



Veterinary Medicines Guidance Note

Wholesale Dealers Authorisations for 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. Basic information about the scope of the Regulations and the requirement for marketing authorisations is given in VMG Note 1: *An Introduction to Marketing Controls on Veterinary Medicines*. This note describes the arrangements for wholesale dealer's authorisations (WDAs).

WHOLESALE DEALER'S AUTHORISATIONS (WDAs)

LEGAL PROVISIONS

3. The provisions specifically relating to WDAs are set out in the Regulations. Failure to comply with the provisions of the Regulations, e.g. the duties of the wholesale qualified person, is a criminal offence and may result in prosecution.

MEANING OF WHOLESALE DEALING

4. For the purposes of the Regulations, wholesale dealing means the procurement, holding or wholesale distribution (whether or not for profit) of a veterinary medicine to retailers or other wholesale dealers. It does not include:
 - the supply by an authorised manufacturer or marketing authorisation holder respectively, of veterinary medicines they have manufactured or to which their marketing authorisation relates; and
 - small quantities of medicines supplied by one retailer to another, provided the value of the total amount supplied in any one year does not exceed five percent of the supplier's turnover for veterinary medicines for that year. *This is intended to allow retailers to supply products to each other without additional regulation where this is necessary to alleviate supply problems that could be detrimental to animal welfare.*

REQUIREMENTS FOR OBTAINING A WHOLESALE DEALER'S AUTHORISATION

5. In order to obtain a WDA, wholesale dealers must have at their disposal:
 - technically competent staff;

- suitable and sufficient premises for the storage, handling and distribution of the medicines; and
 - a nominated Responsible Person – known as a Wholesale Qualified Person (WQP)
6. Holders of a WDA are also required to:
- have an emergency recall plan will ensure effective implementation of the recall from the market of any relevant medicinal products where such recall is:
 - (i) ordered by the VMD or by the competent authority of any other EEA State; or
 - (ii) carried out in co-operation with the manufacturer of, or the holder of the marketing authorisation for, the product in question;
 - maintain records for at least 3 years and make them available for inspection by a duly appointed inspector;
 - Procure veterinary medicinal products only from authorised manufacturers or wholesale dealers;
 - Supply veterinary medicines in accordance with the wholesale dealer's authorisation to persons lawfully permitted to receive them; these are:
 - (i) retailers who are authorised to supply those veterinary medicines to the public in accordance with the Regulations (please refer to Veterinary Medicines Guidance Note 3 for further information);
 - (ii) holders of Wholesale dealers Authorisations relating to those medicines;
 - only supply an authorised veterinary medicinal product for which there is a marketing authorisation for the time being in force in respect of that product; and the sale or offer for sale is in accordance with the provisions of that authorisation.
 - carry out a stock audit at least annually;
 - ensure proper stock turnover;
 - comply with the principles of good distribution practice (GDP) as if the veterinary medicinal products were medicinal products for human use, as set out in *EU Guidelines on Good Distribution Practice (GDP) of medicinal products for human use (94/C63/03) and Rules and Guidance for Pharmaceutical Manufacturers and Distributors*; and
 - provide information or samples to a duly appointed inspector on demand.
7. A satisfactory inspection is required before a WDA may be granted. The site in question must be:
- weatherproof;
 - secure and lockable;
 - clean;
 - free from contaminants; and

- capable of fulfilling the storage requirements of all veterinary medicinal products to be stored there as detailed in the marketing authorisation (MA).
8. Holders of a WDA who import veterinary medicines, which are not authorised in the UK, must first ensure that an import certificate has been obtained from the VMD unless the imported medicines are to be exported immediately. Guidance on import certificates is contained in VMG Note 7 Import certificates schemes.
 9. Holders of a WDA who import a UK-authorised veterinary medicine from another Member State must notify the holder of the marketing authorisation for that product of the import, unless the importing wholesaler is also the holder of the relevant marketing authorisation. Further guidance on this type of import is in Veterinary Medicines Guidance Note 6, which is available on the VMD website.

HOW TO APPLY FOR A WHOLESALE DEALER'S AUTHORISATION

10. Application forms are available on the VMD website (www.vmd.gov.uk).
11. Application forms will be processed by the VMD within 90 days of receipt.
12. An applicant for a WDA is required to supply information in relation to the following:
 - name and address of applicant;
 - the different classes of product to which the WDA will relate, i.e. whether the products are:
 - (i) Prescription Only Medicines - Veterinary (POM - V);
 - (ii) Prescription Only Medicines – Veterinary Surgeon, Pharmacist, SQP (POM-VPS);
 - (iii) Non-Food Animal - Veterinary Surgeon, Pharmacist, SQP (NFA-VPS); and
 - (iv) Authorised Veterinary Medicine - General Sales List (AVM-GSL). *(including other types of products such as those that are marketed under the Small Animal Exemption Scheme (SAES), registered homeopathic remedies)*
 - address of each site from which wholesale distribution (i.e. procurement, storage, sale, supply or export of medicinal products) takes place together with an indication of the general range of medicinal products to be stored at each.
 - a description of the facilities and equipment available at each site for storing the medicinal products and distributing products from or between the sites.

- a description of the arrangements at each site for ensuring a satisfactory stock turnover.
 - the name, address, and qualifications of the Wholesale Qualified Person; and
 - details of an emergency plan for the recall of defective products and a description of arrangements for keeping records of all products received or dispatched.
 - WDA holder are also required to have a documented Quality System (refer to Annex to this document).
13. The VMD will only issue a WDA when it is satisfied, following an inspection of the site(s), that the information contained in the application is accurate and in compliance with the requirements of the legislation.
14. For further advice on how to complete the application form please contact Sam Ward on tel: 01932 338496.

RESPONSIBLE PERSON - WQP

WQP Requirements

15. The WQP is responsible for safeguarding product users against potential hazards arising from poor distribution practices - as a result, for example, of supplying suspect products, poor storage or failure to establish the bona fides of suppliers and purchasers.
16. A WDA holder must have at his disposal, at all times, the services of a WQP who;
- has adequate knowledge of the activities to be carried out and of the procedures to be performed under the authorisation; and
 - has experience in those procedures and activities.
17. There is no statutory requirement for the WQP to be a pharmacist, although this is desirable. However, he/she should have access to pharmaceutical knowledge and advice when it is required and have personal knowledge of:
- The relevant provisions of the Regulations;
 - Articles 76-85 of Directive 2001/83/EC as amended on the Community Code relating to medicinal products for human use, as amended;
 - European Commission Guidelines on good distribution practice of medicinal products for human use (94/C 63/03);
 - The conditions attached to the WDA for which he/she is nominated;

The products traded under the authorisation and the conditions necessary for their safe storage and distribution;

- The categories of persons to whom products may be distributed; and
- The Quality System and Standard Operating Procedures employed by the WDA holder.

18. Where the WQP is not a pharmacist, or eligible to act as a Qualified Person (QP) (as defined in Directive 2001/82/EC as amended), he should have at least one year's practical experience in both or either of the following areas:
 - (a) Handling, storage and distribution of medicinal products.
 - (b) Selling, supplying or procuring medicinal products.
19. In addition, the WQP should have at least one year's managerial experience in controlling and directing the activity of the wholesale distribution of medicinal products on a scale, and of a kind, appropriate to the licence for which nominated.
20. It is for the VMD to determine if a particular WQP the appropriate knowledge and experience for the scale and nature of the wholesale distribution operation to which he is nominated.
21. The WQP does not have to be an employee of the WDA holder but he must be at his/her continuous disposal. Where the WQP is not an employee there should be a written contract that specifies his/her responsibilities, duties, authority and so on.
22. The WDA Holder shall:
 - notify the VMD of the name, address, qualifications and experience of the person who will carry out the functions of the WQP
 - notify the VMD of any changes to the WQP
 - not permit any person to act as the WQP other than the person named on the authorisation

Duties of the WQP

23. The WQP should impose a quality management programme which complies with GDP guidelines to ensure that the conditions of the WDA are met. The WQP should ensure that:
 - the conditions under which the authorisation has been granted have been and are being complied with, and
 - the products being handled are maintained in accordance with the requirements of their Marketing Authorisations
24. To carry out his/her responsibilities the WQP should:

- have a clear reporting line to either the WDA holder or, where the WDA holder is a company, to the Managing Director;
 - have access to all areas, sites, stores and records which relate to the licensable activities being carried out;
 - regularly review and monitor all such areas, sites, etc. or have delegated arrangements whereby he receives written reports that such actions have been carried out on his behalf. For example, where the WDA covers a number of sites the WQP may have nominated deputies. However, the WQP should assure himself and the VMD that the necessary controls and checks are in place. The WQP remains responsible and he should personally carry out the delegated functions at least once a year;
 - focus on the management of licensable activities, the accuracy and quality of records, compliance with established standard operating procedures, the quality of handling and storage equipment and facilities, and the standards achieved; and
 - keep appropriate records relating to the discharge of his responsibilities.
25. The WDA holder should ensure that there is a written Standard Operating Procedure (SOP) for receiving advice and comment from the WQP and recording the consequent action taken.
26. Should it prove impossible to resolve a disagreement between the licence holder and the WQP with regard to the statutory duties and responsibilities of the responsible person under the licence, the VMD should be approached for advice. Whilst a joint referral is clearly to be preferred, either party may approach the VMD for advice independently. If a WQP finds that he is in difficulty over his statutory responsibilities and the activities being carried out under the licence he should, in strict confidence, consult the VMD.

INSPECTIONS

27. Holders of a WDA for veterinary medicines are subject to regular inspections by the VMD. Inspection enables the VMD to confirm that WDA holders are complying with the conditions of their authorisation, with the provisions of the Regulations and with the requirements of Good Distribution Practice (GDP).

Amongst other things, VMD Inspectors are empowered to:

- inspect the premises, organised arrangements and procedures used in the storage and distribution of medicinal products;
- interview key personnel named on licences;
- take samples; and
- examine any documentation or records relating to the manufacture, assembly, storage and distribution of veterinary medicinal products.
- It is a requirement of both EC and UK national legislation that WDA holders shall make their premises available for inspections by the Licensing Authority at any reasonable time.

28. A fee is charged for these inspections. See Section 44 - Fees.
29. Following an inspection, the VMD Inspector prepares a report of his findings. A letter is sent to the applicant or authorisation holder noting any non-compliances found and asking for proposals to remedy them. In the most serious cases the report is referred to the Licensing Authority for consideration of more formal action which can include the refusal i.e. refusal before a WDA is granted, making a variation to an existing licence, suspension or revocation of a WDA, or suspension or revocation of part of a WDA or take action relating to the activities or omissions of the WQP.
30. Failure to comply with the Regulations may result in the suspension, compulsory variation or revocation of the WDA by the Secretary of State. WDA holders reserve the right to appeal against such decisions made by the Secretary of State.

RECORD KEEPING REQUIREMENTS

31. Holders of a WDA must keep detailed records for all incoming and outgoing transactions, including disposals, for at least three years. The records may be in the form of purchase and sales invoices, or on a computer, or in any other form, which provides as a minimum the following information:
 - the date and nature of the transaction;
 - the identity of the veterinary medicinal product;
 - the manufacturer's batch number;
 - the expiry date;
 - the quantity; and
 - the name and address of the supplier or recipient;
32. Holders of a WDA are required to carry out a detailed audit at least once a year. The audit must reconcile all incoming and outgoing veterinary medicinal products with products currently held in stock with any discrepancies being recorded.
33. If discrepancies have occurred, for example, from spillage or breakage it is for the individual concerned to consider whether any discrepancies are acceptable or whether further action may be required.

CONTRACTING SUPPLY TO ANOTHER WDA HOLDER

34. When a WDA Holder is acting as a third party storage and distribution site for another WDA holder, an appropriate technical agreement needs to be in place between the two businesses (and made available to Inspectors). The technical

agreement needs to fully describe where the responsibility for various aspects of GDP rests, whether with the contract giver or the contract acceptor.

35. Specifically, the agreement should formalise which party is responsible for checking and recording that the customer is authorised to receive veterinary medicines; which party would take responsibility for initiating recalls and which party deals with any complaints from the customer relating to the products delivered.
36. As an example – WDA holder 'A' places an order with WDA holder 'B' for direct delivery to a retail business 'C'. In this scenario WDA holder 'A' receives payment from business 'C' for goods which have never actually been handled by WDA holder 'A' and therefore WDA holder 'A' cannot confirm that their own GDP responsibilities have been met in relation to the products being distributed. In fact WDA holder 'B' is providing the storage and distribution facility on behalf of WDA holder 'A'.
37. The account holder would also be expected to name the supplying WDA as a contracted-out warehousing function on his own WDA and to perform annual inspections at the contracted WDA under the terms of the technical agreement. Where no such technical agreement exists, then delivery should only be made to the authorised WDA premises of the account holder placing the order.
38. If no technical agreement is in place, the requirements of the Veterinary Medicines Regulations will not be met in relation to compliance with GDP and it is likely that enforcement action will be taken against both WDA holders involved. Such action could result in a temporary suspension of all related WDAs until the matter is resolved.

VALIDITY OF AUTHORISATIONS

39. Once issued, a WDA is valid indefinitely, subject to regular satisfactory inspection and compliance with all the legal requirements. However, a WDA will lapse if the holder does not deal in veterinary medicines for five years.
40. A WDA may be suspended or revoked if the requirements are not complied with.
41. The VMD may revoke, vary or suspend a WDA when a condition of that authorisation is no longer being met. Where it appears that public safety is at risk it may also suspend the WDA with immediate effect for a period of up to three months. This suspension may be renewed for further periods of up to three months if the VMD considers this necessary.
42. Where an authorisation is refused, suspended, compulsorily varied or revoked, the applicant will be offered the opportunity to appeal (see VMG Note 11).

VARIATION OF AUTHORISATIONS

43. Before changes to the information contained in the authorisation documents, such as material alterations to the premises or distribution methods, can be made, an appropriate variation application must be submitted to and approved by the VMD. Failure to comply with this requirement could result in the authorisation being suspended, revoked or compulsorily varied.

FEES

44. A fee is normally charged for handling applications (including applications for variations) and for inspections. Wholesale Dealer's are also subject to an annual fee. Details on the relevant fees can be found in the Veterinary Medicines Regulations, which are available on the VMD website (www.vmd.gov.uk).
45. Fee reductions apply in respect of applications, annual fees and inspection fees for businesses whose annual turnover (meaning gross value of all veterinary medicinal products sold) is less than £35,000.

FURTHER GUIDANCE

46. Further detailed guidance on requirements for manufacturers, including information on Good Distribution Practice (GDP) is produced by the MHRA in the publication *Rules and Guidance for Pharmaceutical Manufacturers and Distributors* (commonly known as "the orange guide"), which is updated periodically and is available from the Stationery Office (Tel 0171 873 9090). There is a charge for this publication.

ANNEX 1

Guidance for manufacturers and distributors re:

CONTROL AND MONITORING OF STORAGE AND TRANSPORTATION TEMPERATURES

Legislation and good practices oblige pharmaceutical manufacturers and distributors to exercise control over the distribution chain to ensure that the quality of medicines is maintained. Critical in this regard is control of the environmental conditions under which medicines are stored and transported. The MHRA's recommendations concerning the control and monitoring of storage and transportation temperatures were published in The Pharmaceutical Journal in July 2001 (1). A summary of these is given below.

Introduction

1. EU requirements and guidelines on Good Distribution Practice (GDP) require distributors to 'ensure that storage conditions are observed at all times, including during transportation'. The requirements are applicable not only to medicines that need to be stored at low temperatures (known as cold chain products) but also to medicines that should be stored below 25° or 30° C (known as temperate chain products). In addition an increasing number of products require storage and transportation at sub-zero temperatures and the application of appropriate controls to these is equally important. What follows gives guidance on how compliance with relevant standards of good practice may be achieved.

Cold Storage

2. Many medicinal products require storage at controlled low temperature. Some of these such as vaccines, insulins, blood products and some products of biotechnology can be denatured by freezing and thus must be maintained within a narrow temperature range above freezing point.

3. The temperature in small refrigerators used to store medicines should be measured continuously and the maximum and minimum temperatures recorded daily. Sufficient space should be maintained to permit adequate air circulation. If the refrigerator is filled to capacity the effect on temperature distribution should be investigated. Refrigerators used for vaccines and other sensitive products should be capable of maintaining the temperature between 2°C and 8°C with the minimum of intervention. Temperature monitoring of these should be by electronic max/min thermometer, with an accuracy of + – 0.5°C, which should be readable from outside the unit. Refrigerators should not be sited in an environment where extremes of temperature (i.e. <10°C or >32°C) will affect their performance.

4. Large commercial refrigerators and walk-in cold rooms should be monitored with an electronic temperature-recording device that measures load temperature in one or more locations, depending on the size of the unit. Portable data-loggers that can be downloaded onto a computer may be used instead of a fixed device. Records should be checked daily. Internal air temperature distribution should be mapped on installation in the empty and full state and annually thereafter under conditions of normal use.

Products should not be stored in areas shown by temperature mapping to present a risk (e.g. in the airflow from the refrigeration unit). Condensate from chillers should not be collected inside the unit.

5. Temperature alarms should be fitted to large and walk-in units and those smaller units used to store products at risk from freezing.

Controlled room temperature storage

6. The simplest monitoring would be with a max/min thermometer placed at a strategic location and read, recorded and reset at least weekly, more frequently during periods of exceptionally hot or cold weather. With the exception of very small stores, temperatures should be recorded at low and high levels. Continuous temperature recording is recommended for large warehouses. Self-contained storage areas within warehouses, (e.g. CD store, flammables store) should be included in temperature monitoring programmes.

7. All warehouses should be temperature mapped to determine the temperature distribution under extremes of external temperature. Mapping should be repeated every two to three years and after any significant modification to the premises, stock layout, or heating system. Medicines should not be stored in areas shown by temperature mapping or other consideration to be unsuitable, e.g. at high level in poorly insulated stores, or next to heaters.

Transportation

Cold-chain goods

8. The route and time of transportation, the local seasonal temperatures and the nature of the load should all be considered when arranging cold-chain distribution. For small volumes of cold-chain goods insulated containers may be used, in which case it is vital that products damaged by freezing are prevented from coming into direct contact with ice packs at subzero temperatures.

9. Larger volumes of cold-chain goods should be shipped in refrigerated transport, particularly if transit times may be prolonged. Temperatures within loads of products at risk from freezing should be strictly controlled and monitored with recording probes or individual temperature monitoring devices, giving consideration to the temperature gradient within the load. The temperature records for each consignment should be reviewed and there should be a procedure for implementing corrective action in the case of adverse events.

10. Distributors should ensure that consignments of cold-chain goods are clearly labelled with the required storage/transport conditions. Receivers should satisfy themselves that the goods have been transported under appropriate conditions and should place them in appropriate storage facilities as soon as possible after receipt.

Other goods

11. Consideration should be given to the possible extremes of temperature inside uninsulated, unventilated delivery vehicles and precautions should be taken to protect all products from heat challenge. This includes representatives' samples kept in car boots and goods distributed using postal services.

Systems Checks and Calibration

12. Any systems whose performance is critical to preserving the product should be tested and demonstrated to achieve what is intended. Measuring and recording devices that are used in critical areas (e.g. temperature monitoring of storage and transport facilities for coldchain goods at risk from freezing) should be calibrated at least annually against a traceable reference device. Records should include pre and post-calibration readings and details of any adjustments made or corrections to be applied. Alarms should be checked for correct functioning at the designated set temperatures.

Reference

(1) Taylor J, Recommendations on the control and monitoring of storage and transportation temperatures of medicinal products. *The Pharmaceutical Journal*, 28 July 2001, Volume 267, pages 128-131.

ANNEX 2

WDA Quality System – Guidance re Requirements & Scope of Inspection

- Quality system documented to include:-
 - Organisational chart
 - Management commitment statement
 - Wholesale Dealer Qualified Person (WQP)
 - Role, responsibility, duties, authority
 - Line to authorisation holder or MD
 - Qualifications and experience
 - SOP for reporting to authorisation holder or MD
 - WQP reports to management/self audits
 - Recording system to enable full traceability
 - Verification of suppliers
 - Verification of customers
 - Storage – facilities, in particular:-
 - Cold chain products, monitoring of temperatures, calibration of temperature monitoring devices
 - Transport; including cold chain products; validation trials
 - Avoidance and contamination
 - Stock rotation
 - Picking of correct products and despatch
 - Tracing of defective products
 - Complaints and recall
 - Dealing with returns, non-conformance and defective products and their disposal or quality checks before resale
 - Training of personnel
 - Cleaning and vermin plan
 - Anti-counterfeit policy
- Inspectors to Check:-
 - Quality system and work instructions
 - Internal audits / management reports from WQP
 - Temperature monitoring devices
 - Effective, accurate, calibrated, position, recorded adequately
 - Cleaning records and vermin plan
 - Purchase records (bona-fides of supplier)
 - Sales records (bona-fides of customers)
 - Complaints and recalled product records
 - Storage of VMPs
 - Adequate / suitable storage
 - Clearly identified
 - Temperature controlled

- Cleanliness
- Controlled drugs securely stored
- Temperature sensitive products
- Quarantine area for non-conforming products
- Security of premises
- WDA holders details and sites accurate and up to date
- WQP contract
- Check products in stock are authorised
- Check if products reflected in authorisation
- Check if SICs/STCs handled
- Check if parallel imports/specials handled
- Any recalled, damaged, non-conforming, counterfeit products

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