



The EFGCP Report on
The Procedure for the Ethical Review of Protocols
for Clinical Research Projects in Europe
(Update: March 2008)

Serbia

1. What laws or regulations apply to an application for conducting a clinical trial in Serbia?

No single legislation covers all biomedical research. The following are relevant: The Medicines and Medical Devices Law, Regulation on Clinical Trials, Data Safety Protection law, Insurance Law.

2. Which government, legal or authoritative body or bodies is or are responsible for the establishment and/or accreditation of (research) ethics committees for reviewing clinical trials for investigational medicinal products, their supervision and quality? Are there different (research) ethics committees reviewing other projects?

Research Ethics Committees (LECs) are established by Scientific Boards of health centres. No accreditation available. QC is covered inside hospitals by their own QC/QA procedures. At university centres, LECs review both CTs and research projects, whether sponsored or academic.

3. What is the process for achieving clinical trial authorisation from the competent authority in Serbia?

The sponsor of the clinical trial submits the application to the appropriate LEC and to the competent authority (CA the Medicines and Medical Devices Agency of Serbia, <http://www.alims.sr.gov.yu>). The CA reviews and assesses clinical trials as the “expert reviewer” and decides within 60 days, with a possible “clock stop” to obtain supplementary information. If the LEC vote is negative, or documentation is invalid or insufficient, the CA issues a legal document prohibiting the clinical trial.

4. What is the process for obtaining ethical review of a clinical trial protocol by a competent (research) ethics committee in Serbia?

The sponsor of the clinical trial submits the application to the relevant LEC. The LEC acts and decides, usually within 35 days.

5. Is there a single organisation to which to apply for ethical review of a clinical trial for an investigational medicinal product, regardless of whether this is for a single site or multiple sites?

No.

6. What is the website for the organisation that issues guidelines on the ethical review of a clinical trial for an investigational medicinal product?

<http://www.alims.sr.gov.yu>

The website of the Serbian Medicines and Medical Devices Agency.

<http://www.zdravlje.sr.gov.yu>

The website of the Serbian Ministry of Health.

7. Is there a procedural interaction between the national or local competent authority and the (research) ethics committee during the approval process?

No, the LEC review and approval precedes the CA assessment.

8. Does the application to the EC and to the competent authority have to be submitted in parallel, or, if not, in which order?

CA will not consider an application before the first positive LEC opinion.

9. How many (research) ethics committees are there in Serbia?

Most of the hospitals/clinics have to have their own LEC that reviews applications for CTs. There are approximately 19 LECs in Serbia.

10. How are ECs funded in Serbia? Do they charge fees? If yes what is their scale of fees?

LECs are permitted by law to charge fees. Usually fees are only charged for applications sponsored by industry. Academic applications are free of charge. Fees are between 0 and €1,200.

11. Who is responsible for submitting the request for ethical review to the competent ethics committee for single-site and for multi-site clinical trials?

Usually a sponsor has to submit the request, but the principal investigator, a contract research organisation or an academic sponsor can also do so.

12. How is a "single opinion" achieved for multi-site studies?

By agreement of the decisions made by LECs. But this does not yet work in practice.

13. How many members serve on an EC?

5-9.

14. How many members constitute a quorum?

Majority of appointed number, i.e. 50%+1

15. How are EC members appointed?

They are appointed by the authority responsible for the establishing of the LEC; this may be the university, hospital, or the institution outside the universities.

16. How is the independence of members ensured?

By their SOPs. Total independence is not possible.

17. How are conflicts of interest of EC members avoided?

The law requires that the LECs have an SOP setting up regulations for cases of conflict of interests.

18. What backgrounds and/or qualifications of members are actively sought?

Members need to have specific qualifications, although there is no official rule for the qualifications requirements:

- balance between male and female members;
- for each application, a physician (or a dentist) in that specific field has to be involved, in addition to a physician who is not associated in any way with the trial and is not a medical doctor of the institution where the trial is to take place;
- a member of the nursing staff, a pharmacist, someone who has ethical expertise (e.g. a member of the clergy), a lawyer, a member of an recognised patient representative group and a statistician.

19. How do ECs obtain specialist expertise?

- LECs are required to have one member present who specializes in the medical area of the CT that is under assessment;
- by asking for an external expert review; the law specifies that in cases where the expertise of the members is insufficient, the LEC has to have procedures for obtaining an expert review. Additionally for paediatric CTs, it is stated by law that there must be an expert present who has paediatric expertise. The same is required for CTs in psychiatry and emergency medicine.

20. What are the training requirements for members of ECs?

There is generally no specific education, nor training requirements.

21. What training programmes are available for EC members in Serbia?

GCP courses, ethics as a subject at medical schools, as well as e.g. EFGCP.

22. What are the timelines for the assessment of single- and multi-site studies?

60 days with one possible “clock-stop”. For Phase IV clinical trials, with a single clock stop, the time lines are 30 days.

23. How are substantial amendments submitted during the review process dealt with?

Substantial amendments have to be reviewed within 60 days.

24. How does an EC assess the suitability of investigators and of sites?

According to the EU and local Directives, the investigator has to provide a CV. The authorities have established minimum requirements regarding the necessary qualifications of investigators.

25. How are the requirements for (research) ethics committees to review the contractual or financial arrangements in clinical trials for both investigators and hospitals handled?

The law requires that the EC should evaluate the basic aspects of the financial arrangements and contracts. In some centres another body is responsible for such matters.

26. How are the requirements for ethics committees to review the compensation arrangements for study subjects handled?

Compensation for subjects is evaluated in the review procedure.

27. Is there an ongoing quality assurance process (e.g. audits, inspections, internal SOP) for (research) ethics committees in Serbia?

A GCP Inspector(ate) exist within Serbian Agency. The Serbian Agency and Serbian Ministry of Health/MoH are the authorities entitled to carry out inspections in these fields.

28. Is there an appeal mechanism?

Yes. A limited appeal mechanism to the CA has been introduced since the implementation of the European GCP Directive.

29. How do ECs deal with SUSAR reports and Annual Safety Reports?

Half of them think that SUSARs should not be sent to LECs. However, LECs are required to forward SUSARs to the national Pharmacovigilance Centre Department of the Serbian Agency.

30. How are 'substantial amendments' defined?

In accordance with EU regulations.

31. What are the indemnity insurance requirements for research projects?

This is regulated by local insurance law, and insurance must be provided by local agency.

32. What are the indemnity insurance requirements for ethics committee members themselves?

There are no specific requirements for insurance of EC members.

33. How is informed consent obtained from vulnerable subjects who are potentially to be involved in a clinical trial?

For medicinal trials, where the subject is unable to give informed consent, the Clinical Trials Regulation make provision for consent to be given by a personal or professional legal representative, subject to a number of detailed criteria.

- if it is not possible to appoint a legal representative
- no information is available to indicate that a patient would refuse participation
- research is important for the validation of data

- the drug or medical device is meant for an emergency situation
- the trial is for the benefit of the patient (or there is no risk at all)
- the trial has the approval of the LEC and CA
- the LEC and CA have expertise in emergency medicine
- the interests of the patient are deemed more important than public interest
- public interest has been publicly shared (e.g. as a poster info about the CT at the department where the study is conducted and /or information on the website of the hospital)
- the patient has to be asked immediately after regaining consciousness for further participation, otherwise her participation in the trial has to be stopped.

For all other patients who are not able to consent, such as children or mentally compromised patients, the parents or legal representative have to give assent instead. The child and the parent have to be informed according to their ability to understand and asked for assent.

34. How do ECs assess the progress and outcome of research projects that they have approved?

By annual and other reports.

35. How does the EC ensure reception of the Annual Safety Report and the Summary of the Final Report of a research project that it has approved?

No processes yet in place, other than procedure for in-house registering of all received correspondence.

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