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ANNEXES 1 to 4

**ANNEXES**

**to the proposal for a**

**REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL**

**on veterinary medicinal products**

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**ANNEXES**

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**REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL**

**on veterinary medicinal products**

## ANNEX I

## Administrative information referred to in Article 7(1)(a)

### 1. Applicant

1.1. Name or business name and address or registered place of business of the person responsible for placing the product on the market

1.2. Name and address of manufacturer (s)

1.3. Name and address of the sites involved in the different stages of the manufacturing

1.4. Name and address of importer, if relevant

### 2. Identification of the veterinary medicinal product

2.1. Proposed name of the veterinary medicinal product

2.2. Active substances

2.3. Strength

2.4. Pharmaceutical form

2.5. Route of administration

2.6. Method of administration

2.7. Target species

### 3. Manufacturing and pharmacovigilance information

3.1. Proof of a manufacturing authorisation

3.2. Identifier or reference number of pharmacovigilance system master file

### 4. Product information

4.1. Draft summary of the product characteristics drawn up in accordance with Article 30

4.2. Description of the final presentation of the product, including packaging and labelling.

4.3. Draft text of the information to be provided in the immediate packaging, outer packaging and the package leaflet in accordance with Articles 9-14 of this Regulation.

**5. Other information**

5.1. List of countries in which a marketing authorisation has been granted for the veterinary medicinal product

5.2. Copies of all the summaries of product characteristics as included in the terms of marketing authorisations granted by Member States, if relevant

5.3. List of countries in which an application has been submitted or refused

5.4. List of countries where the veterinary medicinal product is to be placed on the market, if relevant

5.5. Critical expert reports on quality, safety and efficacy

## ANNEX II

## Technical requirements referred to in Article 7(1)(b)

## PART 1 - Technical requirements for veterinary medicinal products other than biologicals

### 1.1. INTRODUCTION

The technical documentation shall include a detailed and full description of the tests, studies and trials conducted or referred to, including the methods used. The data shall be relevant and of sufficient quality to demonstrate the quality, safety and efficacy of the veterinary product.

Data shall be sufficient to establish:

- the veterinary medicinal product's dosage for the various animal species, its pharmaceutical form, its method and route of administration and its shelf life

- any precautionary and safety measures to be taken when storing the veterinary medicinal product, administering it to animals or disposing of waste, together with an indication of potential risks that the veterinary medicinal product might pose to the environment, to public and animal health;

- the withdrawal period in the case of veterinary medicinal products intended for food-producing species;

- the therapeutic indications, contra-indications and adverse events.

The application shall contain a description of the testing methods employed by the manufacturer, the results of pharmaceutical (physico-chemical, biological or microbiological) tests and safety tests, including tests assessing the potential risks posed by the medicinal product for the environment. In addition, results of residue tests, pre-clinical studies and clinical trials shall also be submitted.

Where relevant, studies shall be submitted providing information on the direct or indirect risks to human health, food safety or animal health of the use of the antimicrobial product in animals, as well as an assessment of the effects of risk mitigation measures proposed by the applicant to limit antimicrobial resistance development.

Pharmacological tests, toxicological tests, residue tests and safety tests shall be carried out in conformity with the provisions related to good laboratory practice (GLP) laid down in Directive 2004/10/EC of the European Parliament and of the Council[1] and Directive 2004/9/EC of the European Parliament and of the Council[2].

The environmental risk assessment connected with the release of veterinary medicinal products containing or consisting of Genetically Modified Organisms (GMOs) within the meaning of Article 2 of Directive 2001/18/EC shall be provided in the dossier. The information shall be presented in accordance with the provisions of Directive 2001/18/EC.

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[1] Directive 2004/10/EC of the European Parliament and of the Council of 11 February 2004 on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances (OJ L 50, 20.2.2004, p. 44).

[2] Directive 2004/9/EC of the European Parliament and of the Council of 11 February 2004 on the inspection and verification of good laboratory practice (GLP) (OJ L 50, 20.2.2004, p. 28).

Experiments on animals other than clinical trials shall be conducted in accordance with Directive 2010/63/EU.

The application shall, where necessary, include information regarding pharmacovigilance system.

For applications submitted through the centralised procedure, the formats made available by the Agency must be used for the submission of the dossier.

## 1.2. QUALITY DOCUMENTATION

### 1.2.1. BASIC PRINCIPLES AND REQUIREMENTS

The quality data shall include for the active substances and for the finished veterinary medicinal product the following information:

- description of the manufacturing process,

- characterisation and properties,

- quality control procedures and requirements,

- stability,

- description of the composition,

- development of the veterinary medicinal product.

All test procedures shall fulfil the criteria for analysis and control of the quality of the starting materials and the finished product. The results of the validation studies shall be provided.

Information shall be submitted describing all test procedures used in sufficiently precise detail for the tests to be reproduced in control tests, carried out at the request of the competent authority; any special apparatus and equipment having been used shall be described in adequate detail.

The formulae of the laboratory reagents shall be indicated, supplemented, if necessary, by the method of preparation. Where test procedures are included in the European Pharmacopoeia or the pharmacopoeia of a Member State, the description of test procedures may be replaced by a detailed reference to the pharmacopoeia in question.

Where relevant, chemical and biological reference material of the European Pharmacopoeia shall be used. If other reference preparations and standards have been used, they shall be identified and described in detail.

Where an active substance of the veterinary medicinal product has been included in a medicinal product for human use authorised in accordance with Directive 2001/83/EC, a quality overall summary provided for in module 2, point 2.3. of the Annex I to this Directive may replace the documentation related to the active substance or the product, as appropriate.

Where the competent authority has publicly announced that the chemical, pharmaceutical and biological/microbiological information for the finished product may be included in the dossier in the Common Technical Document (CTD) format laid down only, the detailed and critical summary on the results of pharmaceutical tests required for the manufacture of the veterinary medicinal product may be presented in the quality overall summary format.

Where an application concerns limited markets, the CTD format may be followed without prior agreement of the competent authorities.

## 1.2.2. DATA SET REQUIREMENTS FOR QUALITY

### A. Qualitative and quantitative composition

A.1. Qualitative particulars of the veterinary medicinal product

A.2. Qualitative particulars of the container and its closure

A.3. Usual terminology

A.4. Quantitative particulars

A.5. Development pharmaceutics

### B. Description of the manufacturing method

### C. Control of starting materials

C.1. Active Substances

(i) Active substances listed in pharmacopoeias

(ii) Active substances not in a pharmacopoeia

(iii) Physico-chemical characteristics liable to affect bioavailability

C.2. Excipients

Documentation shall be submitted to show that colouring matters for inclusion in veterinary medicinal products satisfy the requirements of Directive 2009/35/EC of the European Parliament and of the Council[3] except where the application for a marketing authorisation concerns certain veterinary medicinal products for topical use, such as insecticidal collars and ear tags.

Documentation shall be submitted to show that colouring matters used meet the purity criteria laid down in Commission Directive 2008/128/EC[4].

C.3. Container-closure systems

(i) Active substance

(ii) Finished product

C.4. Substances of biological origin

### D. Control tests carried out at intermediate stages of the manufacturing process

### E. Tests on the finished product

E.1. General characteristics of the finished product

E.2. Identification and assay of active substance(s)

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[3] Directive 2009/35/EC of the European Parliament and of the Council of 23 April 2009 on the colouring matters which may be added to medicinal products (OJ L 109, 30.4.2009, p. 10).

[4] Commission Directive 2008/128/EC of 22 December 2008 laying down specific purity criteria concerning colours for use in foodstuffs (OJ L 6, 10.1.2009, p. 20).

E.3. Identification and assay of excipient components

E.4. Safety tests

**F. Stability tests**

F.1. Active substances(s)

F.2. Finished product

## 1.3. SAFETY DOCUMENTATION

### 1.3.1. BASIC PRINCIPLES AND REQUIREMENTS

The safety documentation shall include an assessment of:

(a) the potential toxicity of the veterinary medicinal product and any risk of undesirable effects which may occur under the proposed conditions of use in animals; these shall be evaluated in relation to the severity of the pathological condition concerned;

(b) the potential harmful effects to humans of residues of the veterinary medicinal product or active substance in foodstuffs obtained from treated animals and any difficulties these residues may create in the industrial processing of foodstuffs;

(c) the potential risks which may result from the exposure of human beings to the veterinary medicinal product at any stage of the lifecycle of the veterinary medicinal product.;

(d) the potential risks for the environment resulting from the use of the veterinary medicinal product;

(e) the potential risks relating to the development of antimicrobial resistance.

The safety documentation shall show that mathematical and statistical procedures have been used in designing the pre-clinical studies and clinical trials and in evaluating the results. Additionally, information shall be provided regarding the therapeutic potential of the product and about the hazards connected with its use.

In some cases it may be necessary to test the metabolites of the parent compound where these represent the residues of concern.

An excipient used in the pharmaceutical field for the first time shall be treated like an active substance.

Where the veterinary medicinal product is intended for use in food-producing animals, the residue documentation shall show:

(a) to what extent, and for how long residues of the veterinary medicinal product or its metabolites persist in the edible tissues of the treated animal or in milk, eggs and/or honey obtained therefrom;

(b) that it is possible to establish realistic withdrawal periods which can be observed under practical farming conditions;

(c) that the analytical method(s) used in the residues depletion study are sufficiently validated to provide the necessary reassurance that the residues data submitted are suitable as the basis for a withdrawal period.

An environmental risk assessment shall be submitted regarding any undesirable effects which the use of the veterinary medicinal product may have on the environment and the risk of such effects. The assessment shall also identify any precautionary measures which may be necessary to reduce such risk.

This assessment shall normally be conducted in two phases. The first phase of the assessment shall always be performed and the second phase shall be performed if necessary. The details of the assessment shall be provided in accordance with accepted guidance. The assessment shall indicate the potential exposure of the environment to the product and the level of risk associated with any such exposure taking into account in particular the following items:

(a) the target animal species, and the proposed pattern of use,

(b) the method of administration, in particular the likely extent to which the product will enter directly into the environment,

(c) the possible excretion of the product, its active substances or relevant metabolites into the environment by treated animals; persistence in such excreta,

(d) the disposal of unused veterinary medicinal product or other waste product.

In the second phase, further specific investigation of the fate and effects of the product on particular ecosystems shall be conducted, in accordance with established guidance. The extent of exposure of the product to the environment, and the available information about the physical/chemical, pharmacological and/or toxicological properties of the substance(s) concerned, including metabolites, shall be taken into consideration.

### 1.3.2. DATA SET REQUIREMENTS FOR SAFETY

**A. Safety tests**

A.1. Precise identification of the product and of its active substance(s)

A.2. Pharmacology

A.2.1 Pharmacodynamics

A.2.2. Pharmacokinetics

A.3. Toxicology

A.3.1. Single-dose toxicity

A.3.2. Repeat-dose toxicity

A.3.3. Tolerance in the target species

A.3.4. Reproductive toxicity including developmental toxicity

A.3.4.1. Study of the effects on reproduction

A.3.4.2. Study of developmental toxicity

A.3.5. Genotoxicity

A.3.6. Carcinogenicity

A.4. Other requirements

A.4.1. Microbiological properties of residues (potential effects on the human gut flora, potential effects on the microorganisms used for industrial food processing)

A.4.2. Observations in humans

A.4.3. Development of resistance

A.5. User safety

A.6. Environmental risk assessment

A.6.1. Environmental risk assessment of veterinary medicinal products not containing or consisting of genetically modified organisms

A.6.2. Environmental risk assessment for veterinary medicinal products containing or consisting of genetically modified organisms

**B. Residue tests**

B.1. Metabolism and residue kinetics

B.1.1. Pharmacokinetics (absorption, distribution, metabolism, excretion)

B.1.2. Depletion of residues

B.2. Residue analytical method

## 1.4. EFFICACY DOCUMENTATION

### 1.4.1. BASIC PRINCIPLES AND REQUIREMENTS

The result of pre-clinical studies and clinical trials shall be included.

The pharmacological activity and the tolerance of the product shall be included through pre-clinical studies.

The clinical trials shall demonstrate or substantiate the efficacy of the veterinary medicinal product at the dosage regimen via the route of administration and specify its indications and contra-indications according to species, age, breed and sex, its directions for use as well as any adverse events which it may have.

Experimental data shall be confirmed by data obtained under normal field conditions.

Clinical trials shall be carried out with control animals (controlled clinical trials), unless it is justified to carry out the clinical trials without control animals. The efficacy results obtained shall be compared with those from the target animal species that have received a veterinary medicinal product authorised in the Union for the same indications for use in the same target animal species, or a placebo or no treatment. All the results obtained, whether positive or negative, shall be reported.

Established statistical principles shall be used in protocol design, analysis and evaluation of clinical trials, unless justified.

All veterinary clinical trials shall be conducted in accordance with a detailed trial protocol.

Clinical field trials shall be conducted in accordance with established principles of good clinical practice and in accordance with the principles of replacement, reduction and refinement of animal testing.

Before the commencement of any field trial, the informed consent of the owner of the animals to be used in the trial shall be obtained and documented. In particular, the animal owner shall be informed in writing of the consequences of participation in the trial for the subsequent disposal of treated animals or for the taking of foodstuffs from treated animals. A copy of this

notification countersigned and dated by the animal owner shall be included in the trial documentation.

Unless a blind field trial is conducted, the provisions on the labelling of formulations intended for use in veterinary field trials shall apply by analogy. In all cases, the words 'for veterinary field trial use only' shall appear prominently and indelibly upon the labelling.

### 1.4.2. DATA SET REQUIREMENTS FOR EFFICACY

**A.Pre-clinical requirements**

A.1. Studies demonstrating pharmacological activity;

A.2. Studies demonstrating the pharmacodynamic mechanisms underlying the therapeutic effect;

A.3. Studies demonstrating the main pharmacokinetic profile;

A.4. Studies demonstrating target animal safety;

A.5. Studies investigating resistance.

Should unexpected results occur during the course of the tests, those results shall be explained in detail.

**B. Clinical requirements**

B.1. Composition of the product batches used

B.2. Target species tolerance

B.3. Bibliographical information

## PART 2 - Technical requirements for biological veterinary medicinal products

### 2.1. INTRODUCTION

The technical documentation shall include a detailed and full description of the studies conducted or referred to, including the methods used. It shall be ensured that the data available are relevant and are of sufficient quality to fulfil the requirements.

Data submitted shall be sufficient to establish:

- the dosage for the various animal species for which the veterinary medicinal product is intended, its pharmaceutical form, its method and route of administration and its proposed shelf life.

- the reasons for any precautionary and safety measures to be taken when storing the veterinary medicinal product, administering it to animals or disposing of waste, together with an indication of potential risks that the veterinary medicinal product might pose to the environment, to public and animal health;

- an indication of the withdrawal period in the case of veterinary medicinal products intended for food-producing species.

- the therapeutic indications, contra-indications and adverse events.

The application shall contain a description of the testing methods employed by the manufacturer, the results of pharmaceutical (physico-chemical, biological or microbiological) tests and safety tests, including tests assessing the potential risks posed by the medicinal product for the environment. This impact shall be studied and consideration shall be given on a case-by-case basis to specific provisions seeking to limit it. In addition, results of residue tests, pre-clinical studies and clinical trials shall also be submitted.

Pharmacological, toxicological, residue and safety tests shall be carried out in conformity with the provisions related to good laboratory practice (GLP) laid down in Directive 2004/10/EC and Directive 2004/9/EC.

Experiments on animals, except clinical trials, shall be conducted in accordance with Directive 2010/63/EU.

The environmental risk assessment connected with the release of veterinary medicinal products containing or consisting of Genetically Modified Organisms (GMOs) within the meaning of Article 2 of Directive 2001/18/EC shall be provided in the dossier. The information shall be presented in accordance with the provisions of Directive 2001/18/EC.

The application shall, where necessary, include information regarding pharmacovigilance system.

For applications submitted through the centralised procedure, the formats made available by the Agency must be used for the submission of the dossier.

## 2.2. QUALITY DOCUMENTATION

### 2.2.1. BASIC PRINCIPLES AND REQUIREMENTS

All analytical test procedures must be described in sufficient details to enable the procedures to be repeated if necessary (e.g. by an official laboratory). All procedures need to be validated by the applicant and the results of the validation studies must be provided.

Applications for immunologicals shall contain information on diluents needed for making the final vaccine preparation.

An immunological veterinary medicinal product shall be regarded as one product even when more than one diluent is required so that different preparations of the final product can be prepared, which may be for administration by different routes or methods of administration. Diluents may be packed together with the vaccine vials or separately.

### 2.2.2. DATA SET REQUIREMENTS FOR QUALITY

**A. Qualitative and quantitative composition**

A.1. Qualitative particulars

A.2. Usual terminology

A.3. Quantitative particulars

A.4. Product development

A.5. Containers

**B. Description of manufacturing method**

**C. Production and control of starting materials**

C.1. Starting materials listed in pharmacopoeias

C.2. Starting materials not listed in a pharmacopoeia

C.2.1. Starting materials of biological origin

C.2.2. Starting materials of non-biological origin

C.2.3. Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies

**D. Control tests during the manufacturing process**

**E. Control tests on the finished product**

E.1. General characteristics of the finished product

E.2. Identification of active substance(s)

E.3. Batch titre or potency

E.4. Identification and assay of adjuvants

E.5. Identification and assay of excipient components

E.6. Safety tests

E.7. Sterility and purity test

E.8. Residual humidity

E.9. Inactivation

**F. Batch to batch consistency**

**G. Stability tests**

**H. Other information concerning genetically modified organisms**

## 2.3. SAFETY DOCUMENTATION

### 2.3.1. BASIC PRINCIPLES AND REQUIREMENTS

The safety tests shall be carried out in the target species.

The safety tests shall show the potential risks from the biological veterinary medicinal product, which may occur under the proposed conditions of use in animals. Those risks shall be evaluated in relation to the potential benefits of the product. Certificates of compliance with Good Laboratory Practice shall accompany relevant studies.

The safety documentation shall be used for assessment of the potential risks which may result from the exposure of human beings to the veterinary medicinal product, for example during its administration to the animal.

Where immunological veterinary medicinal products consist of live organisms, especially those which could be shed by vaccinated animals, the potential risk to unvaccinated animals of the same or of any other potentially exposed species shall be evaluated. In the case of live vaccine strains which may be zoonotic, the risk to humans shall be assessed.

The environmental risk assessment shall evaluate the potential harmful effects, which the use of the product may cause to the environment and identify any precautionary measures, which may be necessary to reduce such risks.

This assessment shall normally be conducted in two phases. The details of the assessment shall be provided in accordance with established guidance. The first phase of the assessment shall always be performed and shall indicate the potential exposure of the environment to the product and the level of risk associated with any such exposure, taking into account in particular the following items:

— the target animal species and the proposed pattern of use,

— the method of administration, in particular the likely extent to which the product will enter directly into the environment,

— the possible excretion of the product, its active substances into the environment by treated animals, persistence in such excreta,

— the disposal of unused or waste product.

Where the conclusions of the first phase indicate potential exposure of the environment to the product, the applicant shall proceed to the second phase and evaluate the potential risk(s) that the veterinary medicinal product might pose to the environment. Where necessary, further investigations on the impact of the product on soil, water, air, aquatic systems, non-target organisms shall be carried out.

### 2.3.2. DATA SET REQUIREMENTS FOR SAFETY

**A. Pre-clinical studies**

A.1. Safety of the administration of one dose

A.2. Safety of one administration of an overdose

A.3. Safety of the repeated administration of one dose

A.4. Examination of reproductive performance

A.5. Examination of immunological functions

A.6. Special requirements for live vaccines

A.6.1. Spread of the vaccine strain

A.6.2. Dissemination in the vaccinated animal

A.6.3. Reversion to virulence of attenuated vaccines

A.6.4. Biological properties of the vaccine strain

A.6.5. Recombination or genomic re-assortment of strains

A.7. User safety

A.8. Residue tests

A.9. Interactions with other veterinary medicinal products

**B. Clinical trials**

**C. Environmental risk assessment**

**D. Assessment required for veterinary medicinal products containing or consisting of genetically modified organism**

## 2.4. EFFICACY DOCUMENTATION

### 2.4.1. BASIC PRINCIPLES AND REQUIREMENTS

All efficacy studies shall be conducted in accordance with a fully considered detailed protocol, which shall be recorded in writing prior to commencement of the study. Pre-established systematic written procedures for the organisation, conduct, data collection, documentation and verification of efficacy trials shall be required.

All efficacy studies and trials shall be described in sufficiently precise details so as to be reproducible in controlled studies or trials, carried out at the request of the competent authorities.

Efficacy studies carried out in the laboratory shall be controlled trials, including untreated control animals unless this is not justified for animal welfare reasons and efficacy can be otherwise demonstrated. In general, these laboratory studies shall be supported by trials carried out in field conditions, including untreated control animals.

### 2.4.2. DATA SET REQUIREMENTS FOR EFFICACY

**A. Pre-clinical studies**

A.1. Quality data on the product batches used

A.2. Description of the study

**B. Clinical trials**

B.1. Qualitative data on the product batches used

B.2. Description of the trial

**C. Bibliographical information**

## 2.5. VACCINE ANTIGEN MASTER FILES

A Vaccine Antigen Master File means a stand-alone part of the marketing authorisation application dossier for a vaccine, which contains all relevant information on quality concerning each of the active substances, which are part of this veterinary medicinal product. The stand-alone part may be common to one or more monovalent and/or combined vaccines presented by the same applicant or marketing authorisation holder.

## 2.6. MULTI-STRAIN DOSSIERS

For foot-and-mouth disease, avian influenza and bluetongue vaccines a multi-strain dossier shall be submitted.

A multi-strain dossier means a single dossier containing the relevant data for a unique and thorough scientific assessment of the different options of strains or combinations of strains permitting the authorisation of vaccines against antigenically variable viruses.

# PART 3 - Technical requirements for homeopathic veterinary medicinal products

## 3.1. INTRODUCTION

The requirements as described in Part 1 shall apply to the homeopathic veterinary medicinal products referred to in Article 88 with the following modifications.

## 3.2. QUALITY

### 3.2.1. TERMINOLOGY

The Latin name of the homeopathic stock described in the marketing authorisation application dossier shall be in accordance with the Latin title of the European Pharmacopoeia or, in absence thereof, of an official pharmacopoeia of a Member State. Where relevant the traditional name(s) used in each Member State shall be provided.

### 3.2.2. CONTROL OF STARTING MATERIALS

The particulars and documents on the starting materials, i.e. all of the materials used from the first step of production of the homeopathic stock through to the final dilution to be incorporated into the finished homeopathic veterinary medicinal product, accompanying the application shall be supplemented by additional data on the homeopathic stock.

The general quality requirements shall apply to all of the starting and raw materials as well as intermediate steps of the manufacturing process up to the final dilution to be incorporated into the finished homeopathic product. Where a toxic component is present, this shall be controlled if possible in the final dilution. However, if this is not possible because of the high dilution, the toxic component shall normally be controlled at an earlier stage. Every step of the manufacturing process from the starting materials up to the final dilution to be incorporated into the finished product must be fully described.

In case dilutions are involved, these dilution steps shall be done in accordance with the homeopathic manufacturing methods laid down in the relevant monograph of the European Pharmacopoeia or, in absence thereof, in an official pharmacopoeia of a Member State.

### 3.2.3. CONTROL TESTS ON THE FINISHED MEDICINAL PRODUCT

Any exception to the general quality requirements shall be duly justified by the applicant.

Identification and assay of all the constituents that may have a toxicological effect shall be carried out. If it can be justified that identification and/or an assay on all the toxicologically relevant constituents is not possible e.g. due to their dilution in the finished medicinal product the quality shall be demonstrated by complete validation of the manufacturing and dilution process.

### 3.2.4. STABILITY TESTS

The stability of the finished product shall be demonstrated. Stability data from the homeopathic stocks are generally transferable to dilutions or potentisations obtained thereof. If no identification or assay of the active substance is possible due to the degree of dilution, stability data of the pharmaceutical form may be considered.

## 3.3. SAFETY

The requirements on safety set out in Part 1 shall apply to the registration of homeopathic veterinary medicinal products referred to in Article 88, without prejudice to the provisions of Regulation (EC) No 470/2009 for substances included in the homeopathic stocks intended for administration to food-producing animal species.

Any missing information must be justified, e.g. justification must be given why demonstration of an acceptable level of safety can be supported although some studies are lacking.

# ANNEX III

## Requirements for abridged and reduced dossiers for marketing authorisation applications

### 1. Generic veterinary medicinal products

Applications for generic veterinary medicinal products shall contain the documentation referred to in Annex I, quality data and data demonstrating that the product has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicinal product and data showing bio- equivalence with the reference medicinal product.

All immediate-release oral pharmaceutical forms shall be considered to be the same pharmaceutical form.

Every claim in the summary of product characteristics not known from or inferred from the properties of the medicinal product and/or its therapeutic group shall be discussed in the non-clinical or clinical overviews and summaries and substantiated by published literature, additional studies or both.

The following information shall be submitted as part of an application:

— the grounds for claiming essential similarity,

— a summary of impurities present in batches of the active substance(s) as well as those of the finished medicinal product (and where relevant decomposition products arising during storage) as proposed for use in the product together with an evaluation of these impurities,

— an evaluation of the bio-equivalence studies or a justification as to why studies were not performed,

— if applicable, additional data in order to demonstrate the equivalence of safety and efficacy properties of different salts, esters or derivatives of an authorised active substance shall be

provided by the applicant; those data shall include evidence that there is no change in the pharmacokinetics or pharmacodynamics of the therapeutic moiety and/or in toxicity, which could influence the safety/efficacy profile.

For generic veterinary medicinal products intended to be administered by intramuscular, subcutaneous or transdermal routes, the following additional data shall be provided:

— evidence to demonstrate equivalent or differing depletion of residues from the administration site, which may be substantiated by appropriate residue depletion studies,

— evidence to demonstrate target animal tolerance at the administration site, which may be substantiated by appropriate target animal tolerance studies.

**2. Similar biological veterinary medicinal products**

Where a biological veterinary medicinal product which is similar to a reference biological veterinary medicinal product does not meet the conditions in the definition of generic medicinal product, information to be supplied shall not be limited to pharmaceutical, chemical and biological data, supplemented with bio-equivalence and bioavailability data. In such cases, additional data shall be provided, in particular on the safety and efficacy of the product.

**3. Bibliographic applications**

For veterinary medicinal products the active substance(s) of which has/have been in 'well-established veterinary use' as referred to in Article 20, with documented efficacy and an acceptable level of safety, the following is required:

A. Information as listed in the Annex I.

B. Quality data.

C. Detailed scientific bibliography addressing all aspects of the safety and efficacy.

D. Post-marketing experience with other products containing the same constituents.

It shall not be allowed to refer to scientific literature in accordance with paragraph 1 if the application provides for a new indication of a substance in well-established use.

Assessment reports published by the Agency as an outcome of the evaluation of applications for maximum residue limits in accordance with Regulation (EC) No 470/2009 may be used as appropriate scientific literature referred to in paragraph 1, in particular for the purpose of demonstrating the safety of the active substance.

**4. Combination veterinary medicinal products**

Data as described in Annex II shall be provided for the combination veterinary medicinal product. It shall not be necessary to provide studies on the safety and efficacy of each active substance. It shall nevertheless be possible to include information on the individual substances in the application for a fixed combination.

The submission of data on each individual active substance, in conjunction with the required user safety tests, residues depletion studies and clinical studies on the fixed combination product, may be considered a suitable justification for omitting data on the combination product, based on animal welfare grounds and unnecessary testing on animals, unless there is suspected interaction leading to added toxicity.

Where applicable, information regarding the manufacturing sites and the safety evaluation of extraneous agents shall be provided.

**5. Informed consent applications**

Applications based on Article 19 shall contain the data described in Annex I, provided that the marketing authorisation holder for the original veterinary medicinal product has given the applicant his consent to refer to the safety and efficacy data dossier of that product. In this case, there is no need to submit quality, safety and efficacy detailed and critical summaries.

**6. Documentation for applications in exceptional circumstances**

A marketing authorisation may be granted subject to certain specific conditions and restrictions requiring the applicant to introduce specific procedures, in particular concerning the safety and efficacy of the veterinary medicinal product, when, as provided for in Article 22, the applicant can show that he is unable to provide comprehensive data on the efficacy and safety under normal conditions of use.

## ANNEX IV

## CORRELATION TABLE

Directive 2001/82/EC

| Directive 2001/82/EC | This Regulation |
|---|---|
| Article 1 | Article 4 |
| Article 2(1)<br>Article 2(2)<br>Article 2(3) | Article 2(1)<br>Article 3<br>Article 2(2),(3),(4) |
| Article 3 | Article 2(4) |
| Article 4(2) | Article 120 |
| Article 5 | Article 5 |
| Article 6 | Article 7(4) |
| Article 7 | Article 119 |
| Article 8 | Article 119, 121 |
| Article 9 | Article 8 |
| Article 10 | Article 115 |
| Article 11 | Articles 116, 117 |
| Article 12 | Article 7 |
| Article 13(1)<br>Article 13(2),(3),(4) | Article 16<br>Article 18 |
| Article 13a | Article 20 |
| Article 13b | Article 17 |
| Article 13c | Article 19 |
| Article 14 | Article 30 |
| Article 16 | Article 88 |
| Article 17 | Article 89 |
| Article 18 | Article 90 |

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