Bundesamt für
Sicherheit im
Gesundheitswesen
BASG

Guidance for submission and authorisation of clinical trials for veterinary medicinal products

Content:

1 APPLICATION FOR APPROVAL OF A VETERINARY CLINICAL TRIAL

1.1 Content of the application

An application for the approval of a clinical trial of a veterinary medicinal product in accordance with Article 9 of Regulation (EU) 2019/6 shall contain in addition to the cover letter, the complete application form F_Z135_Application Form_Clinical_Trial_veterinary' and the documents as listed in the Annex to the application form.

The cover letter must either be signed by the applicant and the duly completed application form by the sponsor and the head of study electronically or provided as a scanned signed original.

The sponsor is responsible for the accuracy and completeness of the information contained in the signed application form, including the documents specified in the Annex.

1.2 Submission of the request

The application form and the documents required for the evaluation shall be submitted electronically via CESP. The documents must be divided into individual folders Part 1 — Part 4), as listed below.

The copy function should not be restricted in all submitted PDF documents, except for scanned documents. This prevents from any unnecessary parallel submission of information in Word format.

General information on CESP submissions can be found under "Electronic Submission".

1.2.1 Technical advice on CESP submission:

1.2.1.1 Entries in the delivery file:

in the field "Regulatory Activity:" Clinical trial

in the field "Comment:"

- at submission of the application: Application_YYYYMMDD
- in case of subsequent submission for validation: (submission of missing documents, if necessary) Response_VAL_YYYYMMDD_VNR
- in the case of subsequent submission after validation: (resolving of technical deficiencies after validation, if necessary; notification of changes, final report) Response_YYYYMMDD_VNR

1.2.1.2 The following folder structure should be used:

P1

1a-admin-info
Cover letter, application form (linked), proof of qualification of the head of study, declaration of consent for animal owners (linked), other administrative information/data

1b-spc_investigational veterinary medicinal product
SPC and/or information on the investigational veterinary medicinal product

1c-spc_control product
SPC and/or information on the control product

P2

Quality documentation (linked)

P3

3a user safety

Documentation on user safety and special precautions for users including for pet owners and people living in the same household

3b residue studies

Documentation on residue studies (linked)

3c withdrawal period

Documentation on withdrawal period (linked)

P4 Efficacy documentation

4a-preclin

Documentation on pharmacology, toxicology, target animal safety, dose justification

4b-clin

Clinical trial documentation (linked)

1.3 Confirmation of receipt

An acknowledgement of receipt including the assigned own procedure number will be sent by e-mail to the applicant's e-mail address provided in the application form at:

- Initial application

Confirmations of receipt by e-mail of the assigned procedure number will also be sent to:

- Submission of requested additional information
- Request for substantial modifications to the study protocol
- Submission of the opinion of the Ethics and Animal Welfare Commission
- Notification of the end of the clinical trial or notification of a temporary halt/early termination or non-start of the clinical trial
- Submission of the final report after completion of the study

In the case of requests concerning the procedure, the assigned procedure number must always be indicated.

Important: Correspondence with the applicant shall be made exclusively to the address indicated in the application form under the field "applicant". The timeliness of the information is the responsibility of the sponsor.

1.4 Opinion of the responsible Ethics and Animal Welfare Committee ("ETK")/Animal testing permit

A clinical trial may not be started until the animal study has been approved and a positive opinion has been received by the responsible Ethics and Animal Welfare Committee. The required submission to the competent ETK may be made before or simultaneously with the submission of the application to the BASG, but not thereafter. The date of submission to the responsible ETK must be indicated in the cover letter (cover letter) and the application form. If already available, the opinion of the ETK should be attached to the application documents.

If a rejection is made by the ETK, the application for approval of the clinical trial will be refused by negative decision of the BASG (see 3.4.3.).

Information on submission can be found on the following websites:

- Ethics and Animal Welfare Committee of the University of Veterinary Medicine Vienna

  https://www.vetmeduni.ac.at/
- Austrian Federal Ministry of Education, Science and Research (https://www.bmbwf.gv.at/Themen/Forschung/Forschung-in-%C3%96sterreich/Services/TierV.html)

1.5 Studies with other/additional requirements

For clinical trials of veterinary medicinal products for gene therapy or veterinary medicinal products containing genetically modified organisms (GMOs/GMOs), in addition to submission to the BASG, an application at the Austrian Federal Ministry of Social Affairs, Health, Care and Consumer Protection (BMSGPK) is required.

Clinical trials of veterinary medicinal products against animal diseases pursuant to §16 Tierseuchengesetz also require an approval by the BMSGPK.

If the BMSGPK refuses to carry out such studies, the application for approval of the clinical trial shall also be refused by negative decision by the BASG, provided that this has already been submitted to the BASG (see 3.4.3.).

2 FEES

Applications to conduct a clinical trial are subject to a fee. The applicable fee rate can be found on the website of the BASG (see BASG-fee-rate). The fees are indexed.

By default, the invoice will be issued to the applicant who will be charged as a party subject to payment. If the recipient of the invoice or the party liable to pay is not identical to the applicant, this must be clearly indicated in the cover letter. It is necessary to distinguish to whom the invoice is to be sent and to whom the invoice is to be issued (if possible, with these wordings).

3 VALIDATION AND ASSESSMENT BY THE AUTHORITY

Important: Correspondence with the applicant shall be made exclusively to the address indicated in the application form under the field "applicant". The timeliness of the information is the responsibility of the sponsor.

3.1 Validation phase

The sponsor must submit a complete application for approval of the clinical trial. The check of the validity of the application with regard to the formal completeness of the submitted dossier should be completed by the BASG within 14 days (validation period). Within this period, an application which has not been properly received (= formally not complete), the applicant may be requested by e-mail to provide the missing or corrected documents. The application shall be deemed to be correct only after receipt of all requested or revised documents via CESP.

The valid application (= formal completeness) will be confirmed by a positive validation letter from the BASG. The validation letter will be sent by e-mail to the applicant.

3.2 Assessment phase

The date of formal completeness defines the start of the assessment period. The BASG then verifies the basic justification and relevance of the project and the requirements for the manufacture of investigational veterinary medicinal products in accordance with Good Manufacturing Practice (GMP) or an equivalent manufacturing practice. The study plan for the clinical trial is assessed based on the data submitted with the application (considering the Guideline on the principles of regulatory acceptance of 3Rs (replacement, reduction, refinement) testing approaches (EMA/CHMP/CVMP/JEG-3Rs/450091/2012)) and other evidence. The evaluation of the application shall take place within 60 days.

If the clinical examination is to be carried out on animals used for the production of food, the scientific assessment submitted on the requested withdrawal periods shall be assessed by the BASG within the prescribed 60-day time limit, so that the animals themselves or their products can enter the food chain after the end of the study.

If the requirements are fulfilled and there are no substantial deficiencies determined during the assessment, the BASG will authorise the application for approval of the clinical trial by means of a positive decision (see 3.3.1).

Should substantial deficiencies be determined during the assessment, the required information/documents will be notified to the applicant by a list of questions (LOQ) pursuant to § 13(3) AVG (see 3.3.2) by e-mail. The applicant shall submit the requested additional information as required according to the list of question within a period of 90 days set by the BASG from the receipt of the request. If the required documents are not submitted within this period or are not complete, the application for approval of the clinical trial will be refused by a negative decision (see 3.3.3). In case of a satisfactory response to the open questions, the BASG will authorise the application for approval of the clinical trial by means of a positive decision (see 3.3.1).

3.3 Conclusion by the BASG/End of Procedure

3.3.1 Authorisation of the application for approval of a clinical trial

An application shall be deemed approved if a positive opinion has been issued by the ETK and no objection has been made by the BASG within the 60 days from the date of formal completeness (positive validation). All applications are subject to an issued license by the BASG. The applicant will receive a written decision by e-mail.

Applications under section 1.5, which require also a permission by the BMSGPK and the ETK and which have already been approved by them, will also be authorised by the BASG by means of a positive decision if no objection has been raised by the BASG itself.

3.3.2 List of Questions (LOQ) in accordance with § 13(3) AVG

The sponsor shall be informed by a list of questions (LOQ) that the submitted documentation and data are insufficient or do not apply to the state of scientific evidence and/or the requested clinical trial is not appropriate for demonstrating the safety and/or efficacy of a veterinary medicinal product. The LOQ will be sent electronically to the e-mail address of the applicant's address entered in the application form. Within a period of 90 days, the application has to be amended accordingly by submitting the required information/documents. The responses to the LOQ must be made in writing and must be submitted to the assigned procedure number together with any amended documents by CESP. If the sponsor fails to comply with the amendment or if the LOQ has not been adequately addressed, the application of the approval of the clinical trial will be rejected by a negative decision made by the BASG (see 3.3.3).

If the responses to the LOQ are satisfactorily addressed, the approval procedure will be concluded by the BASG by issuing a positive decision, which the applicant will receive by e-mail.

3.3.3 Rejection of the application for approval of a clinical trial

The BASG shall declare the rejection by means of a negative decision if the objections to the application for approval of the clinical trial, which were communicated to the applicant in the LOQ, have not been satisfactorily resolved within the set time limit.

Accordingly, the BASG must declare the rejection by means of a negative decision if the ETK or the BMSGPK has confirmed a negative opinion.

4 REPORTING OBLIGATIONS OF THE APPLICANT DURING THE CONDUCT OF THE CLINICAL TRIAL

4.1 Substantial modifications to the Study Plan

All major amendments, in particular those affecting the safety of the study animals, on the quality or safety of the investigational veterinary medicinal product, on the interpretation of the test results or on the overall scientific value of the study, shall be notified to the BASG without delay. The amendment must contain a cover letter with a summary and justification of the modifications made, as well as the amended documents. All documents must be submitted via CESP to the assigned procedure number. The updated parts of the dossier shall be presented in the initial dossier and with the highlighting of the

amendments (track change mode). Furthermore, the main changes must be summarised, described and justified separately.

The BASG shall carry out the assessment of the modified dossier within a 60-day review period, provided that the scope of the change permits that. In case that the assessment period of 60 days is considered insufficient for the BASG due to the scope of the amendment, the study must be submitted again. The initial application for approval of the clinical trial will be rejected by a negative decision.

4.2 Other modifications

Other non-substantial changes to the study plan should be reported to the BASG informally by e-mail to basg-heve@basg.gv.at.

If an amendment concerns the application form, an updated version of the application form must be submitted via CESP without delay in order to ensure that this information is up-to-date.

4.3 Reporting of suspected adverse events

All reports of suspected adverse events from clinical trials for veterinary medicinal products shall be included in the Union Pharmacovigilance Database in accordance with the requirements of Article 76(1) and (2) of Regulation (EU) 2019/6 and the Guideline on veterinary good pharmacovigilance practices, Modules: "Collection and recording of suspected adverse events for VMPs".

The marketing authorisation holder or head of study is obliged to report any suspected adverse events observed during the study at the latest within 30 days of the completion of the final study report to the Union pharmacovigilance database or to the BASG.

5 END OF THE CLINICAL TRIAL

When the study is finalised according to the study plan, the sponsor must send an e-mail to basg-heve@basg.gv.at within 30 days after the end of the study.

In the event of an early termination, i.e. in case of a discontinuation or non-start of the study, the sponsor shall report on the early termination or non-start of the clinical trial to the BASG within 15 days, clearly stating all the reasons for the deviation. The notification must also be made by e-mail to basg-heve@basg.gv.at.

6 REPORTING OBLIGATIONS AFTER COMPLETION OF THE CLINICAL TRIAL

The sponsor shall ensure the completion of a clinical trial summary report within one year of the end of the study. The final report has to be submitted to the BASG via CESP indicating the procedure number of the initial application for approval of this clinical trial.

7 LABELLING OF INVESTIGATIONAL VETERINARY MEDICINAL PRODUCTS

The sponsor shall make available the sufficiently characterised and labelled investigational veterinary medicinal product which has been manufactured in accordance with the Operations Ordinance pursuant to § 62 of the Austrian Medicines Act (AMG) or, if the investigational substance was not manufactured in Austria, in accordance with internationally recognised standards.

Investigational veterinary medicinal products, except in justified cases for carrying out a study, shall contain, the following information on the labelling, indicated on the containers and, where used, on the outer package in user-friendly writing, generally understandable in German and in a sustainable manner:

1. Name of the sponsor or the applicant, address and telephone number (including contact person),
2. Name and strength of the investigational veterinary medicinal product;
3. Batch identification/number,

4. Pharmaceutical form,
5. Content by weight, volume or package size,
6. Target species(s),
7. Route(s) of administration,
8. Dosage regime including dose interval, duration of treatment or in accordance to an accompanying document or the instruction of an investigator,
9. Withdrawal period for investigational preparations intended for food-producing animals;
10. Expiry date preceded by the abbreviation "Exp {mm/yyyy}" or, if the nature of the investigational veterinary medicinal product permits, date of retesting;
11. Protocol number/study ID that allows identification of the clinical trial, the testing site(s), the investigator and the sponsor, unless included in an accompanying document that can be handed over to the person concerned;
12. For preparations intended for use in veterinary clinical trials, the words: 'for veterinary clinical trial use only' shall appear prominently and indelibly;
13. Storage conditions or special storage precautions;
14. Note that the investigational veterinary medicinal product should be kept out of the sight and reach of children, provided that the investigational veterinary medicinal product is intended to be administered by the animal keeper;
15. Special precautions for disposal of unused investigational veterinary medicinal product, information on other take-back schemes for the disposal or other special precautions to avoid any risks to the health of unaffected persons and to the environment.

In case of small containers, at least the information referred to in points 1, 2, 3, 7, 9, 11, 12 shall be contained. The information referred to in No. 1-15 may also be included in an accompanying document. The information referred to in point 12 shall be clearly visible and indelible on the containers.

8 IMPORT/SHIPMENT OF INVESTIGATIONAL VETERINARY MEDICINAL PRODUCTS

According to § 6(2) of the Austrian Medicines Import Act (AWEG 2010), the shipment of medicinal products within the European Economic Area (EEA) does not require any notification for clinical studies of veterinary medicinal products.

Investigational preparations for clinical trials manufactured or authorised in Switzerland and transported from Switzerland to Austria, do not require notification either (see § 6(2) and § 14(8) AWEG).

Provided that veterinary medicinal products manufactured outside the EEA have been released to the EU by a Qualified Person, the above provisions are also applicable.

Irrespective of the provisions of the AWEG 2010 and irrespective of the country of origin and marketing authorisation status, an import certificate from the BMSGPK is required in all cases for medicinal products and blood products containing narcotic drugs or psychotropic substances (https://www.sozialministerium.at/en/).

9 ANNEXES TO THE APPLICATION FORM

Summary of the documents and documents to be attached to the application:

1. Cover letter signed by the applicant electronically or as a scanned signed original
2. Current Summary of Product Characteristics (SPC) of the investigational veterinary medicinal product (if the investigational (veterinary) medicinal product is authorised)
3. Current Summary Product Characteristics (SPC) of the control product (for controlled studies with positive control group)
4. Documentation on pharmaceutical quality and manufacturing of the investigational veterinary medicinal product including GMP, GMP equivalent or QP declaration
5. Clinical Trial Study Plan, incl. GCP compliance according to VICH GL 9 Good Clinical Practices

6. Preclinical documentation (pharmacology, toxicology, user safety data)
7. Scientific justification of the proposed withdrawal period (if necessary) and data on residue studies (if available)
8. Information on the target animal safety
9. Information on the dose justification
10. Statistical protocol according to EMA/CVMP/EWP/81976/2010-Rev.
11. Information for the head of study ("investigator's brochure"): including Reference Safety Information (RSI) on the investigational medicinal product, if no SPC exists
12. Proof of qualification of the head of study
13. Recruitment methodology
14. Information letter for the pet owner
15. Declaration of consent of the pet owners or holders of the study animals
16. Opinion of the responsible Ethics and Animal Welfare Committee (ETK)/Animal testing permit
17. Opinion of the BMSGPK in studies with GMOs or investigational medicinal products against animal diseases pursuant to §16 Austrian Animal Diseases Act (if applicable)
18. Other investigators involved in this study
19. Others, please specify (e.g.: BMSGPK import certificate for investigational veterinary medicinal products with addictive or psychotropic substances)

10 Contact

If you have any questions, please contact the following e-mail address: basg-heve@basg.gv.at

11 Links

- Regulation (EU) 2019/6 on veterinary medicinal products and repealing Directive 2001/82/EC: REGULATION (EU) 2019/6
- Austrian Medicines Product Act — AMG; BGBl No 185/1983 as amended: AMG
- Labelling Ordinance 2008; BGBl. II No 174/2008 as amended: Labelling Ordinance
- Austrian Medicines Import Act 2010 — AWEG 2010; BGBl. I No 79/2010 as amended: AWEG
- Austrian Regulation on Fees (Verordnung des Bundesamtes für Sicherheit im Gesundheitswesen über den Gebührentarif gemäß GESG): https://www.basg.gv.at/ueber-uns/gebuehrentarif
- Austrian Federal Ministry of Social Affairs, Health, Care and Consumer Protection (BMSGPK) https://www.sozialministerium.at/
- Austrian Federal Ministry of Education, Science and Research https://www.bmbwf.gv.at/Themen/Forschung/Forschung-in-%C3%96sterreich/Services/TierV.html
- Ethics and Animal Welfare Committee of the University of Veterinary Medicine Vienna https://www.vetmeduni.ac.at/
- Guideline on the principles of regulatory acceptance of 3Rs (replacement, reduction, refinement) testing approaches (EMA/CHMP/CVMP/JEG-3Rs/450091/2012): https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-principles-regulatory-acceptance-3rs-replacement-reduction-refinement-testing-approaches_en.pdf
- Guideline on statistical principles for clinical trials for veterinary medicinal products (pharmaceuticals) EMA/CVMP/EWP/81976/2010-Rev.1: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-statistical-principles-clinical-trials-veterinary-medicinal-products-pharmaceuticals-rev-1_en.pdf
- Guideline on veterinary good pharmacovigilance practices (VGVP), Modules: Collection and recording of suspected adverse events for veterinary medicinal products EMA/306663/2021: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/guideline-veterinary-good-pharmacovigilance-practices-vgvp-module-collection-recording-suspected_en.pdf

- VICH GL9 Good clinical practices VICH GL9 Good clinical practices: https://www.ema.europa.eu/en/vich-gl9-good-clinical-practices