Guidance

Animal Test Certificates

Guidance on Animal Test Certificates (ATCs) required to carry out the field trial of a veterinary medicine in animals (clinical trial) in the UK.

Clinical trials in animals

The Veterinary Medicines Regulations 2013 (VMR) define a veterinary medicine as:

- any substance or combination of substances presented as having properties for treating or preventing disease in animals;
- any substance or combination of substances which may be used in or administered to animals with a view either to restoring, correcting, or modifying physiological functions by exerting a pharmacological, immunological, or metabolic action, or to making a medical diagnosis; or
- any substance or combination of substances that may be used for the purpose of euthanising an animal.

A clinical trial is a study usually conducted in client-owned animals, that aims to examine under field conditions the safety and/or efficacy of a veterinary medicine under normal conditions of animal husbandry or as part of normal veterinary practice.

You need an Animal Test Certificate (ATC) to carry out a clinical trial of a veterinary medicine in animals in GB and/or NI. You must submit an application for an ATC to the VMD.

The types of medicinal product falling under the definition of a veterinary medicine and tested during a clinical trial might include: a veterinary medicine under development, an authorised veterinary medicine, or a human medicine.

ATCs in the UK

An Animal Test Certificate (ATC) permits:

- the use of a medicine during a clinical trial, including the use of a medicine outside the terms of its marketing authorisation
- the procurement and supply of that medicine
- the import of any medicine specified in the certificate in accordance with the conditions of that certificate
- the produce from treated animals to enter the food chain if appropriate
- the use of randomisation and/or blinding within the study protocol
- the administration of a placebo product

There are three different types of application that can be used to obtain an ATC (type-A, type-B, and type-S). The type of ATC application required is dependent on several factors; these are set out below.

Types of ATC application

Commercial clinical trials

Commercial clinical trials are usually conducted by the pharmaceutical industry to generate the data required to support a marketing authorisation (MA) application. This may be a new MA application for a veterinary medicinal product under development, or a change to an existing MA for an authorised product. To obtain an Animal Test Certificate (ATC) for a commercial clinical trial you will need to submit a type-A or type-B ATC application.

Non-commercial clinical trials

Practising vets or researchers may wish to carry out a non-commercial and typically small-scale clinical trial of a medicine. Such a study may be conducted to inform clinical practice or be undertaken for academic purposes. To obtain an ATC for these types of non-commercial clinical trial you will need to submit a type-S ATC

application. However, where the criteria for a type-S ATC application cannot be met, a type-B ATC application is usually required.

Further details regarding the types of ATC application are provided below.

Type-A

You should submit a type-A ATC application if you wish to conduct a commercial clinical trial of a medicinal product that is already authorised (has an existing MA) for veterinary or human use in the UK or an EEA member country, and one of the following applies:

1. The product is a biological veterinary medicine (inclusive of immunological products and exclusive of human medicines) and the clinical trial is to be conducted in animals of the target species included in the existing MA, using a dosing regimen authorised for that species (or a lower dose) and the authorised route of administration.
2. The product is a non-biological veterinary medicine, the clinical trial is to be conducted in animals from a food-producing species, and the dosing regimen to be tested (dose, frequency of administration, and duration of a treatment course) is the same as (or lower than) the dosing regimen authorised for use in that species via the same route of administration.
3. The product is a non-biological veterinary medicine or human medicine, and the clinical trial is to be conducted in a companion animal species.

Where the criteria for a type-A ATC application cannot be met, a type-B ATC application is usually required.

Type-S

You should submit a type-S ATC application if you are a practising vet or researcher wishing to carry out a small-scale non-commercial clinical trial of a veterinary medicine or a human medicine and one of the following applies:

1. Biological veterinary medicine: The medicinal product is a biological veterinary medicine (inclusive of immunological products and exclusive of human medicines) with an existing MA granted in GB, NI, or an EEA member country and the clinical trial is to be conducted in animals of the target species included in the existing MA, using a dosing regimen authorised for that species (or lower) and the authorised route of administration.
2. Non-biological product studied in non-food animals: The medicinal product is a non-biological veterinary medicine or a human medicine and has an existing MA granted in the UK, Australia, Canada, an EEA member country, Japan, New Zealand, and/or the USA and the clinical trial is to be conducted in non-food animals (companion animals or other animals, including their products, declared to never enter the food chain).
3. Non-biological product studied in food-producing animals: The medicinal product is a non-biological veterinary medicine or a human medicine with an existing MA granted in the UK and/or an EEA member country and the trial is to be conducted in food-producing animals, and one of the following applies:

a) The clinical trial is to be conducted in a species included in the existing MA, the dosing regimen to be tested (dose, frequency of administration, and duration of treatment course) is the same as (or lower than) the dosing regimen authorised for use in that species via the same route of administration, and the associated withdrawal periods set out in the SPC will be observed.

b) The medicinal product contains only substances that are listed in Table 1 of the Annex to Commission Regulation 37/2010 (for NI) or the GB MRL list (for GB), and an appropriate withdrawal period has been set. For a type-S ATC application, withdrawal periods may be determined by reference to the principles set out in VMD guidance concerning the setting of withdrawal periods under the prescribing cascade.

c) The clinical trial is to be conducted in Horses, the active substance(s) tested are listed as ‘essential for the treatment of equidae or are substances bringing added clinical benefit’ according to regulation (EC) 122/2013, and a 6 month withdrawal period will be applied.

Where the criteria for a type-S ATC application cannot be met, a type-B ATC application is usually required. Should the criteria set out above not apply, it is recommended that you contact us at postmaster@vmd.gov.uk before submitting an ATC application.

Sample size

Small-scale non-commercial clinical trials will usually involve no more than 25 animals treated with the test product. However, where it is necessary to permit meaningful statistical analyses, larger sample sizes may be accepted, where adequate justification has been provided.

Design

To ensure robust study design and appropriate consideration of how to reduce, refine and replace the use of animals, the work should be conducted to recognised quality standards for published research, such as the Defra Joint Code of Practice for Research (JCoPR). In addition, the VMD expects that the work will be the subject of an ethical review.

Before initiating your trial, you should inform the MA holder of the authorised product under investigation. On completion of the trial, we expect that the results will be reported in compliance with the principles set out in the Animal Research: Reporting In Vivo Experiments (ARRIVE) Guidelines.

Type-B

You should submit a type-B ATC application where the nature of a clinical trial or the medicinal product(s) under investigation do not meet the criteria set out above for either a type-A (commercial clinical trial) or a type-S (small-scale non-commercial clinical trial) ATC application.

Tables to determine type of ATC application required

Contact us at postmaster@vmd.gov.uk if after using these tables you are still unsure which type of application to apply for.

Commercial clinical trials

Reference	Question	If Yes	If No
Q1.	Is the product authorised as a veterinary medicine or human medicine in the UK or an EEA member country?	Yes, go to Q.2	No = type-B
Q2.	Is the product a biological (including immunological and excluding human medicine) veterinary medicine?	Yes, go to Q.3	No, go to Q.4
Q3.	Is the trial to be conducted in the species included in the existing MA, using a dosing regimen authorised for that species (or lower), via the authorised route of administration?	Yes = type-A	No = type-B
Q4.	Is the trial to be conducted exclusively in non-food animals?	Yes = type-A	No, go to Q.5

Reference	Question	If Yes	If No
Q5.	Is the clinical trial to be conducted in a species of food producing animal included in the existing marketing authorisation for the medicinal product, using the dosing regimen authorised for that species (or lower), via the authorised route of administration, and observing the withdrawal periods in the SPC?	Yes = type-A	No = type-B

Small-scale non-commercial clinical trials in non-food animals

- companion animals
- horses declared never to enter the food chain
- other animals (including their products) declared to never enter the food chain

Reference	Question	If Yes	If No
Q1.	Is the product a biological (including immunological and exclusive of human medicine) veterinary medicine?	Yes, go to Q.2	No, go to Q.4

Reference	Question	If Yes	If No
Q2.	Is the product authorised as a veterinary medicine in the UK or an EEA member country?	Yes, go to Q.3	No = type-B
Q3.	Is the trial to be conducted in the species included in the existing MA, using a dosing regimen authorised for that species (or lower), via the authorised route of administration?	Yes = type-S	No = type-B
Q4.	Is the product authorised as a veterinary medicine or human medicine in the UK, Australia, Canada, an EEA member country, Japan, New Zealand, or the USA?	Yes = type-S	No = type-B

Small-scale non-commercial clinical trials in food producing animals

Reference	Question	If Yes	If No
Q1.	Is the product a veterinary medicine or a human medicine authorised in the UK or an EEA member country?	Yes, go to Q.2	No = type-B
Q2.	Is the product a biological (including immunological and excluding human medicines) veterinary medicine?	Yes, go to Q.3	No, go to Q.4
Q3.	Is the clinical trial to be conducted in the species included in the existing MA, using a dosing regimen authorised for that species (or lower), via the authorised route of administration?	Yes = type-S	No = type-B
Q4.	Is the veterinary medicine to be used in a species included in the existing MA, using a dosing regimen authorised for that species (or lower), via the authorised route of administration, and observing the withdrawal periods in the SPC?	Yes = type-S	No, go to Q.5

Reference	Question	If Yes	If No
Q5.	Are the pharmacologically active substances in the medicinal product listed in Table 1 of the Annex to Commission Regulation 37/2010 or on the GB MRL list?	Yes, go to Q.6	No, go to Q.7
Q6.	Will an appropriate withdrawal period be applied? An appropriate withdrawal period should be at least as long as the label withdrawal period and may be longer in accordance with the principles set out under schedule 4 (paragraph 2) of the Veterinary Medicines Regulations 2013.	Yes = type-S	No = type-B
Q7.	If the medicine is to be used for the treatment of horses, are the active substances listed as ‘essential for the treatment of equidae’ according to regulation (EC) 122/2013, and will a 6 month withdrawal period be applied?	Yes = type-S	No = type-B

When an ATC is not required

In certain situations an Animal Test Certificate (ATC) is not required.

A clinical trial involving a non-medicinal therapy does not require an ATC. For example, an ATC is not required for a clinical trial of a surgical intervention or a food supplement if the product(s) to be tested does not fall within the definition of a veterinary medicine when used in accordance with the study protocol. The definition of a veterinary medicine is set out under the Veterinary Medicines Regulations 2013 (VMR).

The retrospective analysis of clinical observations is not a clinical trial and therefore does not require an ATC.

A clinical trial carried out by a vet who will administer a veterinary medicine in accordance with the provisions of the prescribing 'cascade' or a clinical trial involving a veterinary medicine used fully in accordance with its Summary of Product Characteristics (SPC) may not require an ATC.

However, an ATC would be required if the study design prevented the prescribing vet from using their professional judgement during clinical decision making (for example, due to the use of randomisation), or when the medicines used during a clinical trial will not be labelled in accordance with the VMR (as might be necessary to facilitate the 'blinding' of study participants).

You can find more information on The Cascade: Prescribing unauthorised medicines.

Studies licensed in full by the Home Office under the Animals (Scientific Procedures) Act 1986 (ASPA), including laboratory studies, do not require an ATC if they are conducted in non-food animals or animals (including their products) declared never to enter the food chain.

Furthermore, for those studies in food-producing animals that have been licensed in full under the ASPA, an ATC is not required provided the veterinary medicine to be used has a marketing authorisation (MA) in GB, NI, or the EEA and is to be administered in accordance with this MA.

The authorised dosing regimen for the species and route of administration must be used, or a lower dose, and the withdrawal periods set out in the SPC must be observed.

If these criteria are not met, then a type-B ATC application to determine or justify an appropriate withdrawal period should be applied for.

Further information on how the Home Office regulates the use of animals in research can be obtained from the Home Office Animals (Scientific Procedures) Inspectorate and associated online guidance.

Number of clinical trials and products per ATC

Each clinical trial requires a separate Animal Test Certificate and should normally only study one therapeutic indication in a single species. Exceptions include clinical trials of ectoparasiticides, endectocides, or multivalent vaccines.

A clinical trial may involve more than one product if:

- the second product is a placebo control product
- the second product is a positive control that is authorised in the UK or at least one EEA member country for administration to the same species for the same indication
- the second product is a human medicine, its use is well supported by literature references, and there is no suitable authorised veterinary medicine
- the medicinal products are of the same pharmaceutical form and contain the same ingredients, but they differ in the strength or dosage of the active or inactive ingredients
- the medicinal products are vaccines and differ only in the inclusion or exclusion of particular antigens under study
- the medicinal 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 an allergy are manufactured by the same method from closely related substances, for example, pollen
- more than one product is expected to be required to produce therapeutic efficacy, for example, the administration of sedative or analgesic combinations or allergens.

Assessment of the application

When you submit an ATC application, we will conduct a benefit:risk assessment based on the data you provide. This assessment focuses on the risks associated with the proposed clinical trial and whether adequate safeguards are in place to ensure the safety of:

- the animals participating in the clinical trial
- those people using the medicines or handling treated animals
- the consumers of produce derived from treated animals
- the environment (where applicable)

For commercial clinical trials, applicants must confirm that the clinical trial will be carried out in accordance with the VICH guideline on Good Clinical Practices (GCP). Small-scale non-commercial clinical trials should also be conducted in compliance with GCP guidance where possible; however, it is recognised that this may not be possible in all situations.

If the benefit:risk assessment concludes positively and any other concerns have been addressed, the ATC application will be approved. We will send your Animal Test Certificate, verifying that the trial has been approved, although this may be subject to a number of conditions that will be specified on the certificate.

How to apply

Prior to submission

Before submitting your ATC application, you should first contact our Regulatory Affairs Section for more information and advice at postmaster@vmd.gov.uk.

If you require a meeting to discuss the ATC application, you should include ‘Request a company meeting’ in the subject line. A meeting is particularly important for those applications that concern the use of a biological or immunological product.

You must contact us before submitting applications involving veterinary medicines containing genetically modified (GM) organisms. A clinical trial in animals involving the deliberate release of GM organisms into the environment requires both an ATC and consent granted by the Secretary of State for the Environment before the trial can start.

This can take up to 90 calendar days, or longer if further information is needed from you, so you will need to apply for this well ahead of the ATC application.

Submission

You should submit your ATC application electronically using the VMDS Secure Messaging Service.

Validation

All applications are validated upon receipt to check that everything has been provided before we begin our assessment. It is up to you to identify and submit all the necessary information in support of your application. If the submission is incomplete, we may not be able to progress your application.

Supporting Data

The data and documents required in support of an ATC application will differ depending on the type of ATC application used (type A, B, or S).

Data requirements are listed in the respective application forms. Do not submit any data or information that has not been asked for; doing so will delay the application process. However, failing to submit full copies of any cited references (including cited scientific literature) may also delay the application process.

Evidence of an ethics committee approval should be provided, if available.

Target species safety and efficacy

Data to support the safety of veterinary medicines after administration to the target species are required for all applications.

For ATC applications that concern a non-biological veterinary medicine, data supporting the safety of the proposed product in the target species must, as a minimum, support safety of the medicinal product when it is administered according to the dose, dosing regimen, and route of administration proposed for the clinical trial.

As an exception to these requirements, for type-A or type-S ATC applications that concern a clinical trial of a veterinary medicine authorised in the UK or EEA and where the medicinal product(s) will be used in the authorised target species, it may not be necessary to submit target species safety data.

For a non-biological veterinary medicine to be eligible for such an exemption, the medicinal product should be used via the authorised route of administration and according to the authorised dosage regimen (dose, frequency of administration, and duration of treatment course) or lower.

Furthermore, consideration should be given to any special characteristics of the target population for a clinical trial and whether safety under the proposed conditions of use during the proposed clinical trial raise any concerns.

All type-B ATC applications for a biological veterinary medicine should be accompanied by a GLP compliant study to support safety.

For all ATC applications you need to provide evidence to support a reasonable expectation of efficacy when the test product is used in accordance with the trial protocol. For example, reference to laboratory efficacy studies, challenge studies, or pilot clinical trials under field conditions may be necessary.

ATC applicants may cross refer to relevant studies in the dossier of an authorised veterinary medicine provided they have a right of access.

The evaluation of field safety and/or efficacy may include the taking of a blood sample prior to the administration of a medicinal product to

establish a baseline for parameters. It may also include additional sampling at key points after administration of the medicinal product to monitor these parameters, but this must be clinically justified.

It is anticipated that animals treated during a veterinary field trial with the medicinal product under investigation will be compared with a control group. Therefore, the veterinary field trial may include either:

- a group of animals designated as positive controls and treated with an existing veterinary medicine, an established procedure, or a human medicine provided its use is well supported and there is no suitable authorised veterinary medicine; or
- a group of animals designated as negative controls and treated with a placebo product or another type of negative control, provided this is adequately justified. In such cases, the study protocol must include adequate safeguards for animal welfare and accord with the principles of the 3Rs

Manufacturing information

Clinical trials to be conducted under an ATC obtained via a type-B ATC application must comply with the current revision of the Note for guidance on minimising the risk of transmitting animal spongiform encephalopathy agents via human and veterinary medicinal products (EMEA/410/01). You must provide appropriate information to confirm that this is the case.

Protocol

For type-A or type-B ATC applications, a clinical trial protocol must be submitted. We do not approve trial protocols but will review them to ensure that any safety issues are adequately addressed. You must ensure that the results of your clinical trial, carried out in accordance with the submitted protocol and under the ATC issued, will be appropriate for any subsequent MA applications.

For a type-S ATC application, the senior investigator and two veterinary surgeons independent of the trial must review the protocol. They must sign a declaration (section 6 of the application form) to confirm that, in their opinion, the study is ethical and is to be

conducted in accordance with the RCVS Code of Professional Conduct and ‘recognised veterinary practice’.

Consent form

For a type-A or type-B ATC application a blank example owner consent form must be submitted. Informed consent is a documented process by which an owner, or owner’s agent, voluntarily confirms the owner’s willingness to allow their animal(s) to participate in a particular study, after having been informed of all aspects of the study that are relevant to the decision to participate.

The consent form should be written in plain English and include at least the following:

a) Confirmation that the owner understands:

- the nature of the trial and the purpose of the treatment
- that animals are participating in a clinical trial using a medicinal product that has not been authorised or is being used ‘off-label’
- that their animal(s) may not receive active treatment as part of the clinical trial if a negative control or placebo control group are being included
- that they can withdraw their animal from the trial at any time without prejudice to the future veterinary care of the animal

b) A statement from the vet concerned confirming that if the animal is not responding to treatment that they may treat the animal at any time to maintain an appropriate level of veterinary care

c) Confirmation that the owner has fully understood the consent form

d) The owner’s consent to the inclusion of their animal(s) in the clinical trial

Labelling

Medicinal products administered in accordance with an Animal Test Certificate (ATC) are subject to the normal labelling requirements set out in the Product Literature Standard.

For authorised veterinary medicines you should use the approved labelling but with a small over label to indicate any amended directions or warnings, the ATC number, and the words “Veterinary clinical trial use only” to ensure accountability in line with GCP requirements.

We expect labels to contain the following minimum information in English:

- the words “For veterinary clinical trial use only”
- name or other designation of the medicinal 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 medicinal 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 a food-producing species (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 the identity of the medicinal products, including placebo products, used in the trial are blinded

You can use a package leaflet if there is insufficient space on the label to include all required text.

For a type-S ATC application you must submit for assessment a statement of the user and target species safety warnings that will

appear on the product label and/or leaflet. It is your responsibility to ensure that the product label and/or leaflet conform to VMD requirements.

However, a statement of the warnings is not required for GB, NI, EEA, or EU authorised veterinary medicinal products for which the labels and product literature are in English or if the medicinal product is to be administered directly by the investigator and there is no subsequent risk to other persons and adverse effects are not likely to occur after the animal has left the investigator's direct supervision.

Additional guidance on the warnings can be found in annex 1 of the application form (type-S ATC application form).

Example labels can be found on the ATC application forms page.

Application Forms

- Apply for a new certificate
- Apply to change a certificate
- There is no application form to renew a certificate

Post authorisation surveillance

Safety, quality and efficacy

During a clinical trial, if evidence becomes available which casts doubt on the safety, quality, or efficacy of the veterinary medicine(s) involved or alters the benefit:risk assessment we may revoke, suspend, or compulsorily vary the Animal Test Certificate (ATC).

If we become aware that an ATC holder has changed the approved test product formula or the clinical trial protocol (e.g., dosing regimen, critical design elements relating to safety monitoring, or named personnel) without our prior approval, the ATC will be suspended immediately. The suspension will remain in force until the changes have been approved, or the medicinal product is brought into line with the terms and conditions of the certificate.

Pharmacovigilance

You are responsible for reporting adverse events (AEs) to us and a person responsible for pharmacovigilance, usually a vet, must be named in your application. They will have overall responsibility for investigating and monitoring any suspected AEs and, when necessary, reporting them to us.

You must put in place appropriate arrangements to ensure that 'blinding' of products does not interfere with pharmacovigilance responsibilities and that study personnel notify the responsible person if AEs occur, which must be reported to us within 30 days of the event.

AEs as a result of a substance used under an ATC could include, but are not limited to:

- death or increased rates of death in a species for which there is an accepted death rate
- life-threatening clinical signs
- persistent or significant disability/incapacity
- congenital anomalies or birth defects
- permanent or prolonged signs in the animal(s) treated
- a reaction involving a human

Suspected lack of efficacy must also be reported. See Veterinary Pharmacovigilance: your responsibilities for further information on reporting adverse events.

You should keep appropriate records of AEs that may occur following administration of the medicine, control or placebo including those which are not serious. A summary of all the AEs that occur during a clinical trial must be submitted for review if the associated ATC is to be renewed.

For studies conducted under GCP the clinical trial protocol should include the procedures for observing animals and should ensure observations are sufficient to allow the detection of AEs. The protocol should include the appropriate action to take when AEs are observed, how these AEs should be recorded in study documentation, and the procedures to follow when reporting AEs to the sponsor.

Variations to ATCs

If you wish to make any changes to your certificate, you must submit an Animal Test Certificate (ATC) variation application. Only certain changes may be made by way of a variation and these permitted changes are listed in the application forms available at Apply to change an animal test certificate. All other changes will require submission of a new ATC application.

Where a new application is necessary to accommodate the changes to an ATC obtained following a type-B ATC application, the timescales for a new type-A ATC application will apply as long as the product formula, target species, and the purpose of the trial remain the same.

We recognise that some test sites cannot be set up until an outbreak of a particular disease occurs and in such cases an ATC may be issued for a maximum number of sites and animals, on the condition that you notify us of the test sites' details as soon as they are known.

These details should include the name and address of the test site, the exact number of animals included at the site, and the name of the site investigator. There will be no charge for this.

Renewals to ATCs

An Animal Test Certificate (ATC) is valid for 2 years. If the trial is not finished within this period, you can apply to renew your certificate. There is no application form for the renewal of an ATC, but you must email a letter to s.response@vmd.gov.uk requesting the renewal at least one month before your ATC expires.

If a certificate is not renewed by the expiry date it will cease to be valid and, to continue the clinical trial, you would need to submit a new ATC application.

The ATC renewal letter should include a justification for why the ATC needs to be renewed, any variations made to the ATC, a copy of the certificate itself, the ATC number, any relevant information concerning the progress of the clinical trial, and a summary account of any adverse events observed.

Application timescales

Further information about ATC application timescales can be found on the Timetables for national applications page.

Fees

Once an application has passed validation, you will be sent an invoice for the fee. For further information regarding fees, see the Fees applied to animal medicine authorisation applications page.

Contact us

For all other enquiries that concern ATCs please email: postmaster@vmd.gov.uk