedure by Germany and the Netherlands who considered no acceptable data in the environmental risk assessment has been provided on: n-octanol:water partition coefficient (K_{ow}); soil adsorption coefficient (K_{oc}); soil degradation; bioaccumulation (BCF); toxicity to dung insects, and therefore the environmental risk assessment cannot be finalised. Furthermore, appropriate risk mitigation measures (RMMs) were considered missing in the product information as a consequence of the identified unacceptable risk to aquatic organisms.

This referral under Article 33(4) of Directive 2001/82/EC was made due to concerns that the applicant had not satisfactorily demonstrated the environmental safety of Deltanil 10 mg/ml Pour-on Solution for cattle and sheep and Deltanil 100 mg Spot-on Solution for cattle due to lack of pivotal data without which it is not possible to conclude on the environmental safety of the products.

2. Assessment of the data submitted

In order to address the concerns raised by the referral, the applicant provided an environmental risk assessment (ERA) in accordance with VICH guidelines GL6¹ and GL38² and in accordance with the CVMP guideline in support of VICH guidelines GL6 and GL38 (EMA/CVMP/ERA/418282/2005)³. Scientific justifications were provided for the cases of deviations from guidelines and a number of peer reviewed publications were submitted. Additionally, RMMs have been considered and proposed for the risk identified for dung insects. On the basis of the ERA no other RMMs were proposed by the applicant. Considering the data submitted, the Committee concluded as follows on issues raised in the notification received from Germany and the Netherlands.

¹ VICH GL6: Guideline on Environmental Impact Assessment (EIAS) for Veterinary Medicinal Products – Phase I (CVMP/VICH/592/98) –

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/10/WC500004394.pdf

² VICH GL38: Guideline on Environmental Impact Assessment for Veterinary Medicinal Products Phase II (CVMP/VICH/790/03) –

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/10/WC500004393.pdf

³ CVMP Guideline on environmental impact assessment for veterinary medicinal products in support of the VICH guidelines GL6 and GL38 (EMA/CVMP/ERA/418282/2005) –

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/10/WC500004386.pdf

An ERA was provided for the Deltanil products, which was in accordance with VICH and CVMP guidelines. It provided all the information required to be able to make a conclusion on the environmental risk presented by the use of the products. The ERA was complete in terms of data requirements and quality of data.

Deltamethrin residues will be introduced into the environment following direct excretion onto pasture. As the active substance is an ectoparasiticide a Phase II ERA was presented.

As deltamethrin has a n-octanol/water partition coefficient (K_{OW} , expressed as $\log K_{OW}$) of >5.1 , its bioaccumulation potential, potential for being considered a persistent, bioaccumulative and toxic (PBT) compound and secondary poisoning were addressed as required by the VICH and CVMP guidelines. Data from an acceptable study gave a bioconcentration factor of 510 l/kg which is below the value of 2000 l/kg which would indicate a potential to bioaccumulate. A screening for PBT properties as required by the CVMP guidelines indicated that deltamethrin did not fulfil the criteria for either 'P' or 'B' although it is considered to be 'T'. Overall deltamethrin was not considered to be a PBT compound. Evaluation of secondary poisoning showed the risk quotient (RQ) values for terrestrial and aquatic predators were <1 and further assessment was not required.

Deltamethrin was shown to have a half-life in soil of 72 days based on acceptable published data. The adsorption/desorption of deltamethrin was determined by the HPLC method which showed that deltamethrin was expected to be non-mobile in soil. The high soil adsorption coefficient (K_{OC} , expressed as $\log K_{OC}$) of >4.2 suggests that any deltamethrin which enters the aquatic environment will move to the sediment. No degradation rate for deltamethrin in sediment was required in order to complete the ERA, but some information in the published literature suggests that in some sediments degradation occurs with a half-life in soil of about 10 days (Åkerblom *et al.* 2008)⁴. However, it was considered that information on the possible accumulation of deltamethrin in sediments should be communicated to the user in the product information.

A new study was carried out on earthworms according to the recommended OECD guideline and a predicted no effect concentration (PNEC) was derived using the accepted assessment factor (10). Comparison of the predicted environmental concentration (PEC) value for soil with the PNEC showed that the RQ for the soil compartment was <1 and no further assessment was required. As the $PEC_{\text{groundwater}}$ was below 0.1 µg/l no further assessment for the water compartment was required.

Acceptable data on the acute toxicity of deltamethrin to dung fly larvae and adult beetles were provided which indicated that RQ values for dung insects were in the order of 90 – 10 000. Published data from a field study using a pour-on deltamethrin product indicated that the effects of deltamethrin can persist for a number of weeks and have the potential to affect dung insect populations in some circumstances. No additional studies were carried out in order to further refine the risk as guidance in this area is not currently available. Consequently in order to mitigate the risk for dung insects RMMs were included in the SPC in sections 4.5.iii and 5 (Environmental properties).

New acute OECD studies were carried out on aquatic organisms followed by an OECD chronic study with daphnia. Using these data PNECs were derived using the appropriate assessment factors. These PNECs were compared with the PEC values (calculated using agreed methods) for surface water exposed via drainage through soil, via direct excretion by cattle and via loss from the fleece of sheep. The RQ values for surface water were <1 for all target animal types. Based on acceptable published data for sediment species the RQ for sediment was <1 . No further assessment of risks to surface water and sediment was necessary and no RMMs were needed.

⁴ Åkerblom *et al.* (2008), Deltamethrin toxicity to the midge *Chironomus riparius* Meigen – Effects of exposure scenario and sediment quality. *Ecotox. Environm. Safety* 70:53-60

3. Benefit-risk assessment

Direct therapeutic benefit

The benefit of the products is that treatment and prevention of infestations by lice and flies on cattle; ticks, lice, keds and established blowfly strike on sheep and lice and ticks on lambs can be carried out using the products. The efficacy of Deltanil has been demonstrated according to current rules during the decentralised procedure. Efficacy was not assessed in this referral procedure.

Risk Assessment

Quality, target animal safety, user safety and residues were not assessed in this referral procedure, as no concern was notified by the reference Member State.

Environmental risk

An ERA in accordance with VICH and CVMP guidelines was provided which contained a mixture of published and bespoke studies from the applicant and addressed all aspects of environmental risk. The use of the products was not expected to pose a risk for soil, groundwater and surface water. A risk for dung insects was identified by the ERA and RMMs were proposed to address the risk.

Risk management or mitigation measures

The RMMs and warnings in the Summary of Product Characteristics (SPC) and package leaflet address the risk to dung insects by advising on the frequency of re-treatments and the duration of deltamethrin excretion. The warnings are appropriate. As a result of this referral it was considered that due to the high adsorption coefficient (K_{oc}) of deltamethrin the following environmental information should also be added to the previously agreed warning sentence in the SPC (section 5 Environmental Properties) and the package leaflet (section 15 Environmental Properties) "...and may accumulate in sediment".

Evaluation of the benefit-risk balance

The benefit-risk balance is considered positive for both Deltanil 10 mg/ml Pour-on Solution for cattle and sheep and Deltanil 100 mg Spot-on Solution for cattle.

Grounds for the granting of the marketing authorisations for Deltanil 10 mg/ml Pour-on Solution for cattle and sheep and Deltanil 100 mg Spot-on Solution for cattle

Having considered all the overall submitted data in writing the CVMP concluded that the ERA for Deltanil Pour-On and Spot-on products shows that the products are not expected to pose a risk for the environment when used as recommended in the product information including the recommended RMMs. The benefit-risk for the products can be considered to be positive.

Therefore, the CVMP recommended the granting of the marketing authorisations for Deltanil 10 mg/ml Pour-on Solution for cattle and sheep and Deltanil 100 mg Spot-on Solution for cattle with amendment to the Summaries of Product Characteristics and package leaflets of the reference Member State. The amended Summaries of Product Characteristics and package leaflets of the reference Member State are set out in Annex III.

Annex III

Amendments in the relevant sections of the Summaries of Product Characteristics and package leaflets

The valid Summary of Product Characteristics, labelling and package leaflet are the final versions achieved during the Coordination Group procedure with the following amendments:

Add the following text in the relevant sections of the product information:

Summary of Product Characteristics

5 Environmental properties

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Add, where applicable, "Deltamethrin is toxic to aquatic organisms and honey bees and may accumulate in sediment."

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Package leaflet:

15. ENVIRONMENTAL PROPERTIES

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Add, where applicable, "Deltamethrin is toxic to aquatic organisms and honey bees and may accumulate in sediment."

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