

Guide to Registration of Homeopathic Veterinary Medicinal Products



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1 SCOPE

This guidance is intended for those companies wishing to obtain registration for the marketing of homeopathic medicinal products for veterinary use in Ireland. It covers the criteria for registration as set out in Regulation (EU) 2019/6 ('the Regulation'), includes information taken from other EU Directives as appropriate, and is applicable from 28 January 2022. It provides advice on the administrative aspects of the registration scheme and gives guidance on how the application should be made.

Regulation (EU) 2019/6 recognises the special characteristics of homeopathic veterinary medicinal products, especially the constituents of those products. In this regard, Article 86 of the Regulation describes the establishment of a simplified registration system for homeopathic veterinary medicinal products.

A 'homeopathic veterinary medicinal product' is defined in the Regulation as 'a veterinary medicinal product prepared from homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence thereof, by the pharmacopoeias used officially in Member States'.

This guidance does not attempt to answer every question a company may have, and the HPRA can provide advice on individual queries and products by contacting vetinfo@hpra.ie.

2 PURPOSE AND SCOPE OF THE REGISTRATION SCHEME

2.1 The purpose of the scheme

The homeopathic veterinary medicines registration scheme is a simplified regulatory procedure which enables companies to market certain homeopathic veterinary medicinal products in Ireland. The basis for the scheme is set out in Regulation (EU) 2019/6.

The supply of veterinary medicinal products in Ireland is governed under the provisions of the relevant national legislation and associated EU legislation. It is unlawful for any veterinary medicinal product to be placed on the market in Ireland except in accordance with a product authorisation or registration granted by the HPRA or the European Commission or, in exceptional cases, by the Department of Agriculture, Food and the Marine. Under the provisions of these regulations, a product marketing authorisation may only be granted where satisfactory evidence of safety, quality and efficacy has been established. In the case of homeopathic veterinary medicinal products which satisfy all the conditions specified in Article 86 of Regulation (EU) 2019/6, a simplified product registration may be granted where satisfactory evidence of safety and quality has been established.

2.2 Products outside the scope of the registration scheme

Products which do not satisfy all the conditions set out in Article 86 of Regulation (EU) 2019/6 are outside the scope of the registration scheme and require a marketing authorisation from the HPRA in accordance with the standard requirements for quality, safety and efficacy.

In addition, the following are outside the scope of Regulation (EU) 2019/6, as amended, and are therefore not covered by this registration scheme:

- Products for use in the treatment of humans
- Products prepared in accordance with a magistral or officinal formula (i.e. those prepared in a pharmacy in accordance with a veterinary prescription for an individual animal or small group of animals)

2.3 Existing homeopathic veterinary medicinal product registrations

The registration of homeopathic veterinary medicinal products granted in accordance with Directive 2001/82/EC before 28 January 2022 shall be deemed to have been issued in accordance with Regulation (EU) 2019/6 and are, as such, subject to the relevant provisions of Regulation (EU) 2019/6.

Registered homeopathic veterinary medicinal products placed on the market in accordance with Directive 2001/82/EC may continue to be made available until 29 January 2027, even if they are not in compliance with Regulation (EU) 2019/6.

2.4 Products eligible for registration

The homeopathic registration scheme applies to homeopathic medicinal products for veterinary use which are intended to be placed on the market and which fulfil the criteria specified in Regulation (EU) 2019/6. To be eligible for registration, a homeopathic veterinary medicinal product must satisfy all the following criteria:

- It must be prepared from homeopathic stocks in accordance with a homeopathic manufacturing procedure described by the European Pharmacopoeia or, in the absence of such a description, by any pharmacopoeia used officially in an EU member state.
- It must be administered by a route of administration described in the European Pharmacopoeia or in the absence thereof, by any of the pharmacopoeias currently used officially in Member States.
- There must be no specific therapeutic indication included in the labelling or in any information relating to the product (i.e. promotional material).

- The product must bear the scientific name of the stock or stocks from which it is prepared; if the product is composed of two or more stocks, the scientific names of the stocks may be supplemented by an invented name.
- It must be sufficiently dilute to guarantee safety; it must contain no more than one part per 10,000 of the mother tincture.
- In the case of homeopathic veterinary medicinal products intended for food-producing animal species, the active substances shall be those pharmacologically active substances allowed in accordance with Regulation (EC) No 470/2009 and any acts adopted on the basis thereof.

2.5 Who should apply for registration

If a homeopathic medicinal product is to be marketed in Ireland under the registration scheme, a registration certificate must be held by the person responsible for placing it on the market. Applications for registration under the scheme may be made by any person who wishes to place a product on the market. A registration for a homeopathic veterinary medicinal product shall only be granted to an applicant established in the Union. Companies should also be aware of the need for the following authorisations and registration requirements:

2.5.1 Registration holders and manufacturers

All sites of registration holders, manufacturing sites, distribution sites, etc., must be registered in the EMA's Organisation Management Service (OMS) as part of SPOR data management services. When registered, each site will be given a LOC ID which should be included in the application forms. If any of the relevant organisations or sites are not already registered, you will need to register it with the EMA. Further information is available on the EMA's IRIS platform website at <https://iris.ema.europa.eu/locations/>.

2.5.2 Manufacturers

A company which manufactures, or which proposes to manufacture, homeopathic veterinary medicinal products must hold a manufacturer's authorisation. 'Manufacture' includes all processes carried out while making the product, including diluting, mixing and quality control. A manufacturer's authorisation is also needed for 'assembly' (e.g. filling and labelling containers), and for third country imports, from a country outside the European Economic Area (EEA).

The HPRA is the competent authority for evaluating applications for manufacture of homeopathic veterinary medicinal products in the case of those products which are manufactured in Ireland. Where products are manufactured in other Member States, the national competent authority of the Member State concerned has the responsibility to grant the manufacturing authorisation.

2.5.3 Importers

A company which imports homeopathic veterinary medicinal products from countries outside the EEA needs a manufacturer's authorisation as described above.

2.5.4 Wholesalers

A company which acts as a wholesaler, or which proposes to do so for the supply of homeopathic veterinary medicinal products for the purpose of resale (other than those it manufactures itself), will need a wholesaler's authorisation. Authorisations to wholesale veterinary medicines in Ireland may be obtained from the Department of Agriculture, Food and the Marine.

3 HOW TO APPLY FOR REGISTRATION

3.1 Application form

Applications should be made on the appropriate HPRA application form accompanied by the data specified in this guide. A separate application form should be completed for each series of dilutions and for each pharmaceutical form for which you seek registration. For combination products, please complete a separate form for each formulation.

The application form is available under the 'Make a submission' section of the HPRA website at www.hpra.ie.

3.2 Registration numbers

Before submitting the application(s) you will need:

- a company number, and
- a product number for each product you wish to register.

These numbers are combined to produce a provisional registration number, e.g. HoVR 01/001, (where HoVR represents homeopathic veterinary registration, 01 is the number allocated to the company and 001 is the product number). This registration number is provisional until the application has been determined and the registration granted or rejected. This number gives no indication of product status.

Provisional registration numbers can be obtained by contacting the Receipts and Validation section of the HPRA.

If an applicant company already holds veterinary product authorisations, then it should use the company number already allocated.

3.3 Where to send the application

The preferred format for applications for registration of homeopathic veterinary medicinal products is an electronic format. Hard copy submissions can be accepted, if electronic submission is not possible.

For details on sending the application to the HPRA, please see the HPRA 'Guide to Electronic Submissions – Veterinary Medicines' available on the HPRA website under 'Regulation', and 'Guidance documents'.

Applications must be accompanied by the correct fee and fee application form - see the 'Guide to Fees for Veterinary Products' on the HPRA website for details of the fees and the method of fee payment. The fee should be sent on the same day as the application form and data. The application will not be considered until the fee has been paid. All fees must be paid in full and any associated bank charges are for your own account.

4 THE APPROVAL PROCESS

4.1 Assessment of the application

When the application and fee have been received, the assessor will check the validity and eligibility of the application. The HPRA will inform you if the product is not eligible for registration under the scheme.

The data accompanying the application will be assessed and if this is satisfactory the HPRA will issue a registration certificate. If there are deficiencies in the application, the assessor will inform you and resolve these, wherever possible, so that a registration certificate can be granted.

4.2 Issue of registration certificates

Following approval, the registration certificate will be sent to you electronically. On receipt, you will be able to market the registered homeopathic product citing the HoVR registration number on the label.

4.3 Timescales for approval

In accordance with Regulation 2019/6, the procedure of registration of a homeopathic veterinary medicinal product shall be completed within 90 days of the submission of a valid application.

5 ACCOMPANYING DATA

5.1 Data required

Under Article 87 of Regulation (EU) 2019/6, the following information must be provided to demonstrate the pharmaceutical quality and batch-to-batch homogeneity of the products concerned:

Product details

- Scientific name (or other name used in a pharmacopoeia) of the homeopathic stock(s)
- Pharmaceutical form
- Route of administration
- Degree of dilution to be registered

Production and control of homeopathic stocks

- A dossier describing how the homeopathic stock(s) are obtained and controlled
- Bibliographic justification of the homeopathic nature and use of the stock(s)
- If the product contains biological substances, a description of the measures taken to ensure the absence of pathogens

Production and control of the dosage form

- A manufacturing and control file for each pharmaceutical form
- A description of the method of dilution and potentisation

Stability of the dosage form

- Data concerning the stability of the homeopathic veterinary medicinal product

Manufacturing authorisation covering the veterinary medicinal product concerned

- A manufacturing authorisation covering the veterinary medicinal product concerned

Registration by other EU Member States

- Copies of any registrations or authorisations obtained for the same homeopathic veterinary medicinal product in other EU Member States. (Note that if the product is registered or authorised or an application is under examination in another Member State, the application may have to be made via mutual recognition.)

Labelling

- The text to appear on the package leaflet, outer packaging and immediate packaging of the homeopathic veterinary medicinal products to be registered.

Withdrawal period

- Proposed withdrawal period with justification

More detailed advice on the data required for homeopathic registration is provided in this guide under Appendix A, Quality and Control of Homeopathic Stocks, and Appendix B, Manufacture and Control of Dosage Forms.

5.2 Presentation of data

A series of dilutions relating to one pharmaceutical form may be covered by one set of data. For example, one set of data is acceptable for Arnica tablets at dilutions of 6x, 6c, and 30c, and a second set of data for Arnica drops at 6x, 6c, and 30c. A single registration certificate will then be issued for each set. A subsequent potency of one of these products submitted later will attract an additional fee and be covered by a separate certificate.

5.3 Format of presentation

Data should be submitted in two separate volumes.

Volume 1 should include:

- Application form
- Manufacturing authorisation(s)
- Any registrations or authorisations issued by other EU member states
- The text to appear on the package leaflet and labelling

Volume 2 should include:

- Production and control of homeopathic stocks
- Production and control of the dosage form
- Stability of the dosage form
- Proposed withdrawal period with justification

There is no requirement for an expert report.

5.4 Homeopathic stocks

The homeopathic stock should be named with reference to an appropriate pharmacopoeial monograph. Information should be provided on the source material (e.g. name of supplier, batch data), details concerning the preparation of the homeopathic stock, and batch data. In some cases, additional information may be requested before the application is approved.

If no monograph is available for the material or the homeopathic stock, a suitable in-house specification should be developed, set out in a manner similar to that of a pharmacopoeial monograph. Adequate justification should be given for this specification. Homeopathic stocks should be prepared by a homeopathic manufacturing method described in an appropriate pharmacopoeia.

Reference should be made to the European Pharmacopoeia (Ph. Eur.), French or German Homeopathic Pharmacopoeias, or to the Homeopathic Pharmacopoeia of the United States.

The homeopathic use of the stocks used to prepare the medicinal product should be justified by reference to a recognised homeopathic Materia Medica.

5.5 Dosage form

Where the diluted homeopathic stock is to be added to a base (e.g. cream, ointment or pilule) details of the manufacture of that formulation must be provided.

If the information applies to more than one product produced by the same company it can be provided as a formulation master file.

5.6 Stability

Stability testing (in accordance with VICH/CVMP guidelines) of the dosage form is necessary to ensure that the finished product specifications are met throughout the claimed shelf life under the designated storage condition. Evidence will be required to show that the dosage form remains stable over the claimed shelf life at a specified temperature.

6 MANUFACTURE AND WHOLESALE

6.1 Manufacturer's authorisation

Article 88 of Regulation (EU) 2019/6 requires all manufacturers of veterinary medicinal products, including importers of products from outside the EEA, to hold an appropriate authorisation. In Ireland the authorisation is in the form of a manufacturer's authorisation, issued by the HPRA or the Competent Authority of another Member State. To obtain an authorisation, an applicant must complete an application for a manufacturer's authorisation (found under the 'Make a submission' section of HPRA website).

The HPRA will only issue an authorisation when it is sure the information contained in the application is accurate. It will be conditional on the holder being able to meet approved standards of Good Manufacturing Practice (as per 'The Rules governing Medicinal Products in the European Union, Volume 4. Medicinal Products for Human and Veterinary use: Good Manufacturing Practices').

6.2 Compliance with Good Manufacturing Practice

Detailed guidelines on the principles of good manufacturing practice (GMP) are published by the European Commission in the 'Guide to Good Manufacturing Practice for Medicinal

Products'. Holders of manufacturers' authorisations are required to manufacture medicinal products in accordance with the principles and guidelines of GMP.

6.3 Import authorisation

Article 88 of Regulation (EU) 2019/6, requires all importers of medicinal products from outside the EEA countries to hold an authorisation. In Ireland the authorisation is in the form of a manufacturer's authorisation. Applicants should have available the services of a Qualified Person (Article 97 of Regulation (EU) 2019/6).

6.4 Qualified Persons

Article 97 of Regulation (EU) 2019/6 requires the holder of a manufacturer's authorisation to appoint a Qualified Person (QP) who is to be named on the licence. The QP's duties are specific and are intended to ensure that every batch of medicinal products has been manufactured and/or assembled and checked in accordance with legal requirements. A QP has a personal responsibility for ensuring that the required tests and controls are carried out and must sign or certify, for each batch, that the appropriate tests have been carried out and that it complies with the relevant requirements.

Article 97 of Regulation (EU) 2019/6 prescribes the qualifications for appointment as a QP. Candidates for appointment as a QP must meet specific educational and vocational requirements.

6.5 Inspection

Article 123 of Regulation (EU) 2019/6, 'Controls', applies to homeopathic veterinary medicinal products. This article requires the competent authority to ensure, by inspection at appropriate intervals, that manufacturing authorisation holders (manufacturers and importers of veterinary medicinal products) and holders of a registration(s) for homeopathic veterinary medicinal products are complying with the legal requirements.

Inspectors are empowered to inspect all authorised sites, to take samples and to examine all relevant documents. Following an inspection, the authorisation holder or registration holder will be informed in writing of any case of non-compliance and will have the opportunity to submit comments.

7 SALE AND SUPPLY

7.1 Route of sale and supply

The system by which medicines are classified as prescription only medicine (POM), licensed retailer (LR) or companion animal medicine (CAM) applies equally to registered homeopathic

products. The classification of a homeopathic product is to be determined at the time of registration, on a product-by-product basis. Essentially the same rules will be followed for registered homeopathic products as apply to all veterinary medicinal products.

8 VARIATION, RENEWAL AND SUSPENSION OF CERTIFICATES

8.1 Application for variations

Where changes to a certificate of registration or the data supplied with the application are to be changed, the homeopathic veterinary medicinal products registration(s) should be varied in accordance with the classifications laid down in the 'EMA/CMDv Guidance on the details of the classification of variations requiring assessment according to Article 62 of Regulation (EU) 2019/6 for veterinary medicinal products and on the documentation to be submitted pursuant to those Variations'. Applications for variations requiring assessment are made using the [EU Application form](#).

Where the changes are relevant to homeopathic veterinary medicinal products and are classified under Commission Implementing Regulation (EU) 2021/17 (i.e. as variations not requiring assessment), the change(s) should be submitted via the Union Product Database (UPD) as a variation not requiring assessment.

8.2 Duration of validity of registration certificates

A registration for a homeopathic veterinary medicinal product shall be valid for an unlimited period.

8.3 Refusal

The HPRA may refuse an application for a product registration where:

- a) The applicant fails to submit information, documents, samples or other materials in accordance with Regulation (EU) 2019/6.
- b) The HPRA is satisfied, following examination of such information, documents, samples or other materials that:
 - the information contained in or furnished in connection with the application is found to be incorrect or inadequate, or
 - the product may be harmful under normal conditions of use, or
 - the qualitative or quantitative composition of the product to which the application relates is not as declared by the applicant, or
 - the labelling or package leaflet does not comply with the provisions of Regulation (EU) 2019/6.

8.4 Suspension and revocation

A certificate of registration may be suspended or revoked if, for example, the product proves to be harmful in the normal conditions of use, where its composition is not as declared or where any material or information provided in connection with the application is found to be incorrect.

8.5 Withdrawal from the market

The HPRA may require a product to be withdrawn from the market if, for example, it proves harmful in the normal conditions of use, if its composition is not as declared or if details of controls have not been provided as requested.

A certificate holder may also voluntarily withdraw a certificate of registration by applying to the HPRA.

9 LABELLING

9.1 Labelling of registered products

Labelling should be legible, indelible and comprehensive. It should be either in the English language only or in English and one or more other languages (provided that the same particulars appear in all languages).

The labelling of all containers and packages must include clear mention of the words 'homeopathic veterinary medicinal product'.

In addition, specific information is required on the labelling, as set out in Regulation (EU) 2019/6. The labelling of registered homeopathic veterinary medicinal products cannot include any other information.

General guidance on labelling requirements is given in Appendix C of this guide and guidance on the labelling requirements for registered homeopathic products and labelling of small containers can be found in Appendix D of this guide.

9.2 Small containers

All the required particulars must appear on either the container or the package; there is no stipulation as to where specific items must appear, if all the specified information is present. Where the container itself is not more than 50 ml, reduced labelling as specified in Appendix D of this guide, may be applied.

9.3 Leaflets

Homeopathic veterinary medicinal products must be supplied with a leaflet. It must contain all the particulars required for the correct use of the product in accordance with labelling, and no other information.

Article 16 of Regulation 2019/6 prescribes the details to be included in the package leaflet of homeopathic veterinary medicinal product.

9.4 Changes to approved labelling

All changes to labelling including those which relate to particulars on the registration certificate must be submitted as a variation for approval before implementation. Changes to labelling caused by related changes to the registration certificate should be submitted with the variation application.

10 PHARMACOVIGILANCE

In relation to the reporting of suspected adverse events following use of a registered homeopathic veterinary medicinal product, the requirements are the same as for veterinary medicinal products authorised by the standard means. The legislative requirements are set out in Section 5 (Articles 73-81) of Regulation (EU) 2019/6.

The requirements include, but are not limited to:

- having an appropriate pharmacovigilance system in place to permit collecting, collating, evaluating and reporting of suspected adverse events in a timely manner,
- having in place a pharmacovigilance system master file (PSMF) that describes in detail the pharmacovigilance system and how compliance with good pharmacovigilance practice is ensured,
- designating a qualified person responsible for pharmacovigilance (QPPV) who shall be located in the EU and be responsible for pharmacovigilance of the registered homeopathic veterinary medicinal product,
- report all suspected adverse events following use of the product within 30 days,
- perform signal management in accordance with Article 81 of Regulation (EU) 2019/6 and record results of the signal management for the product at least annually.

Further details and guidance relating to pharmacovigilance can be obtained from relevant guidelines available on the European Medicine's Agency's website.

APPENDIX A QUALITY AND CONTROL OF HOMEOPATHIC STOCKS

A1 Introduction

Applications to register homeopathic veterinary medicinal products must include robust documentation on both the production and control of the homeopathic stock and the final dosage form. Due to the inherently low concentrations of active substances in homeopathic preparations, quality control tests conducted solely on the finished product often provide limited insight into batch consistency or pharmaceutical quality, therefore detailed information on the stock preparation should be provided. The quality, reproducibility, and homogeneity of the homeopathic stock should be demonstrated through controlled procedures, validated processes, and appropriate documentation supporting the consistent quality of the finished product and compliance with Article 87 of Regulation (EU) 2019/6.

A2 Preparation of stocks

Homeopathic stocks must be prepared in accordance with a manufacturing method set out in a homeopathic pharmacopoeia. Where the manufacturing process departs from that of the pharmacopoeia, other justification should be provided. The European Pharmacopoeia, the German Homeopathic Pharmacopoeia, the Homeopathic Pharmacopoeia of the United States and homeopathic monographs cited in the French Pharmacopoeia may be used. Applicants should refer to the appropriate section of the homeopathic pharmacopoeia.

Raw materials and vehicles used should be of an appropriate pharmacopoeial quality unless adequately justified (see section below on raw materials).

The quantity of raw material and vehicles used for each batch should be specified. If batch sizes vary, then a representative batch size should be stated.

The nature of containers used for the maceration process should be described, together with the times and conditions used.

A3 Control of starting materials

Raw Materials - specifications

Raw materials used should comply with the section on raw materials set out in individual monographs of a homeopathic pharmacopoeia.

In some instances, it may be necessary to include controls additional to those specified in the individual monograph, for example:

Plant material

- Microscopic examination
- Limit tests for pesticides and micro-organisms
- Description of the part of the plant used

Zoological material and minerals of natural origin

- Bioburden controls or absence of pathogens with reference to transmissible agents

Where no monograph exists, applicants will be required to draw up a suitable monograph for the raw material, considering the following characteristics as appropriate to the nature of the raw material (which may be botanical, zoological or chemical in origin).

- Description, identity, name and appearance
- Assay
- Melting point, solubility
- Microbiological contamination
- Impurities (including sulphated ash, foreign material)
- Loss on drying

In some cases, for example certain minerals or organic substances, it may be necessary to refer to the European Pharmacopoeia.

Established guidelines should be taken into account, for example the Committee for Human Medicinal Products (CHMP) guidelines on biological and botanical raw materials and the Homeopathic Medicinal Products Working Group (HMPWG) of the Heads of Medicines Agencies documents on 'Points to consider on Safety of Homeopathic Medicinal Products from Biological Origin' and 'Points to consider on Non-clinical Safety of Homeopathic Medicinal Products of Botanical, Mineral and Chemical Origin'. Additional information should be provided as appropriate.

Supporting data

Applicants should provide data to demonstrate compliance with the proposed monograph (batch data or certificates of analysis for three batches). Where additional controls are necessary, evidence should be provided to show that these controls are met.

Where it is necessary for an applicant to establish a monograph, the controls and limits applied should be justified and analytical methods validated.

Supporting data for plant material should include details of the source of the material, cultivation and time of harvesting. Details of any drying procedure used and any treatment to reduce levels of microbial contamination should be stated. It is preferable for plant material to be grown organically (see guideline on Good Agricultural and Cultivation Practices (GACP)). Supporting data for zoological material should include information on the collection, treatment and storage of the source material.

Vehicles

Vehicles used for the preparation of homeopathic stocks should be of an appropriate pharmacopoeial quality unless justified.

A4 Control of stocks

Applicants should provide satisfactory evidence in the form of batch data or certificates of analysis to demonstrate that the stock meets the agreed specification.

Where a stock is not the subject of an approved monograph, the specifications used to control the stock should be adequately justified and analytical methods validated.

Where additional controls are used for monographed stocks, evidence should be provided to show that these are adhered to.

A5 Stability of stocks

Evidence of stability should be provided unless stocks are freshly prepared for immediate use.

The stability of homeopathic stocks should be established with due reference to the specification used to control the stock at the time of preparation.

Stability should be monitored over a storage period in controlled conditions (e.g. temperature and humidity – VICH/CVMP stability guidelines) and an appropriate shelf life established, based on the results. This work may be carried out on an on-going basis, and applicants may wish to extend the shelf life in the light of available information.

Manufacturers of stocks should provide clear advice concerning storage conditions, for example, below 25°C, protected from light. Diluted stocks should be assigned the same shelf life (expiry date) as the original stock.

A6 Justification of the homeopathic use of the stock

Reference should be made to a suitable Materia Medica such as Clarke or Boericke. Where a stock has not been included in a Materia Medica, appropriate literature references should be provided.

APPENDIX B MANUFACTURE AND CONTROL OF DOSAGE FORMS

B1 Introduction

Applications to register homeopathic veterinary medicinal products should be accompanied by supporting data on the production and control of the dosage form as laid down in Regulation (EU) 2019/6; the provisions of the quality standards applied to homeopathic medicines are similar to those applied to all other medicinal products for veterinary use. The special nature of homeopathic products is such that where manufacturing processes for dosage forms are standardised, the supporting data can be held in a master file on the formulation to which the applicant may cross-refer. Due to the extremely low levels of stocks present in the dosage form, it is particularly important to ensure that adequate planning and in-process control is applied to the manufacturing process to ensure batch homogeneity. These guidelines outline the general requirements for the accompanying data, taking account of the variety of homeopathic dosage forms, which are subject to registration.

B2 Formulation master files

Applicants may choose to present data on 'inert' or 'un-medicated' dosage forms in the form of a formulation master file to which they may cross-refer following its approval.

The formulation master file should contain the following information:

- Formulation details
- Development pharmaceuticals
- Container to be used for marketing
- Method of manufacture, in-process controls, including application of the diluted stock
- Specification of inert or un-medicated dosage form
- Batch data of inert or un-medicated dosage form
- Stability of inert or un-medicated dosage form

B3 Formulation

Complete Composition

Full details of the formulations should be provided for each product, including the theoretical composition of excipients in the final formulation.

Development Pharmaceuticals

Details should be provided of any development work, which is relevant to the formulation such as preservative efficacy data for topical creams, oral liquids and eye drops. The role of the excipients should be described.

Container

A description of the container and closure should be provided, including specifications.

B4 Manufacture

Applicants should refer to the method set out in a named homeopathic pharmacopoeia and should provide supplementary information as set out below. Applicants will be expected to comply with GMP requirements (as per 'The Rules governing Medicinal Products in the European Union, Volume 4. Medicinal Products for Human and Veterinary use: Good Manufacturing Practices').

Batch size and manufacturing formula

Details of a typical batch size should be provided. The quantity of stock to be added to the dosage form, and the degree of dilution of the stock prior to it being added should be declared.

Manufacturing process

The key elements of the manufacturing process and any standard operating procedures used should be summarised. Any sterilisation procedures should be described.

In-process controls

Where in-process controls are used, these should be stated, for example during the dilution process.

Process validation

Information on process validation should be made available, especially concerning more complex dosage forms. For sterile products (eye drops) an accepted pharmacopoeial method should be used.

Specifications

Specifications of excipients to be used in the un-medicated dosage form should be declared. Container specifications should be listed.

B5 Finished product specification

The finished product specification should control the organoleptic and physical characteristics of the product. An identity test should be included for the stock at low dilutions. The finished product specification should take account of any special characteristics of the dosage form. For example, creams might include a control for preservatives and eye drops should be sterile.

Analytical Controls

All methods used should accord with a pharmacopoeia (e.g. Ph. Eur.). Where a pharmacopoeial method is not available or appropriate, a suitable, validated alternative should be used.

Batch Data

Batch data should be made available for at least three batches, which should preferably be at production scale.

B6 Dilution and potentisation

Details of the homeopathic method used for dilution and potentisation should be provided, together with the method used to incorporate the diluted stock into the un-medicated dosage form. Validation data should be provided to demonstrate that the process consistently yields a uniform product. The quality and quantity of diluent should be described, and the details of any in-process controls provided.

B7 Stability studies

Stability studies should be carried out in the container for marketing and should be conducted at a controlled temperature or range of temperatures (VICH Guidelines). The extent of testing to be carried out will require careful consideration and will depend upon the nature of the product. Examples of what might be required include preservative efficacy data for creams, or maintenance of alcohol content for oral liquids.

The stability of tablets or granules medicated using high dilution of stock can be established and the results extrapolated to other tablets provided an identical container and manufacturing process are used. The same principle applies to liquid products of similar composition.

For more complex dosage forms such as creams or multi-dose eye drops, stability should be evaluated for individual products.

APPENDIX C GENERAL LABELLING REQUIREMENTS

General labelling requirements are laid out in Regulation (EU) 2019/6.

Legibility

Labelling should be legible, indelible and comprehensive. It should be either in the English language only or in English and one or more other languages (provided that the same particulars appear in all languages). Companies should supply an undertaking that the other language(s) provide the same particulars.

Print size or type

There is no minimum print size laid down by regulations. All labels must be easily read under normal circumstances, and companies must have regard to this when considering print size, colour and layout.

Concertina and fold-out labels/leaflets

This type of leaflet/label attached to a container is acceptable so long as the specific labelling requirements of the homeopathic registration scheme are met.

Information on inner surface of packaging

Information printed on the inner surface of packaging is not acceptable. All the labelling requirements must be shown on the outer surface of the packaging.

APPENDIX D LABELLING OF REGISTERED HOMEOPATHIC PRODUCTS

The particulars to appear on the immediate package (immediate labelling), outer package (outer labelling) and package leaflets of homeopathic veterinary medicinal products, are outlined below.

Where there is no outer packaging, all the information referred to below must appear on the immediate packaging.

No other information should be included, as provided for by Regulation (EU) 2019/6.

Immediate labelling

- a) the scientific name of the stock or stocks followed by the degree of dilution, using the symbols of the European pharmacopoeia or, in the absence thereof, of the pharmacopoeias used officially in Member States. Where two or more stocks are present the scientific name can be supplemented by an invented name.
- b) the name or company name of the registration holder (i.e. the registration certificate holder)
- c) the route of administration
- d) the pharmaceutical form
- e) special storage precautions, if any
- f) the target species
- g) if applicable, the withdrawal period, even if such period is zero
- h) the words 'homeopathic veterinary medicinal product'
- i) the expiry date in the format: 'mm/yyyy', preceded by the abbreviation 'Exp'
- j) the manufacturer's batch number, preceded by the word 'Lot'

Outer labelling

- a) the scientific name of the stock or stocks followed by the degree of dilution, using the symbols of the European pharmacopoeia or, in the absence thereof, of the pharmacopoeias used officially in Member States. Where two or more stocks are present the scientific name can be supplemented by an invented name.

- b) the name or company name of the registration holder (i.e. the registration certificate holder)
- c) the route of administration
- d) the pharmaceutical form
- e) special storage precautions, if any
- f) the target species
- g) if applicable, the withdrawal period, even if such period is zero
- h) the words 'homeopathic veterinary medicinal product'
- i) the expiry date in the format: 'mm/yyyy', preceded by the abbreviation 'Exp'
- j) the manufacturer's batch number, preceded by the word 'Lot'
- k) the contents by weight, volume, or number of immediate packaging units of the homeopathic veterinary medicinal product
- l) the warning to 'Keep out of the sight and reach of children'
- m) the warning 'For animal treatment only'
- n) a recommendation to read the package leaflet
- o) the registration number specified in the certificate of registration

Package leaflet

- a) the scientific name of the stock or stocks followed by the degree of dilution, using the symbols of the European Pharmacopoeia or, in the absence thereof, of the pharmacopoeias used officially in Member States. Where two or more stocks are present the scientific name can be supplemented by an invented name.
- b) the name or company name and permanent address or registered place of business of the registration holder and, where appropriate, of the manufacturer
- c) the method of administration and, if necessary, the route of administration
- d) the pharmaceutical form

- e) special storage precautions, if any
- f) the target species and, where appropriate, dosage for each such species
- g) a special warning, if necessary, for the homeopathic veterinary medicinal product
- h) the registration number specified in the certificate of registration
- i) withdrawal period, if applicable
- j) the statement 'homeopathic veterinary medicinal product'

Small immediate labelling

Where the immediate packaging units are too small to contain in a readable form the information referred to under 'Immediate labelling' the labelling requirement for small immediate packaging units is as follows:

- a) the scientific name of the stock or stocks followed by the degree of dilution, using the symbols of the European pharmacopoeia or, in the absence thereof, of the pharmacopoeias used officially in Member States. Where two or more stocks are present the scientific name can be supplemented by an invented name.
- b) the manufacturer's batch number, preceded by the word 'Lot'
- c) the expiry date in the format: 'mm/yyyy', preceded by the abbreviation 'Exp'
- d) the statement 'homeopathic veterinary medicinal product'

Small immediate packaging units must have an outer packaging and package leaflet containing all the information outlined above, including those already stated on the small immediate packaging units.