

3 Regulation

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Introduction

3.1. In the UK, sales of prescription-only veterinary medicinal products form part of a larger market, about 30 per cent of which is supply of non-prescription medicines. In order that this context may be seen, this chapter outlines the regulation of prescription and non-prescription veterinary medicines with the exception of medicated feedingstuffs and the pre-mixes or intermediate products used in their manufacture. (Products of the latter kinds form a discrete group, about 6 per cent of total veterinary medicine sales, outside the terms of reference of the inquiry and supplied through channels different from those used for other veterinary medicines.)

3.2. The way in which veterinary medicines are regulated has considerable impact on their supply. Regulatory requirements must be satisfied before a veterinary medicine can be introduced into the market and the distribution classification resulting from the regulatory process determines who may sell it to animal owners.

3.3. Individuals, businesses and premises involved in the manufacture, prescription, dispensing, sale, supply and administration of veterinary medicines can also be subject to regulation, according to their function.

Scope of regulation

3.4. The manufacture, distribution, sale, supply, prescription, dispensing and administration of human and veterinary medicines in the UK is governed by a significant body of law, most of it made at European level and either transposed into UK law or having direct effect. Though the legal framework applies throughout the EC (and in the European Economic Area countries, Norway, Iceland and Liechtenstein), the resulting regulatory functions are divided between national and transnational bodies. Small but significant areas of national discretion remain.

3.5. No veterinary medicine may be supplied or administered in the UK unless it has a current MA. (There are limited exceptions to this, though not significant in this inquiry.) Each MA stipulates the species and conditions for which the veterinary medicine may be used. There may be several MAs in respect of the same veterinary medicine. This can happen if it is marketed under more than one name or by more than one veterinary manufacturer, either under licence or because it is a copy of an out-of-patent medicine (a 'generic'). An MA may only be held by a person established in the EC, normally the person responsible for the primary marketing of the product within the UK. Annually, between 80 and 90 MAs are given in the UK. Only a minority, approximately ten per year, are completely new to the UK, the majority being new formulations, presentations, brandings or indications of active substances already authorized for veterinary use here.

3.6. No veterinary medicine may be granted MA until its safety, quality and efficacy have been demonstrated in accordance with detailed requirements set out in EC law. Efficacy is to be judged against the claims made by the MA applicant. Because virtually all veterinary medicines are hazardous if used incorrectly, safety is a key factor in their regulation. It embraces risk to the treated animal, other animals that may come into contact with it, persons administering it, consumers of food from treated animals and the environment. Nevertheless safety is not to be judged in absolute terms. The preamble to the principal European Directive dealing with veterinary medicines¹ notes: 'The concepts of harmfulness and therapeutic efficacy can be examined only in relation to one another and have only a relative significance, depending on the progress of scientific knowledge and the use for which the medicinal product is intended.'

3.7. The assessment of quality relates mainly to the processes by which the product is, or will be, manufactured and the testing and other procedures by which its ongoing conformity with its specification will be assured. The method used to establish shelf life is also assessed.

3.8. Veterinary medicines that meet criteria for POMs laid down in EC law² may only be supplied to the public by a veterinary surgeon or in accordance with a veterinary surgeon's prescription—in either

¹Council Directive 2001/82/EC.

²See paragraph 3.35.

case for the treatment of an animal or herd under the veterinary surgeon's care. Member states have discretion to extend, but not to narrow, these criteria. This has not been done in the UK, though the criteria have been interpreted in more detail in guidance prepared by the Veterinary Products Committee (VPC).

3.9. EC law also requires a veterinary prescription for new products containing ingredients first used in an authorized veterinary medicine less than five years ago unless the national authority is satisfied that none of the criteria referred to in the previous paragraph apply.

3.10. Member states may make stipulations regarding the allowable channels of distribution of these and all other veterinary medicines. Most, including the UK, have defined schemes of distribution classification covering all veterinary medicines, though these schemes differ. The same medicine may be prescription-only in one country but not in another.

3.11. EC law also requires member states to set up arrangements for the surveillance of adverse reactions to veterinary medicines and of their residues in food (the latter also covering certain environmental contaminants). These arrangements are not further described here as they come into play only after medicines have reached the end of the supply chain (though the information they generate can affect products' future regulatory status).

Regulation of veterinary medicines

3.12. EC Council Directive 2001/82/EC and Council Regulations (EEC) 2377/90 and 2309/93 between them set out the framework of EC law governing the regulation of veterinary medicines. In particular, these enactments:

- define the meaning of 'veterinary medicinal product';
- require such products to be authorized before they may be marketed or used;
- specify in detail the technical requirements to be satisfied before authorization may be granted;
- require the determination of MRLs for all active ingredients to be administered to food-producing animals;
- stipulate timing and other aspects of authorization procedures at EC and national level;
- specify descriptions of veterinary medicines that may be supplied by retail only in accordance with a veterinary prescription;
- require control of the production and assembly of veterinary medicines; and
- require ongoing pharmacovigilance.

Routes to marketing authorization

The centralized procedure

3.13. There are three routes to MA. First, the European Commission has power to grant MA and has established the independent European Medicines Evaluation Agency (EMA) to manage the necessary assessments. This route to MA—the 'centralized procedure'—is mandatory for certain categories of veterinary medicine, optional for some others and unavailable for everything else. Embedded within the EMA and formally part of it is the Committee for Veterinary Medicinal Products (CVMP), a committee of independent experts, two of whom may be nominated by each member state. It is responsible for the scientific examination of each application once the EMA has accepted the dossier as being within its legal competence and has verified that it addresses all the aspects required by EC law together with the required supporting information.

3.14. In each case the CVMP appoints, from among its members, a rapporteur and co-rapporteur (applicants may suggest names, though the CVMP makes its own decisions and notifies them to the applicant). The rapporteur is responsible for the assessment of the dossier, using a team selected from a panel of some 400 independent veterinary experts. The rapporteur's assessment is scrutinized by the co-rapporteur and submitted to the CVMP. After further stages the CVMP prepares a formal Opinion (which it must adopt no later than 210 days from receipt of a valid application, disregarding waiting time while the applicant responds to requests for further information). The Opinion goes to the European Commission for consideration, leading to formal decision-making. MAs under the centralized procedure take the form of European Commission Decisions (or European Council Decisions in disputed cases) having direct effect in all member states and are published in a Community Register. At 17 December 2002 it listed 34 current MAs granted through the centralized procedure, some covering more than one presentation of the medicine.

The national procedure

3.15. Second is the national procedure, in the UK much as it was before relevant European law took effect though authorization criteria laid down in EC law now govern the technical details. The national procedure may be used only when the veterinary medicine in question has no MA in any other member state and is not of a kind that must go through the centralized procedure. Its use is becoming infrequent as use of the decentralized procedure (see below) increases.

3.16. In the UK the VMD (an Executive Agency of Defra) assesses national applications for MA. In novel cases, or where it is minded to refuse the application, other than on grounds of illegality, it takes advice from the independent VPC. Formal MA is given by any one or more of the Ministers responsible for Health or Agriculture in the jurisdictions of the UK.

The decentralized procedure

3.17. The third route to MA is the European 'decentralized procedure' (sometimes called the 'mutual recognition procedure') which enables a single product dossier of test results and other details to be submitted in support of MA applications to any number of member states. It applies, and is then mandatory, when the veterinary manufacturer of a medicine:

- with national authorization in a single member state wishes to market the product in one or more other member states; or
- with no MA in any EC country, wishes, from the outset, to obtain MA in more than one member state at the same time.

3.18. In the former case, the veterinary manufacturer applies for MA to the competent authorities of each additional member state in which it wishes to market the product: these states are then the 'concerned member states' (CMS) for this instance of the decentralized procedure. The member state responsible for the initial MA of the product is the 'reference member state' (RMS). Where the product has no prior authorization in the EC, the applicant selects and applies to a member state to act as RMS, identifying the CMSs from which it also wishes to obtain MA. The national authority of this RMS is then responsible for the assessment of the application and, if it is successful, for granting MA in its country.

3.19. Once MA has been granted by the RMS, the applicant may then ask each CMS to mutually recognize it: the CMSs are allowed 90 days in which to reach a decision. Within that period the CMSs must reach a common agreement to grant or refuse MA. Upon agreement to grant MA, each country then gives MA under its national law and makes such stipulations governing distribution in its territory as it thinks fit, consistent with EC law (see paragraph 3.35). The product, as marketed in all of these countries, must be identical apart from its authorization number and the language of its labelling and inserts.

3.20. Dispute resolution procedures are laid down for cases in which agreement cannot be reached: if objections are upheld, MA may not be granted in any EC country and its existing MA must be withdrawn. Some veterinary manufacturers told us that to reduce this risk they had come to favour certain countries, including the UK, as RMS because the rigour of their assessments made successful challenge

unlikely. The VMD told us that France, Germany or the UK had been RMS in around 90 per cent of decentralized applications so far dealt with and that the UK was RMS in some 60 per cent of cases in which it had been involved. Figures provided by the National Office of Animal Health (NOAH) indicated that the proportion of decentralized cases in which France, Germany or the UK was RMS had fallen, from 91 per cent in 1999 to 64 per cent in 2000 and 46 per cent in 2001.

Maximum residue limits

3.21. For each species of food-producing animal for which a product is authorized, the MA specifies a withdrawal period between its last administration and the point at which the treated animal, or products such as milk and eggs obtained from it, may enter the human food chain. Withdrawal periods are determined during the regulatory assessment on the basis of test results provided by the applicant. They are such as to ensure that all potentially harmful residues of pharmacologically active ingredients will then be below their respective MRL. The European Commission, through the EMEA, sets all MRLs, which are generally species- and tissue-specific and must be used by the authorities of all member states. No veterinary medicine may be authorized for use in a food-producing species unless all requisite MRLs have been determined.

Abridged procedures

3.22. Under each of the three routes the MA applicant has to provide detailed information about the product and furnish the results of testing in accordance with the relevant technical requirements. However, there are circumstances, such as the authorization of a generic of an existing authorized medicine, in which the results of new toxicological and pharmacological tests and clinical trials are not required. These abridged procedures cover three cases:

- (a) *The 'essentially similar' case.* If the MA application relates to a product that is demonstrated to be essentially similar to another product already given MA by the same authority, the dossier for the existing product can be used in support of the new application, in so far as the holder of the original MA agrees. A patent-holder might allow its use, for example, when wishing to license another veterinary manufacturer to market a rebranded version of the patented product.
- (b) *The 'bibliographic' case.* The MA application relates to a product whose ingredients have a well-established medicinal use with recognized efficacy and an acceptable level of safety demonstrated by means of detailed references to scientific literature. This procedure is rarely used.
- (c) *The 'generic' case.* This case resembles the 'essentially similar' case described above with the following differences:
 - (i) the MA of the existing reference product may have been given by any EC authority;
 - (ii) to the extent that the product and its reference product differ (for example, in aspects of formulation such as the excipients used), evidence must be provided to show the bio-equivalence of the product and the essentially similar reference product; and
 - (iii) re-use of the existing dossier does not require the agreement of the MA holder provided that the MA has been in force for six years or, in the case of high-technology products, ten years (the 'data protection period'). There is no necessary connection between the time at which patent protection ceases and the end of the data protection period, which member states may extend to ten years in all cases. The UK has done so.

This procedure is used mainly by veterinary manufacturers wishing to copy a medicine whose data protection period has expired. (An application would be rejected if the existing product were still subject to data protection.)

Renewal of marketing authorizations

3.23. MAs, including a few remaining product licences given under the Medicines Act 1968 and in force when product licensing was superseded by MA on 1 January 1995, are valid for five years, after which they must be renewed. Information to update elements of the original dossier must accompany applications for renewal.

3.24. From time to time the detailed technical requirements and test methods specified for MA assessments are brought up to date to reflect scientific advances, including greater understanding of the safety and efficacy of medicines (especially of the environmental and human health impacts of pharmaceutical residues). The updating of dossiers is interpreted by some EC authorities, including the VMD, as entailing the submission of test results where necessary to bring the dossier fully into line with current requirements as set out in guidelines prepared by scientific committees of the EMEA.

Authorization of imports

3.25. Veterinary medicines entering the EC from third countries must gain MA before they may be marketed. No mutual recognition arrangements exist though discussions on the harmonization of authorization requirements, led by the EC, USA and Japan, are taking place through the International Committee on Veterinary Harmonization.

3.26. Veterinary medicines authorized through the centralized procedure may be marketed anywhere in the EC provided labelling and inserts are worded as approved by the EMEA in the language of the country in which they are sold. In all other cases products authorized in one member state may not legally be imported into another without MA from the importing country. This extends to products authorized through the decentralized procedure in both exporting and importing countries. (The decentralized procedure leads to separate MAs given by the national authorities of the RMS and each CMS which, though they all relate to an identical medicine, are valid only in the country concerned. For example, such a product authorized in France cannot legally be imported into and sold in the UK because its authorization number and the language of its labelling and insert differ from the UK product.) We were encouraged to hear of discussions on the dual labelling of products with authorizations granted under the decentralized procedure in the UK and the Republic of Ireland.

3.27. European enactments do not provide simplified MA procedures to cater for intra-EC importing. However, as a result of a ruling by the European Court of Justice in the *De Peijper* case,¹ national authorities have power to grant MA to imports, subject to suitable safeguards, without applying the full requirements specified in EC legislation.

3.28. In the UK, the VMD has established a scheme for the MA of parallel imports (MAPI). It applies to products authorized, using the full criteria, in the exporting country and which are the same as a product already authorized in the UK. In this context 'same' is closer to 'equivalent' than 'identical'. However, the imported product and its UK-authorized twin must be manufactured by, or under licence to, the same company or by companies in the same group working to the same specification. (The applicant for the MAPI does not have to be associated with this company or group or with the holder of either of the existing MAs though in that case it could face difficulties in establishing the case.)

Regulatory fees

3.29. The fees charged by the VMD depend upon the MA path chosen by the applicant (national, decentralized, abridged, renewal) and reflect the complexity of the case. Fees are designed to achieve overall full cost recovery; the maximum at 4 October 2002 (for a major national authorization) was £20,085. The EMEA's fee for the centralized authorization of a single presentation of a pharmaceutical product is €100,000 (approximately £67,000); for a vaccine the fee is half this. There are extra charges for additional strengths and presentations of the product. The EMEA told us that a proposal to increase EMEA's charges by 16 per cent was under consideration.

¹CJEC 20.5.76, Case 104/75, 1976.

3.30. These charges can be compared with product development costs, which we were told could approach US\$100 million in the case of a new active substance, and UK launch and other non-regulatory costs which, in the 33 examples reported to us, averaged just under £200,000.

3.31. Commercialization of a product cannot begin until regulatory processes are complete; the time taken to obtain MA, unlike regulators' fees, is a significant factor when veterinary manufacturers judge whether to launch a product in Europe and in particular whether to launch it in the UK. The VMD's target is to determine all new MAs within 210 clock-days (the number of days the application spends within the VMD, excluding time spent by the applicant providing further information or answering questions raised by the VMD). It met this target in over 99 per cent of cases in each of the last three years.

3.32. Veterinary manufacturers reported the lapse of time between an application for MA in the UK and its granting. The average, of 35 cases spread over the three years to the end of 2000, was just under 24 months. (The median interval was lower, just 16 months, reflecting the preponderance of simpler, and therefore quicker, cases in the sample.)

Classification

3.33. Strictly speaking, the term 'classification' refers to the distinction between medicines that may be supplied only in accordance with a veterinary prescription (or by a veterinary surgeon to an animal or herd under his or her care) and those not subject to this restriction. However, the term is also commonly used to refer to the distribution classifications described in the following paragraphs. These distribution classifications are not harmonized within the EC and have exclusively national relevance.

3.34. For medicines other than pre-mixes for medicated feedingstuffs, four distribution classifications are used in the UK:

- (a) *POM—Prescription-only*: May not be supplied except by a veterinary surgeon or by a pharmacy in accordance with a veterinary surgeon's prescription—in either case for the treatment of an animal or herd under the veterinary surgeon's care and administered by him or her or in accordance with his or her directions.
- (b) *P—Pharmacy*: May be supplied, without prescription, by a pharmacy (or by a veterinary surgeon for the treatment of an animal or herd under the veterinary surgeon's care).
- (c) *PML—Pharmacy and Merchants' List*: (Unlike the others, this distribution classification has no human medicine counterpart.) May be supplied, without prescription, by a pharmacy, veterinary surgeon (for the treatment of an animal or herd under his or her care), registered agricultural merchant or (if a wormer for cats, dogs or horses) a registered saddler.
- (d) *GSL—General Sale List*: May be supplied, without prescription, by any retailer.

'P' is the default distribution classification under the Medicines Act 1968 and applies if no other distribution classification is given as part of an MA.

EC prescription-only criteria

3.35. The criteria for POM classification¹ laid down in EC legislation are that the product:

- (a) is subject to official restrictions on supply or use, such as:
 - (i) restrictions resulting from the implementation of the relevant United Nations convention on narcotic and psychotropic substances; and

¹Directive 2001/82/EC Article 67.

- (ii) restrictions on the use of veterinary medicinal products resulting from EC law;
- (b) is one in respect of which special precautions must be taken by the veterinarian to avoid any unnecessary risk to:
 - (i) the target species;
 - (ii) the person administering the product to the animal;
 - (iii) the consumer of foodstuffs obtained from the treated animal; and
 - (iv) the environment;
- (c) is intended for treatments or pathological processes which require a precise prior diagnosis or the use of which may cause effects which impede or interfere with subsequent diagnosis or therapeutic measures; or
- (d) is a magistral formula intended for animals (ie a medicine prepared in a pharmacy in accordance with a prescription for an individual animal).

3.36. In addition, a prescription shall be required for new veterinary medicines containing an active substance which has been authorized for use in a veterinary medicine for less than five years unless, having regard to the information or particulars provided by the applicant, or experience acquired in the practical use of the product, the competent authorities are satisfied that none of the criteria in paragraph 3.35 applies.

UK interpretation of the EC prescription-only criteria

3.37. In the UK, the EC criteria are interpreted in administrative guidelines produced by the VPC. These are that a prescription shall be required:

- (a) when diagnosis of the condition for which the product is intended would be beyond the competence of the livestock owner or accurate diagnosis (including in particular differential diagnosis) is required so that medication appropriate to the circumstances can be administered and the necessary veterinary advice given;
- (b) when the product needs to be administered by the veterinary surgeon in person or under his or her supervision, for example because it is a therapeutic antimicrobial agent or an injectable preparation for small animals; or because of other legal provisions; or the method of administration is novel;
- (c) when the product's toxicity may present a safety hazard in animals or man; when the risk/benefit ratio of using the product is finely balanced; when the substance has a significant activity on the central nervous system, for example anaesthetics, tranquillizers or where it significantly alters the animal's physiology;
- (d) when careful monitoring of the use of the product is required (this would normally apply to all new ingredients for up to five years and could apply to known active ingredients authorized for administration by a new route); and
- (e) when the substance is controlled under the Misuse of Drugs Act 1971 or allied legislation, or the active ingredient is classified prescription-only for human use.

3.38. The UK has been readier than many member states to make use of the provision referred to in paragraph 3.36 allowing, where it is safe to do so, the early reclassification of medicines that were initially classified prescription-only because they were novel.

3.39. All veterinary medicines classified POM in the UK are specified in a Statutory Instrument¹ which applies the classification and secures that the relevant provisions of the Medicines Act apply as they should to these medicines. This Statutory Instrument is periodically updated; all current centralized authorizations are specified, including all such authorizations issued after the finalization of the draft Statutory Instrument.

General Sale List criteria

3.40. Section 51 of the Medicines Act 1968, applicable to human and veterinary medicines, provides for the GSL distribution classification to be given to products that can, with reasonable safety, be sold or supplied other than by, or under the supervision of, a pharmacist. In the case of veterinary medicines this is modified by the further proviso that the product can with reasonable safety be sold or supplied other than by a registered agricultural merchant.

3.41. Veterinary medicines classified GSL are specified in a statutory instrument, updated as necessary.²

3.42. Veterinary medicines whose properties fall between the POM and GSL criteria may be sold or supplied without a prescription. The default P distribution classification applies to those medicines that may only be sold by or under the supervision of a pharmacist or veterinary surgeon (in the latter case, only for the treatment of an animal or herd under his or her care). Otherwise medicines in this intermediate group are classified PML (in practice, this is the great majority of them).

Pharmacy and Merchants' List criteria

3.43. The PML distribution classification, now established by the Medicines (Exemptions for Merchants in Veterinary Drugs) Order 1998, is a variant of the P distribution classification aimed at the supply of veterinary medicines to farmers and others who keep animals as a business. Veterinary medicines classified PML may be sold, to a person who keeps animals for the purposes of carrying on a business, by a registered agricultural merchant or, if a cat, dog or horse wormer, a registered saddler from premises which are registered and subject to annual inspection by the Registration Authority (in Great Britain, the RPSGB; in Northern Ireland, the Department of Health, Social Services and Public Safety for Northern Ireland). Each sale of a PML medicine must be made under the authority of an SQP—see paragraph 3.91.

3.44. PML medicines may also be sold from a pharmacy (with each sale by, or under the supervision of, a pharmacist) or by a veterinary surgeon for the treatment of an animal or herd under his or her care. They are legally identified in a list kept by the Secretary of State for the Environment, Food and Rural Affairs.

Classification process

3.45. As part of its assessment of applications for MA, the VMD considers what distribution classification to give. Products falling within the VPC's guidelines for prescription-only medicines are classified POM. In all other cases the VMD, with advice from the VPC as necessary, makes a judgement based on its assessment of risk in the light of factors such as the properties of the product, its intended use and means of administration and the views of the MA applicant. The VMD takes into account the welfare of animals treated with the product but does not consider factors affecting the welfare of animals needing treatment. For example, evidence to the inquiry shows that most veterinary surgeons apply lower percentage mark-ups to medicines classified PML than to POMs (see paragraph 6.149). Whether or not a medicine is intrinsically costly, a non-POM classification is likely to lead to a lower retail price, and therefore a greater likelihood of treatment and, so long as this does not lead to misuse, improved animal welfare. The VMD and the VPC do not consider this to be an aspect of efficacy when they judge a product's distribution classification.

¹The most recent is The Medicines (Veterinary Drugs) (Prescription Only) Order 2001 (SI 2001/1646).

²The most recent is the Medicines (Veterinary Drugs) (General Sale List) Order 2001 (SI 2001/1645).

Reclassification

3.46. Unless a product is legally required to be permanently classified POM, the MA holder may at any time apply to the relevant national authorizing authority for a change of distribution classification. Supporting evidence, which may include new test results, is likely to be required. In the case of a product having UK MA and which was initially classified POM because an ingredient, or the method of administration, was new, the VMD is willing to consider applications for reclassification earlier than five years after first MA, making use of the discretion in the final leg of the EC POM specification (see paragraph 3.36).

3.47. Several veterinary manufacturers have said to us that products authorized through the centralized procedure must necessarily be permanently classified as prescription-only. This is mistaken: the EC prescription-only criteria apply whatever route is used to obtain MA. Their effect is to require all the veterinary medicines currently eligible for the centralized procedure to be classified, at least initially, as prescription-only. Many products which are novel, in their active ingredients or method of administration, may use the centralized procedure and in some cases could be legally reclassified as non-prescription-only after five years. Whether this happens or not is a matter for the judgement of the CVMP and the Authorities of the EC and will be reflected in the specific terms of each centralized authorization.

3.48. Member states have no power to deviate from the terms of a centralized authorization. But subject to those terms it remains open to member states to set national distribution requirements. If, therefore, a centrally-authorized product were to be classified, or reclassified, as not prescription-only it appears that, for national purposes, the UK could apply one of its non-POM distribution classifications, P, PML or GSL.

The cascade

3.49. It will sometimes happen that there is no veterinary medicine authorized for the treatment of a particular combination of species and condition. In these circumstances a veterinary surgeon may make use of the 'cascade', which allows him or her, or a person acting under his or her direct responsibility, to administer to a particular animal or small number of animals:

- (a) a veterinary medicine authorized in the UK for use in another animal species or for another condition in the same species;
- (b) if there is no such veterinary medicine as described in (a) above, a product authorized for use in the UK in a human being; or
- (c) if there is no such human medicine as described in (b) above, a veterinary medicinal product prepared by an authorized person in accordance with a veterinary prescription. (In the UK 'an authorized person' means a pharmacist or the veterinary surgeon having the animal or herd under his or her care.)

Where the animal concerned is food-producing, the medicine may only contain substances found in a veterinary medicine already authorized in the UK for such animals. The veterinary surgeon must specify an appropriate withdrawal period.

Regulation of participants in the supply chain

Elements of the supply chain

3.50. For the purposes of our inquiry, we distinguish three levels in the supply of veterinary medicines (for simplicity, disregarding supply to research institutions, zoos and some other specialized, small-scale users). The levels are:

- (a) manufacturer supply to wholesalers, veterinary practices, agricultural merchants and some end-users, such as industrial-scale poultry producers, who employ veterinary surgeons;
- (b) wholesaler supply to veterinary practices, pharmacies, agricultural merchants and saddlers; and
- (c) veterinary surgeon, pharmacy, agricultural merchant, saddler and other retailer supply to animal owners such as farmers and pet owners.

Wholesaler licensing, outlined in paragraphs 3.66 and 3.67, governs the particular distribution classifications of veterinary medicines in which individual wholesalers may trade. At retail level, the distribution classification of a medicine plays a key part in determining the individuals or businesses permitted to supply it.

Supply of veterinary medicines

3.51. Some 2,000 veterinary medicines are authorized for sale in the UK. Table 3.1 breaks these down between the four distribution classifications referred to in paragraph 3.34 and gives corresponding sales in 2001 (at manufacturers' prices to wholesalers). The numbers of medicines classified POM does not take account of authorizations granted or withdrawn after the date specified in SI 2001/1646 (30 March 2001).

TABLE 3.1 Breakdown of MAs and sales by distribution classification

| <i>Distribution classification</i> | <i>Number of MAs listed at 21.11.02</i> | <i>Percentage of all listed MAs</i> | <i>Sales, year ended 31.12.01 (£m)</i> | <i>Percentage of sales</i> |
|------------------------------------|---|-------------------------------------|--|----------------------------|
| POM | 983 | 48 | 231.8 | 72 |
| P | 14 | 0.7 | 1.3 | 0.4 |
| PML | 411 | 20 | 75.3 | 23.5 |
| GSL | 630 | 31 | 12.2 | 3.8 |

Sources: VMD published MA listings; NOAH (sales data).

3.52. Except for those classified GSL, almost all veterinary medicines reach end-users (mainly farmers and owners of companion animals) in one of two ways: from a veterinary surgeon (or surgery) or from an agricultural merchant or saddler (neither of whom may supply POMs).

3.53. This twofold structure is repeated at wholesale level where a sharp distinction exists between two groups of wholesalers. 'Veterinary' wholesalers (the term has no regulatory or legal significance) supply all types and distribution classifications of veterinary medicines as well as a wide range of non-medicinal products used in veterinary practice. They deal almost exclusively with veterinary surgeons and practices. 'Trade' wholesalers supply non-POM veterinary medicines alongside many other agricultural products. They seldom, if ever, supply to veterinary surgeons and practices, their customers being agricultural merchants, saddlers, outlets selling GSL medicines and some end-users.

Overview: other EC countries

3.54. Only the Republic of Ireland has a scheme of distribution classifications resembling that in the UK. The Irish scheme includes an additional distribution classification, POM(E), which allows a product to be sold not only by a veterinary surgeon for an animal under his or her care but also under the direct supervision of a pharmacist without a veterinary prescription.

3.55. In Germany, the great majority of veterinary medicines are classified POM and retailed by veterinary surgeons. The remainder are available through pharmacies or may have a 'free' distribution classification, equivalent to GSL in the UK, allowing sale by any type of retailer. The position is similar in France, though there are exceptions: some prescription-only medicines, specified in secondary legislation, may be supplied by a *groupement* to its members provided this is in accordance with a health plan agreed and controlled by a veterinary surgeon. French law also allows unrestricted sale of external parasiticides for companion animals.

3.56. In Belgium, all veterinary medicines may only be retailed by a pharmacy. More than 90 per cent of the total are classified POM and so require a veterinary prescription. The position is similar in Denmark, save that stocks obtained from a pharmacy may be supplied to farmers by a veterinary surgeon for animals under his or her care. In Portugal, all veterinary medicines are classified POM and may be supplied by a veterinary surgeon to animals under his or her care or by a pharmacy in accordance with a veterinary prescription. Authorized farmer groups, which must employ a veterinary surgeon, may buy medicines direct from veterinary manufacturers or wholesalers.

Manufacturers

Overview

3.57. Eighty-five companies are shown in SI 2001/1646 as holding UK or centralized MAs for veterinary medicines classified POM. Eighteen of them account for almost 90 per cent of UK sales of veterinary medicines, their individual shares ranging from 0.7 to 14.4 per cent. Only three of the major international manufacturers of veterinary medicines manufacture in the UK; the remainder operate here as sales and marketing organizations supplying medicines made elsewhere.

3.58. Although most sales by manufacturers are to wholesalers, there is some direct supply to veterinary practices as well as to agricultural merchants and end-users (to neither of whom manufacturers may supply POMs unless the business employs a veterinary surgeon).

Regulation of manufacturing

3.59. ‘Manufacture’ is defined in the Medicines Act 1968 broadly to mean the making of a medicinal product. This report uses ‘manufacturer’ in the different sense, defined in the glossary, to refer to a person who is not necessarily a maker of veterinary medicinal products. Paragraphs 3.60 to 3.62 outline the licensing of manufacture in its Medicines Act sense, but using ‘production’ and cognate terms in its place. Paragraph 3.66 adopts the same usage.

3.60. Before a veterinary medicine can be given MA the authorizing authority must be satisfied that it is produced in accordance with criteria set out in EC law. If production takes place within the territory of the EC the maker, whether or not the MA holder, must have authorization from the relevant national authority allowing it to produce the medicine. ‘Producing’ includes partial production and, other than at retail level, processes such as dividing up, packaging, labelling and presentation. In the UK this authorization is by means of licensing under the Medicines Act 1968. The Medicines Control Agency (MCA—an executive agency of the Department of Health) has this responsibility in respect of human medicines. The VMD’s parallel responsibility for veterinary medicines is subcontracted to the MCA, except in the case of veterinary immunological products where the VMD inspects premises, though the resulting licences under the Medicines Act are issued by the MCA on the VMD’s behalf. Licences specify the dosage forms to which they apply and are for the production of human medicines, veterinary medicines or both. Every premises on which production takes place must be licensed (a single licence may cover several sets of premises in the same ownership).

3.61. The licensing procedure entails inspection of the premises and reinspections, normally at two-yearly intervals while the licence remains in force. Licensed producers must have permanent and continuous access to a Qualified Person whose duty it is to ensure that each batch of product is produced in accordance with its MA and to so certify each batch in a register.

3.62. If the premises are outside UK jurisdiction, a licence as such cannot be issued by the UK authority. Where the premises are elsewhere in the EC the MCA relies upon acceptance by the national authority. In other cases the MCA either relies upon the mutual recognition agreements that exist with a number of non-EC countries or arranges an inspection visit to the overseas premises. These procedures are separate from the VMD’s procedures for granting MA: it is up to the applicant to coordinate the two so that before granting MA, the VMD can verify that the place of production has been found to be satisfactory. A formal variation of the MA is required if the place of production is to be changed.

Responsibilities of MA holder

3.63. The grant of MA places its holder under a number of legal duties. Broadly, these relate to:

- (a) maintenance of product quality including its conformity to the Summary of Product Characteristics set out in the MA;
- (b) pharmacovigilance;
- (c) notification of the authorizing authority of any change liable to require a variation of the MA;
- (d) confining supply of veterinary medicines to purchasers who may lawfully acquire them, having regard to each medicine's distribution classification;
- (e) retention of the product dossier for at least five years after authorization ceases;
- (f) withdrawal of the product, or particular batches, from the market if so directed by the authorizing authority; and
- (g) provision of samples or information in response to a request by the authorizing authority.

Wholesalers

Overview

3.64. The wholesale supply of POMs to veterinary surgeons, veterinary practices and pharmacies is undertaken exclusively by five veterinary wholesalers (see paragraph 3.53) who also supply veterinary medicines with other distribution classifications as well as other veterinary requisites.

3.65. All these wholesalers handle the products of all manufacturers and stock their complete ranges of veterinary medicines. Almost all their customers are veterinary surgeons and veterinary practices, though some of them also supply the few pharmacies that offer a veterinary service.

Regulation of wholesalers

3.66. Any person in the UK who buys veterinary medicines for wholesale distribution in the UK or elsewhere in the EC requires a wholesale dealer's licence that names all the premises from which their business is carried on. Wholesale dealer's licences are held not only by the wholesalers mentioned above but also by many agricultural merchants and UK manufacturers who supply veterinary medicines that they have not produced, but have bought from others, chiefly from their parent company.

3.67. Wholesale dealer's licences are granted by the MCA. They distinguish between the supply of human and veterinary medicines and between the different classes and distribution classifications of products. Licence holders may only deal in accordance with the scope of their licence. The licensing procedure includes an initial inspection of the premises and reinspections, normally at four-year intervals.

Retail-level suppliers

Veterinary surgeons and practices

Overview

3.68. A very high proportion of the supply of POMs to end-users takes place through veterinary practices. There are just under 2,000 veterinary practices in the UK, operating from around 3,200 locations. They vary in size, ranging from a veterinary surgeon working alone through partnerships of two or more veterinary surgeons to corporate practices with many tens of surgeries spread over areas as

populous as Greater London. A minority of veterinary surgeons delivering animal healthcare services, including treatment with POMs, work not in a veterinary practice but elsewhere, for example as employees of animal charities, large corporate food producers and zoos.

Role of veterinary surgeons

3.69. When presented with a patient, a veterinary surgeon's first task is to determine the animal's need, through clinical examination and diagnosis if it is ill or by the application of healthcare principles if the objective is prevention. He or she must then decide whether treatment is needed, whether it should include medication and if so what.

3.70. Any medicine to be administered to the animal must be authorized unless there is no such medicine available for the species and condition in question. In that case the veterinary surgeon will need to have recourse to the cascade (see paragraph 3.49) and the medicine must be administered by him or her or under his or her direct responsibility.

3.71. If a non-POM is to be used (whether or not under the cascade), the client may choose to buy it from the veterinary surgeon or from another source in accordance with its distribution classification. If the veterinary surgeon decides that a POM must be used, the client may either buy it from the veterinary surgeon (usually the most convenient option if the medicine requires veterinary administration, for example if it is an injectable) or may obtain a prescription to be dispensed in a pharmacy.

3.72. Under the law as it stands the only veterinary surgeon who may supply or prescribe a POM (or a medicine under the cascade) for a particular animal or herd is a veterinary surgeon under whose care it is.

Regulation of veterinary surgeons

3.73. A veterinary surgeon is a person who is a registered member of the RCVS. To obtain this membership a person must successfully complete professional training recognized by the RCVS. With certain exceptions (including veterinary students and nurses), nobody who is not a veterinary surgeon may practise veterinary surgery, ie they may not, in particular:

- (a) diagnose diseases in or injuries to animals;
- (b) give advice based on such diagnosis;
- (c) carry out medical or surgical treatment of animals; or
- (d) perform surgical operations on animals.

3.74. The legal obligations of veterinary surgeons in relation to veterinary medicines are outlined below. At professional level, a veterinary surgeon may be disciplined through the RCVS's disciplinary procedure if found to have engaged in disgraceful professional conduct, to have been convicted of a criminal offence rendering him or her unfit, in the opinion of the RCVS disciplinary committee, to practise, or to have registered fraudulently. The RCVS does not have power to impose penalties for anything less though standards of conduct are set out in its advisory *Guide to Professional Conduct* (which also summarizes veterinary surgeons' main legal obligations). Failure to follow this advice is not necessarily either unlawful or disgraceful but may be taken into consideration in disciplinary procedures that can lead to a member's being suspended or struck off and so losing his or her right to practise, possibly permanently.

3.75. Veterinary surgeons' role in respect of the prescribing and supply of veterinary medicines flows from the Medicines Act 1968 and regulations made under it. The Act's basic provision is that human and veterinary medicines, other than those on a GSL, may only be sold at a pharmacy by, or under the supervision of, a pharmacist (section 52). Although this basic provision contains no requirement for a prescription, there are further provisions having the effect that:

- (a) any authorized medicine may be sold by a veterinary surgeon for administration by him or her, or under his or her supervision, to an animal or herd under his or her care (section 55(3));
- (b) medicines of a class or description specified by order as prescription-only may *only* be supplied:
 - (i) on veterinary prescription at a pharmacy by, or under the supervision of, a pharmacist (the prescribing veterinary surgeon must certify that the prescription is for an animal or herd under his or her care); or
 - (ii) without prescription, by a veterinary surgeon for administration, to an animal or herd under his or her care, by him or her or in accordance with his or her directions (section 58);
- (c) any other exceptions specified by order (this power has been used to create the PML distribution classification—see paragraph 3.34) (section 57); and
- (d) medicines of a class or description specified by order as GSL products may be sold from any premises (but see paragraph 3.93) without the involvement of a pharmacist and without prescription (section 51).

3.76. The RCVS *Guide to Professional Conduct* contains provisions relevant to veterinary surgeons' role in the supply of medicines. One relates to the provision of prescriptions and states:

Veterinary surgeons are encouraged to make their clients aware that veterinary medicines may be obtained on prescription from other suppliers, for example pharmacies, and should not unreasonably refuse to supply prescriptions if clients wish to purchase veterinary medicines from other suppliers. A reasonable charge may be made for prescriptions, which may only be issued for animals under the care of the prescribing veterinary surgeon.

Another deals with itemized accounts:

The professional/client relationship is one of mutual trust and respect, under which a veterinary surgeon must: ... provide fully itemised accounts if requested.

A third deals with the provision of cost information before treatment begins:

Discussion should take place with the client, covering a reasonable range of treatment options and prognoses, and the likely costs in each case ... the owner should be warned that additional costs may arise if complications occur.

If during the course of treatment it becomes evident that an estimate or a limit set by the client is likely to be exceeded the client should be contacted.

3.77. The RCVS must investigate all complaints within its jurisdiction made against its members, however trivial they may appear. It must take similar action when a conviction is reported to it. In the majority of cases the member's response will reveal that a misunderstanding has arisen and enable the RCVS to resolve the complaint by correspondence. It is, however, incumbent upon members to respond constructively to the allegations. Persistent failure to do so will in itself raise a misconduct issue. Members may indicate that they choose to exercise their 'right to silence' and the complaint may then go forward un rebutted.

3.78. There is no specific regulation of veterinary surgeries or their dispensaries although veterinary surgeons are required to keep records of all incoming and outgoing transactions relating to veterinary medicinal products (other than GSL products) supplied by retail for use in food-producing animals. A detailed audit must be carried out annually. Records of incoming and outgoing veterinary medicines must be reconciled with current stores and discrepancies recorded. The State Veterinary Service is responsible for inspecting veterinary surgeries' compliance with these provisions; enforcement is the responsibility of the VMD. The RCVS *Guide to Professional Conduct* recommends the keeping of case records for all patients, including records of the medicines prescribed, supplied or administered. It also makes recommendations about the standard of surgeries.

3.79. Virtually all veterinary surgeons carrying out farm animal work are appointed by Defra as LVIs to carry out monitoring and inspection work in connection with the regulation of food production. Such veterinary surgeons' performance of these functions are subject to periodic checks by the State Veterinary Service.

Pharmacies and pharmacists

Overview

3.80. There are approximately 12,000 community pharmacies in Great Britain and a little over 500 in Northern Ireland, all of which may lawfully dispense POMs in accordance with a veterinary surgeon's prescription provided that dispensing is carried out by, or under the supervision of, a registered pharmacist. All other distribution classifications of veterinary medicine may also be supplied.

3.81. A small number of specialist veterinary pharmacies exist, at least two of which trade on the Internet. As the law stands, they may not dispatch POMs until they have received the written prescription bearing the original signature of the prescribing veterinary surgeon. Work is in hand to allow the use of electronic or faxed prescriptions for human medicine which could easily be extended to the veterinary sphere.

Regulation of pharmacies and pharmacists

3.82. A person may act as a pharmacist in Great Britain (and lawfully dispense all veterinary medicines from a registered pharmacy) only if registered by the RPSGB. In Northern Ireland a pharmacist must be registered by the Pharmaceutical Society of Northern Ireland. In either case registration is obtained by examination, taken after successfully completing an approved four-year degree course followed by a year's practical experience. The two societies have a mutual recognition arrangement to allow pharmacists to move easily between Northern Ireland and Great Britain.

3.83. There is no formal category of 'veterinary pharmacist', though the few specialist businesses mentioned above use the term. However, the two pharmaceutical societies insist that specialist pharmacists, including specialists in veterinary pharmacy, must be competent in their specialism. Although specific specialist training is not always necessary, pharmacists may study for the Diploma in Agricultural and Veterinary Medicine offered by the RPSGB.

3.84. A pharmacist may dispense medicines only from a registered pharmacy. Pharmacies are registered by the two pharmaceutical societies who inspect them as part of registration and reinspect on average at intervals of 18 months.

3.85. Pharmacists may dispense a POM only in accordance with a veterinary surgeon's prescription. If the prescription specifies a particular branded product, the pharmacist may not substitute any other medicine for it. Where the prescription is for a generic and does not use a brand name, the pharmacist may dispense any product meeting that description that is authorized for the species and condition in question. Pharmacists are subject to the same record-keeping and annual reconciliation requirements as veterinary surgeons (see paragraph 3.78).

Agricultural merchants and saddlers

Overview

3.86. The Medicines (Exemptions for Merchants in Veterinary Drugs) Order 1998¹ defines an agricultural merchant as 'a person who carries on a business involving in whole or in part the sale of agricultural requisites, being things used for soil cultivation or keeping of animals for production of food or game, equipment for collecting produce from animals kept for production of food, things for the maintenance of that equipment and protective clothing'.

¹SI 1998/1044.

3.87. Just under 1,000 premises in the UK are registered for the supply of PML medicines by some 500 agricultural merchant businesses. They are suppliers to the farming industry, operating in proximity to it, but also supply PML medicines for cats, dogs and horses to owners of companion animals as well as to relevant businesses. Animal health amounts to between 15 and 25 per cent of the business of agricultural merchants as a whole, though individually the proportion ranges from 10 to 90 per cent.

3.88. The Regulations mentioned above also define a saddler as ‘a person carrying on a business involving in whole or in part the sale of saddlery requisites, being products and equipment and things for the maintenance of that equipment, for keeping horses or ponies, including human clothing for that purpose’. Some 175 saddlery businesses operate from premises registered for the supply of PML wormers for cats, dogs and horses. They may not supply other PML medicines.

3.89. Underlying the PML distribution classification is the view that end-users will be knowledgeable keepers of animals. Accordingly agricultural merchants may only sell PML products to a person whom they know, or have reasonable cause to believe, keeps animals by way of a business. Wormers for cats, dogs or horses may only be sold to keepers of the animal in question (though not necessarily kept by way of business) for use on such an animal.

Regulation of agricultural merchants, saddlers and their premises

3.90. The RPSGB and, in Northern Ireland, the Department of Health, Social Services and Public Safety for Northern Ireland are responsible for registering premises where an agricultural merchant or saddler supplies veterinary medicines classified as PML. The business as such is not subject to registration and is unaffected by a change of ownership—though this must be notified as it is a criterion for registration that the owner is a fit and proper person for the sale of PML medicines. Annual registration is required and premises are inspected at intervals of about 18 months.

3.91. Each sale of a PML medicine must be authorized by an SQP. In this context an SQP is a person included in the relevant part of the register of SQPs kept by the Animal Medicines Training Regulatory Authority (AMTRA). A person may only be included in the register after having completed a training course recognized by AMTRA in relation to the SQP role in an agricultural merchant or saddler as the case may be. The SQP must adhere to a Code of Practice issued by AMTRA.

3.92. Like veterinary surgeons, agricultural merchants and saddlers are required to keep transaction records and to reconcile them annually with stocks. These requirements apply in respect of all PML medicines, including those supplied for non-food animals.

Other retailers

3.93. GSL veterinary medicines may be sold by any retailer subject only to the requirement that the premises on which they are stored and from which they are sold must be capable of being closed to the public. There is no specific compliance monitoring of the requirement.

Future developments in regulation

3.94. This inquiry has taken place concurrently with two other reviews which overlap it in a number of ways. The European Commission has been reviewing the principal EC legislation on human and veterinary medicines and has made formal proposals for change. At much the same time the Government, as part of its Action Plan for Farming, commissioned an independent review of the dispensing by veterinary surgeons of POMs (the Marsh review). The Government’s formal response was published on 10 December 2002.

3.95. Because the state of competition in the supply of POMs was not an explicit issue before either of these reviews, their perspectives differ from that of this inquiry for which competition is central. Nevertheless, and especially in regard to regulation, we have quite frequently been led to consider matters on which the reports of the Marsh review or the European Commission (or both) have made

recommendations. The following paragraphs summarize aspects of the European Commission's review which we consider have implications for competition in the supply of veterinary POMs. Appendix 3.1 presents a similar summary of the Marsh review's recommendations.

Proposed revision of European law

3.96. The European legislation establishing the EMEA and creating the centralized procedure for MA came into force on 1 January 1995. It added significantly to the body of European medicines law (human and veterinary) as it then existed and required the European Commission to report within six years on its operation. The Commission's report, accompanied by formal proposals for legislative change, was presented to the Council of Ministers on 26 November 2001. The European Commission's explanatory memorandum indicates that the main purposes of the proposals are to reduce regulatory barriers, promote fuller harmonization and reverse the decline in the range of species and conditions for which there are authorized veterinary medicines. The proposals are now under discussion within the legislative processes of the EC and could be enacted, though not necessarily in force, by the end of 2003.

3.97. A number of the European Commission's proposals, if adopted, could affect competition in the supply of POMs in the UK. Below we briefly outline the proposals we believe will have the biggest potential effects on competition—in some cases to improve it, in others not:

- (a) MAs to be valid indefinitely in the absence of field evidence of harm.
- (b) MAs to be voided if marketing is delayed beyond two years from authorization, or if there is a hiatus in marketing of more than two years.
- (c) All medicines for food animals to be prescription-only.
- (d) All medicines containing an active ingredient authorized for veterinary use for less than seven years to be prescription-only with no provision for discretionary earlier downward reclassification.
- (e) The data protection period to be at least ten years in all cases, irrespective of the earlier lapse of patent protection, and 13 years in the cases of bee and fish medicines.
- (f) This ten-year data protection period to be extended by one year for each new food animal species added after the initial grant of MA, up to a maximum of three additional years, provided the MA holder was the original applicant for MRL determination of the active ingredient.
- (g) Separate food-animal and non-food-animal cascades now specified: horses may be treated as non-food animals if a declaration is made that the animal is never intended for food use.
- (h) For food animals the second leg of the cascade is broadened to include use of a medicine authorized in another member state for the same species for the same or a different condition.
- (i) The centralized procedure is widened:
 - (i) by making it mandatory for all veterinary medicines containing a new active ingredient not previously incorporated in any veterinary medicine authorized in the EC; and
 - (ii) by making it optional if the product shows significant therapeutic, scientific or technical innovation or if centralized authorization is of interest to patients or animal health at EC level.
- (j) Generics of centrally-authorized medicines may be authorized by member state authorities.