HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Guide to
Registration of Veterinary Medicinal Products for Pets that qualify for registration under Article 5(6) of Regulation 2019/6

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~~This guide does not purport to be an interpretation of law and/or regulations and is for guidance purposes only.~~

CONTENTS

1 SCOPE

This guidance is intended for those companies wishing to obtain registration for the marketing of veterinary medicinal products in Ireland~~, which~~ that are intended for the following animals which are exclusively kept as pets: aquarium or pond animals, ornamental fish, cage birds, homing pigeons, terrarium animals, small rodents, ferrets and rabbits; that qualify for registration under Article 5(6) of Regulation 2019/6. ~~It~~

This guidance covers the criteria for registration~~. It~~ and provides advice on the administrative aspects of the registration scheme ~~and gives~~, as well as guidance on how the application should be made and the registration maintained.

This guidance does not attempt to answer every question a company may have, and the HPRA can provide advice on individual queries and products as required. A list of contact points is provided in ~~Appendix A~~section 11.

All qualifying veterinary medicinal products that are registered nationally must, in accordance with Article 4 of Regulation 2019/6, be listed in the European Medicines Agency's (EMA's) Union Product Database (UPD). Applicants should refer to the SPOR on-boarding guidance available on the EMA website and register to the Referential Management Services (RMS) and Organisational Management Services (OMS). Additional clarification of the requirements for the UPD should be obtained from the EMA.

This guidance has been developed in advance of the underpinning national legislation being available. The guidance will be amended once that legislation is available. ~~Accordingly, the guidance remains draft and is subject to change should it be necessary.~~ It is provided to applicants to assist in the preparation of applications and to clarify the HPRA's approach to such applications ahead of the ~~application of Regulation 2019/6 on 28 January 2022~~introduction of new national legislation.

2 PURPOSE AND SCOPE OF THE REGISTRATION SCHEME

2.1 ~~The~~ Purpose of the scheme

The registration scheme ~~in respect of qualifying veterinary medicinal products~~ described in this guidance is a simplified regulatory procedure which enables companies to register and market certain qualifying veterinary medicinal products in Ireland. The supply of veterinary medicinal products in Ireland is regulated by the provisions of national ~~(revised SI to be added here)~~ and EU legislation (Regulation 2019/6). It is unlawful for any veterinary medicinal product to be placed on the market in Ireland except in accordance with a product marketing authorisation or registration granted by the HPRA or the European Commission or, in exceptional cases, in accordance with a licence issued by the Department of Agriculture, Food and the Marine~~.~~ (DAFM). In the case of veterinary medicinal products for pets that qualify for an exemption from

the need for a marketing authorisation under Article 5(6) of Regulation 2019/6, a simplified product registration may be granted by the HPRA where satisfactory evidence of compliance with the requirements outlined in section 5 of this guidance has been established.

2.2 Products eligible for registration

The registration scheme applies to veterinary medicinal products which are intended to be placed on the Irish market and which fulfil the criteria specified in Article 5(6) of Regulation 2019/6. To be eligible for registration, a qualifying product must meet **all** the following criteria:

- Indicated only for use in the following animals which are exclusively kept as pets: aquarium or pond animals, ornamental fish (fish kept in closed water systems), cage birds (e.g. birds kept in cages or aviaries), homing pigeons (pigeons kept for racing or exhibition), terrarium animals (reptiles, amphibians and arthropods kept in tanks and cages – including animals free-living in domestic gardens), small rodents (domestic mammals of the order rodentia), ferrets and rabbits (i.e. pet rabbits).
- ~~Containing~~Contains active substances that are not subject to veterinary prescription under Article 34 of Regulation 2019/6.
- ~~Containing~~Contains only active substances that are known pharmaceutical substances.
- ~~Are~~ Administered to animals orally or topically (excluding products that are administered in the eye) and not by other routes of administration.
- Measures are in place to prevent unauthorised use of the products in other animals, that is, they are labelled appropriately and presented in pack sizes suitable for a single course of treatment.
- Are manufactured according to Good Manufacturing Practice (GMP) by an authorised manufacturer.

2.3 Products outside the scope of the registration scheme

Products which do not satisfy all of the conditions set out in Article 5(6) of Regulation 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. These include:

- Products that are not intended for the species of animals identified in Article 5(6) of Regulation 2019/6 as being exclusively kept as pets, e.g. those that are intended for administration to other species of animals and animals which are used to produce food for human consumption, including medicines for chickens, ducks and turkeys.
- Products that are subject to a veterinary prescription. Article 34 of the Regulation details the conditions for classifying a product as subject to veterinary prescription.
- Products containing novel substances, or stem cells or biological agents.
- Products that are intended for administration to animals other than by oral or topical routes.

2.4 Who should apply for registration

If a qualifying 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 Irish market. Prospective applicants should also be aware of the need for the following authorisations:

Manufacturers
A company which manufactures or which proposes to manufacture such products must hold a manufacturer's authorisation. 'Manufacture' includes all processes carried out in the course of making the dosage form, packaging (e.g. filling and labelling), and quality control. The HPRA is the Competent Authority for evaluating applications for manufacture 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. Where products are manufactured in from a country outside the European Economic Area (EEA) a certificate of ~~Good Manufacturing Practice (GMP)~~GMP by the competent authority concerned is required.

Importers
A company which imports veterinary medicinal products from countries outside the EEA needs a manufacturer's ~~/~~ /importers' authorisation (MIA) as described above. A MIA is also needed for physical receipt and batch certification of a product which has been imported from a third country, i.e. from a country outside the EEA.

Wholesalers
A company which acts as a wholesaler or which proposes to do so for the supply of products for the purpose of resale 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 (DAFM).~~DAFM.

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 (see section 5). A separate application form should be completed for each product for which you seek registration.

The application form, is available on the 'Publications and Forms' section of www.hpra.ie.

3.2 Where to send the application

~~Send one electronic copy of the application form and the supporting data (see section 5 below) to:~~

~~Receipts and Validation Section: submissions@hpra.ie~~

Please see the HPRA '*Guide to Electronic Submissions – Veterinary Medicines*' for details on sending the application to the HPRA.

3.3 Fees

Applications must also be accompanied by the appropriate fee - see the HPRA 'Guide to fees for veterinary products' on the 'Publications and Forms' section of www.hpra.ie for details of the fees and the method of fee payment (fees will ~~only~~ be listed when the ~~necessary~~ national legislation is ~~known~~finalised). 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 REGISTRATION PROCESS

4.1 Processing of the application

When the application (as per section 5 below) and fee have been received, the validity and eligibility of the application will be checked. The HPRA will inform you if the product is not eligible for registration under the scheme.

Once the application has been validated it will then be scheduled for internal review. The supporting data accompanying the application will be reviewed. If there are deficiencies in the application, you will be informed and given an opportunity to address the deficiencies identified.

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 this guideline.

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 proposed product does not satisfy the requirements of Article 5(6) of Regulation 2019/6, or
   - the product may be harmful under the proposed 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 this guideline.

Failure to satisfactorily address any deficiencies identified will result in the application for registration being refused. Where deficiencies are satisfactorily resolved, the HPRA will issue a registration certificate.

4.2 Issue of registration certificates

Following approval, the registration certificate will be sent to you. On receipt you will be able to market the registered product citing the registration number on the label. The registration will be valid for an indefinite period provided that the product remains fully consistent with the application that has been registered by the HPRA.

4.3 Timescales for registration

The HPRA will take all appropriate measures to process applications within 60 days of submission of a valid application.

5 ACCOMPANYING DATA

5.1 Data required

The following information must be provided in support of an application for registration of the products concerned:

Applicant details

- Name and address of the applicant.
- Confirmation that the applicant is legally established in an EU Member State, and presuming so, the name and address of the EU address for the applicant (if different from above).
- Contact details for correspondence with the HPRA (name, email address).
- Location and contact details for the Qualified Person responsible for Pharmacovigilance.
- All organisation details in the application form must be registered in the EMA's Organisation Management Service (OMS) before an application can be made to the HPRA. The applicant should provide the Org-ID and LOC-ID received from the OMS. If any of the relevant organisations or sites are not already registered, they will need to be registered with the EMA. Further information is available at https://iris.ema.europa.eu/locations/.
- Reference number of the pharmacovigilance system master file (PSMF) relating to the product.

Product details

- Scientific name (or other name used in a pharmacopoeia) of the active substance(s)
- Pharmaceutical form
- Pack size(s) being offered for sale
- Full qualitative and quantitative composition of the product
- *Product specification
- Route(s) of administration
- Target species
- Indication(s) for use
- Dosage

- Any warnings or precautions considered necessary to ensure correct and safe use of the product

*The product specification shall consist of:
1. Assay for active substance(s) with a limit of ~~+/-~~ ± 5.0 % using an analytical method validated in-line with VICH GL 2: Validation of analytical procedures: methodology
2. Those parameters included on the relevant Ph. Eur. dosage form monograph

So for example:

The specification for an oral solution shall contain:
- active content ~~+/-~~ ± 5 %
- the relevant uniformity of dose test (there are ~~5~~five listed in the Ph. Eur. depending on the type of product)

The specification for a tablet shall contain:
- active content ~~+/-~~ ± 5 %
- the relevant uniformity of dose test (there are ~~3~~three listed in the Ph. Eur. depending on the type of product)

Manufacturing authorisation covering the veterinary medicinal product concerned
- A copy of the GMP certificate (or EudraGMP reference) for each site involved in the manufacture~~/~~/packaging~~/~~/importation of the product should be provided. For manufacturing sites in non-EEA countries, a copy of the GMP certificate should be provided.

Registration by other EU Member States
- Copies of any registrations or authorisations obtained for the same veterinary medicinal product in other EU Member States.

Labelling ~~&~~and package leaflet
- Labelling and package leaflet texts (preferably electronic versions).

Other data
- Confirmation that a pharmacovigilance system is in place that fulfils EU requirements including a ~~Pharmacovigilance System Master File (~~PSMF~~)~~ in accordance with Chapter ~~5~~V of Regulation ~~(EU)~~ 2019/6.

6 MANUFACTURE, IMPORTATION AND WHOLESALE

6.1 Manufacturer's ~~/~~/importer's authorisation

Article 88~~.~~(1) of Regulation 2019/6 requires all manufacturers of medicinal products, including importers of products from outside the EEA, to hold an appropriate authorisation

(manufacturer's/importer's authorisation (MIA~~).~~)). In Ireland, the MIA is issued by the HPRA. To apply for an MIA, an applicant must complete an application form (see the 'Publications and Forms' section of www.hpra.ie). An applicant should have available the services of at least one Qualified Person (Article 97 of Regulation 2019/6) – see ~~also~~section 6.3 below.

The HPRA will only issue an MIA when it is satisfied that the information contained in the application is accurate and the manufacturing site is in a position to comply with the principles and guidelines of Good Manufacturing Practice (*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

MIAs are required to manufacture medicinal products in accordance with the principles and guidelines of Good Manufacturing Practice and in accordance with the marketing authorisation or registration, as appropriate. Further information on the manufacture and control of dosage forms is given in Appendix A of this guide.

6.3 Qualified persons

Article 97 of Regulation 2019/6 requires the holder of an MIA to have permanently at its disposal the services of at least one Qualified Person (QP) who is to be named on the licence. The ~~QPs~~QP's duties are specific and are intended to ensure that every batch of medicinal products has been manufactured and/or imported 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 certify each batch.

Article 97 also prescribes the qualifications for appointment as a QP. Candidates for appointment as a QP must meet specific educational and vocational requirements.

6.4 Inspection

Articles 90 and 123 of Regulation 2019/6 require the Competent Authority to ensure, by way of inspection before granting an MIA and by way of controls (including routine ongoing inspections at intervals based on risk), that MIA holders are complying with the legal requirements. Article 88~~.~~(4) requires the competent authority to record the MIAs in the relevant EU database of manufacturing and wholesale distribution. Inspectors are empowered to inspect all authorised sites, to take samples and to examine all relevant documents. Following an inspection, the authorisation holder will receive a copy of the inspector's report. The MIA holder will be promptly informed in writing by the competent authority of any case of non-compliance identified through the controls and shall have the opportunity to submit comments within a time limit set by the competent authority. Where there is an acceptable outcome to the inspection process, a certificate of ~~Good Manufacturing Practice~~GMP will be published on the EU database.

7 SALE AND SUPPLY

7.1 Route of sale and supply

The system by which medicines are classified nationally as licensed merchant (LM) or companion animal medicine (CAM) applies equally to qualifying veterinary medicinal products to be registered under Article 5(6) of Regulation 2019/6. The classification of a qualifying product will be determined at the time of registration, on a product-by-product basis. Essentially the same rules will be followed for registered products under Article 5(6) of Regulation 2019/6 as apply to all veterinary medicinal products.

8 UPDATING, SUSPENSION, REVOCATION AND WITHDRAWAL OF REGISTRATIONS

8.1 Updates to applications

Changes to a registered product or the data supplied with the application must be submitted to the HPRA for approval before implementation. Further details on the variation procedure will be provided in due course.

8.2 Duration of certificates

Registration certificates are valid indefinitely provided that the product remains consistent with that registered by the HPRA.

8.3 Suspension and revocation

A registration may be suspended or revoked if, for example, the product proves to be harmful under 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 or the product no longer remains consistent with that registered by the HPRA.

8.4 Withdrawal from the market

The HPRA may require a product to be withdrawn from the market if, for example, it proves harmful under normal conditions of use, if its composition is not as declared, if the product (including labelling) no longer remains consistent with that registered by the HPRA or if details of controls have not been provided as requested.

A certificate holder may also voluntarily withdraw a product's registration, which should be notified to the HPRA.

9 LABELLING

9.1 Labelling of registered products

The labelling of all containers and packages must include the HPRA registration number.

General guidance on labelling is given in ~~the appendices to~~Appendix B of this document.

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, as long as all the specified information is present and is legible. Where the container itself is not more than 50 ml, reduced labelling may be applied and will be determined during the application review process.

9.3 Package leaflets

The supply of a package leaflet with the product is optional. However, if all the recommended information cannot be included on the immediate label in a legible format, a leaflet is recommended and it must contain all the particulars required for the correct use of the product. No other information than that registered with the HPRA may be included.

9.4 Changes to approved labelling and package leaflets

All changes to labelling and/or package leaflets including those which relate to particulars on the registration certificate must be submitted to the HPRA for approval before implementation.

10 PHARMACOVIGILANCE

In relation to the reporting of adverse events following use of a registered 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 of Chapter IV 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 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.

11 ~~APPENDIX A~~ CONTACT POINTS WITHIN THE HPRA

Veterinary Sciences Department: vetinfo@hpra.ie
Receipts and Validation Section: submissions@hpra.ie
Compliance Department: compliance@hpra.ie

APPENDIX ~~B~~A MANUFACTURE AND CONTROL OF DOSAGE FORMS

AC1 Introduction

Applications for registration of qualifying veterinary medicinal products for pets under Article 5(6) of Regulation 2019/6 should be accompanied by supporting data on the production and control of the dosage form as laid down in Regulation 2019/6~~;~~.

AC2 Formulation

Complete Composition
Full details of the formulations should be provided for each product.

Container
A description of the container and closure should be provided.

Finished Product Specification
The finished product specification should be provided.

AC3 Manufacturing control

Although details of the manufacturing process are not required to be submitted, the manufacturer should define, validate and control the manufacturing process in accordance with the requirements in the EU GMP Guide.

APPENDIX ~~C~~B GENERAL LABELLING REQUIREMENTS

General labelling requirements are laid out in Regulation 2019/6 for veterinary medicinal products. Although the requirements are not explicitly stated as being directly applicable to veterinary medicinal products to be registered in accordance with Article 5(6) of Regulation 2019/6, the HPRA recommends that similar information be included on the labelling and package leaflet of products to be registered in accordance with ~~Art~~Article 5(6).

Further information is available in the HPRA 'Guide to Product Literature Standard (PLS) for Veterinary Medicinal Products'. This guide for applicants to assist in the creation of mock-ups for regulatory approval is available on the HPRA website.

Outer packaging

It is recommended that the following minimum information is included on the outer package:

- Name of the veterinary medicinal product
- ~~Name and strength~~Statement of the active substance(s)
- ~~Pack~~Package size
- Target species (if not included in the name)
- Indication(s)
- Route(s) of administration
- Expiry date
- ~~General~~Special storage ~~precaution~~precautions
- The words "Read the package leaflet before use", or other appropriate reference~~.~~
- The words "For animal treatment only"
- The words "Keep out of the sight and reach of children"
- Name of the registration holder
- Registration number
- Batch number

If there is no outer package, then it is recommended that all of the above particulars are included on the immediate package.

Immediate packaging

It is recommended that the following information is included on the immediate package:

- Name of the veterinary medicinal product
- ~~Name and strength~~Statement of the active substance(s)
- Target species (if not included in the name)
- Route(s) of administration
- Expiry date
- ~~General~~Special storage ~~precaution~~precautions
- Name of the registration holder
- Registration number
- Batch number

For small immediate packaging (e.g. blisters, strips, small single-dose containers) or where the container itself is not more than 50 ml, reduced labelling may be considered. In this case, it is recommended that at least the following is included for small containers:

- Name of the veterinary medicinal product
- ~~Name and strength~~Quantitative particulars of the active substance(s)
- Batch number
- Expiry date

Package leaflet

It is recommended that the following minimum information is included on the package leaflet:

- Name of the veterinary medicinal product
- Qualitative and quantitative composition of the active substance(s)
- Target species
- Indication(s) for use
- Contraindications~~/~~
- Special warnings (including any special precautions for use ~~or potential adverse reactions~~)
- Adverse events
- Dosage for each species, route(s) and method~~(s)~~ of administration
- ~~General~~Advice on correct administration
- Special storage ~~precaution~~precautions
- The words "Keep out of the sight and reach of children"
- ~~Disposal advice~~
- Special precautions for the disposal of unused product or waste materials, if any
- Name of the registration holder and of the manufacturer responsible for batch release, if different
- Registration number
- The method of sale and supply (classification route, see below)
- The date when the package leaflet was last approved by the HPRA~~.~~
- Registration holder or its representative, as appropriate, for the reporting of suspected adverse events

The method of sale and supply, LM or CAM, should appear within a box symbol on the package leaflet. It may also be included in the outer packaging and immediate packaging. The method of sale and supply on the package leaflet and label (in the absence of a package leaflet) is written in full with each first initial capitalised. That is, CAM should be followed by 'Companion Animal Medicine', and LM should be followed by 'Licensed Merchant' (this advice is based on ~~SI~~S.I. No 786 of 2007, but may be changed once new national legislation is available ~~in 2022~~).

If there is no package leaflet, then it is recommended that all of the above particulars are included on the outer/immediate package, including:

- The words "For animal treatment only"
- Pack size
- Batch Number

- Expiry date

APPENDIX ~~D~~C LEGISLATION

EU

Regulation (EU) 2019/6~~.~~

Irish

New national legislation is awaited at time of writing ~~in May 2021.~~this guide.

Note: This is not a comprehensive list of all the relevant regulations, further details available on Office of the Attorney General website.