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Guideline on data requirements for authorisation of immunological veterinary medicinal products in exceptional circumstances

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This guideline replaces the CVMP related guidelines ("Guideline on requirements for an authorisation under exceptional circumstances for vaccines for emergency use against bluetongue" (EMEA/CVMP/IWP/37267/2008) and the "Guideline on requirements for an authorisation under exceptional circumstances for vaccines for use in birds against avian influenza" (EMEA/CVMP/IWP/222624/2006)). Specific requirements for vaccines against avian influenza and bluetongue are included in the Annex, Table 2 and Table 3.

Keywords	***Immunological veterinary medicinal products, veterinary vaccines, exceptional circumstances, new veterinary regulation***

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
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Executive summary

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 introduces specific provisions for applications in exceptional circumstances (Article 25).

The general aim of this guideline is to define minimum data requirements for the demonstration of quality, safety and efficacy of immunological veterinary medicinal products (IVMPs) for applications submitted under Article 25 of Regulation (EU) 2019/6.

It is the intention of the guideline to provide comprehensive guidance on the essential requirements for such applications.

A summary of possible reductions in data requirements for applications for IVMPs in exceptional circumstances is presented in the Annex of this guideline.

1. Introduction (background)

In the European Union (EU), marketing authorisations for IVMPs are based on the requirements of Regulation (EU) 2019/6, Article 8 with the requirements for technical documentation necessary for demonstrating quality, safety and efficacy detailed in Annex II of the Regulation (Commission Delegated Regulation (EU) 2021/805 of March 2021 amending Annex II to Regulation (EC) No. 2019/6 of the European Parliament and of the Council). However, Article 25 of Regulation (EU) 2019/6 provides for a derogation from Article 8, whereby, in exceptional circumstances related to animal or public health, an applicant may submit an application which does not meet all requirements of Article 8, and for which it can be argued that the benefit of the immediate availability on the market of the veterinary medicinal product concerned to the animal or public health outweighs the risk inherent in the fact that certain quality, safety or efficacy documentation has not been provided.

This 'exceptional use' provision has been introduced into the legislation to address potential availability concerns in the face of an outbreak or recognition of the threat of an outbreak of new or re – emerging infectious diseases in Europe with the potential for severe impact on animal or public health. Eligibility for submission under Article 25 of Regulation (EU) 2019/6 (Applications in exceptional circumstances) will be determined on a case-by-case basis where the immediate availability and distribution of an IVMP on the market and the possibility for rapid vaccination is considered of crucial relevance for outbreak control and/or disease eradication.

In case of emergencies, Member States of the EU can allow use of IVMPs without authorisation according to Article 110 of Regulation (EU) 2019/6: "2. By way of derogation from Article 106(1) of this Regulation, and in the absence of a veterinary medicinal product as referred to in Article 116 of this Regulation, in the event of an outbreak of a listed disease as referred to in Article 5 of Regulation (EU) 2016/429 or an emerging disease as referred to in Article 6 of that Regulation, a competent authority may allow the use of an immunological veterinary medicinal product not authorised within the Union." However, there are many risks associated with the use of unauthorised IVMPs in relation to the absence of certain data that would normally be provided in support of a marketing authorisation application submitted in accordance with Article 8 of Regulation (EU) 2019/6 (see CVMP reflection paper on the risks that should be considered prior to the use of unauthorised vaccines in emergency situations, (EMA/CVMP/IWP49593/2013)).

Therefore, the introduction of a legal basis for the issuing of marketing authorisations in exceptional circumstances and the provision of clear guidance for applicants and assessors on the minimum data

requirements for all relevant parts of the application dossier for a marketing authorisation of IVMPs in exceptional circumstances is considered highly beneficial.

Notwithstanding, it needs to be demonstrated that for objective and verifiable reasons certain quality, safety or efficacy documentation required in accordance with Annex II of Regulation (EU) 2019/6 cannot be provided. Furthermore, it has to be stated clearly in the summary of product characteristics that based on the lack of comprehensive data only a limited assessment of quality, safety and efficacy has been conducted.

This guideline should provide a comprehensive guidance on data requirements for applications for IVMPs in exceptional circumstances related to animal or public health and provide some flexibility to applicants to quickly formulate appropriate IVMPs, which nevertheless meet the minimum requirements regarding quality, safety and efficacy. The decision to grant a marketing authorisation in exceptional circumstances with a reduced data set will be made on the basis of an individual benefit-risk assessment dependent on the specific circumstances.

2. Scope

This guideline applies to marketing authorisation applications for IVMPs in exceptional circumstances.

The objective of the guideline is to define the minimum data requirements for applications in exceptional circumstances for all relevant parts of the dossier to support applications for authorisation of IVMPs under Article 25 of Regulation (EU) 2019/6.

Because the marketing authorisation may be granted subject to one or more requirements for the marketing authorisation holder such as introduction of conditions or restrictions, notification of adverse events to the competent authority or conduct of post-authorisation studies, it should be considered in which cases these requirements are an appropriate substitute for data that would typically be provided in support of an application for marketing authorisation.

Such requirements for individual IVMPs will be set on a case-by-case basis. It is emphasised that procedural aspects including establishing criteria for re-examination and validity of a marketing authorisation in exceptional circumstances are not in the scope of the guideline."

3. Legal basis and relevant guidelines

Requirements for a marketing authorisation application are laid down in Article 8(1) (b) of Regulation (EU) 2019/6 and are specified in Title IIIb 'Requirements for immunological veterinary medicinal products' of Annex II of the Regulation.

This guideline should be read in conjunction with the introduction and general principles of Annex II to Regulation (EU) 2019/6, the European Pharmacopoeia (Ph. Eur.) and all other relevant EU and VICH guidelines.

Exceptional circumstances

Articles 25 and 26 of Regulation (EU) 2019/6 introduce a specific legal basis for the concept of a marketing authorisation in exceptional circumstances for veterinary medicinal products, also specifying the terms which need to be fulfilled for applications and marketing authorisations in exceptional circumstances:

Article 25

"*By way of derogation from point (b) of Article 8(1), in exceptional circumstances related to animal or public health, an applicant may submit an application which does not meet all requirements of that point, for which the benefit of the immediate availability on the market of the veterinary medicinal product concerned to the animal or public health outweighs the risk inherent in the fact that certain quality, safety or efficacy documentation has not been provided. In such a case, the applicant shall be required to demonstrate that for objective and verifiable reasons certain quality, safety or efficacy documentation required in accordance with Annex II cannot be provided."*

Article 26

1. In the exceptional circumstances referred to in Article 25, a marketing authorisation may be granted subject to one or more of the following requirements for the marketing authorisation holder:

(a) a requirement to introduce conditions or restrictions, in particular concerning the safety of the veterinary medicinal product;

(b) a requirement to notify to the competent authorities or the Agency, as applicable, of any adverse event relating to the use of the veterinary medicinal product;

(c) a requirement to conduct post-authorisation studies.

2. Where a veterinary medicinal product has been granted a marketing authorisation in accordance with this Article, the summary of product characteristics shall clearly state that only a limited assessment of quality, safety or efficacy has been conducted due to the lack of comprehensive quality, safety or efficacy data.

This is also reflected in Annex II of Regulation (EU) 2019/6 under section IV.7. - Applications in exceptional circumstances:

"In exceptional circumstances related to animal or public health, a marketing authorisation may be granted under Article 25 for a veterinary medicinal product, subject to certain specific obligations, conditions and/or restrictions.

For such applications, the applicant shall submit Part 1 as described in this Annex, together with a justification as to why the benefit of the immediate availability on the market of the veterinary medicinal product concerned outweighs the risk inherent in the fact that certain quality, safety or efficacy documentation has not been provided.

For Parts 2, 3 and 4, certain quality, safety or efficacy data required by this Annex may be omitted, if the applicant justifies that those data cannot be provided at the time of submission. For the identification of the essential requirements for all such applications, the relevant guidance published by the Agency shall be taken into account.

Post-authorisation studies may be requested as part of the conditions for marketing authorisation, and shall be designed, conducted, analysed and presented according to the general principles for quality, safety and efficacy tests set out in this Annex, and relevant guidance documents, as applicable depending on the issue to be addressed in the study."

4. Minimum data requirements for an authorisation in exceptional circumstances

4.1. General requirements

The requirements as mentioned in section IIIb of Annex II to Regulation (EU) 2019/6 and the relevant Ph. Eur. general chapters and monographs apply to all IVMPs. However, for IVMPs authorised in exceptional circumstances certain quality, safety and efficacy data may be omitted. Detailed information on minimum data requirements for IVMPs authorised under exceptional circumstances is listed below and possible reductions in requirements are summarised in Table 1 in the Annex.

Provision of lacking and/or additional data to address critical deficiencies in the pre-authorisation data set may be required within a defined timeframe following authorisation.

The IVMP must be manufactured under GMP conditions.

If manufacturing of a vaccine, which allows differentiation between vaccinated and naturally infected animals (DIVA) is possible, this type of vaccine is preferred. In such cases, where the marker claim is reliant on in vitro diagnostic tests, sufficient data on the diagnostic tests shall be provided to allow adequate assessment of the claims related to the marker properties.

No formal critical expert reports for each part are requested, however the applicant should present a summary of the submitted documentation together with a discussion on the 'benefit of the immediate availability on the market' of the IVMP and justification for any data gaps. This should be included in Part 1C of the dossier.

The requirements of the guideline on vaccine platform technology master files (vPTMF), including possible data reductions/omissions foreseen, are applicable in case an already certified vPTMF is used for an application under exceptional circumstances.

A vaccine must only contain active substances (one or more) that are epidemiologically relevant to the disease outbreak or the threat for the emerging disease situation concerned. For IVMPs containing a GMO, this guideline is applicable for quality and efficacy requirements. For safety, the requirements of Directive 2001/18/EC must be met. In line with the latter Directive, it is acceptable for an applicant to submit data, which has been generated for similar GMO constructs already authorised to fulfil part of the requirements for safety. Where such a construct is part of a vPTMF, the certificate obtained may be used to fulfil the respective safety requirements.

Data from similar/comparable IVMPs, which are already authorised, may be acceptable in some cases mentioned below under quality, safety and efficacy requirements.

4.2. Quality requirements (Part 2)

2A. Qualitative and quantitative composition

Information regarding the qualitative and quantitative particulars of all the constituents / IVMP ingredients has to be provided.

Quantification of the active substances in the finished product is compulsory in line with Annex II of Regulation (EU) 2019/6 (e.g. number of organisms, specific protein content, mass, number of International Units (IU) or units of biological activity). For inactivated vaccines, this should be the antigen content after inactivation. However, if appropriate antigen quantification is not available, the

quantification of antigen before inactivation may be considered as long as a correlation with vaccine efficacy can be demonstrated.

2B. Description of the manufacturing method

A description of the manufacturing process should be given, including the identification of the key stages in the production process. The information should include relevant data to prove consistency of the manufacturing process and details concerning precautions taken to ensure the homogeneity and consistency of each batch of the finished product.

The process of the blending should be described with the quantitative particulars of all the substances used, including an example for a representative production batch.

Full inactivation in case of an inactivated vaccine has to be demonstrated; it is essential to demonstrate absence of residual live virus/bacteria in the vaccine. The inactivation step has to be validated.

The use of two pilot/R&D [1] batches to validate the consistency of production process is acceptable (to be verified with a 3rd batch at industrial scale later).

2C. Production and control of starting materials

For materials of animal origin, including seed materials, cell seeds, batches of serum and other material originating from animal species, freedom of extraneous agents and compliance with the relevant monographs of the Ph. Eur. (5.2.5, 5.2.8, 0062) have to be demonstrated. The testing program may be reduced and replaced by a valid risk assessment in line with Ph. Eur. monograph 5.2.5. For master seeds, extraneous agents testing is requested only for those agents that may occur in the source species. Any TSE risk has to be evaluated in case source materials originating from ruminants are used.

In case of a live attenuated vaccine, the stability of the attenuation characteristics of the seed has to be described.

Vaccine production shall be based on a seed lot system and on established cell seeds, whenever possible.

2D. Control tests during the manufacturing process

The methods of control used during manufacturing process shall be described, documented and the results provided, unless otherwise justified, with a view to verifying the consistency of the manufacturing process and the final product.

For inactivated or detoxified vaccines, inactivation or detoxification shall be tested during each production run. The control of inactivation (or detoxification) is essential to ensure that no residual live pathogenic organism or toxic material is present in the vaccine. This test should be validated.

2E. Control tests on the finished product

Finished product testing has to be performed in order to demonstrate quality of the product. The control tests carried out on the finished product should be fit for purpose (no full validation requested).

A relevant batch potency test which is fit for purpose is considered a critical element for the quality of the IVMPs. A quantification of the active substance shall be carried out on each batch to show that

[1] Pilot batch: small scale industrial batch, but in full compliance with the production process described in the licensing dossier.
R&D batch: batch produced under laboratory conditions but in full compliance with the production process described in the licensing dossier

each batch will contain the appropriate antigen content to ensure an acceptable level of safety and efficacy.

Visual inspection is mandatory and appropriate specifications regarding appearance control must be set.

Sterility and purity control of the finished product to demonstrate the absence of contamination by extraneous agents or other substances should be shown according to section IIIb.2E of Annex II.

2F. Batch- to- batch consistency

Batch-to-batch consistency should be proven since inconsistencies may lead to unexpected safety issues or an unacceptable loss of efficacy. Data from two pilot/R&D batches representative of routine production must be provided, including the batch protocols describing the results of the tests performed during production and on the finished product.

2G. Stability tests

A justification for the proposed shelf life and the recommended storage conditions for the active substance and the finished product should be provided.

Results of one pilot/R&D batch is acceptable (results of one industrial batch to be provided later).

Stability data relating to similar IVMPs could be used to define a shelf life.

Stability data on one final container size is acceptable provided the selected presentation is justified by the applicant.

Where a shelf life is proposed in the absence of real-time studies relating to the specific product under consideration, the maximum shelf life shall be determined case-by-case. When not available pre-authorisation, data to confirm the proposed shelf life and the recommended storage conditions for the active substance and the finished product should be provided post-authorisation.

4.3. Safety requirements (Part 3)

For pre-clinical safety studies (laboratory safety studies), the Good Laboratory Practice (GLP) requirements can be lifted provided the protocols and reports allow a satisfactory assessment of the trials. The numbers of animals used should be following the requirements of Ph. Eur. 5.2.6, unless otherwise justified.

The batch used for safety testing shall be taken from batches produced according to the manufacturing process described in Part 2. Safety data generated using pilot/R&D batches will be accepted.

For inactivated IVMPs, the use of standard batches (it is not required to use a batch of maximum antigen content) is possible in safety studies. The safety and efficacy studies may be combined in the same pre-clinical (laboratory) study, using the same batch(es) of the IVMP.

For live IVMPs, the use of the least attenuated passage level is not required. The titre used in the studies should be adequately justified.

Safety tests must be performed in all recommended target species for the most sensitive categories and of minimum age recommended for vaccination. Extrapolation from one category or even species to another or one route of administration to another would be possible based on scientific justification for all safety studies. Each recommended route and method of administration should be tested. A worst-case scenario for route and method of administration may be used, if scientifically justified.

Safety of an overdose for live IVMPs and of first re-vaccination are not required. Demonstration of safety of the primary vaccination schedule is sufficient.

Studies for the examination of reproductive performance may be omitted. If such studies are not performed, relevant warnings should be given in the SPC. Whenever data related to other IVMPs of similar composition (excipients and adjuvants) and a similar vaccination schedule are available these data could be used as supportive data to fulfil the requirements with regard to reproductive performance.

Any available data on safety from non-target species should be submitted as supportive documentation. In case a live attenuated vaccine is used, safety aspects for non-target species and the environment have to be addressed. If specific relevant studies have been conducted, the data should be submitted.

A live attenuated organism is still able to replicate in the vaccinated animal and may cause some signs of disease. In case the attenuated agent is spread to the environment, non-vaccinated animals including non–target species may be affected. Published literature may be used to address this issue. In the absence of adequate scientific literature, the relevant studies may be required to evaluate spread to unvaccinated target animals and potentially non-target species which could be highly susceptible to the vaccine strain.

In case of live vaccines for zoonotic diseases used for food-producing animals, the study of dissemination is required to detect where the vaccine strain is present in the animal's body and if the organism persists at the administration site.

Increase in or reversion to virulence shall be investigated in case of a live attenuated vaccine. The stability of the attenuation characteristics has to be described.

The potential of live attenuated strains to recombine/reassort with field strains should be addressed.

User risk assessment must be provided accompanied by supportive documentation. This risk assessment should cover human exposure (i.e. persons who may come in contact with vaccinated animals). If specific preparation activities of the products are required (e.g. dissolution, filling into special devices) this should be taken into consideration in the user risk assessment.

To obtain a marketing authorisation for a veterinary medicinal product intended for food-producing species in the EU, a maximum residue limit (MRL) must be established in advance for all substances that are pharmacologically active at the dose that is intended to be administered to the target species. Substances considered not to be pharmacologically active, should be entered into the list of substances considered as not falling within the scope of Commission Regulation (EC) 37/2010. An excipient that is not listed in either Table 1 of or is not in the out-of-scope list, can only be used in a veterinary medicinal product intended for food producing species if it is concluded that the substance cannot be expected to show pharmacodynamic activity at the dose at which it is/will be administered to the target animal. For any IVMP component (e.g. preservatives, adjuvants, zoonotic vaccine strains), consumer safety has to be addressed. Where possible, well established adjuvants and other excipients should be used to formulate the IVMP.

Clinical trials are not required. Safety data from previous use in the field (use of an IVMP not authorised in the EU according to Article 110 (2)) and/or from use in the field outside the EU should be provided, if available.

4.4. Efficacy requirements (Part 4)

Appropriate information regarding immunogenicity and relevance of the vaccine strain to the current epidemiological situation in the field is required to verify the benefit of availability of the vaccine.

The expected degree and nature of protection should be addressed. An acceptable level of efficacy will be established on a case-by-case basis using a benefit/risk approach taking into account the available data.

The batch used for efficacy testing shall be taken from batches produced according to the manufacturing process described in Part 2. Efficacy data generated using pilot/R&D batches will be accepted.

For inactivated IVMPs, the use of standard production batches (it is not required to use a batch of minimum antigen content) is possible in efficacy studies. The safety and efficacy studies may be combined in the same pre-clinical (laboratory) study, using the same batch(es) of an IVMP.

For live IVMPs, the efficacy studies may be combined with one-dose pre-clinical (laboratory) safety studies. The use of the maximum passage level is not required. The titre used in the studies should be adequately justified.

Efficacy should be demonstrated in laboratory conditions by a challenge model in all recommended target species and categories recommended for vaccination unless scientific/literature data can be provided demonstrating that extrapolation from one species to another species or from one category of a species to another category of the same species is possible.

The IVMP should be administered by each recommended route and method of administration. Extrapolation from one route of administration to another may be acceptable if scientifically justified. If not all routes of administration are covered by appropriate data, this should be reflected in the SPC.

The challenge agent should be relevant to the European epidemiological context of the disease for which the IVMP is intended.

If an indicator of protection is used, the challenge may be omitted. For an indicator to be acceptable as a correlate of IVMP efficacy, it shall be demonstrated that a sufficient correlation exists between the indicator measured and the claimed protection in the target species. An indicator of protection should be shown to play a substantial role in the immune response, relevant for protection of the target species against the disease concerned. The methods used to evaluate the parameters of efficacy (for example detection of the post-challenge viremia or serology) should be fit for purpose. Methods such as virus isolation and RT-PCR would normally allow satisfactory follow-up.

Definition of the onset of immunity after primary vaccination schedule is a crucial parameter to allow appropriate use under exceptional circumstances. A proposal of a vaccination schedule taking into consideration particular aspects like primary vaccination or vaccination of particular groups, e.g. pregnant animals, has to be provided and the recommended vaccination schedule has to be justified.

Serological data may be appropriate to demonstrate duration of immunity. The absence of establishment of the duration of immunity is acceptable and must be clearly indicated in the SPC.

A lack of data regarding maternal derived antibodies and their effect on IVMP efficacy may be acceptable, however, in such cases a clear statement in the SPC is necessary.

Clinical trials are not required. Data on previous use in the field (according to article 110 (2)) should be provided, if available.

4.5. Product information

The SPC is an essential part of a marketing authorisation.

Where a veterinary medicinal product has been granted a marketing authorisation in accordance with Article 25 of Regulation (EU) 2019/6, the SPC shall clearly state that only a limited assessment of quality, safety or efficacy has been conducted due to the lack of comprehensive data.

In line with Article 35(1)(j)(ii) of Regulation (EU) 2019/6, the SPC will carry the following statement: *"Marketing authorisation granted in exceptional circumstances and therefore assessment based on customised requirements for documentation"*.

The QRD veterinary annotated product information template is also applicable for veterinary medicinal product granted a marketing authorisation in accordance with Article 25. Standard statements, given in the template should be used whenever they are applicable. This concerns the SPC, the labelling and the package leaflet.

Details on the data which have not been provided by the applicant (i.e. the data gaps) will be included and made publicly available in the European public assessment report.

5. Annex

Table 1: Reduced data requirements for IVMPs intended for authorisation in exceptional circumstances

Please note that the numbering of the table refers to the numbering in Section IIIb of Annex II to Regulation (EU) 2019/6.

No. of section	Section title	Reduced data requirements
1. SUMMARY OF THE DOSSIER		
	General requirements	A summary of the submitted documentation together with a discussion and justification for any data gaps should be provided (no formal critical expert reports requested). In any case when essential data are not available, this data gap has to be reflected in the SPC. The possible data reductions/omissions foreseen in the guideline on vaccine platform technology master files (vPTMF) are applicable in case an already certified vPTMF is used for an application in exceptional circumstances.
2. QUALITY DOCUMENTATION		
2.A	Product description	For inactivated IVMPs, if it is not possible give the amount of antigen after inactivation, the quantification of antigen before inactivation may be considered as long as a correlation with vaccine efficacy can be demonstrated
2.B	Description of the manufacturing method	The use of two pilot/R&D batches to validate the consistency of production process is acceptable (to be verified with a 3rd batch at industrial scale later).
2.C	Production and control of starting materials	For master seeds, extraneous agents testing is requested only for those agents that may occur in the source species.
2.E	Control test on the finished product	The control tests carried out on the finished product should be fit for purpose (no full validation requested).
2.F	Batch-to-batch consistency	Data from two pilot/R&D batches must be submitted, including the batch protocols describing the results of the tests performed during production and on the finished product.

No. of section	Section title	Reduced data requirements
2.G	Stability tests	Results of one pilot/R&D batch is acceptable (results of one industrial batch to be provided later). Stability data relating to similar IVMPs could be used to define a shelf life. Stability data on one final container size is acceptable provided the selected presentation is justified by the applicant.
3. SAFETY TESTS		
3.A	General requirements	GLP requirements can be lifted provided the protocols and reports allow a satisfactory assessment of the trials. The numbers of animals used should be following the requirements of Ph. Eur. 5.2.6, unless otherwise justified. The safety and efficacy studies may be combined in the same pre-clinical (laboratory) study, using the same batch(es) of an IVMP. For inactivated IVMPs, the use of standard production batches (no maximum antigen content necessary) is possible. For live IVMPs, the use of the least attenuated passage level is not required. The titre used in the studies should be adequately justified. The use of pilot/R&D batches is possible. Any available data on safety from non-target species should be submitted as supportive documentation.
3.B	Pre-clinical studies (laboratory safety studies)	
3.B.2	Safety of one administration of an overdose	Safety of an overdose for live IVMPs is not required.
3.B.3	Safety of the repeated administration of one dose	Safety of first re-vaccination is not required. Demonstration of safety of the primary vaccination schedule is sufficient.

No. of section	Section title	Reduced data requirements
3.B.4	Examination of reproductive performance	Studies for the examination of reproductive performance may be omitted. If such studies are not performed, relevant warnings should be given in the SPC. Whenever data related to other IVMPs of similar composition (excipients and adjuvants) and a similar vaccination schedule are available these data could be used as supportive data.
3.B.5	Examination of immunological functions	Studies for the examination of immunological functions may be omitted. If necessary, relevant warnings should be included in the SPC.
3.B.6.1	Spread of vaccine strain	Published literature may be used to fulfil this requirement. In the absence of adequate scientific literature, the relevant studies should be performed to evaluate spread to unvaccinated target animals and potentially non-target species which could be highly susceptible to the vaccine strain.
3.B.6.2	Dissemination in the vaccinated animal	Data not required unless the vaccine strain is shown to spread. Published literature may be used to fulfil this requirement. In the absence of adequate scientific literature, the relevant studies should be provided. In the case of live vaccines for zoonotic diseases used for food producing animals, data on dissemination is necessary.
3.C	Clinical trials (field studies)	Clinical (field) studies are not required. Data on previous use in the field should be provided if available.

No. of section	Section title	Reduced data requirements
4. EFFICACY DOCUMENTATION		
4.A	General requirements	Scientific/literature data can be provided demonstrating that extrapolation from one species to another or from one category of a species to another category of the same species is possible. Extrapolation from one route of administration to another may be acceptable if scientifically justified. If not all routes of administration are covered by appropriate data, this should be reflected in the SPC. The safety and efficacy studies may be combined in the same pre-clinical (laboratory) study, using the same batch(es) of an IVMP. For inactivated IVMPs, the use of standard production batches (no minimum antigen content necessary) is possible. For live IVMPs, the efficacy studies may be combined with one-dose pre-clinical (laboratory) safety studies. The use of the maximum passage level is not required. The titre used in the studies should be adequately justified. The use of pilot/R&D batches is possible.
4.B	Pre-clinical studies (laboratory trials)	The methods used to evaluate the parameters of efficacy (for example detection of the post-challenge viremia or serology) should be fit for purpose. If an indicator of protection is used, the challenge may be omitted. For an indicator to be acceptable as a correlate of IVMP efficacy, it shall be demonstrated that a sufficient correlation exists between the indicator measured and the claimed protection in the target species. An indicator for protection should be shown to play a substantial role in the immune response, relevant for protection of the target species against the disease concerned.

No. of section	Section title	Reduced data requirements
		Omission of studies such as duration of immunity is acceptable, provided that it is made clear in the SPC that the data are not available.
		Omission of studies such as effect of maternally derived antibodies (MDA), are acceptable, provided that it is stated in the SPC that the data are not available.
4.C	Clinical trials (field trials)	Clinical (field) studies are not required. Data on previous use in the field should be provided if available.

Table 2: Specific reduced data requirements for vaccines against avian influenza

Please note that the numbering of the table refers to the numbering in Section IIIb of Annex II to Regulation (EU) 2019/6.

No. of section	Section title	Data requirements
1. SUMMARY OF THE DOSSIER		
	General requirements	For an avian species to be included in the section "Target Species" of the SPC the outlined safety and efficacy data have to be provided. If only incomplete but relevant safety and efficacy data is available for a given species this will be stated elsewhere in the SPC. The use of conventional live vaccines is not acceptable.
2. QUALITY DOCUMENTATION		
2.A	Product description	The active ingredient can be live recombinant virus or bacteria, an inactivated antigen (conventional inactivated viruses or obtained by reverse genetics systems) or a subunit antigen. The origin of the vaccine strain(s) is not relevant as long as protection against the epidemiologically relevant H5 and/or H7 highly pathogenic avian influenza virus strains is induced.
2.D	Control tests during the manufacturing process	To test for complete inactivation, sequential passage through two groups of eggs will probably be sufficient. If the applicant has experience with inactivation of other influenza strains, the evidence of which should be provided, demonstration of complete inactivation at 67% of the total time allowed will be sufficient. Otherwise, a full set of data with intermediate values will be necessary.
2.E	Control test on the finished product	The control of the finished product including a description of the safety and titre or potency tests (correlated with the antigen content) performed on the finished product in SPF chickens, the limits of acceptance and a declaration of the applicant that certifies that the results are within the specifications should be provided.
2.G	Stability tests	The usual requirements for stability should be put in place as soon as possible for the vaccine. In the meantime, supporting data of the experience with other influenza vaccines for veterinary use would be acceptable with a maximally granted shelf life of 12 months.

No. of section	Section title	Data requirements
3. SAFETY DOCUMENTATION		
3.B.2.	Safety of one administration of an overdose	For live recombinant vaccines the safety of the administration of an overdose to birds of the minimum age recommended for vaccination should be demonstrated in laboratory studies for all recommended target species (e.g. chickens, ducks and turkeys). For inactivated vaccines, if data are available with other vaccines of similar composition (excipients and adjuvants) in the same or a similar range of target species these could be used to fulfil the requirements.
4. EFFICACY DOCUMENTATION		
4.A	General requirements	All available data on efficacy for species other than the indicated target species should be provided, with special attention to ducks and turkeys. A high degree of protection against mortality and clinical signs of disease is expected. A significant reduction of excretion and transmission of the challenge virus is a major goal. The level of reduction of excretion of challenge virus shown in laboratory studies should be sufficient to give an expectation of an acceptable level of performance in the field. If data on vaccination in the face of infection is available this should be provided in order to be reflected in the SPC if relevant. The onset of immunity should be as rapid as possible to allow the use of the vaccine in emergency conditions. As a minimum, challenge at one time point after vaccination is required. It is expected that the duration of immunity induced by the vaccine should cover the economic life of the target species. Serology may be sufficient as long as a titre that has been shown to be efficacious for the species in question is maintained for the duration claimed. Any need for revaccination should be justified and all relevant data should be provided.

Table 3: Specific reduced data requirements for vaccines against bluetongue

Please note that the numbering of the table refers to the numbering in Section IIIb of Annex II to Regulation (EU) 2019/6.

No. of section	Section title	Data requirements
1. SUMMARY OF THE DOSSIER		
		For a species to be included in the section "Target Species" of the SPC the outlined safety and efficacy data have to be provided. If only incomplete but relevant safety and efficacy data are available for a given species this will be stated elsewhere in the SPC
2. QUALITY DOCUMENTATION		
2.G	Stability tests	The usual requirements for stability should be put in place as soon as possible for the vaccine. In the meantime and in the absence of data, a maximum shelf life of 12 months may be granted. The use of stability data of a BTV vaccine containing other serotypes but having the same composition in adjuvants and excipients may be used to define the shelf life.
3. SAFETY DOCUMENTATION		
3.A	General requirements	Due to the expected large use of this type of vaccine, the examination of reproductive and lactating performances after vaccination should be carried out. Whenever data related to other vaccines of similar composition (excipients and adjuvants) and similar vaccination schedule are available these data could be used to fulfil the requirements with regard to reproductive performance

No. of section	Section title	Data requirements
4. EFFICACY DOCUMENTATION		
4.A	General requirements	The main parameter of efficacy of the vaccine is a prevention in viraemia post-challenge accompanied by the absence of clinical signs (if relevant). If it is not possible to achieve this goal, the acceptable level of efficacy will be established on a case by case basis using a risk/benefit approach taking into account for example available data on level of reduction of viraemia, reduction of clinical signs, prevention or reduction of transplacental infection. The methods used to detect the post-challenge viraemia should be validated. Methods such as virus isolation and RT-PCR would normally allow satisfactory follow up. BT vaccines, which would allow the differentiation between infected and vaccinated animals, would be desirable to allow a DIVA vaccination campaign. For these `marker' vaccines where the marker claim is reliant on in vitro diagnostic tests, sufficient data on the diagnostic tests shall be provided to allow adequate assessment of the claims related to the marker properties.