

Based on Article 51 paragraph 4 of the Law on Medicines and Medical Devices (*Official Gazette of the Republic of Serbia*, No. 84/04 and 85/05 – other law),

The Minister of Agriculture, Forestry and Water Management hereby passes

THE RULES GOVERNING CLINICAL TRIALS OF MEDICINES USED
EXCLUSIVELY IN VETERINARY MEDICINE

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I. BASIC PROVISIONS

Article 1

These Rules shall regulate the terms and manner of conducting clinical trials of medicines used exclusively in veterinary medicine (hereinafter: veterinary medicines), as well as the procedure and contents of the documents required for approving clinical trials of veterinary medicines.

Article 2

The provisions of these Rules may not be applied to post-marketing non-interventional clinical trials of veterinary medicines.

Article 3

The terms used in these Rules shall have the following meaning:

- 1) Clinical trial of a veterinary medicine means a trial conducted on a target animal species or a specific category of animals, with a view to discovering, establishing or verifying clinical, pharmacological or pharmacodynamic effects of one or more investigational medicines, as well as testing the absorption, distribution, metabolism and excretion of one or more veterinary medicines in order to establish their safety, efficacy and therapeutic effects;
- 2) Post-marketing interventional clinical trial of a veterinary medicine means a trial in which the veterinary medicine is applied under the conditions contained in the marketing authorisation for the veterinary medicine, requiring additional diagnostic procedures, as well as the monitoring procedures defined in the protocol on the clinical trial of the veterinary medicine;
- 3) Post-marketing non-interventional clinical trial of a veterinary medicine (pharmacoeepizootiological testing) means a trial in which a veterinary medicine is applied under the conditions contained in the marketing authorisation for the veterinary medicine and in which the selection of the animal is not determined in advance by a clinical trial protocol, but rather is a part of the established treatment practice, the prescription of the veterinary medicine being clearly separated from the decision to include the animal in the trial. Additional diagnostic or monitoring

- procedures are not applied, while the received results are analysed through epizootiological methods;
- 4) Multi-centre clinical trial is the clinical trial of a veterinary medicine conducted under a single protocol at more than one trial site by more than one investigator, irrespective of whether the trial sites are in the same country or in different countries;
 - 5) Investigational veterinary medicine means a pharmaceutical form or formulation of an investigational active substance or combination of substances, as well as a veterinary medicine which has a marketing authorisation when the form or the packaging is changed or when it is used in a manner different from that approved in the authorisation, when the veterinary medicine is tested to be applied for a new indication, or when it is used for obtaining new information on the approved application of the veterinary medicine in question;
 - 6) Comparative medicine means an investigational veterinary medicine or a veterinary medicine from the market, constituting active control with which the investigational veterinary medicine is compared.
 - 7) Investigational animal means an animal on which clinical trials of a veterinary medicine are conducted, regardless of whether the animal uses the investigational veterinary medicine or is included in order to control the use of the veterinary medicine, i.e. if the animal is administered a veterinary medicine with which the investigational veterinary medicine is compared;
 - 8) Sponsor of the clinical trial of a veterinary medicine means the manufacturer, financier of the clinical trial, as well as the investigator conducting the clinical trial; the sponsor is responsible for conducting the clinical trial of a veterinary medicine;
 - 9) Site of the clinical trial of a veterinary medicine means a veterinary institution or a facility or space in which animals are held or bred, which meet the requirements concerning the personnel, equipment and premises for treating animals and in which the clinical trial of a veterinary medicine is conducted;
 - 10) Institution for the clinical trial of a veterinary medicine is a veterinary institute or a legal person conducting clinical trials of veterinary medicines under the law;
 - 11) Contract Research Organisation (CRO) means a legal or natural person concluding a contract with the sponsor of the clinical trial of a veterinary medicine, based on which the legal or natural person assumes all or a part of the sponsor's powers, and is responsible for the assumed powers in conducting the clinical trial of a veterinary medicine;
 - 12) Investigator in a clinical trial means a person that is directly involved in the clinical trial of a veterinary medicine and that is responsible for the tasks entrusted to him/her in conducting the clinical trial of a veterinary medicine;
 - 13) Chief investigator means a person responsible for conducting the clinical trial of a veterinary medicine in an institute for clinical trials of veterinary medicines;
 - 14) Investigator's brochure means a document containing analytical, pharmacological-toxicological, immunological and clinical data on an investigational veterinary medicine that are important for investigating the effects of the veterinary medicine on an animal;

- 15) Clinical trial protocol (hereinafter: the protocol) means a document that contains the objectives, design, methodology, statistical considerations and organisation of clinical trials of veterinary medicines, criteria for including an animal in a trial and therapy, as well as precautions, all under Good Clinical Practice guidelines for clinical trials of veterinary medicines;
- 16) Protocol amendments mean a document on amendments to the protocol or a formal explanation of the protocol;
- 17) Documentation of a clinical trial means complete records in any form (including written, electronic, magnetic and optical recordings, as well as scans, X-ray, electrocardiograms, etc.), describing or recording the methods applied, conduct of a trial and its results, all undertaken activities and factors affecting the clinical trial of a veterinary medicine;
- 18) Report on a clinical trial of a veterinary medicine means a document on the entire investigation of the therapeutic, prophylactic or diagnostic efficacy of an investigational veterinary medicine, listing clinically and statistically significant consolidated data, findings and analyses of the received trial results; in other words it means a written report on the development, results and conclusions of a trial in accordance with Good Clinical Practice guidelines for clinical trials of veterinary medicines;
- 19) Report on the development of the clinical trial of a veterinary medicine means a report on the trial results and an assessment arising from the conducted analyses within a specific time interval in the course of the clinical trial;
- 20) Good Clinical Practice in clinical trials of veterinary medicines (GCP) means a set of internationally recognised ethical and professional standards concerning the quality of planning, implementing, documenting, reporting and conducting clinical trials on animals, ensuring the protection and welfare of animals and the protection of the rights of the animal's owner, in order to reach valid clinical conclusions, at the same time extending adequate protection to the participants in the trial;
- 21) Inspection of the implementation of Good Clinical Practice guidelines in clinical trials of veterinary medicines means a procedure through which the Medicines and Medical Devices Agency of Serbia (hereinafter: the Agency) controls if a clinical trial is conducted in accordance with the trial protocol, Good Clinical Practice guidelines for clinical trials of veterinary medicines and with the positive regulations, at the clinical trial site, in an institute for clinical trials of veterinary medicines, or in the premises of another legal or natural person to which the sponsor has transferred powers or a part of powers in the clinical trial of a veterinary medicine, or, as required, at other relevant sites;
- 22) Consent of the animal's owner means the owner's dated and signed written statement whereby he/she confirms his/her consent to the effect that a clinical trial of a veterinary medicine should be conducted on an animal owned by him/her, made voluntarily upon receiving oral and written information on all aspects of the trial, which is relevant for making a decision on the animal's inclusion in the clinical trial;
- 23) Ethics Committee means an independent body whose duty is to ensure the protection of the rights, safety, welfare and health of the animals included in a

- clinical trial. The Committee's composition and functioning, as well as operational and other regulations pertaining to the Committee, must be in accordance with Good Clinical Practice guidelines for clinical trials of veterinary medicines;
- 24) Standard Operating Procedures (SOP) mean detailed written instructions for achieving the uniformity of all procedures in conducting clinical trials of veterinary medicines;
 - 25) Auditor means a specially qualified person who independently assesses, on behalf of the sponsor, compatibility of all activities concerning a clinical trial of a veterinary medicine with the protocol, the sponsor's Standard Operating Procedures (SOP), Good Clinical Practice guidelines for clinical trials of veterinary medicines, the law and these Rules;
 - 26) Auditing report means the auditor's written report on the results of the conducted audit;
 - 27) Monitor means a specially qualified person monitoring the conduct of clinical trials of veterinary medicines, guaranteeing that the development, documentation and reports on a clinical trial of a veterinary medicine are in accordance with the protocol, the sponsor's Standard Operating Procedures (SOP), Good Clinical Practice guidelines for clinical trials of veterinary medicines and positive regulations;
 - 28) Monitor's report means the monitor's written report to the sponsor of a clinical trial of a veterinary medicine upon each visit to the trial site, as well as a report on all other data concerning the clinical trial, in accordance with the sponsor's Standard Operating Procedures (SOP);
 - 29) Ensuring the quality of clinical trials of veterinary medicines means all planned and systemic activities undertaken to ensure the conduct of a clinical trial, as well as entering, storing and analysing data under Good Clinical Practice Guidelines for clinical trials of veterinary medicines and under positive regulations;
 - 30) Adverse reaction to a veterinary medicine in a clinical trial means any harmful and unintended response to the veterinary medicine which occurred in the course of the clinical trial and which is related to any dose of the veterinary medicine used in the prophylaxis, diagnosis or treatment of an illness or with a view to improving or modifying physiological functions;
 - 31) Serious adverse reaction to a veterinary medicine in a clinical trial is any harmful and unintended response to the veterinary medicine which may occur in the course of the clinical trial, resulting in reduced ability or congenital anomalies or a birth defect, prolonged or persistent symptoms in the treated animals, as well as direct life threat, including death;
 - 32) Untoward adverse reaction means a response to a veterinary medicine whose nature, gravity or outcome are not known or described in the summary of characteristics of the veterinary medicine or in the investigator's brochure, and are not to be expected in view of the known pharmacological characteristics of the veterinary medicine;
 - 33) Adverse event in a clinical trial means any adverse occurrence which took place in the course of administering a veterinary medicine and for which a cause-and-effect link with the application of the veterinary medicine may not be proved. An

- adverse occurrence means any unintended or adverse sign (e.g. abnormal laboratory findings), a symptom or an illness, chronologically connected with administering the medicine;
- 34) Serious adverse event in a clinical trial means an adverse occurrence which took place in the course of the clinical trial of a veterinary medicine for which a causal link with receiving or administering the veterinary medicine has not been proven, and which results in significantly reduced ability or congenital anomalies or a birth defect, prolonged or persistent symptoms in the treated animals, as well as direct life threat, including death;
- 35) Observance of the adopted design of a clinical trial means abiding by all requirements of the trial design, Good Clinical Practice in clinical trials of veterinary medicines and by positive regulations.

II. TERMS AND MANNER OF CLINICAL TRIALS OF VETERINARY MEDICINES

1. COMMON PROVISIONS

Article 4

The objective of clinical trials of veterinary medicines shall be to demonstrate and confirm the effect of a veterinary medicine upon administering the recommended dose, to establish indications and contraindications of a veterinary medicine in accordance with the species, breed, age, gender and category of the animal, as well as to establish the manner of development of any adverse reaction which may occur in the course of the clinical trial of a veterinary medicine, as well as safety and tolerance of a veterinary medicine within the prescribed manner of use.

Article 5

Clinical trials of veterinary medicines also include the clinical segment of investigating bioavailability or bioequivalence of veterinary medicines.

Bioavailability or bioequivalence from paragraph 1 of this Article shall be assessed if:

- 1) the therapeutic range of a veterinary medicine is narrow;
- 2) anomalies which can be connected with pharmacodynamic characteristics of a veterinary medicine, occurred in previous clinical trials;
- 3) the sponsor wants to prove essential similarity with the veterinary medicine which is on the market.

Article 6

In clinical trials of veterinary medicines used for improving animal productivity, the following is particularly assessed:

- 1) animals' health status;
- 2) daily increase of animals' body weight;
- 3) quantity and quality of animal products.

Article 7

Clinical trials of veterinary medicines are conducted on animals, with an animal control group.

Pharmacological or pharmacodynamic effects of a veterinary medicine are compared with the animal control group to which no therapy was prescribed, i.e. with the effects of the comparative veterinary medicine which has the marketing authorisation and whose therapeutic effect has been verified.

Article 8

Possible effects of veterinary medicines on the environment, on the residues of veterinary medicines in products from treated animals, on the fate of the animals used in trials, as well as on the safety of the people involved in trials, shall be monitored in the course of clinical trials of veterinary medicines.

Article 9

Results of clinical trials of veterinary medicines shall be reached through quantitative or conventional clinical methods.

In order to verify the results from paragraph 1 of this Article, statistical methods shall be used.

The received results from paragraph 1 of this Article, whether positive or negative, shall be reported to the Agency.

Article 10

Clinical trials of veterinary medicines shall be conducted only on the samples manufactured and controlled in accordance with Good Manufacturing Practice guidelines and labelled as follows: "For the purpose of clinical trial".

Documentation on each batch of an investigational veterinary medicine shall be kept for at least five years from the termination of the clinical trial.

Article 11

Documentation concerning clinical trials of veterinary medicines shall be kept by the Agency under its Professional Secret Act.

2. SPONSORS OF CLINICAL TRIALS OF VETERINARY MEDICINES

Article 12

The sponsor of the clinical trial of a veterinary medicine (hereinafter: the sponsor) shall perform the following tasks:

- 1) preparing complete documentation necessary for obtaining the licence for the clinical trial of a veterinary medicine, i.e. documentation required for amendments to the protocol or to the licence for the clinical trial of a veterinary medicine;
- 2) appointing the chief investigator who should sign a statement to the effect that he/she accepts the proposed protocol, and signing a piecework contract with the chief investigator for conducting the clinical trial of a veterinary medicine under the law and these Rules;
- 3) determining the site of the clinical trial of a veterinary medicine at which the trial is to be conducted, and ensuring contractual consent on the use of the premises, equipment and personnel for conducting the trial;
- 4) negotiating, before the clinical trial commences, the indemnity payable to the animal's owner in case of damage caused by the clinical trial;
- 5) ensuring sufficient pre-clinical and clinical data on the investigational veterinary medicine, submitting them to the chief investigator in an appropriate form;
- 6) informing the chief investigator, the Agency and the Ethics Committee on all new relevant data concerning the investigational veterinary medicine;
- 7) ensuring data on the quality of the investigational veterinary medicine, as well as data on the previous pre-clinical and clinical trials of the veterinary medicine;
- 8) informing the Agency and the Ethics Committee on all serious adverse reactions to the investigational veterinary medicine and adverse events in a clinical trial, under the regulations on adverse reactions to the veterinary medicine;
- 9) ensuring the supervision of the conduct of a clinical trial by appointing a monitor and, as required, an auditor in the clinical trial of a veterinary medicine;
- 10) informing the Agency and the chief investigator in a timely fashion on amendments to the protocol on the clinical trial of a veterinary medicine, under positive regulations;
- 11) informing the Agency in a timely fashion on the development of the clinical trial of a veterinary medicine, its termination, discontinuation or suspension.

Article 13

In addition to the tasks from Article 12 of these Rules, the sponsor of the clinical trial of a veterinary medicine shall have the duty to ensure a sufficient quantity of the investigational veterinary medicine.

The veterinary medicine from paragraph 1 of this Article must be labelled and the outer packaging must contain at least the following particulars:

- 1) name of the veterinary medicine, its brand name, INN or generic name, strength or some other identification mark;
- 2) manufacturer's name
- 3) expiry date;
- 4) batch number;
- 5) other necessary marks concerning the investigational target species of the veterinary medicine.

The outer packaging of the veterinary medicine from paragraph 1 of this Article must be labelled as follows: "For the purpose of clinical trial".

3. CONTRACT RESEARCH ORGANISATION

Article 14

The sponsor of the clinical trial of a veterinary medicine may transfer, by virtue of a contract, all powers or a part of powers in the clinical trial to a contract research organisation (hereinafter: the CRO), which should discharge all obligations undertaken by the contract on the sponsor's behalf.

The CRO shall be established as a legal person without a registered office in the Republic of Serbia, which may perform a part of its contractual obligations taken over from the sponsor through an authorised representative to the Republic of Serbia, with whom it shall conclude a piecework contract under the law.

Article 15

Within the obligations undertaken in the clinical trial of a veterinary medicine, the CRO must perform all activities that would have been performed by the sponsor of the clinical trial if he had not transferred all powers or a part of powers in the clinical trial to the CRO.

The CRO's authorised representative to the Republic of Serbia shall perform only those tasks for which he/she was authorised by the CRO by virtue of a contract.

The CRO, or its authorised representative to the Republic of Serbia, shall exercise the transferred powers or a part of powers in the clinical trial of a veterinary medicine under the law, these Rules, as well as Good Clinical Practice guidelines for clinical trials of veterinary medicines.

Article 16

The CRO shall be obliged to submit to the Agency a proof that it has been entered in the register of the Republic of Serbia's competent authority, or an adequate proof that it performs its activities under the regulations of the country where it is seated.

The CRO shall be obliged to submit to the Agency a verified copy of the contract defining the scope of powers transferred from the sponsor of the clinical trial of a veterinary medicine to the CRO.

The CRO's authorised representative to the Republic of Serbia shall be obliged to submit to the Agency a verified copy of the contract defining the scope of powers exercised by him/her on behalf and for account of the CRO.

The CRO, or its authorised representative to the Republic of Serbia, shall be responsible for the transferred powers or a part of powers in the clinical trial of a veterinary medicine, in which the transfer of powers or a part of powers to the CRO or its authorised representative to the Republic of Serbia, shall not free the sponsor of the clinical trial of a veterinary medicine from the ultimate responsibility for conducting the clinical trial.

4. CHIEF INVESTIGATOR AND INVESTIGATIVE TEAM IN THE CLINICAL TRIAL OF A VETERINARY MEDICINE

Article 17

The chief investigator of the clinical trial of a veterinary medicine shall be a person who is, at a minimum, the holder of the degree of the Faculty of Veterinary Medicine and who specialises in a field in which the investigational veterinary medicine is primarily applied, or who has a teaching or research title in the field of veterinary medicine.

The chief investigator in the clinical trial of veterinary medicines must have additional knowledge in the field of Good Clinical Practice in clinical trials of veterinary medicines.

Apart from the chief investigator from paragraph 1 of this Article, the team conducting the clinical trial of a veterinary medicine may include persons who hold, at a minimum, the degree of the Faculty of Veterinary Medicine.

Article 18

Before the clinical trial commences, the chief investigator shall:

- 1) submit to the sponsor his/her curriculum vitae and documents testifying to his expertise and skills required for the post of the chief investigator;
- 2) sign a statement that he/she is acquainted with the characteristics of the investigational veterinary medicine, as well as with the objective of the clinical trial to be conducted under the attached protocol and positive regulations;
- 3) sign with the sponsor of the clinical trial of a veterinary medicine a piecework contract for conducting the clinical trial of veterinary medicine under the law;
- 4) submit to the sponsor a list of investigative team members.

Article 19

Within the procedure of nominating members of the investigative team from Article 18 item 4 of these Rules, the chief investigator shall acquaint investigative team members with the protocol, pre-clinical and clinical data on the veterinary medicine, as well as with test lists.

Article 20

The chief investigator and the investigative team shall perform the following tasks in the course of the clinical trial of a veterinary medicine:

- 1) determine a sufficient number of animals in accordance with the criteria laid down by the protocol for involving animals in the clinical trial;
- 2) provide explanations to animal owners orally and in writing, in a user-friendly manner, about data on the investigational veterinary medicine, the purpose and design of the conduct of the clinical trial, dangers and benefits for animals, the animal selection method, an approximate number of animals and other possible forms of treatment, as well as their advantages and disadvantages;
- 3) before the commencement of the clinical trial of a veterinary medicine, obtain from the animal owner his/her voluntary written consent specifying that animals possessed by him/her may participate in the clinical trial;
- 4) administer the investigational veterinary medicine to animals or enable other persons to administer the investigational veterinary medicine according to the dosage regimen defined by the protocol;
- 5) ensure accuracy, completeness, readability and up-to-datedness of the data related to the clinical trial of a veterinary medicine, as well as the confidentiality of data available for supervision by the sponsor and the Agency.

Article 21

In the course of the clinical trial of a veterinary medicine the chief investigator shall be obliged to:

- 1) fix the starting and closing dates of the clinical trial of a veterinary medicine in agreement with the sponsor of the clinical trial, as well as inform the clinical trial sponsor of the discontinuation of the clinical trial of a veterinary medicine;
- 2) appropriately store the investigational veterinary medicine, keep records of the dispensing and consumption of the investigational medicine samples, as well as store unused samples of the medicine in a prescribed manner, and destroy them in agreement with the sponsor of the clinical trial of a veterinary medicine;
- 3) in the case of an immediate threat to the animal, inform the sponsor of the clinical trial of a veterinary medicine that the clinical trial was discontinued;

- 4) prepare a report on the completed clinical trial of a veterinary medicine and submit an interim report on the clinical trial, if necessary and upon the Agency's request.

If need be, the chief investigator shall be obliged to propose an amendment to the trial protocol, and in case the proposed amendment is approved, he/she shall be obliged to ensure that all those involved in the clinical trial are informed of the approved amendment to the protocol and that the treatment is resumed in accordance with the trial protocol amendment.

Article 22

The chief investigator shall keep records of each animal involved in the clinical trial.

The chief investigator shall inform the members of the investigative team during the clinical trial of the problems in the conduct of the clinical trial of a veterinary medicine.

Investigative team members shall inform the chief investigator of adverse reactions to the investigational veterinary medicine or adverse events and necessary measures that should be undertaken in order to protect the health of the animals.

Article 23

The chief investigator, investigative team members, as well as experts of other relevant profiles (graduate pharmacists, specialists in medical biochemistry, statisticians and the like) shall sign with the sponsor of the clinical trial of a veterinary medicine piecework contracts, which shall contain, in addition to other statutory elements, the amount of remuneration for the performance of tasks in the clinical trial of a veterinary medicine.

5. ETHICS COMMITTEE

Article 24

The Ethics Committee shall comprise at least five members, who have relevant qualifications and experience in evaluating scientific and medical aspects and ethical principles of the welfare of animals used in clinical trials of veterinary medicines.

For the purpose of preventing conflict of interest, only those members of the Ethics Committee who are not investigators in a particular clinical trial and who

are independent from the sponsor shall be eligible to vote, i.e., to give their opinion on issues related to the clinical trial of a veterinary medicine.

The composition, tasks, operational and other documents related to the work of the Ethics Committee must be in line with Good Clinical Practice guidelines for clinical trials of veterinary medicines.

Article 25

The clinical trial of a veterinary medicine may commence if the Ethics Committee has passed a positive decision on the conduct of the clinical trial of a veterinary medicine before the commencement of the clinical trial of a veterinary medicine.

Before passing the positive decision referred to in paragraph 1 of this Article the Ethics Committee shall consider:

- 1) relevance and design of the clinical trial of a veterinary medicine;
- 2) rationale for the clinical trial of a veterinary medicine, i.e., evaluation of the envisaged benefits and risks for the health of animals;
- 3) protocol;
- 4) expertise of the chief investigator and the investigative team;
- 5) investigator's brochure;
- 6) capacities of the institution for the conduct of the clinical trial of a veterinary medicine;
- 7) proof that the sponsor has negotiated the amount of indemnity to be paid to the owner of the animal in case damage is inflicted by the clinical trial.

If the Ethics Committee fails to take a positive decision on the conduct of the clinical trial of a veterinary medicine, the Agency shall not issue a licence for the clinical trial of that medicine.

Article 26

In the case of multi-centre clinical trials conducted in the Republic of Serbia, the Ethics Committee may propose to the sponsor of the clinical trial of a veterinary medicine, or the chief investigator, to suspend further conduct of the clinical trial in a specific institution where the clinical trial of a veterinary medicine is conducted, if there are well-founded reasons for that.

Article 27

For a multi-centre clinical trial of a veterinary medicine conducted in several countries, a positive decision on the conduct of the multi-centre clinical trial of a veterinary medicine shall be passed by each of those countries or their respective competent Ethics Committees.

Article 28

The Agency may, before issuing a licence for the conduct of the clinical trial of a veterinary medicine, ask for an additional opinion of the Ethics Committee on the submitted application for the conduct of the clinical trial of a veterinary medicine, i.e., on all contentious issues that may arise in the course of the conduct of the clinical trial of a veterinary medicine.

6. LICENCE FOR THE CLINICAL TRIAL OF A VETERINARY MEDICINE

Article 29

The sponsor of the clinical trial of a veterinary medicine who does not have a marketing authorisation for a veterinary medicine, shall submit to the Agency, before the commencement of the clinical trial, an application for approval of the clinical trial of a veterinary medicine.

An application for approval of the clinical trial of a veterinary medicine shall contain:

- 1) cover letter from the sponsor;
- 2) completed form of the application for approval of the clinical trial of a veterinary medicine;
- 3) data on the sponsor of the clinical trial of a veterinary medicine;
- 4) proof that the CRO is registered with the competent authority in the Republic of Serbia in the register of legal entities or entrepreneurs or proof of the performance of the activity under the regulations of the country where the CRO has its registered office;
- 5) notarized copy of the contract on the assignment of all or part of the powers to the CRO or an authorised representative of the CRO in the clinical trial of a veterinary medicine;
- 6) protocol of the clinical trial of a veterinary medicine;
- 7) findings about adverse reactions to a veterinary medicine;
- 8) investigator's brochure (an overview of previous pre-clinical trials and clinical experience) including an assessment of the maximum residue level (MRL) and the proposed withdrawal period;
- 9) sample of the test list in Serbian (CRF);
- 10) positive opinion of the Ethics Committee;
- 11) written consent of the institution where the clinical trial of a veterinary medicine is to be conducted;
- 12) documentation about the investigational veterinary medicine, a GMP certificate, a certificate of the analysis, a certificate from the Agency of the performed quality control, labelling of the medicine in the Serbian and original languages, both for the investigational veterinary medicine and for the medicine with which the investigational veterinary medicine is compared;
- 13) brief CV with references of the chief investigator;

- 14) written statement of the chief investigator that he has been informed of the characteristics of a veterinary medicine in the clinical trial and the objective of the clinical trial, as well as that the trial is to be conducted in conformity with the applicable regulations and Good Clinical Practice guidelines for clinical trials of veterinary medicines;
- 15) information sheet for the owner of the animal and a written consent form to be signed by the animal's owner;
- 16) proof that the sponsor has negotiated the amount of indemnity to be paid to the owner of the animal in the event of damage inflicted by the clinical trial;
- 17) list of states where the veterinary medicine was granted the marketing authorisation, if any;
- 18) list of states where the same clinical trial of a veterinary medicine is conducted;
- 19) list of states where a clinical trial of the same veterinary medicine has been approved;
- 20) list of institutions where the same clinical trial of a veterinary medicine is conducted, if it is a multi-centre trial;
- 21) additional information necessary in the procedure for obtaining a licence for the conduct of the clinical trial, which is needed to protect animal health and welfare, upon the Agency's request;
- 22) proof that prescribed fees have been paid to the Agency for the issuance of the licence for the clinical trial of a veterinary medicine.

The form of the application for approval of the clinical trial of a veterinary medicine is attached to these Rules and shall constitute their integral part (Form No. 1).

Article 30

The cover letter referred to in Article 29 item 1) of these Rules shall contain:

- 1) logo, name and address of the sponsor;
- 2) subject or summarized contents of the application for approval of the clinical trial of a veterinary medicine;
- 3) summary of the protocol in Serbian;
- 4) name of the clinical trial of a veterinary medicine;
- 5) name of the investigational veterinary medicine with the specified active substance;
- 6) name of the veterinary medicine with which the investigational veterinary medicine is compared;
- 7) pharmaceutical form and strength of the veterinary medicine;
- 8) manufacturer's name;
- 9) date and signature of the person responsible for the clinical trial.

Article 31

The protocol of the clinical trial of a veterinary medicine referred to in Article 29 item 6) of these Rules shall contain:

- 1) background information;
- 2) basic information;
- 3) objectives and purpose of the clinical trial of a veterinary medicine;
- 4) design of the clinical trial of a veterinary medicine;
- 5) animal selection;
- 6) treatment of animals;
- 7) assessment of efficacy of a veterinary medicine for animals;
- 8) assessment of safety of a veterinary medicine for animals;
- 9) assessment of safety of a veterinary medicine for humans;
- 10) assessment of safety of a veterinary medicine for the environment;
- 11) statistical data;
- 12) information on direct access to original data or documents;
- 13) data on quality control and assurance;
- 14) data on animal protection;
- 15) information on data handling and keeping of documentation;
- 16) data on financing the clinical trial of a veterinary medicine;
- 17) data on the negotiated amount of indemnity to be paid to the animal owner in the event of damage inflicted by the clinical trial;
- 18) manner of publication of the results in the clinical trial of a veterinary medicine;
- 19) other appendices.

Article 32

The investigator's brochure referred to in Article 29 item 8) of these Rules shall contain:

- 1) front page;
- 2) confidentiality statement;
- 3) contents;
- 4) summary;
- 5) introduction;
- 6) physical, chemical and pharmaceutical characteristics of the pharmaceutical form of a veterinary medicine;
- 7) data on the pre-clinical trial of a veterinary medicine;
- 8) data on testing for residues;
- 9) data on the effect of the investigational veterinary medicine on animals;
- 10) conclusion.

Article 33

In addition to the data referred to in Article 32 of these Rules, the investigator's brochure shall also contain information on the quality, safety and efficacy of a veterinary medicine, as well as an assessment of the risk-benefit balance of the investigational veterinary medicine.

The documentation referred to in paragraph 1 of this Article shall relate to the investigational veterinary medicine, as well as to the comparative veterinary medicine used in the trial as active control.

Article 34

The Agency shall examine the completeness of the application for approval of the clinical trial of a medicine within 30 days from the day on which the application was submitted.

If the application referred to in paragraph 1 of this Article is not complete, the Agency shall inform the sponsor in writing to supplement the application with additional data in a specified time limit.

The time limit for the issuance of the licence for the clinical trial of a veterinary medicine shall stop running from the day on which the Agency asked the sponsor to furnish additional data and shall resume from the day on which the sponsor furnished the requested additional data.

If the sponsor fails to furnish additional data in the requested time limit, the Agency shall reject the application for approval of the clinical trial of a veterinary medicine as incomplete.

If the application for approval of the clinical trial of a veterinary medicine is complete, the 60-day time limit for the issuance of the licence for the clinical trial of a veterinary medicine shall start running.

Article 35

If the statutory requirements and the requirements set out in these Rules have been met, the Agency shall grant a licence for the clinical trial of a veterinary medicine.

7. AMENDMENT OF THE PROTOCOL OR LICENCE FOR THE CLINICAL TRIAL OF A VETERINARY MEDICINE

Article 36

The sponsor of the clinical trial shall follow scientific and technological development of the profession, the results of pharmacovigilance and other relevant information and shall, on that basis, propose to the Agency amendments to the protocol or to the licence for the clinical trial of a veterinary medicine.

Article 37

A complete application for amendment of the protocol or of the licence for the clinical trial of a veterinary medicine shall contain:

- 1) cover letter from the sponsor or the CRO, or the authorised representative of the CRO;
- 2) completed form for amendments to the protocol or the licence for the clinical trial of a veterinary medicine;
- 3) documentation related to the amendments to the protocol or the licence for the clinical trial of a veterinary medicine;
- 4) proof that prescribed fees have been paid to the Agency.

The form for the application for approval of amendments to the protocol or the licence for the clinical trial of a veterinary medicine is attached to these Rules and shall constitute their integral part (Form No. 2).

Article 38

The cover letter referred to in Article 37, paragraph 1, item 1) of these Rules shall contain:

- 1) logo, name and address of the sponsor;
- 2) subject: brief information about amendments;
- 3) name of the clinical trial of a veterinary medicine;
- 4) name of the investigational medicine;
- 5) pharmaceutical form, strength and package of the medicine;
- 6) name of the manufacturer of the medicine;
- 7) date and signature of the person responsible for the clinical trial of a veterinary medicine.

Article 39

The Agency shall examine the completeness of the application for approval of amendments to the protocol or the licence for the clinical trial of a veterinary medicine within 30 days from the day on which the application was received.

If the application referred to in paragraph 1 of this Article is not complete, the Agency shall inform the sponsor in writing to supplement the application with additional data in a specified time limit.

The time limit for amending the protocol or the licence for the clinical trial of a veterinary medicine shall stop running from the day on which the Agency asked the sponsor to furnish additional data and shall resume from the day on which the sponsor furnished the requested additional data.

If the sponsor fails to furnish additional data in the requested time limit, the Agency shall reject the application for amending the protocol or the licence for the clinical trial of a veterinary medicine as incomplete.

If the application is complete, the 60-day time limit for amending the protocol or the licence for the clinical trial of a veterinary medicine shall start running.

8. POST-MARKETING INTERVENTIONAL CLINICAL TRIAL OF VETERINARY MEDICINES

Article 40

The sponsor of the clinical trial of a veterinary medicine shall be obliged, before the post-marketing interventional clinical trial of a veterinary medicine has commenced, to inform the Agency in writing about the intention and commencement of the clinical trial of a veterinary medicine which has the marketing authorisation.

The clinical trial referred to in paragraph 1 of this Article shall be conducted in accordance with the approved summary of the characteristics of a veterinary medicine.

In case it has been established in the procedure for inspection of the conduct of the clinical trial of a veterinary medicine from paragraph 1 of this Article that the clinical trial is not conducted in accordance with the approved summary of the characteristics of a veterinary medicine, the Agency shall suspend or prohibit the clinical trial.

9. REPORTING ON THE CONDUCT OF THE CLINICAL TRIAL OF A VETERINARY MEDICINE

Article 41

The chief investigator shall draw up a report on the completed clinical trial of a veterinary medicine, and if necessary, submit a clinical trial interim report at the request of the Agency during the clinical trial of a veterinary medicine.

The report of the investigator shall contain the following data:

- 1) on the animal's owner, on the animal or herd;
- 2) on animal keeping and feeding, including the application of any additives;
- 3) on the history of the illness including the data on the illnesses that developed immediately before or during the trial;
- 4) on the diagnosis and the method for making it;
- 5) on the symptoms and seriousness of the illness under the conventional criteria;
- 6) on the dose of the investigational veterinary medicine, the manner of use, the frequency of administration, the undertaken precautions, etc.;

- 7) on all positive or negative results, with a full report on the clinical picture and findings of diagnostic tests, as well as on any adverse effect;
- 8) on the impact on the behaviour, work or production abilities of the animal;
- 9) on the impact on the quality of products obtained from the investigational animal;
- 10) conclusion about each individual case or, if relevant, a common conclusion for all cases;
- 11) reports on the cases which must carry the date and signature of the investigator.

Article 42

The sponsor of the clinical trial of a veterinary medicine shall report to the Agency on a quarterly basis on the development of the clinical trial of a veterinary medicine.

In the event of the discontinuation of the clinical trial (early termination of the clinical trial, suspension of the clinical trial), as well as of the termination of the clinical trial in the Republic of Serbia or termination of trials in all other countries where the clinical trial is conducted, the sponsor of the clinical trial of the medicine shall inform the Agency of the discontinuation or termination of the clinical trial of a veterinary medicine within 15 days from the day of the discontinuation or termination of the clinical trial of a veterinary medicine (notification about the discontinuation/termination of the clinical trial).

The form for the notification about the discontinuation/termination of the clinical trial of a veterinary medicine is attached to these Rules and shall constitute their integral part (Form No. 3).

Article 43

The sponsor of the clinical trial of a veterinary medicine shall draw up a final report on the results of the clinical trial of a veterinary medicine, to be submitted to the Agency within a year from the day of the termination of the clinical trial of a veterinary medicine.

The report referred to in paragraph 1 of this Article must contain positive and negative results of the clinical trial of a veterinary medicine, on the basis of which an objective assessment shall be made of the clinical trial of a veterinary medicine or benefits and risks for animal health, and of the investigational veterinary medicine, as well as of the safety and efficacy of a veterinary medicine.

Article 44

The sponsor shall keep the documentation of the clinical trial of a veterinary medicine for a period in which that medicine is considered a new medicine or a

medicine with a new manner of application or new indications, which is a period of five years from the day on which the first marketing authorisation was obtained for it or from the day of amendments to the marketing authorisation.

10. MONITORING OF ADVERSE REACTIONS TO THE MEDICINE

Article 45

The monitoring of adverse reactions to the investigational veterinary medicine shall be performed in accordance with the regulations governing the monitoring of adverse reactions to a veterinary medicine.

All adverse reactions to the veterinary medicine during the conduct of the clinical trial shall be reported to the Agency in accordance with the regulations governing the reporting on an adverse reaction to the medicine.

Each serious adverse event during the conduct of clinical trials, which occurs in the investigational animals or which poses a risk for public health must be reported to the Agency immediately.

11. INSPECTION OF THE CONDUCT OF THE CLINICAL TRIAL OF A VETERINARY MEDICINE

Article 46

The Agency shall perform inspection of the conduct of the clinical trial of a veterinary medicine in accordance with the Law on Medicines and Medical Devices, its implementing regulations, as well as with Good Clinical Practice guidelines for the clinical trial of veterinary medicines.

The Agency shall perform inspection of the conduct of the clinical trial of a veterinary medicine on the premises of the sponsor, the CRO, or the authorised representative of the CRO, in respect of the tasks performed by the CRO, or the authorised representative of the CRO, in accordance with the Law on Medicines and Medical Devices, its implementing regulations, as well as in accordance with Good Clinical Practice guidelines for the clinical trial of veterinary medicines.

The inspection of the conduct of the clinical trial of a veterinary medicine shall be performed by an authorised official of the Agency responsible for the tasks related to the clinical trial of veterinary medicines.

Article 47

Before the inspection of the clinical trial of a veterinary medicine commences, the Agency shall notify the sponsor and the chief investigator, as well as the CRO or

the authorised representative of the CRO, of the inspection of the clinical trial of a veterinary medicine.

The Agency shall submit a report to the sponsor on the performed inspection of the conduct of the clinical trial of a veterinary medicine.

Article 48

In the procedure for inspecting the conduct of the clinical trial of a veterinary medicine at the site where the inspection, referred to in Article 46, paragraphs 1 and 2 of these Rules, is performed the Agency may issue a written order to eliminate particular irregularities in the conduct of the clinical trial of a veterinary medicine within a specified time limit.

If these irregularities have not been eliminated in the specified time limit, the Agency may, after the performed inspection, suspend or prohibit the clinical trial if it has established that the clinical trial of a veterinary medicine is not conducted in accordance with the Law on Medicines and Medical Devices and its implementing regulations, as well as with Good Clinical Practice guidelines for the clinical trial of veterinary medicines.

The Agency may suspend or prohibit the clinical trial of a veterinary medicine for which it has issued a licence for the conduct of the clinical trial of a veterinary medicine in the Republic of Serbia, if that is in the interest of animal health, i.e., in the interest of science and society at large.

If, according to the assessment of the Agency, the already initiated clinical trial of a veterinary medicine does not have to be urgently suspended in order to protect animal health, the Agency shall first request data from the sponsor or the chief investigator on the conduct of the clinical trial.

The sponsor or the chief investigator shall be obliged to submit to the Agency the requested data within 15 days from the day on which these data were requested. After that, the Agency shall notify the sponsor, the chief investigator and the Ethics Committee of its decision.

III. TRANSITIONAL AND FINAL PROVISIONS

Article 49

A clinical trial of veterinary medicines initiated before the entry into force of these Rules shall be aligned with the provisions of these Rules within 90 days from the day of entry into force of these Rules.

Article 50

These Rules shall enter into force on the eighth day from their publication in the *Official Gazette of the Republic of Serbia*.

No. 110-00-00178/2007-09
In Belgrade, 26 February 2008

Minister,
Dr Slobodan Milosavljević, m.p.

Form no. 1

Medicine and Medical Devices Agency of Serbia

Vojvode Stepe 458, 11 152 Belgrade, Serbia, tel.: + 381 11/3951156, +381 11/3951157, fax: + 381 11/3951147 e-mail: hygia@alims.sr.gov.yu

Case number:	Received by:
Reception date:	Date of the request for additional documents:
Date of reception of additional documents:	Date of the formal completion of the application:

Filled in by the Medicine and Medical Devices Agency of Serbia

APPLICATION FOR THE AUTHORIZATION OF CLINICAL TRIAL OF A VETERINARY MEDICINE

Name of the clinical trial	
Number of the clinical trial protocol, including the number of amendments, if required	
Sponsor of the clinical trial and a responsible person	Sponsor (name, address, telephone and the fax number, e-mail address): Sponsor is at the same time the manufacturer <input type="checkbox"/>
	An applicant, authorized by the Sponsor to cooperate with the Agency during the trial, if it is not the sponsor (name, address, telephone and the fax number, e-mail address): Responsible person (name, address, telephone and the fax number, e-mail address)

Manufacturer of a veterinary medicine and a	Manufacturer (name, address)
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contact person	Contact person of the manufacturer (name, address, telephone and the fax number, e-mail address)	
Contract research organization (CRO) and a contact person	Contracting research organization (name, address, telephone and the fax number, e-mail address) Responsible person(name, address, telephone and the fax number, e-mail address)	
Supplier or importer of a veterinary medicine	Supplier or importer of veterinarian medicine(name, address, telephone and the fax number, e-mail address)	
Information on veterinary medicine	Name of the veterinary medicine	
	Composition of a veterinary medicine	
	Pharmaceutical form	
	Date of application	Date and number of authorization
	ATCVet code	Stage of clinical trial
	Suggested withholding period	
	The medicine is registered in other countries: no <input type="checkbox"/> yes <input type="checkbox"/>	
	Country, year and licence number:	
	Expiry date:	Storage conditions:
	How the medicine should be used:	Dosage in clinical trial:
Active substance manufacturer(name, address):		
Quantity of active substance per single dosing unit, volume unit or mass unit:		
The investigational medicine no yes		

other countries	Country, licence number, date of issuance:		
Trial is connected with obtaining a marketing authorization for a medicine in the RS	yes <input type="checkbox"/>	no <input type="checkbox"/>	
Exemption of remuneration request	yes <input type="checkbox"/>	no <input type="checkbox"/>	
	(Veterinary medicines rarely used or used for under-represented animal species)		
Purpose and a brief summary of clinical trial protocol			
Duration of a clinical trial	Envisaged date of commencement and termination of clinical trial		
Number and type of animals covered by the clinical trial and a dose of investigational veterinary drug	The institution conducting clinical trial:	Number and species of animals	Dose of veterinary medicine
	Investigational veterinary medicine		
	Veterinary medicine applied in control group		
	Placebo (composition)		
	Multi-centre trial:		

	Total number of animals covered by clinical trial		
	Total number of animals covered by the clinical trial in the territory of the Republic of Serbia		
The institution conducting a clinical trial, the chief investigator and other investigators	The institution conducting the clinical trial of a veterinary medicine (name, address, telephone and fax number, e-mail address)		
	Chief investigator (name, address, telephone and fax number, e-mail address)		
	Chief veterinarian on the ground (if the chief investigator is not a practicing veterinarian): address, telephone and fax number, e-mail address		
	Other investigators included in the clinical trial of a veterinary medicine (Name and surname, qualifications, contact details)		
Monitoring the quality of a trial	yes <input type="checkbox"/>	no <input type="checkbox"/>	
	Monitor <input type="checkbox"/>	Auditor <input type="checkbox"/>	Other <input type="checkbox"/>
	Please, list:		
	STATEMENT OF THE CHIEF INVESTIGATOR		
	I am acquainted with the information on the investigational veterinary medicine, submitted to me by the sponsor of the clinical trial. During the trial, I will keep records about the investigational veterinary medicine or medicines and will, by all means, report to the Medicine and Medical Device Agency of Serbia any adverse event in the clinical trial as well as any amendment to the clinical trial protocol. I am acquainted with “The rules governing clinical trials of medicines used exclusively in veterinary medicine” as well as with the provisions of the Law on Medicines and Medical Devices of the Republic of Serbia		
	Date and signature		
Signature and stamp of the sponsor of the clinical trial of a	I hereby confirm that all above-mentioned information are true The sponsor is under the obligation to submit to the Medicine and Medical Devices Agency of Serbia the final report on the results of the conducted clinical trial of a veterinary medicine, as well as to inform the		

veterinary medicine	Agency forthwith in case of the postponement or discontinuation of the clinical trial of a veterinary medicine		
	Date	Signature of the responsible person of the sponsor	(Seal).

Submitted documentation	Part/page: from-to		Part/page: from-to
Clinical trial protocol	<input type="checkbox"/>	Documentation on the investigational medicine	<input type="checkbox"/>
Investigator's brochure/summary of the characteristics of medicine	<input type="checkbox"/>	GMP certificate	<input type="checkbox"/>
Test list	<input type="checkbox"/>	Biography of the chief investigator(s)	<input type="checkbox"/>
Approval of Ethics Committee(s)	<input type="checkbox"/>	Remuneration slip	<input type="checkbox"/>
Statement by the Board Meeting/Director of the Institution	<input type="checkbox"/>	Other documents	<input type="checkbox"/>
Information sheet for the animals' owner and a written consent in Serbian	<input type="checkbox"/>	Please, list:	<input type="checkbox"/>

The number of pages added by the applicant due to the lack of space within the application form:

Medicine and Medical Devices Agency of Serbia

Vojvode Stepe 458, 11 152 Belgrade, Serbia, tel.: + 381 11/3951156, +381 11/3951157, fax: + 381 11/3951147 e-mail: hygia@alims.sr.gov.yu

Case number:	Received by:
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Date of reception of additional documents:	Date of the formal completion of the application:

Filled in by the Medicine and Medical Devices Agency of Serbia

APPLICATION FOR THE AUTHORIZATION OF THE AMENDMENTS TO THE PROTOCOL, I.E., OF THE APPROVAL OF CLINICAL TRIAL OF A VETERINARY MEDICINE

Amendments to the clinical trial protocol <input type="checkbox"/>		Amendments to the original application for clinical trial <input type="checkbox"/>	
Name of the clinical trial			
Number of clinical trial protocol, including amendments, if required			
Sponsor of the clinical trial and a responsible person	Sponsor (name, address, telephone and fax number, e-mail address)		
	An applicant, authorized by the Sponsor to cooperate with the Agency during the trial, if it is not the sponsor (name, address, telephone and the fax number, e-mail address):		
	Responsible person (name, address, telephone and fax number, e-mail address)		

	Applicant: sponsor <input type="checkbox"/> contract research organization <input type="checkbox"/> investigator <input type="checkbox"/>
Type of the amendment to the clinical trial	
These amendments mostly relate to the safety measures already applied.	yes <input type="checkbox"/> no <input type="checkbox"/>
Reasons for amending clinical trials:	
Amendments arising from animal security	yes <input type="checkbox"/> no <input type="checkbox"/>
Amendments arising from the interpretation of expert documentation/research results	yes <input type="checkbox"/> no <input type="checkbox"/>
Amendments arising from the quality of investigational veterinary medicine	yes <input type="checkbox"/> no <input type="checkbox"/>
Amendments/replacements in conducting or managing a clinical trial:	
Amendments in the inclusion of an additional trial site, replacement of the chief investigator	yes <input type="checkbox"/> no <input type="checkbox"/>
Replacements of the sponsor, legal representative, applicant	yes <input type="checkbox"/> no <input type="checkbox"/>
Amendments in the transfer of chief duties and obligations in a clinical trial	yes <input type="checkbox"/> no <input type="checkbox"/>
Please, state here:	
Other amendments	yes <input type="checkbox"/> no <input type="checkbox"/>
Please, state here:	
Other:	yes <input type="checkbox"/> no <input type="checkbox"/>
Please, state here:	
The content of the amendment of a clinical trial:	
Amendments to the information stated in the application for a clinical trial	yes <input type="checkbox"/> no <input type="checkbox"/>
Amendments to the clinical trial protocol	yes <input type="checkbox"/> no <input type="checkbox"/>
Amendments to other additional documents	yes <input type="checkbox"/> no <input type="checkbox"/>
Please, state here:	

Other:	yes <input type="checkbox"/> no <input type="checkbox"/>
Please, state here:	
Reasons for amendments:	
A brief description of amendments:	

Submitted documentation:			
Remuneration slip	<input type="checkbox"/>	A list of amended documents	<input type="checkbox"/>
A list of suggested amendments	<input type="checkbox"/>	Supporting documentation	<input type="checkbox"/>
Other documents	<input type="checkbox"/>		
Please, list:			

I hereby confirm that all the above mentioned data contained in the application and the supporting documentation are accurate and true and that no significant fact that may affect the security of the participants in a trial and the authenticity of the conclusions has remained undisclosed.	
Name, surname and the title of the responsible person	
Date	Signature of the responsible person

Form no. 3

Medicine and Medical Devices Agency of Serbia
 Vojvode Stepe 458, 11 152 Belgrade, Serbia, tel.: + 381 11/3951156, +381 11/3951157, fax: +
 381 11/3951147 e-mail: hygia@alims.sr.gov.yu

Case number:	Received by:
Reception date:	Date of the request for additional documents:
Date of reception of additional documents:	Date of the formal completion of the application:

Filled in by the Medicine and Medical Devices Agency of Serbia

INFORMATION ON DISCONTINUATION/TERMINATION OF THE CLINICAL TRIAL OF A VETERINARY MEDICINE
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Name of the clinical trial	
Number of the clinical trial protocol, including amendments, if required	
Sponsor of the clinical trial and a responsible person	Sponsor (name, address, telephone and fax number, e-mail address)
	The sponsor is at the same time a manufacturer <input type="checkbox"/>
	An applicant, authorized by the Sponsor to cooperate with the Agency during the trial, if it is not the sponsor (name, address, telephone and the fax number, e-mail address):
	Responsible person (name, address, telephone and the fax number, e-mail address)

	Applicant: sponsor <input type="checkbox"/> contract research organization <input type="checkbox"/> investigator <input type="checkbox"/>
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Termination of a trial

Termination of a trial in the RS yes no Date:

Termination of a trial in all countries where it was conducted yes no Date:

Early termination of a trial yes no Date:

Temporary suspension yes no Date:

The reason for temporary termination of a trial:

Security yes no

Inefficacy yes no

The trial has not commenced yes no

Other yes no

Number of animals still receiving therapy at the moment of discontinuation or early termination of a clinical trial in the RS

In case of discontinuation of a clinical trial or its early termination, please describe briefly in the addendum the following:

- explanation of discontinuation or early termination of a trial
- suggested treatment of animals receiving therapy at the moment of early termination or temporary suspension
- consequences of the early termination of the trial for the analysis of benefit-risk ratio of the investigational medicine

I hereby confirm that all the above-mentioned data are accurate and that clinical

trial reports will be submitted to the Agency and a responsible Ethics Committee within 90 days from the date of the termination of the trial in all countries in which the trial was conducted.

Name, surname and the title of responsible person

Date

Signature of the responsible
person