



Veterinary Medicines Guidance Note

An Introduction to Marketing Controls on Veterinary Medicines

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ASSURING THE SAFETY, QUALITY AND EFFICACY
OF VETERINARY MEDICINES



THESE NOTES ARE ONLY A GENERAL GUIDE AND MUST NOT BE TREATED AS A COMPLETE OR AUTHORITATIVE STATEMENT OF THE LAW ON ANY PARTICULAR CASE

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INTRODUCTION

1. This is one of a series of Veterinary Medicine Guidance (VMG) Notes explaining the requirements under the Veterinary Medicines Regulations ('the Regulations'). The Regulations are revoked and replaced every year, so the references to the Regulations should be read as referring to the ones that are currently in force. Therefore, the date and number of the Statutory Instrument is not shown in the VMG Notes. These VMG Notes will be updated as necessary and the date of the most recent update is shown on the front cover. The Regulations set out the UK controls on veterinary medicines, including their manufacture, advertising, marketing, supply and administration.
2. This VMG Note provides a general introduction to the controls on marketing veterinary medicines, the requirement for a marketing authorisation and obligations placed on the holders of Marketing Authorisations (MAs) in the UK.

LEGISLATION AND GUIDANCE

EUROPEAN COMMUNITY LAW

3. In November 2001, the main Community provisions relating to veterinary medicines, other than medicated feeds and feed additives, were consolidated into a new directive – Directive 2001/82/EC on the Community code relating to veterinary medicinal products. Following an extensive review of the operation of the Community procedures this was amended by Directive 2004/28/EC of 31 March 2004. Any reference to 'the Directive' should be taken as referring to these two amending Directives.
4. Regulation (EEC) No 2309/93 established a Community "centralised" authorisation procedure and a European Agency for the Evaluation of Medicinal Products. Following the review referred to above, this was repealed and replaced by Regulation (EC) No 726/2004. This sets out current provisions for the European centralised authorisation procedure under which the European Commission may issue a marketing authorisation that is valid in all Member States. It also sets out modified provisions for the structure and operation of the European Agency and relevant committees.
5. Additionally, Commission Regulations (EC) No 1084/2003 and 1085/2003 control the variation of MAs issued under the centralised and decentralised/mutual recognition procedures respectively. Separate EU legislation applies to controls on residues of veterinary medicines in animals and foodstuffs, which are outside the scope of this VMG Note.
6. EU legislation on veterinary medicines is published by the European Commission in *The Rules Governing Medicinal Products in the European Union, Volume 5 - Pharmaceutical Legislation, Veterinary Medicinal Products*, which is updated periodically to take account of new legislation. This and other volumes in the same series are available on the Commission website

(<http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev5.htm>) or in print from The Stationery Office Ltd (telephone: 0870 600 5533) or from the Office for Official Publications of the European Communities in Luxembourg (http://publications.europa.eu/index_en.htm). EU legislative documents are also available individually on the internet (http://europa.eu.int/documents/eudralex/index_en.htm).

7. The European Commission has also published guidance on the requirements of the relevant Community law in *the Rules Governing Medicinal Products in the European Union - Notice to Applicants, Veterinary Medicinal Products*, which is available in three volumes. Volume 6A covers procedures for marketing authorisations, volume 6B gives guidance on the presentation and content of the data dossier required in support of an application and volume 6C provides guidelines on various regulatory aspects. These volumes are available as above.
8. This guidance note relates to the provisions as implemented in the UK and its supplements, but does not replace, the Commission guidance in the *Notice to Applicants*, and should be read with it.

SCOPE OF THE VETERINARY MEDICINES REGULATIONS

9. The Regulations control veterinary medicinal products, including pre-mixes for medicated feedingstuffs, which are intended to be placed on the market within the UK. This VMG Note examines what this means.

DEFINITION OF VETERINARY MEDICINAL PRODUCT

10. Because they transpose the requirements of EU legislation, the Regulations use the Community law definition of veterinary medicinal product. Article 1.2 of the Directive defines a "veterinary medicinal product" as:

"(a) any substance or combination of substances presented as having properties for treating or preventing disease in animals; or

(b) any substance or combination of substances which may be used in, or administered to, animals with a view either to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis".

11. Although modified by the Directive, the definition continues to apply to products that are said to be medicinal "by presentation" or medicinal "by function". The Regulations apply the provision in Article 2.2 of the Directive that, where a product falls within both the definition of a veterinary medicinal product and that of another type of product that is subject to other Community legislation, it is subject to the controls of the veterinary medicines legislation. This principle has, to a large extent, been followed for some time. For example, a number of veterinary medicines for the treatment of ectoparasites such as fleas, ticks and lice, which could be regarded as pesticides, have historically been regulated as veterinary medicines.

PRODUCTS EXCLUDED FROM THE SCOPE OF THE REGULATIONS

12. The Regulations do not apply to:
- inactivated immunological veterinary medicinal products that are manufactured from pathogens or antigens obtained from an animal and used for the treatment of that animal or other animals on the same site;
 - veterinary medicines based on radioactive isotopes.

REQUIREMENTS FOR A MARKETING AUTHORISATION

13. The Regulations require that any person who places a veterinary medicinal product on the market does so in accordance with a Marketing Authorisation granted by the Secretary of State or by the European Medicines Agency. In order to be legally placed on the market in the UK a veterinary medicinal product must be the subject of an MA valid in the UK (but see exceptions referred to below).

MEANING OF PLACING ON THE MARKET

14. Placing a product on the market covers a range of activities. This includes sale or supply as well as offering a product, or advertising its availability, for sale or supply.

APPLICATION OF AUTHORISATION REQUIREMENTS

15. The Regulations apply the requirement for a MA in a number of particular circumstances which are set out below.
- Application to Import Products**
It is an offence to import an unauthorised veterinary medicinal product. However, the Regulations provide for exceptions in certain circumstances which are detailed in VMG Note 7.
 - Possession and Supply of Unauthorised Products**
The Regulations provide for exceptions in both the possession and supply of unauthorised products (see VMG Note 23).
 - Application to Herbal Remedies**
Where a herbal remedy falls within the definition of a veterinary medicinal product, it is subject to the Regulations and may not be administered or placed on the market in the UK except in accordance with an MA. Herbal products, which do not fall within this definition, are not subject to control as veterinary medicines in the UK.
 - Application to Homeopathic Remedies**
Veterinary homeopathic remedies that meet criteria specified in the Regulations are eligible for registration under a simplified scheme. Other veterinary homeopathic products may require a marketing authorisation. For further information see VMG Note 9.

ADMINISTRATION OF PRODUCTS

16. The Regulations prohibit the administration of a veterinary medicinal product unless:
- it is the subject of a MA;
 - it has been registered under the simplified scheme for homeopathic remedies or has been notified to the VMD for inclusion on the “grandfather rights” list;
 - it is exempt from the requirements for a marketing authorisation under the small animal exemption scheme;
 - further restrictions apply in the case of food-producing animals.
17. Exceptions are provided for products administered for research purposes in accordance with a certificate granted by the Secretary of State or administered in accordance with the provisions of the Regulations (including the “prescribing cascade”).

MARKETING AND ADMINISTRATION IN EXCEPTIONAL CIRCUMSTANCES

18. The Regulations provide that, where the health situation so requires, the Secretary of State may authorise the marketing or administration to animals of a veterinary medicinal product authorised in a country other than the UK.

ROUTES OF AUTHORISATION

19. There are four routes by which MAs may be obtained. These are summarised below. Except for Provisional Marketing Authorisations the data requirements and criteria for authorisation are the same under each route.

THE CENTRALISED PROCEDURE

20. This is obligatory for high technology products and growth promoters defined in the Annex to EU Regulation 726/2004. It is optional for other innovative veterinary medicines as specified in the Regulations. Under this procedure, applications are made to the European Medicines Agency. MAs are issued by the European Commission and are valid in all EU Member States.

THE NATIONAL PROCEDURE

21. This applies to products not already authorised in the EU and for which authorisation is required in only one Member State. In the UK applications are made to the VMD who issue authorisations. MAs issued under this procedure are valid in the UK only.

MUTUAL RECOGNITION AND DECENTRALISED PROCEDURES

22. These apply where an applicant wishes to obtain authorisations for a product in two or more Member States. If an authorisation has already been issued in the

EU, the holder may apply to one or more Member States to issue identical authorisations on the basis of mutual recognition of the “reference” authorisation.

23. Where an authorisation has not been issued, the applicant may submit identical applications to each Member State in which authorisation is required and request one to act as “reference” Member State (RMS). This is known as the decentralised procedure. MAs are issued by each Member State to which an application is made on the basis of approval of the assessment report and related documents produced by the RMS. A binding arbitration procedure applies where Member States are unable to agree a decision on an application.

PROVISIONAL MARKETING AUTHORISATIONS

24. In accordance with Article 26(3) of the Directive, a Provisional MA may be granted in exceptional circumstances without the provision of a full data dossier (see VMG Note 5). Neither Community nor UK law define “exceptional circumstances” although the Directive provides that such authorisations may only be granted for “objective and verifiable reasons”. The facility may be useful when there is no suitable authorised medicine available to treat a particular disease or to treat a new disease in the UK. A new disease could either be one that has not previously been recorded in the UK, or an existing disease whose pattern has changed to such an extent that existing remedies have ceased to be effective.
25. Provisional authorisations will normally be valid for 1 year and may be subject to special conditions, dependent upon the circumstances prevailing in any individual case. Anyone interested in the possibility of applying for a Provisional Marketing Authorisation should contact the VMD at as early a stage as possible.

PROCEDURES FOR UK MARKETING AUTHORISATIONS

APPLICATION, GRANT AND RENEWAL

26. The Regulations transpose the provisions of Community law concerning MAs, applications for which must be made in accordance with the provisions of the Regulations, and be accompanied by the data specified therein. Further details are given in VMG Note 2.
27. The VMD, acting on behalf of the Secretary of State, is the UK national competent authority for authorising veterinary medicinal products. It considers each application according to either the national or the decentralised/mutual recognition procedures. If the product meets the criteria of safety, quality and efficacy, has a favourable risk/benefit balance and does not contravene any other provision of Community law, an authorisation will be issued. Unless it is a provisional authorisation, it will be valid for 5 years initially.
28. The MA may be renewed if the holder applies for renewal at least 6 months before the end of the 5-year period (see VMG Note 2). Once renewed, the authorisation remains valid indefinitely unless the VMD considers a single additional renewal is

justified on grounds of pharmacovigilance (surveillance of suspected adverse reactions to the product) 5 years after the first renewal.

29. However, where an authorised product is not marketed in the UK for 3 consecutive years, the authorisation will cease to be valid unless, exceptionally, an exemption from this provision is granted on justified human or animal health grounds. Such an exemption might be granted, for example, where a product for treating a sporadically occurring disease had not been marketed because the disease had not occurred during that period. Information on marketing will be received under the pharmacovigilance procedures.

REVOCATION, SUSPENSION AND COMPULSORY VARIATIONS

30. During the validity of the MA, evidence may become available to throw doubt on the safety, quality or efficacy of the product or which alters the risk/benefit assessment. In such circumstances the VMD may revoke, suspend or compulsorily vary the authorisation. The circumstances in which such action can be justified are specified in Article 83 of the Directive and are reproduced in the Regulations. It should be noted that if the VMD becomes aware that a Marketing Authorisation Holder (MAH) has changed any of the authorised specifications of an authorised product without the prior approval of the VMD, the MA will be suspended immediately. The suspension will remain in force until the changes have been approved or the product is brought into line with the authorisation.

APPEALS PROCEDURES

31. The Regulations set out the appeals procedures that apply in the case of refusal, suspension or revocation of an MA for a veterinary medicinal product. VMG Note 11 describes these procedures.

DUTIES ON HOLDERS OF MARKETING AUTHORISATIONS

32. The grant of a MA allows the MAH to place a product on the market within the UK. The MAH must comply with the general law of the UK and with the requirements imposed in the Regulations that the product is placed on the market in accordance with the MA. This requires that:
- the product is manufactured and placed on the market in accordance with the contents of the data dossier supplied with the application, or subsequently amended with the approval of the VMD; and
 - the authorisation holder complies with duties imposed on him by the Regulations and, of course, other applicable laws of the UK.

This includes compliance with labelling requirements as well as distribution controls relevant to the legal distribution category applicable to the product (e.g. POM-V, POM-VPS, NFA-VPS, AVM-GSL) and associated advertising controls. These aspects are explained further in VMG Notes 3 (Distribution categories) and 18 (Product literature) respectively.

SPECIFIC OBLIGATIONS

33. In addition, the Regulations impose a number of specific obligations or duties on MAHs. This section summarises the main requirements. It does not cover those relating to the import of products manufactured outside the Community, nor requirements concerning pharmacovigilance and labelling, which are covered in VMG Notes 13 and 18 respectively.

ALTERATIONS TO MARKETING AUTHORISATIONS/DATA DOSSIERS

34. MAHs are required, in respect of the methods of preparing the product and the control testing methods employed by the manufacturer, to take account of scientific and technical progress. They must introduce any changes that may be required to enable the product to be manufactured and checked by means of generally accepted scientific methods. Any such changes are subject to approval by the VMD, and will be dealt with in accordance with procedures for variations (see VMG Note 4).

35. MAHs are required to immediately inform the VMD of any proposed alteration to the data dossier including the SPC, labels and package leaflets, submitted in support of an MA. Any such changes are subject to approval by the VMD and will be dealt with in accordance with procedures for variations (see VMG Note 4). MAHs should note that all original documents forming part of the efficacy data dossier submitted in support of the MA must be retained for at least 5 years after the product is no longer authorised.

COMPLIANCE WITH DIRECTIONS

36. Several parts of the Regulations require MAHs to comply with directions given to them by the VMD. These include the following:

- cease supply of a product and to ensure that it is withdrawn from the market, either in total or in respect of one or more specified batches as directed;
- comply with any improvement notice served on them by a duly authorised officer in accordance with the Regulations;
- provide sufficient quantities of the substances to enable controls to be made on the identification of the presence of residues of the product;
- provide technical expertise to facilitate the implementation of the analytical method for detecting residues of the product in the national reference laboratory.

OTHER NOTIFICATION REQUIREMENTS

37. Several other Articles of the Directive require notifications to be made. All such notifications should be sent within the time specified to the Information Management section at the VMD. When sending such notifications please remember to include the product name and authorisation number. The main requirements are summarised below.

38. MAHs are required to immediately supply the VMD with any new information that might entail amendment of the data dossier, or the approved SPC, or that might influence the assessment of the benefits and risks of the product concerned,

including any prohibition or restriction imposed by the competent authorities of any country in which the product is marketed.

39. MAHs are required to promptly update information provided in the data dossier on the authorisation position of the product in other countries. This includes details of any applications submitted and of any decisions to grant or refuse an authorisation. Such decisions should be notified as soon as they are known.
40. MAHs are required to notify the VMD of the date of actual placing on the UK market of a product and if the product permanently ceases to be marketed in the UK. In addition, MAHs are required to notify the VMD immediately of any action taken by them to suspend the marketing of a product or to withdraw a product from the market. They must also provide the reasons for such action if it concerns the efficacy of the product or the protection of human or animal health or the environment.

OBLIGATIONS IN RESPECT OF ENFORCEMENT ACTIVITIES

41. The Regulations provide for enforcement. They include provision for the appointment of enforcement officers and powers to carry out enforcement activities including powers of entry, inspection of premises, examination of records and documents, taking of samples and seizure of products. The Regulations require MAHs to allow authorised enforcement officers to carry out their duties and exercise their powers as appropriate.

FURTHER INFORMATION

42. Further information is available from the Veterinary Medicines Directorate, Woodham Lane, New Haw, Addlestone, Surrey, KT15 3LS - Tel: +44 (0)1932 336911; Fax: +44 (0)1932 336618 or E-mail: VMGNotes@vmd.defra.gsi.gov.uk. Veterinary Medicines Guidance Notes and other information, including details of VMD contacts, are available on the VMD website (www.vmd.gov.uk).

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