



Veterinary
Medicines
Directorate

**VETERINARY MEDICINES
GUIDANCE NOTE**

No 6

**ANIMAL TEST
CERTIFICATES**

Last updated July 2013

www.gov.uk

QUICK START GUIDE

1. This Veterinary Medicines Guidance Note (VMGN) is aimed primarily at individuals, organisations and companies who intend to conduct clinical (field) trials of substances that are expected to fall within the definition of a veterinary medicinal product (VMP). The definition of a VMP is provided in the Veterinary Medicines Regulations (VMR). Further guidance on substances that fall within the definition of a VMP is given in Chapter 1 of this document, or Veterinary Medicines Guidance Note (VMGN) 1 Controls of Veterinary Medicines, which is published on the Veterinary Medicines Directorate's (VMD's) website
http://www.vmd.defra.gov.uk/public/vmr_vmgn.aspx
2. In the context of this VMGN, a clinical (field) trial is a study whose purpose is to demonstrate the efficacy and/or safety of a VMP in the intended target species under conditions of field use. Chapter 1 of this document outlines further conditions.
3. An Animal Test Certificate (ATC) authorises the conduct of a clinical trial of a VMP in the United Kingdom.
4. This quick start guide is a summary of the provisions of the VMR; detailed information is found in the body of the VMGN. However, in summary, this note provides guidance on the procedures in place in relation to applications for ATCs of which there are two categories, ATC-A/B (with two types of application process, A and B) and ATC-S, which are authorised on a national basis.
5. The ATC-A/B is mostly appropriate for clinical trials conducted by pharmaceutical companies wishing to generate data for a marketing authorisation (MA) application for a VMP. Further information about MAs is available in VMGN 2 Marketing Authorisations for Veterinary Medicinal Products, which is published on the VMD's website http://www.vmd.defra.gov.uk/public/vmr_vmgn.aspx
In order to obtain an ATC-A/B an applicant may submit a Type A or B application. The application type depends on the current authorisation status of the active substance being investigated and the potential risks to treated animals, users, consumers of products from treated animals and the environment.
6. The ATC-S is specifically intended for small scale research trials conducted by veterinarians. In order to obtain an ATC-S an applicant may submit a Type S application. Specific guidance is given in Annex B of this document.
7. Further guidance on types of applications is given in Chapter 2 of this document. Guidance on the application process and data requirements is provided in Chapter 4.
8. Unless otherwise specified, reference to ATCs throughout this document includes both categories (ATC-A/B and ATC-S).
9. An ATC authorises both the trial itself, the procurement and supply of the veterinary medicine used in it and enables produce from the treated animals to enter the food chain if appropriate.
10. The VMD may consult with Defra and other Government Departments, e.g. the Food Standards Agency (FSA), before approving an ATC.

11. Once an application for a new ATC has been progressed, and the benefit:risk assessment is considered positive, the ATC will be granted. Not all ATCs for which applications are submitted are approved. Some applications for ATCs are refused at the end of the assessment process due to insufficient and/or inadequate supporting data.
12. Following grant of an ATC, it may be subject to a number of post-authorisation requirements including renewal of the ATC, variation procedures that facilitate any proposed changes to the particulars of an ATC and obligations on ATC holders including the requirement to report serious adverse events (AEs). Further information is given in Chapter 5 of this document.
13. All procedures applied to animals during the course of the trial must be consistent with “recognised veterinary practice” and the investigating veterinary surgeon must act in accordance with the Veterinary Surgeon’s Act, otherwise the study will also need to be regulated under the Animals (Scientific Procedures) Act (A(SP)A). Further information is provided in Chapter 1.

FURTHER INFORMATION

- For more information on Animal Test Certificates please contact the VMD’s New Licensing team on 01932 338439 or alternatively contact VMD reception on 01932 336911 and quote “Animal Test Certificates”.

TABLE OF CONTENTS

Contents	Paragraph	Page
Introduction	1	5
Chapter 1: What is an Animal Test Certificate (ATC)?		
Nature of trials that require an Animal Test Certificate and background information	7	6
Validity of an ATC	18	8
Trials NOT requiring an ATC	20	8
Import of a medicinal product	23	9
Chapter 2: Types of Animal Test Certificate (ATC)	24	10
Chapter 3: Labelling of Products Supplied under an ATC	36	15
Chapter 4: The Application Process		
Data Requirements and Validation	43	17
Assessment and Outcome	55	18
Submission	63	19
Timescales	69	20
Fees	82	21
Chapter 5: Post Authorisation Steps		
Terms and Conditions	84	22
Obligations on ATC Holders	86	22
Pharmacovigilance	89	23
Variations	92	24
Fees	99	25
Duration and Renewal of ATCs	101	25
Fees	107	25
Further Information	109	26
ANNEX A: NOTE ON SUPPORTING DATA FOR ATCs USING PHARMACEUTICAL PRODUCTS		27
ANNEX B: SPECIFIC GUIDANCE FOR RESEARCHERS AND PRACTISING VETERINARIANS ON ATC-Ss		34
List of Abbreviations		38

Introduction

1. This is one of a series of Veterinary Medicines Guidance Notes (VMGNs) explaining the requirements under the Veterinary Medicines Regulations (VMR). The VMR are revoked and replaced on a regular basis so reference to them should be read as referring to the ones that are currently in force. Therefore, the date and number of the Statutory Instrument are not shown in the VMGN. This VMGN 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 on the Veterinary Medicines Directorate's (VMD) website http://www.vmd.defra.gov.uk/public/vmr_vmgn.aspx gives basic information about the scope of the VMR and the requirement for MAs, i.e. what constitutes a veterinary medicinal product (VMP).
3. This VMGN provides guidance on the UK's Animal Test Certificate (ATC) scheme.
4. Although this VMGN attempts to cover most issues that are likely to arise in connection with putting together applications for an ATC, we recognise that it is not exhaustive. If you would like further advice in respect of a specific problem concerning an application, please telephone the relevant assessors for advice, or contact the Committee Support Team in order to arrange a meeting with the relevant personnel. Contact details are available on the VMD website www.vmd.defra.gov.uk
5. Please note that guidance is provided in this document for both pharmaceutical and immunological applications. Some parts of the guidance, however, are only relevant to one type of application and these are noted as such.
6. Unless otherwise specified, all documents available on the VMD website will be found in the thematic area, 'Pharmaceutical Industry'.

CHAPTER 1

What is an Animal Test Certificate (ATC)?

Nature of trials that require an Animal Test Certificate and background information

7. Usually, a clinical trial involving the use of a VMP must be the subject of a valid ATC, issued by the VMD, before it can be conducted. The ATC holder must conduct the trial in accordance with the terms of the certificate. Some types of trials which do not require an ATC are detailed at the end of this Chapter.
8. In the context of an ATC, a clinical trial is a study whose purpose is to demonstrate or substantiate the effect of a veterinary medicine after administration using the proposed dosage regimen via the proposed route of administration, and to specify its indications and contraindications according to species, age, breed and sex, its directions for use and any adverse reactions (AEs) that it may have. Clinical trials investigate the efficacy and/or safety of a veterinary medicine under conditions of field use and are usually conducted in client-owned animals.
9. The definition of a (VMP) is given in the VMR, but it has been duplicated below for ease of reference:
 - *Substances or combinations of substances presented as having properties for treating or preventing disease in animals; or*
 - *Substances or combinations of substances that may be used in, or administered to animals with a view either to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis.*
10. Therefore, according to the VMR, VMPs used in clinical trials may include authorised veterinary medicines, authorised human medicinal products, medicinal products authorised outside the UK and formulations in the final stages of product development. The VMD can provide guidance if it is not clear if this definition applies to a particular substance.
11. The purpose of an ATC is:
 - to provide appropriate safeguards for those animals involved in tests and trials;
 - to provide adequate safeguards for those people administering the product (users), people who may consume product from treated animals (consumers) and the environment;
 - to encourage trials and tests to be carried out in the UK by providing a positive environment for research and a rapid system of approval for applications to conduct clinical trials of VMPs in animals.
12. Clinical trials of VMPs are usually conducted in client-owned animals, rather than animals held at research establishments. All procedures applied to animals during the course of the trial must be consistent with “recognised veterinary practice” and the investigating veterinary surgeon must act in accordance with the Veterinary

Surgeon's Act, otherwise the study will also need to be regulated under the Animals (Scientific Procedures) Act (A(SP)A). Further information is available from the GOV.UK website at: <https://www.gov.uk/research-and-testing-using-animals>

- Further information on the definition of “recognised veterinary practice” is available in the *Royal College of Veterinary Surgeons (RCVS) Code of Professional Conduct, (Supporting guidance, section 25.2 – Interface between the Veterinary Surgeons Act 1966 and the Animals (Scientific Procedures) Act 1986)* available at www.rcvs.org.uk
 - Placebos can be included within an ATC provided use does not compromise animal welfare as a result of withholding treatment. The inclusion of placebo treated “control” groups will require A(SP)A authority if likely to cause pain, suffering, distress or lasting harm to the animal.
 - Further information on how investigations are regulated under A(SP)A is available from the *Animals (Scientific Procedures) Inspectorate at the Home Office*.
 - For studies conducted primarily under A(SP)A, an ATC may also be needed if produce from animals treated with an unauthorised VMP will enter the food chain. In these specific circumstances, please contact the VMD directly for further advice.
13. An ATC authorises both the trial itself and the procurement and supply of the veterinary medicine used in it.
 14. Products used in ATCs are subject to the labelling provisions outlined in Chapter 3.
 15. Some applications for ATCs are refused at the end of the assessment process either due to insufficient and/or inadequate supporting data or, if after assessment of all the data provided in support of the application, a negative benefit:risk conclusion is reached. There is a right of appeal for type B applications. For further information please refer to VMGN 9 Guidance on Appeals Against Regulatory Decisions, which is published on the VMD's website
http://www.vmd.defra.gov.uk/public/vmr_vmgn.aspx
 16. The VMD will not approve trial protocols, except to ensure that safety and welfare issues are adequately addressed. It is for applicants to ensure that the results of trials carried out under ATCs will be appropriate for any subsequent applications for an MA.
 17. Due to the investigational nature of an ATC, no charge should be levied for the trial material. However, in exceptional circumstances, and subject to the prior agreement of the VMD, it may be possible to charge a fee to recover the cost of the trial.

Validity of an ATC

18. An ATC is valid for two years following grant of the initial authorisation. In most circumstances it is expected that the authorised trial will have been completed within

that period; however, if the trial is still in progress, the ATC must be renewed in order for it to continue to be considered valid. If an ATC is not renewed by the renewal date it will cease to be valid. Further information about renewal of an ATC is available in Chapter 5.

19. During the validity of the ATC, evidence may become available which casts doubt on the safety, quality or efficacy of the product(s) involved, or which alters the benefit:risk assessment. In such circumstances the VMD may revoke, suspend or compulsorily vary the certificate in the same way that it can for an MA. 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 ATC holder has changed any of the approved specifications of the ATC without the prior approval of the VMD, the ATC will be suspended immediately. The suspension will remain in force until the changes have been approved, or the product is brought into line with the terms and conditions of the certificate.

Trials NOT requiring an ATC

20. Clinical trials involving food-supplements that are not intended for marketing with direct or implied medicinal claims, or other non-medicinal therapies such as surgical interventions, are not within the scope of the VMR and, therefore, do not require an ATC.
21. Veterinary surgeons, on their own initiative, may carry out some types of trials without an ATC. In this case, the investigatory VMP must be administered in accordance with their Summary of Product Characteristics¹ (SPC), or products should be administered in accordance with the provisions of “the cascade” as stated in the VMR. For further information please refer to VMGN 13 Guidance on the Use of the Cascade, which is published on the VMD’s website
http://www.vmd.defra.gov.uk/public/vmr_vmgn.aspx
 If the trial involves products administered under the cascade and the randomisation procedures within a trial prevent the prescribing veterinarian from being able to use their professional expertise and judgement to make a decision on the best treatment for the individual animal, then an ATC is needed. Retrospective analysis of clinical observations is not a trial.
22. For studies conducted without an ATC, the products used must be labelled in accordance with the VMR; if this is not possible an ATC is needed. For further information please refer to VMGN 2 Marketing Authorisations for Veterinary Medicinal Products, which is published on the VMD’s website
http://www.vmd.defra.gov.uk/public/vmr_vmgn.aspx
 For example, for trials where the owner is required to administer a treatment to the animal in a blinded manner an ATC will be required.
23. Investigations made during the early stages of a products development, e.g. pharmacokinetic or dose-finding studies, are usually conducted in animals kept at research establishments. For these types of studies, an ATC is not appropriate and a

¹ The purpose of the Summary of Product Characteristics (SPC) is to provide a clear and unambiguous description of the approved conditions of use of a VMP; it includes information such as the active substance, target species, indications, withdrawal periods etc. SPCs are published in the product information database available on the VMD website.

licence issued by the Home Office under the Animals (Scientific Procedures) Act (A(SP)A) 1986 will be needed. Further information is available from the GOV.UK website at: <https://www.gov.uk/research-and-testing-using-animals>.

Import of a medicinal product

24. The holder of an ATC may import anything specified in the certificate in accordance with the conditions outlined in the certificate.

CHAPTER 2

Types of Animal Test Certificates (ATCs)

25. There are two categories of ATCs: ATC-A/B and ATC-S. Clinical trials are authorised on a national basis.
26. The ATC-A/B is mostly appropriate for clinical trials conducted by pharmaceutical companies wishing to generate data for an MA application for a VMP. In order to obtain an ATC-A/B an applicant may submit a Type A or B application. The application type depends on the current authorisation status of the active substance being investigated and the potential risks to treated animals, users, consumers of products from treated animals and the environment.
27. The ATC-S is specifically intended for small scale research trials conducted by veterinarians. In order to obtain an ATC-S an applicant may submit a Type S application.
28. For all trials, which are primarily intended to generate pivotal data for **future MA applications**, the application must be for an ATC-A/B - either Type A or Type B application, according to Table 1 below:

Table 1: Type A or Type B application?

1.	Is the product already authorised as a human or veterinary medicinal product in a European Union (EU) or European Economic Area (EEA) member state?	Yes → Q. 2	No → Type B
2.	Is the product an immunological/biological product? Is the product a pharmaceutical product?	Yes → Q. 3 Yes → Q. 4	
3.	Is the trial to be conducted in the species included on the existing MA?	Yes → Type A	No → Type B
4.	Is the trial to be conducted in companion animals only?	Yes → Type A	No → Q. 5
5.	Is the trial to be conducted in the authorised food species at the same or a lower dose rate and using the same method of administration?	Yes → Type A	No → Type B

29. For small scale trials conducted by veterinary surgeons as clinical research the type of application required will be for an ATC-A/B, or for an ATC-S, according to Tables 2 and 3 below. ATC-S is intended for research trials that do not need to be conducted in accordance with Good Clinical Practices (GCP²) and involve small numbers of animals.

² GCP: Good Clinical Practices, VICH Topic GL9

30. Trials conducted under an ATC-S should not enrol more than 50 animals to the investigatory product treatment group unless this is clearly justified by statistical aspects of the study design.
31. Trials conducted under an ATC-S will not normally involve immunological products owing to the inherent risks of such products being contaminated with extraneous agents. It is advisable to approach the VMD before making an application for an ATC-S for an immunological/biological product, unless it already has an MA in the EU or EEA.
32. Products used in trials conducted under an ATC-S should usually be administered without alteration to the pharmaceutical form beyond that advised in the SPC; where any alteration is proposed (for example dilution) product quality and hence safety must not be compromised.
33. Researchers are encouraged to contact marketing authorisation holders (MAHs) of authorised VMPs prior to undertaking trials with their products.

Table 2: **Pharmaceutical products** to be tested in:

- Companion animals
- Horses declared never to enter the food chain
- Other (including food species) animals which have been declared never to enter the food chain³

Is the product:			
An EU (incl. UK) or EEA authorised VMP?		Go to Q. 1	
An EU (incl. UK) or EEA authorised Human product?		Go to Q. 4	
A VMP or human product authorised in one of the named third countries?		Go to Q. 5	
None of the above, e.g. a new chemical entity?		Type B	
EU (incl.UK) or EEA authorised VMP			
1.	Is the product to be used in the authorised species?	Yes → Q.2	No → Q. 3
2.	Is the product to be used at the authorised (or lower) dosage regimen which is supported by published literature ⁴ of the <u>efficacy</u> of the active substance in this species for the proposed indications?	Yes Type S	No → Q. 3
3.	Is there published literature supporting the <u>target species safety</u> , and <u>efficacy</u> of the active substance in this species, for the proposed indications and at the proposed dose regimen?	Yes Type S	No Type A
EU (incl UK) authorised Human products			
4.	Is there published literature supporting the <u>target species safety</u> , and <u>efficacy</u> of the active substance in this species, for the proposed indications at the proposed dose regimen?	Yes Type S	No Type A
VMPs and human products authorised in third countries			
5.	Is the product authorised in one of the following countries: United States, Canada, Japan, New Zealand, Australia?	Yes → Q.6	No Type B
6.	Is the product authorised for the same species and indications, using the same dosage regimen? (i.e. VMP only)	Yes Type S	No → Q. 7
7.	Is there published literature supporting the <u>target species safety</u> and <u>efficacy</u> of the active substance in this species for the proposed indications and at the proposed dose regimen?	Yes Type S	No Type B

³ To include zoo animals.

⁴ Refer to Annex A, Notes on supporting data for Type S applications.

Table 3: **Pharmaceutical products to be tested in food species**

Is the product:			
1.	A human or VMP authorised in the EU (incl. UK) or EEA?	Yes → Q.2	No Type B
2.	Is the product a VMP to be used in the authorised species, at the same or a lower dose rate, observing the withdrawal periods in the SPC?	Yes → Q.5	No → Q. 3
3.	Are the pharmacologically active substances in the product listed in Table 1 of the Annex of Commission Regulation (EU) 37/2010, and statutory withdrawal periods are to be applied? ⁵	Yes → Q.6	No → Q. 4
4.	Is the product to be used for the treatment of horses, <u>and</u> the active substances are listed as “essential for the treatment of equidae” according to Regulation (EC) 122/2013 <u>and</u> a 6-month withdrawal period is to be applied? ⁵	Yes → Q.6	No Type B
5.	Is there published literature ⁶ to support the <u>efficacy</u> of the active substance in this species for the proposed indications?	Yes Type S	No → Type A
6.	Is there published literature ⁶ to support the <u>target species safety</u> and <u>efficacy</u> of the active substance in this species, for the proposed indications and at the proposed dose regimen?	Yes Type S	No Type B

34. In general, each individual trial requires a separate ATC as the purpose of the trial should be to generate data in respect of one therapeutic indication and should normally involve a single species of animal. Possible exceptions to this rule would be trials of ectoparasiticides, endectocides or multivalent vaccines. This is because there might be concurrent infestations/infections of more than one species of pathogen/parasite in the same animal and more than one indication would be tested. Individual trials may be multi-centred.

35. A trial may involve more than one product, but only where:

- the second product to be administered is a placebo or a positive control which is authorised for that species and indication in an EU or EEA Member State. In exceptional circumstances, a human authorised product may be used as a control product where use is well supported by literature references and there is no suitable authorised VMP; or
- the products are of the same pharmaceutical form and contain the same ingredient(s) but differ in the strengths or dosages of the active or inactive ingredient(s); or
- for vaccines, the products differ only in the inclusion or exclusion of particular antigens under investigation; or

⁵ For statutory withdrawal periods, refer to the Veterinary Medicines Regulations, Schedule 4. The VMD reserves the right to specify an appropriate withdrawal period.

⁶ Refer to Annex A, Notes on supporting data for Type S applications.

- the products are of two or more dilutions of either the same allergen extract or mixture of allergen extracts used for desensitisation therapy; or the products used for *in vivo* diagnosis of allergy are manufactured by the same method from closely related substances (e.g. pollen); or
 - more than one product is expected to be required to produce therapeutic efficacy, e.g. sedative/analgesic combinations, allergens.
36. Each trial requires a separate application form plus supporting data as appropriate; refer to chapter 4 'The Application Process' for further information.

CHAPTER 3

Labelling of Products Supplied under an ATC

37. An ATC imposes conditions regarding labelling. These conditions require that the product being used as part of the trial is labelled in accordance with the general labelling rules for products subject to an MA. For further information please refer to VMGN 2 Marketing Authorisations for Veterinary Medicinal Products, which is published on the VMD's website
http://www.vmd.defra.gov.uk/public/vmr_vmgn.aspx
Where trials are being conducted according to a blind design, these rules will be relaxed to the extent necessary to allow for this. A package leaflet is required if there is insufficient space on the label to include all relevant text.
38. For ATC-A/B, draft label and package leaflet text should be submitted as part of the application package. This will be assessed and approved during the application procedure. The approved versions must be used for the trial.
39. For ATC-S, the applicant will be required to submit a statement of user and target species safety warnings to appear on the label/leaflet, but otherwise it is the responsibility of the ATC holder to ensure that the labelling/leaflets conform to requirements. Additional guidance on the warnings can be found in Annex 1 of the ATC-S application form.
40. As a general rule the VMD will expect labels to contain the following minimum information in English:
- the words "For Veterinary Clinical Trial Use Only";
 - name or other designation of the product;
 - quantity of product;
 - any restrictions on use;
 - expiry date and, if appropriate, in-use expiry date;
 - directions for use specific to the trial including dosage, frequency, duration, method and route of administration;
 - contra-indications, warnings and precautions, and special instructions for handling and storing the product;
 - instructions for disposal (in most cases, these should state that any unused product and containers should be returned to the trial sponsor);
 - if to be used in species used to produce food (including horses, rabbits and pigeons) either the specified withdrawal period or the words "Not to be Used in Animals for Human Consumption";
 - name and address of ATC holder and ATC number;
 - the manufacturer's batch number;

- a unique code/number identifying the individual container, where appropriate (e.g. where the identity of the products used in the trial are blinded).
41. For authorised VMPs the approved labelling may be used provided it is in English, but a small over label should indicate any amended directions/warnings, the ATC number and the words “Veterinary Clinical Trial Use Only” to ensure accountability in line with GCP requirements.
 42. If any of the above is likely to cause difficulties, particularly in respect of blinded trials, please contact the VMD for guidance.
 43. There are suggested proformas for the labelling of materials to be used in clinical trials on the VMD website. You will need to adapt these as appropriate to take account of the nature of individual studies.

CHAPTER 4

The Application Process

Data Requirements and Validation

44. Application forms for ATC-A/B and ATC-S are available on the VMD website www.vmd.defra.gov.uk. The different application forms and data requirements reflect the difference in complexity of the application types.
45. The data and documents required in support of an application for an ATC-A/B or ATC-S are provided in the application forms and the annexes to this VMGN. To avoid unnecessary delays in the processing of an application, applicants should not submit any additional data that have not been asked for.
46. In the interests of animal welfare, a justification is required for the proposed trial. As trials by their nature will cover only a limited number of animals on a small number of sites, data are not necessary to demonstrate quality, safety and efficacy to the level required in support of an application for an MA. The submission of a full data dossier is not required.
47. Reference to laboratory or target animal efficacy or challenge studies may be necessary. Applicants may make cross-references to relevant studies in the data dossier for an already authorised VMP which is held by the VMD and to which the applicant has a right of access.
48. Applicants should ensure that the procedures and techniques used during the field trial, including sampling, use of placebos and control animals, comply with “recognised veterinary practice” (see Chapter 1 of this document). Placebos can be included within an ATC provided use does not compromise animal welfare. The ATC itself does not relieve the veterinary surgeon from providing normal veterinary care for the animal involved in a trial. Should this be prohibited by the protocol of the trial, or if trial procedures are not compliant with recognised veterinary practice, the Home Office should be consulted regarding the need for an A(SP)A licence.
49. It should be noted that studies conducted under an ATC to investigate the safety of a product should normally be conducted at the proposed dosage, administered for the proposed duration of administration. Target species tolerance studies involving either multiple dosages or an extended dosage period would normally require a licence under A(SP)A.
50. Studies intended to generate data for an MA application should be carried out in accordance with the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (*VICH*) *Topic 9: Guideline on Good Clinical Practices* implemented in the EU in July 2001.
51. It is not a requirement that products used in ATC trials be manufactured under Good Manufacturing Practice (GMP) conditions, although this is encouraged.

52. The VMD will not approve trial protocols, except to ensure that safety and welfare issues are adequately addressed. It is for applicants to ensure that the results of trials carried out under ATCs will be appropriate for any subsequent applications for an MA.
53. For Type B ATC applications, it will be necessary to demonstrate compliance with the latest version of the joint Committee for Proprietary (Human) Medicinal Products/Committee for Veterinary Medicinal Products (CPMP/CVMP) guideline on “Minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products” - EMEA/410/01. The relevant information that should accompany each application consists of a signed declaration in the appropriate format together with a Certificate of Suitability demonstrating compliance with the relevant monograph or the relevant scientific data where appropriate. The formats and the declarations are available on the VMD website.
54. All applications for ATCs are subject to validation; guidance on how to submit a valid application is provided on the VMD website.
55. The onus is on the applicant to identify and submit all the necessary supporting data in their application package. If the application is incomplete it is likely to fail validation.

Assessment and Outcome

56. The VMD will evaluate applications looking particularly at the risks involved in the proposed trials. Our main concerns will be for safety, especially to consumers of produce from the treated animals, to the environment, to people using the product or handling treated animals, and to the animals undergoing the trial.
57. After validation, consideration will be given as to whether additional scientific advice is required. This may be necessary in relation to products containing new active chemical entities not previously approved in the EU or EEA or, in the case of vaccines, live antigens not previously included in the UK authorised product. Although we will aim to do this within the timescales set out in Chapter 4, this may not always be possible as it depends on the dates of committee meetings.

Because the Importation of Animal Pathogens Order 1980 may also apply, VMD will consult Defra’s Animal Health and Welfare Directorate when applications are received relating to agents that are:

- exotic to the UK;
 - notifiable;
 - zoonotic; or
 - may affect statutory or non-statutory surveillance for animal disease.
58. The VMD considers issues of safety to the consumer as part of the assessment. Nevertheless, we may consult other government bodies including the Food Standard Agency (FSA) in relation to food safety, should the need arise. We advise the FSA routinely of all ATC applications for food producing species and send copies of the

dossiers to them. We would normally expect to conduct any such consultations within the usual assessment timescale.

59. For applications involving VMPs containing or consisting of genetically modified organisms the applicant should contact the VMD for advice. Any medicinal trial in animals involving the deliberate release of genetically modified organisms into the environment requires both an ATC and a Part B Experimental Release Licence, which is issued by the Genetically Modified Policy Unit of Defra under Directive 2001/18/EC. The part B experimental release licence is required before a trial may start.
60. In order to expedite progression on an application, it is essential that the responses provided are comprehensive and all pertinent data are provided.
61. If the proposed outcome is to refuse the application, the applicant will be notified of this. For Type B applications the applicant will be given an opportunity to appeal against this decision. Further information about the appeals process please refer to VMGN 9 Guidance on Appeals Against Regulatory Decisions, which is published on the VMD's website http://www.vmd.defra.gov.uk/public/vmr_vmgn.aspx
62. If the outcome is to approve the application, the applicant will be sent a certificate verifying that the trial has been approved subject to a number of conditions that will be specified on the certificate.
63. The ATC may be issued for a single batch of a product for which data solely relating to this batch are provided. Alternatively, it may be issued on the basis of agreed specifications, so that different batches of product may be used in the trial.

Submission

64. 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. Applications must be submitted by the proposed ATC holder who must be the person who takes overall legal responsibility for the trial.
65. If submitted electronically, the application package should be sent on a CD/DVD to the address below, or sent via email (using Eudralink⁷ or not; it is the applicant's choice) to: s.response@vmd.defra.gsi.gov.uk. Please note there is a 40 MB limit on the Eudralink system.
66. There is no set format for the content of electronic submissions, but the PDF file(s) should be held within a main 'ROOT' folder.
67. If submitted in hard-copy the applicant should send four copies of the application package, for each proposed trial, to the following address:

Information Management Section
 Veterinary Medicines Directorate
 Woodham Lane

⁷ Eudralink is a secure electronic system that enables files to be sent over the Internet via a user-friendly Web interface.

New Haw, Addlestone
Surrey
KT15 3LS

68. The application forms are available on the VMD website; these are VMD-created documents for use under this national-only scheme.
69. Queries regarding the submission of applications should be directed to the Information Management team via email to: s.response@vmd.defra.gsi.gov.uk.

Timescales

70. The timescales for dealing with an application for a new ATC 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 for ATC (Type A and Type B) and ATC-S is also provided below.
71. **Applications for ATC (Type A) and ATC-S** are processed on a 30-day timetable. The clock starts upon receipt of an application and is validated within 5 days; 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.
72. Once the application is deemed valid, the clock will continue running and the application will proceed into the assessment phase where the assessor(s) has up to 15 days to either approve or refuse the application, or ask further questions. Whatever the outcome, the applicant will be informed accordingly.
73. In such cases where more data are required, the assessors involved will usually send a combined list of questions to the applicant.
74. If further questions are asked, the applicant will be required to provide responses within 10 days from the date of the letter. It should be noted that the clock continues running during this time. If a response is not received within the given deadline, the application will be considered withdrawn.
75. Upon receipt of the response, the assessor(s) has up to the end of the 30-day timeframe to assess the response and either approve or refuse the application. If approved, formal authorisation documentation will be sent to the applicant within 5 days of assessor sign-off.
76. Except for the validation period, there is no provision for stopping the clock during an ATC (Type A) and ATC-S application procedure.
77. **Applications for ATC (Type B)** are processed on a 50-day timetable. The clock starts upon receipt of an application and is validated within 5 days; 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.

78. Once the application is deemed valid, the clock will continue running and the application will proceed into the assessment phase where the assessor(s) has up to 35 days to either approve or refuse the application, or ask further questions. Whatever the outcome, the applicant will be informed accordingly.
79. If further questions are asked, the clock will stop pending receipt of the response. The applicant will be asked to provide a response within a given deadline (usually three months, or other timescale as agreed by the VMD); if a response is not received within the given deadline, the application will be considered withdrawn.
80. The VMD will keep all requests for additional data to the minimum. In such cases where more data are required, the assessor for each discipline will usually send an individual question letter to the applicant in order to avoid delays and expedite responses; however, the clock will remain stopped until all initial questions have been addressed and a complete response has been received.
81. Upon receipt of a complete response, the clock restarts and the assessor(s) has up to the end of the 50-day timeframe to assess the response and either approve or refuse the application. If approved, formal authorisation documentation will be sent to the applicant within 5 days of assessor sign-off.
82. There is provision for stopping the clock during an ATC (Type B) application procedure if further information/clarification is required.

Fees

83. **The fee should not accompany the application and nor should it be paid in advance of the submission of the application.**
84. Details on the relevant fees can be found in Schedule 7 of the VMR, which is available on the VMD website www.vmd.defra.gov.uk.

CHAPTER 5

Post Authorisation Steps

Terms and Conditions

85. The terms and conditions of the authorised ATC comprise:
- all information submitted with the application
 - additional documents detailing any changes or additions made during the assessment period and
 - any general or special conditions imposed by the VMD
86. Any alterations in the trial that bring it outside the terms and conditions of the ATC will be in breach of the terms and conditions on which the ATC was granted. In such circumstances, either a variation or a new ATC should be obtained. A person carrying out a medicinal test on animals that is not covered by the terms and conditions of an ATC is liable to prosecution. The holder of the ATC is guilty of an offence if he supplies the product for administration that is not within the terms and conditions of the ATC.

Obligations on ATC Holders

87. The issuing of an ATC gives authority for the holder to supply and use the product in accordance with the approved dossier. In the case of studies conducted in compliance with Good Clinical Practice – Veterinarian (GCP-v) the ATC holder should be the Sponsor⁸ or person/organisation to whom they have legally delegated this responsibility. In particular, the ATC holder must observe any special conditions written into the ATC, use the approved product literature and comply with the laws relating to any variations to the terms of the ATC.
88. By signing the application form the ATC holder undertakes:
- to meet the terms and conditions of the ATC;
 - to ensure that Informed Owner Consent is obtained for both participation in the trial and for products not used in accordance with the SPC or unauthorised use of any products used in the trial.
 - to ensure that all procedures conducted under the ATC comply with the RCVS Guide to professional conduct and “recognised veterinary practice” (Code of Professional Conduct, *Supporting guidance, section 25.2, Interface between the Veterinary Surgeons Act 1966 and the Animals (Scientific Procedures) Act 1986*, www.rcvs.org.uk). For Type S ATC, as the protocol is not submitted, the researcher/investigator and at least two other veterinary surgeons, who are

⁸ The Sponsor of a trial is the individual, company or organisation who takes responsibility for the initiation, management and, usually, financing of the clinical trial.

independent of the trial and have a further qualification in the discipline concerned, should provide signed confirmation that they have reviewed the protocol and that they are satisfied that the study is ethical and to be conducted in accordance with these requirements.

- to comply with pharmacovigilance reporting requirements detailed below;
- to notify the VMD of any other information affecting the safety of the test product(s) that becomes available from any source before or during the course of the trial; and
- to notify the VMD of any discontinuation of the trial and the reasons for it.

89. An ATC may be revoked (or, if appropriate, compulsorily varied) if:

- the ATC holder fails to observe any of the terms and conditions of the ATC;
- doubts arise about the safety or quality of the product;
- changes in the conduct of the test have an adverse effect on the safety of the target or other animals, of consumers of the produce of target animals, of users of the product or of the environment;
- information supplied at the time of application is found to have been deficient or incorrect in a material way (i.e. in a way which influenced the VMD's decision).

Pharmacovigilance

90. It is a condition of any ATC that any serious AEs (i.e. any reaction involving a human or which has caused to increased mortality or serious ill-health in treated animals, or birth defects in the offspring of treated animals) to any substance used under an ATC (i.e. test article, control or placebo) must be reported to the VMD within 15 days. For further information please refer to VMGN 11 Pharmacovigilance Guidance on Adverse Events, which is published on the VMD's website http://www.vmd.defra.gov.uk/public/vmr_vmgn.aspx

91. ATC holders should keep appropriate records of AEs that may occur following administration of the test control articles, including those which are not serious. A summary of all AEs that occur during the trial will be required if the ATC is to be renewed. For studies conducted under Good Clinical Practice (GCP) the study protocol should include procedures for observing, recording and reporting AEs.

92. The ATC holder is responsible for reporting AEs to the VMD and must name a person responsible for pharmacovigilance in the ATC application form. This person, usually a veterinary surgeon, must have overall responsibility for investigating any suspected AEs, monitoring them and, when necessary, reporting them to the VMD in accordance with the regulatory requirements in paragraph 89, above. Appropriate arrangements should be put in place to ensure that 'blinding' of products does not interfere with pharmacovigilance responsibilities. The ATC holder should ensure that they are notified promptly by the investigators of serious AEs.

Variations

93. Any changes to the terms or conditions of an ATC must be made by means of a variation, unless otherwise agreed by the VMD.
94. It is not possible to vary an ATC-S. Minor changes may be made by prior agreement and notification to the VMD, but more substantial changes will require a new application. Therefore, this section outlines the procedure for varying an ATC obtained via a Type A or Type B application procedure only.
95. Variation applications may be submitted either electronically, or in hard-copy as per the guidance provided in Chapter 4 ('Submission'). If submitted in hard-copy, two copies of the application package are required.
96. The ATC holder should complete the application form, available on the VMD website, by setting out and justifying the proposed change. Only the types of changes listed below may be dealt with by way of a variation application:
 - the name of the product or the designation by which it is known;
 - name and address of the ATC holder;
 - the name and address of any person in the UK taking part, in the course of a business carried out by him, in the manufacture or assembly of the product and for imported products, the name and address of the manufacturer and assembler of the product in the form imported;
 - a justified increase in the number of animals to be treated with the test product;
 - the inclusion and/or exclusion criteria used in the selection of animals for the test, or the withdrawal of animals from the test;
 - the arrangements for monitoring safety including any instructions, restrictions or precautions to ensure the safety in use and at disposal;
 - the name or qualifications of the overall Monitor of the trials (see VICH guideline on Good Clinical Practice for definition of Monitor);
 - the name of the site Investigator involved in the animal test (see VICH guideline on Good Clinical Practice for definition of Investigator);
 - the name of any additional Investigator and addresses of any additional test sites;
 - product shelf-life;
 - the approved label text.
97. Variation applications will be processed in accordance with the procedure and timescales used for applications for new ATCs (Type A) and ATC-Ss as outlined in Chapter 4 ('Timescales').
98. It is recognised that some tests cannot be set up until an outbreak of a particular disease of interest occurs. In these circumstances an ATC may be issued for a maximum number of sites and animals with the condition that test sites and the exact

number of animals included at each site are advised as they become known. There will be no specific charge for this.

99. All other changes require new ATC applications. However, where an existing UK trial is being modified, as long as the product formula, species and purpose of the trial remain the same, an ATC (Type A) procedure and fee will apply.

Fees

100. The fee should not accompany the application and nor should it be paid in advance of the submission of the application.
101. Details on the relevant fees can be found in Schedule 7 of the VMR, which is available on the VMD website www.vmd.defra.gov.uk.

Duration and Renewal of ATCs

102. An ATC is valid for two years following grant of the initial ATC. In most circumstances it is expected that the authorised trial will have been completed within that period; however, if the trial is still in progress, the ATC must be renewed in order for it to continue to be considered valid. If an ATC is not renewed by the renewal date it will cease to be valid.
103. It should be noted that there is no formal application form for renewal of an ATC.
104. For ATC-A/B, the ATC holder should submit a letter to the VMD requesting renewal of the ATC. The ATC holder should include particulars of the ATC and any variations previously made to it, particulars of the progress of the trial, and a summary account of AEs noted. A justification for renewal of the ATC must also be provided.
105. For ATC-S, the ATC holder should submit a cover letter requesting renewal of the ATC accompanied by a report documenting the reasons and justification for the request and a summary account of AEs noted.
106. Renewal applications may be submitted either electronically, or in hard-copy as per the guidance provided in Chapter 4 ('Submission'). If submitted in hard-copy, two copies of the application package are required.
107. Renewal applications will be processed in accordance with the procedure and timescales used for applications for new ATCs (Type A) and ATC-Ss as outlined in Chapter 4 ('Timescales').

Fees

108. The fee should not accompany the application and nor should it be paid in advance of the submission of the application.
109. Details on the relevant fees can be found in Schedule 7 of the VMR, which is available on the VMD website www.vmd.defra.gov.uk.

Further Information

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

ANNEX A

NOTE ON SUPPORTING DATA FOR ATCs FOR PHARMACEUTICAL PRODUCTS

Supporting Data for Type A & B Applications

The data requirements for an ATC-A/B are detailed on the application form. If data are not available for all areas, this will not necessarily mean that an ATC will not be granted, but a justification for the absence of data should be provided in every case. The VMD reserves the right to request additional data to that listed in this annex for the assessment of the safety of the product, including those aspects of quality that may impact on safety.

The following notes are provided for applications for pharmaceutical products to supplement the information on the application form:

Quality

The following additional data are required for **Type B** applications only:

Qualitative and Quantitative Particulars

The product should be described (colour, shape, dimensions, pharmaceutical form).

A very brief rationale for the selection of the formula for use in the trial should be presented. Any similarities of the proposed trial material with an already authorised product (e.g. same unconventional excipient) should be mentioned.

If a positive control is to be modified for double blinding purposes, information on the nature of the modification should be given together with a consideration of whether the modification has an impact on bioavailability. This may also be relevant for some Type A applications.

Method of Preparation of the Final Product

For non-standard manufacturing processes, a detailed description of critical steps should be provided.

Process validation data are NOT required.

Specification of the Active Substance

For those active substances which are confirmed in the table in section 4.6 of the application form as complying with one of the following Ph. Eur., BP, or the pharmacopoeia of another EU Member State, the United States Pharmacopoeia (USP), or the United States Pharmacopoeia-National Formulary (USP-NF), further information is not generally required. However, where additional controls need to be applied to the active substance due to the nature of the dosage form and method of manufacture (e.g. sterility, particle size) these should be provided.

For those active substances, which do not fall into the categories mentioned above, the active substance specification should be summarised and justified. The summary should indicate each of the tests, the limits applied and the type of test method (e.g. assay, 98.5 - 101.0%, HPLC). Alternatively, a copy of the Certificate of Analysis for the batch used to manufacture the trial material should be supplied together with a justification demonstrating the suitability of the batch for the intended use.

Active Substance Manufacture, Evidence of Structure and Impurities

Additional data are required for novel molecules and for active substances from a source not currently authorised for use in the manufacture of veterinary or human medicines in the EU. Novel molecules in this case are considered to be those substances which have not previously been used in the EU in/on animals or humans.

The additional data which are required are:

- The method of manufacture of the active substance should be summarised. Any substance of animal origin used in the manufacture of the active substance should be clearly identified and their suitability for use in the manufacturing process, in terms of product safety, should be discussed.
- For non-pharmacopoeial active substances, evidence of structure data should be presented together with interpretations.
- Information on the potential impurities of the active substance, their origin and the levels actually observed in batches of the active substance should be presented. Their significance in terms of the safety of the product to be tested should be commented upon.

Control of Other Ingredients

For ingredients that do not comply with the Ph. Eur., BP, or the pharmacopoeia of another EU Member State, USP or USP-NF, specifications should be provided. The specifications should include test and limits and an outline of the method, e.g. gas chromatography.

If a single batch approval ATC is required, for those ingredients not covered by any of the pharmacopoeia listed above, a Certificate of Analysis should be provided. A justification demonstrating the suitability of the material for the intended use should accompany the Certificate of Analysis.

Release Finished Product Specification

Complete analytical methods do not need to be presented. Supporting validation data should NOT be supplied.

An end of shelf-life Finished Product Specification is NOT required.

If a single batch approval is sought, rather than summarising the Finished Product Specification in section 4.10 of the application form, a copy of the Certificate of Analysis of the batch of product intended for use in the trial should be provided.

If a placebo product is to be used in the trial, a simple Finished Product Specification for the placebo should be provided. The Specification should primarily cover physical characteristics, e.g. appearance, dimensions, fill weight/volume and absence of the active substance.

Stability and Shelf Life

A shelf life, and, if appropriate in-use shelf life linked to specified storage conditions, should be proposed and justified. Stability data (chemical and physical) for the proposed formulation should be presented in the form of tabulated results. Stability data on closely related formulations (e.g. different strengths of the proposed dosage form containing the same excipients) may be acceptable with a justification for the use of such data. Similarly, stability data on the same formulation stored in similar packs (e.g. same contact materials but different shapes/sizes) would require a justification.

Although provision of stability data on pilot batches stored under Committee for Medicinal Products for Veterinary Use (CVMP) recommended conditions is desirable, provision of stability data for laboratory batches stored, for example, under ambient conditions may be permitted, depending on the nature of the proposed trial.

The requirements for stability data will depend on the type of product under investigation and the proposed trial. It is acceptable to provide only sufficient data to support a short shelf life, e.g. 3 months, if this is adequate for the purpose of the trial. For trials involving extended periods of time, more stability data will need to be provided. Alternatively, subject to there being a reasonable expectation of good stability based on related formulations, an agreement may be reached on real-time monitoring of stability during the course of the trial.

Human Safety

The following additional data are required for **Type B** applications only:

General

As indicated previously, summary data only are required. The amount of detail to be included depends on the authorisation status of the product or its active substances. Some examples are shown below as a guide, and the application form itself provides further information.

Product containing an active substance authorised for use in another species:

A maximum residue limit (MRL) summary report (if available) could be provided, supplemented with any additional data appropriate to the trial, a user risk assessment and a detailed summary of relevant residues depletion data together with a proposal for a withdrawal period.

Product containing an active substance used in products other than veterinary medicines, e.g. in pesticides:

A summary of a published pesticide assessment, supplemented with any additional data appropriate to veterinary medicines, a user risk assessment and, if relevant, a detailed summary of residues depletion data together with a proposal for a withdrawal period.

Product containing a completely new active substance:

Detailed tabulated or descriptive summary of each study, together with conclusions on user and consumer warnings.

Tabulated summaries may usefully be provided in the formats defined for the safety expert reports which must accompany applications for marketing authorisations.

User Safety

A user risk assessment must be submitted for all applications. This should include a summary of the product's basic toxicity and a consideration of the likely user exposure during the trial.

Consumer Safety

If produce from animals treated during the trial is to enter the food chain, the data provided must demonstrate that the food will contain no harmful veterinary drug residues. Where the pharmacologically active substance of the products to be used appears in Table 1 of the Annex of Commission Regulation (EU) 37/2010, applicants will need to propose a suitable withdrawal period. As an alternative to the presentation of residue depletion studies and depending on the nature of the substance concerned, a relevant withdrawal period may be proposed and justified by the submission of reasoned arguments. Relevant withdrawal periods are at least: 28 days for meat, 7 days for milk and eggs or 500 degree days for fish. Where other pharmacologically active substances are concerned, applicants will need to justify an MRL and withdrawal period.

In exceptional circumstances, applicants may wish to start field trials before sufficient information is available to allow a full assessment of residues. In this case produce from the treated animals may not enter the food chain and applicants must agree to label the product "*Not to be used in Animals for Human Consumption*". The applicant must justify this approach and state how treated animals are to be disposed of to ensure that their products do not enter the food chain.

Environmental Safety

The following additional data are required for **Type B** applications only:

An environmental risk assessment is NOT required for Type B ATCs for companion animals. Completion of sections 1, 2 and 3 of the application form is all that is required.

It is not expected that there will be significant exposure of the environment as a result of the use of a product under an ATC. This is mainly due to the small scale of use, regardless of whether an existing product or a new product is used.

Applicants should provide an environmental risk assessment which demonstrates that environmental exposure to the test product is not extensive. In most cases information on the number of animals on the trial, the number of sites and the dose and duration of treatment will be sufficient to show that exposure will not be significant. The applicant should also consider any other information or environmental risk assessment available for the test product which might be of relevance when preparing their assessment.

In exceptional cases, exposure of the environment may be found to be significant. In these cases a summary report of individual fate and effects studies available should be provided with the risk assessment. These summaries should be sufficient, for the ATC application, but the assessor may ask for a full report of one or more studies, if necessary, to complete the environmental risk assessment.

General information relating to Animal Welfare and Study Design

General animal welfare needs should be taken into consideration, for example, provision must be made for:

- alternative treatment if the product under trial is not efficacious or if unacceptable side effects are observed;
- the blinding code to be broken if necessary, for example, if an animal has a suspected AE and the investigator needs to know whether it has been given the test product, a positive control or a placebo in order to treat the animal correctly;
- treatment of any animal which has had a placebo administered to it, if treatment is required;
- satisfactory safety monitoring in terms of provisions for re-examinations during and following treatment, clinical pathology monitoring, etc.
- availability of normal 24-hour per day emergency service for veterinary care and appropriate arrangements. This is particularly relevant if this service is delegated, to ensure continuity of care and for the blinding code to be broken in the event of an emergency.

The proposed numbers of animals that the test product is to be administered to must be justified and based on statistical requirements and must be the minimum number consistent with the objective for the trial.

A suitably qualified person, usually a veterinary surgeon, must be available to investigate any suspected AEs, treat the animal(s) appropriately and, if necessary, remove it (them) from the trial.

Target Safety Species

Information to support target species safety is required for all applications except Type A where there is an existing EU authorisation for the same species using the same posology. The VMD will need to be sure that safety in the target species is acceptable at the proposed dosage and for the proposed duration of administration, and that there is a reasonable margin of safety.

Efficacy Data

Evidence should be provided to indicate that there is a reasonable expectation that the test product will produce the desired effect and to support the proposed dosing regimen. For example, reference to laboratory and/or pilot studies may be necessary.

Trial Protocol

The trial protocol should include the scientific rationale for the study and clearly state the study objectives.

Trial protocols should be GCP compliant. Whilst the protocol should be submitted to the VMD, the VMD will not approve it. It is for applicants to ensure that the results of trials carried out under ATCs will be appropriate for subsequent applications for MAs, and that accurate records are maintained for company archives.

Supporting Data for Type S Applications

Target Species, Safety and Efficacy Data

Scientific literature, published by a reputable source, should be presented. Ideally, the literature should be derived from peer-reviewed journals but alternative sources may be taken into consideration, for example, papers presented at conferences which have been reviewed by a committee. Other data (e.g. specialist group email discussion lists) may be taken into consideration and will be judged on merit. The literature should provide supportive evidence for the safety and efficacy of the active substance, when used in accordance with the proposed dosage regimen, in the target species.

If there is an existing EU or EEA authorisation for the product in the same species and using the same dosing regimen, target species safety data are not required.

For an “exotic” species, it may be possible to present literature from a related species if its relevance can be justified by the applicant.

Full copies of all references should be submitted; citations alone are not sufficient.

ANNEX B

SPECIFIC GUIDANCE FOR RESEARCHERS AND PRACTISING VETERINARIANS ON ATC-Ss

An ATC-S (Type S ATC) is intended to authorise small scale research trials of human or veterinary medicinal products administered in a clinical/field setting to client-owned animals.

The following is a summary of the guidance already provided throughout this VMGN, but you are also advised to read the Quick Start Guide and general guidance in the VMGN as not all aspects are covered below.

In the context of this guidance note, a clinical trial is a study whose purpose is to demonstrate the effect of a medicinal product in the target species under conditions of field use. Clinical trials are usually conducted in client-owned animals, rather than animals held at research establishments. They may represent the final part of a pharmaceutical company's development programme, the dosing regimen and toxicity profile for the product having been investigated at earlier stages in studies regulated under A(SP)A. However, veterinary researchers may also conduct small scale clinical trials of medicinal products when there is already some supporting evidence of their safety and efficacy available in the public domain. These trials are regulated under the VMR with the aim of providing safeguards to the animals involved, people administering the products, consumers of animal produce and the environment. Providing that certain conditions are met (detailed below), small scale research trials may be authorised under the simplified Type S ATC.

Veterinary surgeons may carry out some types of investigations of VMPs without an ATC, for example, in order to determine the best treatment for an individual animal. In this case, the VMP must be administered in accordance with its Summary of Product Characteristics (i.e. authorised species, indications, dose regimen etc) or the decision for the treatment of each individual animal (or group of animals on the same holding) should be made in accordance with the "Cascade" as stated in the VMR. For further information please refer to VMGN 13 Guidance on the Use of the Cascade, which is published on the VMD's website http://www.vmd.defra.gov.uk/public/vmr_vmgn.aspx

In these types of studies, the products must be labelled in accordance with the VMR, otherwise an ATC is needed. Furthermore, if the trial requires randomisation such that the vet is prevented from using their professional expertise and judgement to make a decision on the best treatment for the individual animal, then an ATC is needed. Retrospective analysis of clinical observations is not a trial.

Trials involving food-supplements which are not intended to investigate direct or implied medicinal claims, or other non-medicinal therapies (such as surgical interventions), are not within the scope of the VMR.

For studies conducted under an ATC-S, all procedures applied to animals during the course of the trial, including sampling, use of placebos and control animals, must comply with "recognised veterinary practice", otherwise the study will also need to be regulated under the Animals (Scientific Procedures) Act (A(SP)A). Placebos can be included within an ATC providing their use does not compromise animal welfare.

- Further information on the definition of "recognised veterinary practice" is available in the RCVS Code of Professional Conduct (Supporting guidance, section 25.2 – Interface between the Veterinary Surgeons Act 1966 and Animals (Scientific Procedures) Act) 1986. Further information on how investigations are regulated

under A(SP)A is available from the Animals (Scientific Procedures) Inspectorate at the Home Office.

In order for a trial to be conducted under an **ATC-S**, the following criteria should apply:

- The investigatory and control products should be human or VMPs that are authorised in the EU, EEA or one of the following third countries: United States of America, Canada, Japan, New Zealand or Australia.
- The data generated are not intended to be pivotal to a future MA application.
- The trial will not enrol more than 50 animals to the investigatory product treatment group, unless clearly justified by statistical aspects of the study design.
- The dosage form will not normally be altered prior to administration, other than as directed in the SPC. Where any alteration is proposed (for example dilution) product quality, and hence safety, must not be compromised. It is recommended that any intended alteration to a dosage form should be discussed with a Quality Assessor at the VMD.
- There should be good quality evidence, preferably as published literature, supporting the safety and efficacy of the active substance in the target species, for the proposed indications and dosage regimen.
- For authorised VMPs to be trialled in food species, if the dose regimen and species are consistent with the SPC, then the withdrawal period indicated in the SPC may be applied. If the dose regimen is not consistent with the SPC, or the product is not authorised in the species, the active substances will be listed in Table 1 of the Annex in Commission Regulation (EU) 37/2010 and the statutory withdrawal period will be applied. The Food Standards Agency is advised routinely of all ATC applications for food producing species.
- For food-producing horses, the active substance may be included in the list of substances essential for the treatment of equidae, Regulation (EC) 122/2013, and a 6-month withdrawal period applied.
- Type S trials will not normally involve immunological products, owing to the inherent risk of such products being contaminated with extraneous agents. It is advised to approach the VMD for discussion before making an application for a Type S ATC for an immunological/biological product unless it already has an MA in the EU.

If the trial does not comply with these criteria, then an application for a Type A or B ATC will be needed.

Researchers are encouraged to contact Marketing Authorisation Holders (MAH) of authorised VMPs prior to undertaking trials with their products.

Application process

Please refer to Chapter 4 for further information on the application process including how to apply, data requirements etc.

Guidance on the requirements for the supporting data for an application for an ATC-S is provided at the end of Annex A of this document and in the ATC-S application form.

The **application form** for an ATC-S is available on the VMD website www.vmd.defra.gov.uk (Pharmaceutical Industry, Applying for a New Authorisation, Application Forms & Related Checklists). The Annex to the application form gives guidance on the type of data required to support target species safety and efficacy, and warnings to be included on labels of products supplied under an ATC.

If you have any difficulties with your application, please contact New Licensing on: 01932 338439.

List of Abbreviations

AE	Adverse Event
A(SP)A	Animals (Scientific procedure) Act 1986
ATC	Animal Test Certificate
BP	British Pharmacopoeia
CPMP	Committee for Proprietary (Human) Medicinal Products
CVMP	Committee for Veterinary Medicinal Products
Defra	Department for Environment, Food & Rural Affairs
EC	European Commission
EEA	European Economic Area
EU	European Union
FSA	Food Standards Agency
GCP	Good Clinical Practice
GCP-v	Good Clinical Practice - Veterinarian
GMP	Good Manufacturing Practice
MA	Marketing Authorisation
MAH	Marketing Authorisation Holder
MRL	Maximum Residue Limit
Ph. Eur.	European Pharmacopoeia
RCVS	Royal College of Veterinary Surgeons
VICH	International Co-operation on Harmonisation of Technical Requirements for Registration of Veterinary Products
USP	United States Pharmacopoeia
USP-NF	United States Pharmacopoeia-National Formulary
VMD	Veterinary Medicines Directorate
VMGN	Veterinary Medicines Guidance Note
VMP	Veterinary Medicinal Product
VMR	Veterinary Medicines Regulations

VETERINARY MEDICINES GUIDANCE NOTE

Veterinary Medicines Directorate
Woodham Lane, New Haw, Addlestone, Surrey KT15 3LS
Telephone (+44) (01932) 336911 Fax: (+44) (01932) 336618
Search for VMD on www.gov.uk