



Veterinary  
Medicines  
Directorate

**VETERINARY MEDICINES  
GUIDANCE NOTE**

**No 15**

**MANUFACTURING  
AUTHORISATIONS**

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[www.gov.uk](http://www.gov.uk)

## **QUICK START GUIDE**

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This Veterinary Medicines Guidance Note (VMGN) is aimed primarily at Manufacturers who are required to comply with the principles of Good Manufacturing Practice (GMP) where appropriate in relation to the following types of authorisation:

### **Manufacturing Authorisation (ManA) – Chapter 1**

Manufacture or importation of authorised veterinary medicinal products (VMP) including manufacture and import for exportation.

### **Manufacturing Extemporaneous Products (Specials) Authorisation (ManSA) – Chapter 2**

Manufacturers of extemporaneous Veterinary Medicinal Products (VMPs) (also known as Specials) for use in accordance with the prescribing Cascade.

### **Autogenous Vaccine Authorisation (AVA-I/S) – Chapter 3**

Manufacture of autogenous vaccines. (A vaccine prepared from a pathogen extracted from a host animal or group which is then used to inoculate the rest of the group)

### **Non Food Animal Blood Banks Authorisation (NFABBA) – Chapter 4**

Collection, storage and supply of whole or fractionated blood for use in animal, which are not used as food.

### **Equine Stem Cell Centre Authorisation (ESCCA) – Chapter 5**

Equine Stem Cell Centres for collection, storage, processing, production and administration of equine stem cells used for autologous treatment of horses.

### **Exemptions for Small Pet Animals**

Placing on the market, manufacture or importation of a product intended for administration to small non food producing pet animals. Further information about the exemption is available in VMGN 12 Exemptions for Small Pet Animals, which is published at [www.gov.uk/government/publications/exemptions-for-marketing-medicines-for-small-pet-animals-vmgn-12](http://www.gov.uk/government/publications/exemptions-for-marketing-medicines-for-small-pet-animals-vmgn-12).

**Please Note:** the guidance in this document is aimed at sites which only handle products covered by the Veterinary Medicines Regulations (VMR). In the case of a site handling both human and veterinary medicines you should also refer to guidance published by the Medicines and Healthcare products Regulatory Agency (MHRA) and direct any enquiries to the Regulatory Information Service on **020 3080 7400** or at [www.mhra.gov.uk/Contactus/RegulatoryInformationService\(RIS\)formedicines/index.htm](http://www.mhra.gov.uk/Contactus/RegulatoryInformationService(RIS)formedicines/index.htm).

## **FURTHER INFORMATION**

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- For more information on Manufacturing Authorisations please contact the Veterinary Medicines Directorate's (VMD's) Inspections Administration Team on 01932 338426 or alternatively contact VMD reception on 01932 336911 and quote "Manufacturing Authorisations".

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## Introduction

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1. This is one of a series of Veterinary Medicines Guidance Notes (VMGNs) explaining the requirements for Marketing Authorisations (MAs) under the Veterinary Medicines Regulations (VMR) which are revoked and replaced on a regular basis, so any references to them should be read as referring to those that are currently in force. Therefore, the date and number of the Statutory Instrument are not shown in this VMGN. The VMGNs will be updated as necessary and the date of the most recent update is shown on the front cover.
2. The VMR set out the UK controls on veterinary medicines including their manufacture, advertising, marketing, supply and administration. VMGN 1 Controls of Veterinary Medicines, which is published at [www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns](http://www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns) gives basic information about the scope of the VMR and the requirement for MA, i.e. what constitutes a veterinary medicinal product (VMP).
3. This VMGN provides guidance on authorisations for Manufacturers who are required to comply with the principles of Good Manufacturing Practice (GMP) in relation to a number of different types of authorisation including **Manufacturing Authorisations (ManA)**, **Administration under the Cascade Authorisations (ManSA)**, **Exemptions for Small Pet Animals Authorisations**, **Autogenous Vaccine Authorisations (AVA-I/S)**, **Non Food Animal Blood Banks Authorisations (NFABBA)** and **Equine Stem Cell Centre Authorisations (ESCCA)**.

**Please note:** the guidance in this document in relation to ManA is aimed at sites that only handle VMPs. In the case of a site handling both human and veterinary medicines you should also refer to guidance published by the Medicines and Healthcare products Regulatory Agency (MHRA) and direct any enquiries to the Regulatory Information Service on **020 3080 7400** or via the website at: [http://www.mhra.gov.uk/Contactus/RegulatoryInformationService\(RIS\)formedicines/index.htm#4](http://www.mhra.gov.uk/Contactus/RegulatoryInformationService(RIS)formedicines/index.htm#4)

4. Further information about ManAs, ManSAs and the Exemptions for Small Pet Animals is available on the VMD website in the thematic area 'Manufacturers, Suppliers, Wholesalers and Distributors'.

## SECTION 1

### Manufacturing Authorisation (ManA)

#### Definitions

6. Under the VMR “manufacture” includes any part of the manufacture of a veterinary medicinal product other than starting materials. The ManA may be granted for the following activities:

**Manufacture** - in relation to a VMP, includes any process carried out in the course of making the product, but does not include dissolving or dispersing the product in, or diluting or mixing it with some other substance used as a vehicle for the purpose of administering it. A ManA is required for both total and partial manufacture, the various processes of dividing up, packaging or presentation and for import from a third country.

*(However, such an authorisation is not required for preparation, dividing up, changes in packaging or presentation where these processes are carried out, solely for retail supply, by or under the supervision of a veterinary surgeon or pharmacist [except for breaking bulk for steriles, which a pharmacist may not do] in a registered veterinary practice premises or pharmacy).*

and/or

**Assembly** - in relation to a VMP, means enclosing the product (with or without other medicinal products of the same description) in a container which is labelled before the product is sold or supplied, or, where the product is already enclosed in the container in which it is to be sold or supplied, labelling the container before the product is sold or supplied in. The over-labelling of medicinal products is an assembly activity and is therefore licensable.

**Import from a third country** - means import from any country other than a European Economic Community (EEC)/European Economic Area (EEA) State.

**Export to a third country** - for ethical reasons the expectation is that veterinary medicines in the UK are made to the same standards irrespective of their intended country of use. Therefore it is considered good practice that manufacturing sites in the UK exclusively producing veterinary medicines intended for export to a Third country will apply for a ManA and will be subject to GMP inspections by the UK Competent Authority to ensure compliance with the European Union (EU) principles of GMP.

**Batch certification** - concerns the activities conducted by a Qualified Person (QP), in determining that a batch of a finished medicinal product is certified within the EEA before release for sale or supply in accordance with the requirements of the Manufacturing Authorisation (MA). The VMD may issue a manufacturer's authorisation solely for the purpose of batch certification to authorise the holder to certify and release batches of products for which he/she holds the MA, where the medicinal product has been manufactured by a contract manufacturer. The QP named on the manufacturer's authorisation granted solely for the purpose of batch certification may either take responsibility for all manufacturing stages conducted by

the contract manufacturer or may take account of the confirmation of the batch by the contract manufacturer's QP.

**Wholesale Supply** - a ManA holder may store and distribute any veterinary medicinal product manufactured or assembled pursuant to his authorisation, without the need for an additional wholesale dealer's authorisation (WDA).

7. Manufacturers and distributors of **specified animal feed additives, premixtures and feedingstuffs** containing **specified feed additives**, and **premixtures and feedingstuffs** containing **VMP**, must be approved by the Secretary of State. This guidance note does not cover this type of manufacture.

Further information and separate guidance is available from the VMD:

tel: 01932 338474 / 338475

email: [inspections@vmd.defra.gsi.gov.uk](mailto:inspections@vmd.defra.gsi.gov.uk)

VMGN 17: [www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns](http://www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns)

8. A ManA is not required:
- for the manufacture of VMPs based on radio-active isotopes;
  - for the manufacture of a veterinary medicine for administration for research purposes in accordance with an Animal Test Certificate (ATC) or a licence issued under the Animals (Scientific Procedures) Act (A(SP)A) 1986.

#### **Duties of the ManA Holder**

9. In order to obtain and maintain a ManA, manufacturers must comply with certain obligations in relation to the manufacture and assembly of veterinary medicinal products. These obligations are set out in Schedule 2, Part 1 of the VMR:
- The VMP must be manufactured in accordance with the MA.
  - The services of the registered QP(s) must be continuously available.
  - The ManA holder must be in possession of a current GMP certificate (and any VMP produced in accordance with GMP).
  - A system of QA (Quality Assurance) and QC (Quality Control) must be in place.
  - Evidence of any control testing performed in accordance with the MA must be made available upon request.
  - The finished product VMP must be labelled with:
    - i. Registered name, strength and pharmaceutical form
    - ii. Batch number
    - iii. Expiry date
    - iv. Storage requirements
    - v. Any warnings required for safe handling of the product
  - A representative sample of the finished VMP must be retained and made available for testing upon request from the competent authority.
10. Where the ManA holder is involved in wholesale supply of the VMP they must:

- Comply with the principles of Good Distribution Practice (GDP).
- Only distribute VMPs registered in the ManA to;
  - i. A holder of a WDA relating to those products;
  - ii. A holder of an authorisation granted by the competent authority of another EEA State authorising the supply of those products by way of wholesale dealing;
  - iii. Any person who may lawfully sell those products by retail or who may lawfully supply them in circumstances corresponding to retail sale; or any person who may lawfully administer those products.
- Ensure the appropriate and continued supply of the VMP that is manufactured or assembled.
- Sell only, or offer for sale or supply, the VMP in accordance and in conformity with a MA unless it is an exempt medicinal product or is distributed to another Member State where it can be legally used as an unlicensed veterinary medicinal product in the Member State concerned.
- Where the VMP is supplied to a person for retail sale or supply, the ManA holder must enclose with the product:
  - i. A document which makes it possible to ascertain the date on which the supply took place;
  - ii. The name and pharmaceutical form of the product supplied;
  - iii. The quantity of the VMP supplied;
  - iv. The names and addresses of the person or persons from whom the products were supplied.

11. The ManA holder must also:

- Inform the VMD of any proposed changes to be made to any personnel or processes registered in the ManA;
- Provide information about the products manufactured under their ManA to the VMD upon request;
- Retain batch documentation and permit access to this documentation by the VMD upon request.

### **Record-keeping requirements**

12. The record requirements are defined in the VMR Part 3, paragraph 21. The records for each batch must include:
- The name of the product;
  - The quantity manufactured, assembled or supplied;
  - The date of manufacture, assembly or supply;
  - The batch number and expiry date;
  - The name and address of the recipient where supplied;
  - All certification provided by the QP related to the batch.
13. All records and certificates must be kept for at least five years from the date that the batch is placed on the market or one year after the expiry of the batch in the case of long shelf-life products.



## Pharmacovigilance

14. Any adverse event (AE) to a VMP, should be reported online at [www.vmd.defra.gov.uk/adversereactionreporting/](http://www.vmd.defra.gov.uk/adversereactionreporting/) or via post to following address:

Department for Environment, Food and Rural Affairs (Defra)  
 Veterinary Medicines Directorate  
 FREEPOST KT 4503  
 Woodham Lane  
 New Haw  
 Addlestone  
 Surrey KT15 3LS

15. For more information relating to pharmacovigilance reporting please refer to VMGN 11 Pharmacovigilance Guidance on Adverse Events, which is published at [www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns](http://www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns).

## Compliance with GMP and GDP

16. **GMP** is defined as “the part of Quality Assurance which ensures that products are consistently produced and controlled in accordance with the quality standards appropriate to their intended use.”
17. *Eudralex volumes 1 to 10* are a collection of guidance, legislation and requirements for both human and veterinary medicinal products:  
[http://ec.europa.eu/enterprise/sectors/pharmaceuticals/documents/eudralex/index\\_en.htm](http://ec.europa.eu/enterprise/sectors/pharmaceuticals/documents/eudralex/index_en.htm)

The principles and guidelines for GMP are defined in ***Eudralex volume 4***:  
[http://ec.europa.eu/health/documents/eudralex/vol-4/index\\_en.htm](http://ec.europa.eu/health/documents/eudralex/vol-4/index_en.htm)

## Transmissible Spongiform Encephalopathy (TSE)

18. The ManA holder must also demonstrate compliance with the *European Commission document EMEA/410/01–Rev 2 ‘Notes for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via veterinary medicinal products’*:  
<http://www.ema.europa.eu/pdfs/human/bwp/TSE%20NFG%20410-rev2.pdf>

## GMP requirements for active substances used as starting materials

19. The Active Substance or Active Pharmaceutical Ingredient (API) must have been manufactured in accordance with *Eudralex Volume 4, Part II*:  
[http://ec.europa.eu/health/files/eudralex/vol-4/2007\\_09\\_gmp\\_part2\\_en.pdf](http://ec.europa.eu/health/files/eudralex/vol-4/2007_09_gmp_part2_en.pdf)

The following materials are exempted from full application of Part II:

- Ectoparasitocidal active substances for veterinary use;
- Substances that are used exclusively for topical application to the unbroken skin of animals and which are ectoparasitocidal, anti-bacterial or anti-fungal agents.

20. Only API sourced from suppliers registered on the MA can be used for VMP manufacture.
21. The suitability of an API supplier must be evaluated by the ManA holder prior to use. This is usually obtained by:

- Supplier Audit;
- Provision of a 'QP statement' certificate of GMP.

## **Personnel**

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### **The Qualified Person**

22. The holder of a ManA must appoint at least one QP, to be named on the authorisation. The appointee must be available on a continuous basis and reside within the EEA. The role and responsibility of the QP is defined in *Eudralex Volume 4, Chapter 2 and Annex 16*.
23. Candidates for appointment as QPs must meet specific educational and vocational requirements. Candidates are usually expected to be members of the Royal Pharmaceutical Society the Royal Society of Chemistry or the Society of Biology, and these professional bodies jointly undertake assessment of the candidate's eligibility on behalf of the VMD. In exception the VMD has the power to appoint a nominee to act as QP on a restricted named site basis only.
24. Each QP is obliged to act in accordance with the *QP Code of Practice* provided by the professional bodies. The QP legal duties are defined in Schedule 2 Part 1 of the VMR.
25. Further guidance on the routine professional duties and responsibilities of the QP is given in *Eudralex Volume 4 Annex 16*.

### **Production Manager**

26. An applicant for a ManA must nominate a suitably qualified Head of Production in the ManA application. The responsibilities of the named Head of Production are defined in *Eudralex Volume 4, Chapter 2*.

### **Quality Controller**

27. An applicant for a ManA must nominate a suitably qualified Head of Quality Control independent of the Production Department. This person may not act as the Production Manager, but can also be named as the QP. The responsibilities of the named Head of Quality Control are defined in *Eudralex Volume 4, Chapter 2*.

## **Powers to Vary, Suspend or Revoke a ManA**

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### **ManA Duration of Validity**

28. Once issued, a ManA is valid indefinitely, subject to regular satisfactory inspection and compliance with legal requirements.

### **ManA Variations (Changes)**

29. The ManA holder must notify VMD of any intended changes (e.g. registered personnel changes, premises alterations, change of site) that could impact upon quality, safety or efficacy of the products manufactured. The ManA holder must submit a variation application to the VMD for approval.

**ManA Suspension and Revocation**

30. The Secretary of State may vary, refuse, suspend, withdraw or revoke a ManA if:
- The holder has not complied with the VMR;
  - The holder has manufactured a VMP which is not authorised by the ManA;
  - The holder has produced a VMP outside the terms of the ManA;
  - The holder has premises and/or equipment which is no longer suitable;
  - The registered QP is not fulfilling his/her duties.
31. Where it appears to the VMD that animal or public safety is at risk it may suspend an authorisation 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.

**Appeals Process**

32. Applicants or ManA holders may appeal against such a decision. The appeal will be heard by an appointed person who will make a recommendation to the Secretary of State. For further information about appeals please refer to VMGN 9 Guidance on Appeals against Regulatory Decisions, which is published at [www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns](http://www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns).

## SECTION 2

### Manufacturing Extemporaneous Products (Specials) Authorisation (ManSA)

#### Introduction

33. This section provides additional advice on the manufacture and supply of unauthorised extemporaneous VMP (also known as 'specials') which have been specially prepared to the order of a veterinary surgeon for use in accordance with the prescribing cascade. Much of the guidance provided in Section 1 is also relevant with regard to Specials manufacture.

The legal basis for ManSA is defined in Schedule 2 Part 4 of the VMR.

34. A veterinary Specials product may only be placed on the market in order to meet the special needs of an individual animal or group of animals. For further information about these restrictions, please refer to VMGN 13 Guidance on the Use of the Cascade, which is published at [www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns](http://www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns).
35. As a rule, an unauthorised medicinal product which is a pharmaceutical equivalent of an available authorised medicinal product should not be placed on the market. A medicinal product should be regarded as a "pharmaceutical equivalent" if:
- (a) it contains the same amount of the same active substance(s), or
  - (b) in the case of liquid dosage forms the same concentration; and
  - (c) it is in the same dosage form; and
  - (d) it meets the same or comparable standards considered in the light of the clinical needs of the patient at the time of use of the product.
36. An authorised VMP obtainable from normal distribution channels in a reasonable time should be considered available for use. If an otherwise suitable authorised product becomes unavailable, it may be necessary for an unauthorised pharmaceutical equivalent to be supplied. This should be seen as a temporary expedient and should not be taken as justification for long term supply. Supply in these circumstances should cease as soon as is practicable, following re-instatement of the suitable authorised product.
37. A Special may only be supplied to veterinary surgeons if all of the following apply:
- (a) there is a genuine order from a veterinary surgeon registered in the UK;
  - (b) the product is formulated in accordance with the requirements of a veterinary surgeon registered in the UK;
  - (c) the product is for administration to an animal under his/her care on his/her direct personal responsibility.
38. The ordering and distribution of Specials should be in response to a clinical need in specific animals. The ordering of Specials should be a direct process between the prescribing vet and the manufacturer and they cannot be supplied via a third party such as a wholesale dealer.

39. All involved in the supply chain should be aware of the unauthorised status of the product. It should be clear from the product's packaging that the product is unauthorised because there will be no MA number on it.

### **Manufacture and Assembly**

40. The manufacturer or assembler of Specials must hold a ManSA granted by the VMD. The manufacturing/assembly site and its operations will be inspected for appropriate compliance with the principles of GMP and the relevant provisions of the VMR.
41. The VMR require that manufacture or assembly is carried out under the supervision of appropriately qualified staff, including a named quality controller and production manager, both of whom are acceptable to the VMD. However, a QP is not required to be named on a ManSA for release of a finished unauthorised product.
42. Release of Specials should be by the quality controller or a nominated deputy. Adequate precautions should be taken to ensure that the product is of the quality required for its intended purpose and that it complies with any relevant pharmacopoeial monograph standards. Written records of manufacture/assembly and supply must be kept for five years and be made available to the VMD on request.
43. The authorisation holder must demonstrate compliance with the European Commission's 'Notes for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via veterinary medicinal products'.
44. Where possible GMP assured API should be used.
45. The authorisation holder shall take all reasonable precautions and exercise all due diligence to ensure that any information he provides to the VMD which is relevant to an evaluation of the safety, quality or efficacy of any medicinal product which he imports handles, stores or distributes is not false or misleading in a material particular.

### **Advertising**

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46. Specials Manufacturing Authorisation (ManSa) holders may advertise the services they provide. ManSa holders cannot promote the specific substances that can be manufactured, however they may provide information on the different types of dosage forms that are available i.e. capsules, syrups, etc.
47. ManSa holders may provide lists of active substances and formulations with prices to veterinary surgeons but only on request.
48. Manufacturers of specials may also provide placebo samples to veterinary surgeons enquiring about their services.

### **Requirements for Testing**

49. Testing should be performed to ensure that products meet in house specifications. For 'one-offs' of non authorised products consistency of manufacture should be demonstrated. As a minimum we would expect a standard procedure that could be

validated even if the end product could itself not be. However, we would expect confirmation of homogeneity if this is appropriate to the preparation.

For one-off extemporaneous preparations limited justification for the expiry data would be required. However we would expect such products to have a short shelf-life to reflect the fact that there are no data to substantiate the validity of the stated expiry date.

However, if the manufacturer is producing a range of “more common” extemporaneous products and they are stored for a length of time waiting for orders we would expect the company to undertake real-time stability studies to justify the proposed shelf-life. Depending on the nature of the products being manufactured we may require data to support the proposed shelf-life and on-going stability studies in accordance with the principles of GMP.

### **Labeling and Record keeping requirements**

50. Holders of ManSA for use under the ‘cascade’ must ensure that the product is labelled with the following, together with any additional information required by the terms of the authorisation:

- the name of the veterinary surgeon who ordered the veterinary medicine;
- a precise description of the veterinary medicinal product;
- the date of production;
- the name of the authorisation holder and the address of the authorised premises;
- the expiry date;
- any necessary warnings;
- instructions for use.

51. Holders of ManSA must keep at least the following records:

- the name and address of the veterinary surgeon who ordered the product;
- a precise description of the veterinary medicinal product;
- the date of production;
- the expiry date;
- the date of supply to the veterinary surgeon.

52. These records must be kept for at least five years.

### **Adverse Events**

53. All adverse events must be reported to the VMD within 15 days.

### **Inspection Frequency**

54. Applications are subject to a pre-approval inspection. The registered facilities and processes are then subject to routine inspection on an ongoing basis. The re-inspection frequency is risk based and derived from the level of compliance with the principles of GMP observed at the last inspection.

## SECTION 3

### Applications and Fees for ManAs and ManSAs

#### Applications

55. If you are considering applying for an authorisation and would like to discuss any issues of concern with an Inspector before submitting your application, please contact the Inspections Administration Team so that this can be arranged on tel: 01932 336911 or email: [inspections@vmd.defra.gsi.gov.uk](mailto:inspections@vmd.defra.gsi.gov.uk).
56. Application forms are available at [www.gov.uk/application-fees-for-animal-medicines](http://www.gov.uk/application-fees-for-animal-medicines).

One copy of the application form and any supporting data should be submitted to the following address:

Inspections Administration Team  
Veterinary Medicines Directorate  
Woodham Lane  
New Haw  
Addlestone  
Surrey  
KT15 3LS

57. An application for a ManA or ManSA should be accompanied by a Site Master File (SMF)  
[http://ec.europa.eu/health/files/eudralex/vol-4/2011\\_site\\_master\\_file\\_en.pdf](http://ec.europa.eu/health/files/eudralex/vol-4/2011_site_master_file_en.pdf)
58. It would help the VMD to process your application more efficiently and speedily if, in addition to paper copies, you could provide an electronic copy of the application or of any parts of it that are available electronically. All word processing formats are acceptable but Microsoft Word held on a CD-ROM is preferred.

#### Application timelines

59. The VMD have 10 days in which to validate the application received, during which time the clock may be stopped when responses to questions are awaited. The VMD then have 90 days to arrange and carry out the pre-approval inspection.

#### Application refusal and appeals process

60. The VMD may refuse to grant an authorisation or may grant an authorisation that is different than that applied for. In such cases the VMD will notify the applicant of its proposals.
61. The notification will set out the reasons for its proposals and give the applicant a period of not less than 28 days to respond. The applicant may either give notice to the VMD of his desire to be heard or make written representations to the VMD with respect to its proposals. Before determining the application the VMD shall give the applicant an opportunity of appearing before, and being heard by, a person appointed for the purpose by the VMD, or shall take those written representations into account, as the case may be. For further information about appeals please refer to VMGN 9 Guidance on Appeals against Regulatory Decisions, which is published at [www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns](http://www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns).

## **Fees**

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62. A fee is normally charged for the assessment of all applications. Details on the relevant fees can be found in the VMR, which are available at [www.gov.uk/veterinary-medicines-regulations](http://www.gov.uk/veterinary-medicines-regulations).
63. Fees are currently payable for the following:
  - (a) Authorisation applications;
  - (b) Authorisation variations;
  - (c) Inspections;
  - (d) Duplicate or multiple GMP Certificates.
64. An annual service charge is also payable.
65. When the VMD plans to make changes to the amount or frequency of fees, authorisation holders are consulted and given the opportunity to comment on the proposals.



## SECTION 4

### Specific Manufacturing Authorisations (AVA, NFABBA and ESCCA)

66. Applications for new AVA, NFABBA and ESCCA (and any variations to these) should be submitted in accordance with the guidance provided at the end of this chapter.

### Autogenous Vaccine Authorisations (AVA)

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67. An AVA relates to the method of production and the premises used to manufacture autogenous vaccines.
68. In order to place on the market an autogenous vaccine manufactured from pathogens or antigens obtained from an animal/s and used for the treatment of that animal and/or other animals within the same epidemiological unit or in the same rearing chain, the manufacturing premises and the method of production must be the subject of a valid AVA.
69. An AVA will only be granted if:
- The product has been inactivated. It is expected that most authorisations will relate to the manufacture of bacterial vaccines. Additional safeguards will be required in respect of most viral vaccines.
  - The VMD is satisfied that the production process will produce a consistent, safe product.
  - The premises are under the supervision of a person who has sufficient qualifications and experience to manufacture the product safely.
  - A veterinary surgeon has confirmed a need and fully justified the use of the AVA in preference to UK or EU authorised products.
70. Manufacturers of autogenous vaccines may apply for two different types of authorisation: AVA-I (Individual), or AVA-S (Standard).
71. An AVA-I covers the production of a single batch of product; an AVA-S covers the on-going production of the products specified in the authorisation.

#### Viral Autogenous Vaccines

72. In the case of viral autogenous vaccines there is a need for a technical framework to give assurance that the associated risks are suitably controlled and that the final vaccines are free from contamination. The requirements for the authorisation of these types of vaccines are detailed below:
- A Manufacturing standard, such as a full GMP certificate or inspection from a VMD inspector. Where a viral vaccine is being produced at a GMP compliant site within the EU, the VMD retains the right to address specific manufacturing issues with the national competent authority and if necessary to carry out a site inspection. This is because although GMP requirements are harmonised, production is not conducted to a harmonised set of requirements such as extraneous agent testing and validation of inactivation kinetics.

- Assurance that the vaccine is an autogenous vaccine, i.e. the vaccine is manufactured from pathogens or antigens obtained from an animal/s and used for the treatment of that animal and/or other animals within the same epidemiological unit or in the same rearing chain. The nature of the animal production industry where the vaccine is intended to be used should be taken into account. The use of the same isolate to produce further batches of vaccine would be on a quality risk basis and tested to determine similarity.
- Complete testing of cell seed to Pharmacopoeia European requirements.
- Inactivation kinetics validation. This must cover the agent in the vaccine but also all possible sources of contamination from the isolate itself as well as potential sources of cross contamination. A risk assessment approach to those viruses which are not likely to be present can be conducted taking into account the geographical source of the isolate, the health status of the animals from which the isolate originated, other isolates handled in the plant and the range of extraneous agents testing of starting materials. A condition of authorisation would include the obligation to update this assessment and validation as appropriate, when any new isolates/starting materials are handled at the plant.
- Extraneous testing of the final product to Pharmacopoeia European requirements where not justified by inactivation kinetics. It may be possible to have derogations on the degree of testing depending on the range of agents covered by the inactivation kinetics validation package and the risk assessment.
- Batch safety test using a double dose of vaccine to be conducted on the site of use of the vaccine with satisfactory results before use of the vaccine batch in the entire group of animals.
- Pharmacovigilance reporting.
- Validation of any tests used for extraneous agents testing should be provided.

### **Validity of an AVA**

73. An AVA-S will be valid continuously subject to satisfactory re-inspection of the premises. The frequency of the inspections will be risk-based and derived from the performance of the AVA-S holder at the last inspection.
74. An AVA-I will be valid for one year from the date it was granted; the single batch of vaccine covered by the AVA-I must be manufactured and placed on the market before the expiry of the authorisation.

### **AVA Variations (Changes)**

75. The authorisation holder must notify VMD of any intended changes (e.g. registered personnel changes, premises alterations, change of site) that could impact upon quality, safety or efficacy of the products manufactured. The holder must submit a variation application to the VMD for approval.

### **AVA Suspension and Revocation**

76. The Secretary of State may vary, refuse, suspend, withdraw or revoke an AVA if:
- The holder has not complied with the VMR;
  - The holder has manufactured a VMP which is not authorised by the AVA;
  - The holder has produced a VMP outside the terms of the AVA;
  - The holder has premises and/or equipment which is no longer suitable;

- The registered QP is not fulfilling his/her duties.

77. Where it appears to the VMD that animal or public safety is at risk it may suspend an authorisation 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.

### **Obligations on AVA Holders**

78. The holder of an Autogenous Vaccine Authorisation is subject to a number of obligations in relation to the labelling of containers of autogenous vaccines, record-keeping, and the reporting of adverse reactions. The requirements for each are outlined in the VMR. AVA holders are also subject to a number of other requirements as outlined below:

#### Target Animal Safety Tests

79. Autogenous vaccines may not be released onto the market before a target animal safety test has been conducted on the premises on which it is intended to administer the vaccine.

#### Batch Release

80. Holders of an AVA-S are subject to the batch release requirements outlined in VMGN 18 Release of Veterinary Medicinal Products to the UK Market [www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns](http://www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns). In summary, the VMD must be notified every time a batch of autogenous vaccine has been placed onto the market. It should be noted that a product may not be placed onto the market until a satisfactory on-farm safety test result has been achieved.

#### Changes to an AVA

81. Any changes to the terms of an AVA-S must be made by means of a variation; the terms include the data and other information provided in support of an application for an AVA-S. For example, a variation must be submitted if you wish to add another vaccine to the list of products already included on the authorisation, or if the name and/or address of the AVA holder changes.

82. An AVA-I may not be varied; the holder of an AVA-I will be required to submit an application for a new authorisation if any of the details change.

### **Non-Food Animal Blood Bank Authorisations (NFABBA)**

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83. An NFABBA authorises the collection, storage and supply of blood, for use in non-food producing animals to meet unforeseen or exceptional needs. The authorisation also permits the blood to be placed onto the market without the need for a MA as long as no medicinal claims are made.

84. The storage and supply of blood constituents obtained by the physical separation of donor blood into different fractions within a closed-bag system is also acceptable under this scheme.

85. Any other means of production of blood products should only be done under a full ManA, and or an MA.
86. An NFABBA will only be granted if the VMD is satisfied that:
- The welfare of the animals used in the collection of blood will be respected
  - The production process will produce a consistent, safe product
  - The blood bank is under the supervision of a veterinary surgeon, or a person that is suitably qualified to operate the blood bank.

### **Validity of an NFABBA**

87. An NFABBA will be valid continuously subject to satisfactory re-inspection of the premises. The frequency of the inspections will be risk-based and derived from the authorisation holder's performance at the last inspection.
88. During the validity of the NFABBA, evidence may become available which alters the risk/benefit assessment of the authorisation. In such circumstances the VMD may revoke or suspend the authorisation. The circumstances in which such action can be justified are specified in the VMR. It should be noted that if the VMD becomes aware that an NFABBA holder is not complying with the terms of the authorisation without the prior approval of the VMD, the NFABBA will be suspended immediately. The suspension will remain in force until the changes have been approved, or the process is brought back into line with the authorisation.

### **NFABBA Variations (Changes)**

89. The authorisation holder must notify VMD of any intended changes (e.g. registered personnel changes, premises alterations, change of site) that could impact upon quality, safety or efficacy of the products manufactured. The authorisation holder must submit a variation application to the VMD for approval.

### **NFABBA Suspension and Revocation**

90. The Secretary of State may vary, refuse, suspend, withdraw or revoke a NFABBA if:
- The holder has not complied with the VMR;
  - The holder has manufactured a VMP which is not authorised by the NFABBA;
  - The holder has produced a VMP outside the terms of the NFABBA;
  - The holder has premises and/or equipment which is no longer suitable;
  - The registered QP is not fulfilling his/her duties.
91. Where it appears to the VMD that animal or public safety is at risk it may suspend an authorisation 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.

### **Obligations on NFABBA Holders**

92. The holder of a NFABBA is subject to a number of obligations in relation to the supply and administration of blood and blood constituents from a blood bank, labelling of containers of blood, record-keeping, and the reporting of adverse reactions. The requirements for each are outlined in the VMR. NFABBA holders are also subject to a number of other requirements as outlined below:

Animal Welfare

93. NFABBA holders should ensure that the health and welfare of the donor animals is respected at all times.
94. In setting up a blood bank it is expected that the animals used as donors will be rescue animals waiting for re-homing or pet animals, and that the blood donation procedure will not require animal sedation. If the donor animals are kept in a colony for the specific purpose of blood donation, or the blood donations require sedation of the animal, then an application for a Home Office Licence under the Animals (Scientific Procedures) Act (ASPA) 1986 and an NFABBA from the VMD will be required.
95. Donor animals should be tested for the absence of certain diseases that may pose a potential risk to transfusion recipients. These tests should be conducted in accordance with veterinary guidelines or following an appropriate risk assessment to ensure that the risk of disease transmission to transfusion recipients is minimised.
96. Donor animals must be certified by the attending veterinary surgeon in relation to their health status at the time of donation. Home Office and RCVS best practice criteria are defined in Annex 1.

**Equine Stem Cell Centre Authorisations (ESCCA)**

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97. An ESCCA authorises premises in the UK used for the collection, storage, processing, production and administration of equine stem cells for use as an autologous treatment for non-food producing horses. It covers manufacturers that operate a cryo-storage facility, or 'bank' of equine derived stem cells, or manufacture stem cells derived products.
98. An ESCCA will only be granted if the VMD is satisfied that:
- The welfare of the animals used in the collection of equine stem cells will be respected;
  - The production process will produce a consistent, safe product;
  - The centre is under the supervision of a veterinary surgeon, or a person that is suitably qualified to operate the centre.

**Validity of an ESCCA**

99. An ESCCA will be valid continuously subject to satisfactory re-inspection of the premises. The frequency of the inspections will be risk-based and derived from the authorisation holder's performance at the last inspection.

**ESCCA Variations (Changes)**

100. The authorisation holder must notify VMD of any intended changes (e.g. registered personnel changes, premises alterations, change of site) that could impact upon quality, safety or efficacy of the products manufactured. The ESCCA holder must submit a variation application to the VMD for approval.

**ESCCA Suspension and Revocation**

101. The Secretary of State may vary, refuse, suspend, withdraw or revoke an ESCCA if:
- The holder has not complied with the VMR;
  - The holder has manufactured a VMP which is not authorised by the ESCCA;
  - The holder has produced a VMP outside the terms of the ESCCA;
  - The holder has premises and/or equipment which is no longer suitable;
  - The registered QP is not fulfilling his/her duties.
102. Where it appears to the VMD that animal or public safety is at risk it may suspend an authorisation 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.

**Obligations on ESCCA Holders**

103. The holder of an Equine Stem Cell Centre Authorisation is subject to a number of obligations in relation to the supply and administration of stem cells, labelling of containers of stem cell products, record-keeping, and the reporting of adverse reactions. The requirements for each are outlined in the VMR. ESCCA holders are also subject to a number of other requirements as outlined below:

Animal Welfare

104. ESCCA holders should ensure that the health and welfare of the horses is respected at all times.

**The Application Process**

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**Data Requirements and Validation**

105. Application forms for applying for new AVA, NFABBA and ESCCA (and variations to these) are available on the VMD website.
106. The information required in support of an application is outlined in the application forms. For new AVAs, or variations to an AVA, the applicant must also provide a Veterinary Surgeon Justification Declaration, which is available on the VMD website.
107. All applications are subject to validation. The onus is on the applicant to identify and submit all the necessary supporting information in their application package. If the application is incomplete it is likely to fail validation.

**Assessment, Timescales and Outcome**

108. The timescales for dealing with an application for a new AVA, NFABBA or ESCCA (and any variations to these) are outlined in the Published Standards, which are available on the VMD Website. More detailed information about the procedures and timescales used for the assessment of applications is also provided below.
109. Applications for new AVA, NFABBA and ESCCA (and any variations to these) are processed on a 45-day timetable from accepting a valid application.

110. The application will be validated within 10 days of receipt; if the application is incomplete the application will either fail validation and the applicant will be asked to resubmit the application, or the validation clock will stop and the applicant will be asked to provide the outstanding data. Once received the validation clock will restart at 0. In both cases, the applicant will be informed accordingly.
111. Once the application is deemed valid, the clock will start running and the application will proceed into the assessment phase where the inspector(s) has up to 45 days to either approve or refuse the application. During this time the clock may stop/start several times in order that an inspection can be carried out and/or if further information/clarification is required from the applicant.
112. If approved, formal authorisation documentation will be sent to the applicant within 10 days of sign-off. If refused, the applicant will be notified accordingly. In this case, the applicant also has a right of appeal against the decision to refuse an application. For further information about appeals please refer to VMGN 9 Guidance on Appeals against Regulatory Decisions,<sup>1</sup> which is published at [www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns](http://www.gov.uk/government/collections/veterinary-medicines-guidance-notes-vmgns).

### Submission

113. Applicants may submit their application packages, which includes the application form and supporting data, to the VMD either electronically (an e-submission), or in hard-copy. We strongly encourage applicants to use the e-submission route.
114. If submitted electronically, the application package should be sent on a CD/DVD to the address below, or sent by email (using Eudralink<sup>1</sup> or not; it is the applicant's choice) to: [s.response@vmd.defra.gsi.gov.uk](mailto:s.response@vmd.defra.gsi.gov.uk). Please note there is a 80 MB limit on the Eudralink system and 25 MB limit on normal emails, i.e. not sent via Eudralink.
115. There is no set format for the content of electronic submissions, but the PDF file(s) should be held within a main 'ROOT' folder.
116. If submitted in hard-copy the applicant should send one copy of the application package to the following address:
- Information Services team  
Veterinary Medicines Directorate  
Woodham Lane  
New Haw  
Addlestone  
Surrey  
KT15 3LS
117. The application forms are available on the VMD website; these are VMD-created documents for use under these national-only schemes.
118. Queries regarding the submission of applications should be directed to the Information Services team via email to: [s.response@vmd.defra.gsi.gov.uk](mailto:s.response@vmd.defra.gsi.gov.uk)

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<sup>1</sup> Eudralink is a secure electronic system that enables files to be sent over the Internet via a user-friendly Web interface.

**Fees**

119. The fee should not accompany the application and nor should it be paid in advance of the submission of the application.
120. Details on the relevant fees can be found in the VMR, which are available at [www.gov.uk/veterinary-medicines-regulations](http://www.gov.uk/veterinary-medicines-regulations).



## SECTION 5 The Inspection Process

### Pre-approval Inspection

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121. A successful pre-approval inspection of the applicant site must be undertaken by VMD inspectors prior to the issue of a Manufacturing Authorisation. Where quality control testing or other activity is contracted to a third party, this site must also be made available for inspection.

### Scheduled Inspection

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122. Manufacturing authorisation holders are subject to inspection on a periodic basis. A risk based approach to inspection frequency is practised. The maximum interval between inspections is 33 months.
123. Production facilities in third countries without a Mutual Recognition Agreement with the EU are also subject to inspection, prior to issue of any GMP certificate.

### Inspection Process (Pre-approval and Routine)

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124. The Inspections Administration team will coordinate a suitable inspection date between the company and inspector.
125. The inspector will issue an agenda in advance of site arrival. The agenda details the key areas for inspection and should be used to prepare for inspections. A template agenda is attached in Annex 2.
126. The VMD will issue an inspection deficiency report within 30 days of the inspection. A template deficiency report is attached in Annex 3.
127. A response to the deficiencies from the company embedded within an electronic copy of the deficiency report is expected within 30 days of report receipt.
128. Following receipt of a satisfactory response to the inspection deficiency report, the VMD will issue a final inspection report and GMP certificate within 90 days of the last day of the inspection. A template GMP report is attached in Annex 4. (GMP certificates are only issued to ManA and Exemptions for Small Pet Animals registered facilities, contract QC test sites and to manufacturing facilities located outside the EEA).

## Further Information

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129. 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 email: [VMGNNotes@vmd.defra.gsi.gov.uk](mailto:VMGNNotes@vmd.defra.gsi.gov.uk). Veterinary Medicines Guidance Notes and other information are available at [www.gov.uk](http://www.gov.uk).

# ANNEX 1

## CRITERIA FOR USE OF BLOOD DONORS FOR NON-FOOD ANIMAL BLOOD BANKS

## **THIS CRITERIA HAS BEEN AGREED WITH THE HOME OFFICE AND THE ROYAL COLLEGE OF VETERINARY SURGEONS**

1. Donations should take place under the supervision of a veterinary surgeon in premises (including specifically adapted vehicles) that provide the appropriate standard of hygiene for the procedures being performed. In addition the appropriate emergency backup must be available should it be required.
2. All donations should adhere to the strict procedures detailed in the company's approved procedures.
3. All donors should be uniquely identified and records kept of all donations to ensure that dogs that present problems at donations can be identified and excluded from further donations where appropriate.
4. Dogs should donate at no greater frequency than 3 monthly intervals.
5. Only dogs that are in a good state of health, do not appear stressed, are compliant and settled and can be handled without excessive restraint will be able to donate.
6. The donors should be examined by a veterinary surgeon prior to blood collection to ensure the dog is in a good state of general health. Blood should not be taken from dogs with a history of surgery or adverse medical conditions in the three months prior to donation, who are on medication, or that are pregnant or whelping or nursing pups at the time of donation.
7. Dogs should not have ever travelled outside the UK.
8. Any blood product not used should be disposed of as waste material.
9. Dogs must not be sedated to facilitate donations.
10. The donors must be a minimum weight of 25kgs to allow up to 450mls of blood to be withdrawn at any one session.
11. The donor should be closely monitored during the donation process. After donating, measures should be taken to reduce risk of haematoma and infection.
12. Donors should be clinically examined after donating and monitored at regular intervals for 1 hour post-donation to ensure they remain healthy and there are no adverse reactions.

# ANNEX 2

## TYPICAL SINGLE DAY INSPECTION AGENDA

**AnyBusiness Ltd****PROPOSED AGENDA FOR GMP INSPECTION****0900am Thursday 1 December 2009**

- **Opening meeting**
  - Introductions
  - General update from the VMD
  - Company and site background (to include product range and background)
  - Scope and confirmation of agenda
  - Follow up from last inspection
  
- **Familiarisation Tour**
  
- **Review of Manufacturing Licences**
  
- **Site master file / site plan review / site familiarisation tour**
  
- **Pharmaceutical quality system**
  - Quality Policy
  - Change control
  - Deviation handling
  - Product Quality Review
  - Quality Risk Management
  
- **Personnel**
  - Key Personnel
  - Training
  
- **Premises and Equipment**
  - Access and security
  - Pest control measures
  - Temperature/ Humidity controls
  - Equipment validation
  
- **Documentation system overview**
  - Structure and controls
  - Starting & Packaging Material specifications
  - Intermediate & Bulk Product specifications
  - Finished Product Specifications
  - Archive arrangements

- **Production**
  - Production areas/processes including warehouse
  - Goods In checks
  - Sampling and Testing
  - Inventory control system
  - Area Clearance
  - Batch Record review
  - Distribution controls
  - Waste disposal
  
- **Quality Control**
  - QC facilities
  - Packaging material and label controls
  - Supplier Assessments
  - TSE statements
  - On going stability arrangements
  - Reference and Retain samples
  - Batch Release
  
- **Outsourced activities**
  - Technical Agreements
  
- **Complaints and Product Recall**
  - Complaint and Recalls process
  
- **Self inspection**
  - Procedure and Schedule
  
- **Any other business**
  
- **Preparation for wrap up meeting**
  
- **Wrap up meeting**

\* Agenda is for guidance only and may be subject to modifications

# ANNEX 3

## TEMPLATE DEFICIENCY REPORT



## DEFICIENCY REPORT

**Inspected site:**

Anybusiness Ltd  
 Unit 1  
 Industrial Estate,  
 Woodbridge,  
 Boxshire,  
 BO3 1AT

Tel: 0123 123 1234  
 Fax: 0123 123 1235

**Activities carried out:** *(Select appropriate activities from those listed below)*

*Manufacture of finished products*  
*Sterile*  
*Non-sterile*  
*Biologicals*  
*Sterilisation of excipient, active substance or medicinal product*  
*Primary packaging*  
*Secondary packaging*  
*Quality control testing*  
*Importing*  
*Batch certification*  
*Storage and distribution*  
*Manufacture of active substance*  
*Other* \_\_\_\_\_

**Inspection date:** 25<sup>th</sup> December 2009

**Inspectors:**

*Inspector A & B*  
 Veterinary Medicines Directorate  
 United Kingdom

**References:**

ManA 12345  
*(enter appropriate manufacturing classification: AVA, NFFABA, ESCC, Cascade, Schedule 6)*

**Introduction:**

*For the company and facility under inspection add:*

- *Brief company and site history*
- *List or summarise authorised products*
- *List products manufactured under contract*
- *Major changes since the last inspection*

*For inspections in non-EEA countries, it should be stated whether the national Competent Authority of the country took part.*

**Brief report of the inspection activities undertaken:***Scope of inspection:*

The inspection was part of the routine re-inspection programme to ensure that Anybusiness Ltd was compliant with the requirements defined in *Eudralex Volume 4 - Medicinal Products for Human and Veterinary Use: Good Manufacturing Practice*. This was the first GMP inspection performed by VMD.

*Inspected facilities:*

Warehouse  
Production Building  
QC laboratory

*Inspected systems and documentation:*

- Manufacturing Authorisation
- Site Master File (SMF)
- Quality Management System (QMS) and documentation hierarchy
- Product Quality Review (PQR)
- Change Management, Deviations (Non Conformance) reporting
- Batch Manufacturing and Packaging Records
- Equipment validation and calibration
- Warehouse and Storage
- Technical Agreements/Contracts
- Complaints and Recall
- Self Inspection

*Specific areas and topics which were not inspected:*

*(List issues which require detailed attention at next inspection)*

**Key personnel met during the inspection:**

John Smith	Site Director
Alan Smith	Qualified Person
Colin Smith	QC Manager

*Follow up of inspection findings from the last inspection:*

The inspection report from the previous inspection was available. A number of deficiencies were raised during the course of the last inspection and the company had responded with action plans to address these issues. During the course of the current inspection it was noted that issues raised previously had largely been addressed. Repeat observations are highlighted in the text below.

### **Inspectors' findings and observations:**

Note: References in parentheses refer to the relevant points in “Eudralex Volume 4: Medicinal Products for Human and Veterinary Use: Good Manufacturing Practice”.

**Summary of deficiencies:** *List all deficiencies even if corrective action has taken place straight away.*

#### **1. Critical deficiencies:**

*‘A deficiency which has produced, or leads to a significant risk of producing either a product which is harmful to the human or veterinary patient or a product which could result in a harmful residue in a food producing animal.’*

#### **2. Major deficiencies:**

*‘A non-critical deficiency which has produced or may produce a product:*

- *which does not comply with its MA*
- *which indicates a major deviation from EU Good Manufacturing Practice*
- *which indicates a major deviation from the terms of the manufacturing authorisation*
- *which indicates a failure to carry out satisfactory procedures for release of batches or (within EU) a failure of the QP to fulfil his legal duties*
- *a combination of several “other” deficiencies, none of which on their own may be major, but which may together represent a major deficiency and should be explained and reported as such.’*

*Pharmaceutical quality system*

2.1 The PQS was deficient in that (GMP reference Chapter 1 – 1.1):

2.2.1 (Enter deficiency details)

2.2.2 (Enter deficiency details)

#### **3. Other deficiencies:**

*‘A deficiency, which cannot be classified as either critical or major, but which indicates a departure from Good Manufacturing Practice. (A deficiency may be “other” either because it is judged as minor or because there is insufficient information to classify it as a major or critical).’*

*Personnel*

3.1 Personnel practices were unsatisfactory in that (Chapter 2 – 2.8);

3.1.1 (Enter deficiency details).

*Premises and Equipment*

3.2 Premises and equipment were unsatisfactory in that (Chapter 3 - 3.4);

3.2.1 (*Enter deficiency details*).

*(Enter other deficiencies under the appropriate remaining section 4 to 9 headings)*

**4. Observations and Comments**

4.1 (*Enter issues that cannot be classified as deficiencies*)

Inspector A  
GMP Inspector  
Veterinary Medicines Directorate

Distribution: Anybusiness Ltd., VMD

# ANNEX 4

## TEMPLATE GMP INSPECTION REPORT

<b>Inspected site:</b>	Anybusiness Ltd  Unit 1 Industrial Estate, Woodbridge, Boxshire, BO3 1AT  Tel: 0123 123 1234 Fax: 0123 123 1235	
<b>Activities carried out:</b>	<i>(Select appropriate activities from those listed below)</i>  <table border="1"> <tr> <td> <i>Manufacture of finished products</i>  <i>Sterile</i>  <i>Non-sterile</i>  <i>Biologicals</i>  <i>Sterilisation of excipient, active substance or medicinal product</i>  <i>Primary packaging</i>  <i>Secondary packaging</i>  <i>Quality control testing</i>  <i>Importing</i>  <i>Batch certification</i>  <i>Storage and distribution</i>  <i>Manufacture of active substance</i>  <i>Other _____</i> </td> </tr> </table>	<i>Manufacture of finished products</i> <i>Sterile</i> <i>Non-sterile</i> <i>Biologicals</i> <i>Sterilisation of excipient, active substance or medicinal product</i> <i>Primary packaging</i> <i>Secondary packaging</i> <i>Quality control testing</i> <i>Importing</i> <i>Batch certification</i> <i>Storage and distribution</i> <i>Manufacture of active substance</i> <i>Other _____</i>
<i>Manufacture of finished products</i> <i>Sterile</i> <i>Non-sterile</i> <i>Biologicals</i> <i>Sterilisation of excipient, active substance or medicinal product</i> <i>Primary packaging</i> <i>Secondary packaging</i> <i>Quality control testing</i> <i>Importing</i> <i>Batch certification</i> <i>Storage and distribution</i> <i>Manufacture of active substance</i> <i>Other _____</i>		
<b>Inspection date:</b>	<i>25<sup>th</sup> December 2009</i>	
<b>Inspectors:</b>	<i>Inspector A &amp; B</i> <i>Veterinary Medicines Directorate</i> <i>United Kingdom</i>	
<b>References:</b>	<i>ManA 12345</i> <i>(enter appropriate manufacturing classification: AVA, NFFABA, ESCC, Cascade, Schedule 6)</i>	

**Introduction:**

*As per deficiency report.*

**Brief report of the inspection activities undertaken:**

*Scope of inspection:*

*As per deficiency report.*

*Inspected facilities:*

*As per deficiency report.*

*Inspected systems and documentation:*

*As per deficiency report.*

*Specific areas and topics which were not inspected:*

*As per deficiency report.*

**Key personnel met during the inspection:**

*As per deficiency report.*

*Follow up of inspection findings from the last inspection:*

*As per deficiency report.*

**Inspectors' findings and observations:**

**A/ Pharmaceutical quality system**

*Describe the management system structure and functionality.*

*Describe the rationale behind cited deficiencies and recommendations.*

**B/ Personnel**

*Describe personnel organisation, experience and approach to training.*

*Describe the rationale behind cited deficiencies and recommendations.*

**C/ Premises and equipment**

*Describe setting, condition and fabric of premises.*

*Describe security, pest control and other product impact processes.*

*Describe the rationale behind cited deficiencies and recommendations.*

**D/ Documentation**

*Describe organisation and functionality.*

*Describe the rationale behind cited deficiencies and recommendations.*

**E/ Production**

*Describe production processes and controls.*

*Describe the rationale behind cited deficiencies and recommendations.*

**F/ Quality control**

*Describe QC area and key processes.*

*Describe starting material controls and finished product release processes.*

*Describe the rationale behind cited deficiencies and recommendations.*

**G/ Outsourced activities**

*Describe associated outsourced activities.*

*Describe the rationale behind cited deficiencies and recommendations.*

**H/ Complaints and recall**

*Describe complaints and recall processes.*

*Describe the rationale behind cited deficiencies and recommendations.*

**I/ Self Inspection**

*Describe self-inspection process.*

*Confirm schedule is in place and current.*

*Describe the rationale behind cited deficiencies and recommendations.*

**J/ Distribution and Shipment**

*e.g. Compliance with GDP.*

**K/ Questions raised relating to the assessment of a MA**

*e.g. Pre-authorisation inspections.*

**L/ Other specific issues identified**

*e.g. Relevant future changes announced by company.*

**M/ Site master file**

*Assessment of SMF if any; date of SMF.*

**N/ Miscellaneous**

*Samples taken.*



**Annexes attached:** *List of any annexes attached.*

Note: References in parentheses refer to the relevant points in “*Eudralex Volume 4: Medicinal Products for Human and Veterinary Use: Good Manufacturing Practice*”.

**Summary of deficiencies:**

**1. Critical deficiencies:**

*As per deficiency report.*

Company response to each deficiency should be inserted in the report under the deficiency.

**2. Major deficiencies:**

*As per deficiency report.*

Company response to each deficiency should be inserted in the report under the deficiency.

**3. Other deficiencies:**

*As per deficiency report.*

Company response to each deficiency should be inserted in the report under the deficiency.

**4. Observations and Comments**

*As per deficiency report.*

Company response to each deficiency should be inserted in the report under the deficiency.

**Recommendation:**

The company have submitted satisfactory responses to the deficiencies raised above; thus the facilities, systems and procedures in place are considered to be in compliance with the requirements of GMP. The inspection frequency detailed below will be subject to review should there be any change in the circumstances of the company or the veterinary products manufactured.

<b>Inspection Findings</b>	<b>GMP Compliance Rating</b> <i>Poor = 1 critical/ <math>\geq</math> 6 Major</i> <i>Acceptable = &lt;6 major</i> <i>Good = 0 major</i>	<b>Maximum Inspection Interval</b> <i>Poor = 12 month</i> <i>Acceptable = 24 month</i> <i>Good = 33 month</i>	<b>Comments</b>
? Critical ? Major ? Other	Poor/Acceptable/Good <i>(delete as appropriate)</i>	12/24/33 <i>(delete as appropriate)</i>	Insert 'None' or rationale for bespoke frequency

**Conclusions:**

The facilities, systems and procedures in place at this site continue to be in compliance with the requirements of GMP. The Manufacturing Authorisation continues to be supported and the inspection is closed out. (*omit for overseas sites and reword for new sites*).

Inspector A  
GMP Inspector  
Veterinary Medicines Directorate

Distribution: Anybusiness Ltd., VMD

## List of Abbreviations

<b>AE</b>	Adverse Event
<b>ATC</b>	Animal Test Certificate
<b>AVA</b>	Autogenous Vaccine Authorisation
<b>Defra</b>	Department for Environment, Food & Rural Affairs
<b>EC</b>	European Commission
<b>EEA</b>	European Economic Area
<b>EEC</b>	European Economic Community
<b>ESCCA</b>	Equine Stem Cell Centre Authorisation
<b>EU</b>	European Union
<b>GMP</b>	Good Manufacturing Practice
<b>GDP</b>	Good Distribution Practice
<b>MA</b>	Marketing Authorisation
<b>Man-A</b>	Manufacturing Authorisation
<b>Man-SA</b>	Manufacturing (Specials) Authorisation
<b>MHRA</b>	Medicines and Healthcare products Regulatory Agency
<b>NFABBA</b>	Non Food Animal Blood Banks Authorisation
<b>QA</b>	Quality Assurance
<b>QC</b>	Quality Control
<b>QP</b>	Qualified Person
<b>TSE</b>	Transmissible Spongiform Encephalopathy
<b>VMD</b>	Veterinary Medicines Directorate
<b>VMGN</b>	Veterinary Medicines Guidance Note
<b>VMP</b>	Veterinary Medicinal Product
<b>VMR</b>	Veterinary Medicines Regulations
<b>WDA</b>	Wholesale Dealers Authorisation

## **VETERINARY MEDICINES GUIDANCE NOTE**

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