Issuer:	Minister of Social Affairs
Type:	regulation
In force from:	18.09.2015
In force until:	31.01.2022
Translation published:	02.05.2017

Procedure for reporting serious adverse events occurring in clinical trials

Passed 17.02.2005 No. 26
RTL 2005, 22, 307
Entry into force 01.03.2005

Amended by the following acts

Passed	Published	Entry into force
09.09.2015	RT I, 15.09.2015, 3	18.09.2015

This Regulation is established on the basis of subsection 90 (8) of the Medicinal Products Act (RT I 2005, 2, 4).

§ 1. Scope of application

(1) This Regulation establishes the procedure for reporting serious adverse events occurring in clinical trials (hereinafter trials) by doctors, dentists or veterinarians conducting trials and manufacturers of medicinal products participating in the trials or by their representatives to the State Agency of Medicines, and in the case of trials of veterinary medicinal products also the Ministry of Agriculture in writing of any serious adverse events occurring in the trials.

(2) The provisions of the Regulations apply to reporting serious adverse events occurring in a clinical trial of a veterinary medical product insofar as this not in conflict with the nature of the trial.

§ 2. Adverse event and adverse reaction

(1) An adverse event means any medical occurrence in a clinical trial subject administered an investigational medicinal product. An adverse event may be any untoward or unexpected change (including laboratory abnormality), symptom or disease which has temporal relevance to the use of the investigational medicinal product but which does not necessarily have a causal relationship with this medicinal product.

(2) An adverse reaction means an adverse event which may have a causal relationship with the administration of such investigational medicinal product. An adverse reaction of a medicinal product means all untoward and unintended responses to an investigational medicinal product related to any dose administered.

(3) A serious adverse event or serious adverse reaction to a medicinal product means any untoward medical occurrence or effect that at any dose:
1) results in death;
2) is life-threatening;
3) results in a need for hospitalisation or prolongation of existing hospitalisation;
4) results in prolonged incapacity for work or persistent or significant disability, or
5) results in a congenital anomaly or birth defect.

(4) Unexpected adverse reaction is an adverse reaction the nature, severity or frequency of which is not consistent with the applicable product information. Applicable product information means a summary of the characteristics of the investigational product for an unauthorised product, or a summary of product characteristics or the package leaflet for an authorised product.

§ 3. Reporting serious adverse events and adverse reactions occurring in clinical trials

(1) Doctors, dentists and veterinarians shall report all serious adverse reactions to a medicinal product and adverse events immediately to the sponsor of the clinical trial in writing in a format provided for in the Annex to this Regulation.

(2) The sponsor shall enter reports on suspected serious unexpected adverse reactions occurring in the clinical trial of an investigational medicinal product or comparator medicinal product in Estonia in the European Pharmacovigilance database and notify the State Agency of Medicines thereof, bearing in mind the following deadlines:
1) suspected unexpected serious adverse reactions that are fatal or life-threatening shall be reported #CP1252# immediately, any case no later than seven calendar days after knowledge by the sponsor of such a case;
2) other suspected unexpected serious adverse reactions which are not fatal or life-threatening shall be reported within fifteen calendar days after knowledge by the sponsor of such a case.

(3) The sponsor of a clinical trial of a veterinary medicinal product shall report any serious unexpected adverse reactions occurring in the clinical trial of an investigational medicinal product or comparator medicinal product in Estonia to the State Agency of Medicines as well as to the Ministry of Agriculture, bearing in mind the deadlines specified in subsection (2).

(4) In reporting serious unexpected adverse reactions, the internationally recognised medical terminology pursuant to the updated version of the Medical Dictionary for Regulatory Activities (MedDRA) shall be used.

(5) In a case specified in clause (2) 1), the data which permit the identification of the subjects, information on the medicinal product or medicinal products used, person who submitted the report and adverse reaction shall be indicated in the immediate report. A complete report on such adverse reaction shall be submitted not later than fifteen calendar days after knowledge of such a case.

(6) A sponsor is required to maintain all reports on adverse reactions submitted to the sponsor by doctors and submit such reports to the State Agency of Medicines at the request of the latter.

(7) If a procedure is used in a clinical trial whereby the persons conducting the trial do not know which medicinal product is administered (double blind procedure), the identification code of the medicinal product shall be broken upon the occurrence of an unexpected adverse reaction. With the consent of the State Agency of Medicines, the identification code of a medicinal product need not be broken.

(8) Once a year, the sponsor is required to submit a written report on serious adverse reactions of the investigational medicinal product identified in any country to the State Agency of Medicines, and in case of veterinary medicinal products, also to the Ministry of Agriculture.

§ 4. Implementing Provisions

(1) Until 31 December 2005, a sponsor may forward the information specified in subsection 3 (2) of this Regulation to the State Agency of Medicines on paper records or electronically, instead of entering the information in the European Pharmacovigilance database.

(2) This Regulation enters into force on 1 March 2005.
* Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (OJ L 121, 01.05.2001, pp. 34–44)

Annex