



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

Slovenia

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

The regulations applying to clinical trials on investigational medicinal products are:

Drug Act (Official gazette, No. 31/06) and Bylaw on Clinical Trials (Official gazette, No. 54/06), which is the Slovenian Directive on Clinical Drug Testing, based on Directive 2001/20/EC.

The Code of Medical Deontology of Slovenia

The Oviedo Convention.

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?

At the national level there is only one research ethics committee, i.e. the National Medical Ethics Committee (NMEC), the members of which are appointed by the Minister of Health for a four-year term. The NMEC has issued Statutory Notes (SN), which can be found on the website <http://www.mf.uni-lj.si/kme-nmec>.

Local ethics committees have recently been set up at university and regional hospitals. The NMEC reviews all biomedical research funded by the State agencies or institutions, all multi-centre and multinational clinical trials, all biomedical research on man conducted in the framework of M.Sc. or D.Sc. theses, as well as all research on man raising important ethical questions. Such projects submitted to local committees must be referred to the NMEC. The local/regional ethics committees are only authorised to review local studies that do not present any serious risk to the participants. They are also invited to preliminarily review the protocols of all studies to be carried

out at the local level, and to monitor their progress after they had been approved by the NMEC.

Research involving gene technology or medically assisted procreation must also be passed by relevant special advisory committees before going to the NMEC for approval.

The NMEC also gives opinions on bioethical issues, advises parliament and assists in formulating relevant laws. It has also produced guidelines for researchers carrying out research involving humans.

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

The application is made by the applicant to the competent authority, the JAZMP. The *authorisation* is required for clinical trials involving advanced therapy medicinal products; for all other clinical trials *notification* is required. The website of the JAZMP is <http://www.jazmp.si>

Approval of the NMEC is one of the required documents before an application is granted.

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

The project proposal should be submitted to the NMEC. Guidelines (also in English) for preparation of the application are available at the NMEC web-site <http://www.mf.uni-lj.si/kme-nmec>. Ethical review is done by the NMEC. The proposal is reviewed by at least one rapporteur (see SN, paragraph 5). Decisions are taken at monthly meetings. Their decisions are sent to the applicants by post well within 60 days of the receipt of application. The decision of NMEC should be sent by the applicant to the CA when available.

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?

Yes, the NMEC. Yes, application is to the National Medical Ethics Committee (NMEC). The website is at www.mf.uni-lj.si/kme-nmec.

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

The website where this information can be found is at <http://www.mf.uni-lj.si/kme-nmec>.

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

Not regularly.

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

The application can be submitted in parallel.

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

One, the NMEC. Local (research) ethics committees have been set up at university and regional hospitals but they are only authorised to review local studies that do not present any serious risk to the participants. They are also invited to give a preliminary review of the protocols of all studies to be carried out at the local level, and to monitor their progress after they had been approved by the NMEC.

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

No fees are charged for review of any (type of) application.

The NMEC has no office or administration of its own. The administrative work is done mainly by its President at the Institute of Clinical Neurophysiology of the Ljubljana Medical Centre. The members of the NMEC are volunteers.

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?

The principal investigator, the sponsor or the CRO may submit the request.

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

As there is only one ethics committee for the approval of IMPs, the NMEC, it always provides the single opinion.

13. How many members serve on an EC?

Thirteen.

14. How many members constitute a quorum?

For opinions on the ethical review of research studies, the quorum is 3 members of the NMEC, 2 of whom must be medical doctors and one a lay person (or an academically educated expert in fields other than medicine), and a consensus must be reached. In case of any ambiguity or disagreement, a minimum quorum is 5 members, at least one of whom must be a non-medical (lay) member. Even then the decision must be confirmed by a majority of all NMEC members; a two-thirds majority of votes of all members shall only be sufficient in exceptional cases.

15. How are EC members appointed?

Candidates are proposed by the Medical Council to the Minister of Health who appoints 13 members.

16. How is the independence of members ensured?

There are no specific measures.

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

Any conflict of interest must be declared by the member. There has been no case of any conflict of interest of a financial nature. Any member who could possibly have a conflict of interest related to a particular project may not participate in the discussion and decision making procedure on that project.

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

Membership is such as to cover the widest possible field of medical research. In addition, the legislation allows that external experts may be appointed.

19. How do ECs obtain specialist expertise?

The majority of academic research is peer reviewed for scientific merit prior to ethical review. In other proposals, specialist expertise is obtained within the NMEC or externally.

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

None.

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

None.

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

Response should be given in 60 days. The applicant receives a reply not later than 3 weeks after the session at which the project is reviewed.

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

They are subject to the same principles of review as a new study.

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

Within the limited population of researchers in Slovenia, their scientific quality and reputation is known. The majority of researchers are also registered at the Ministry of Science. Additionally, researchers' CVs with experience in research are required within their applications. The same is true of the sites.

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?

In principle, financial arrangements should be transparently disclosed to the NMEC. However, professional institutional services should and do take care of the legality.

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

Means of recruitment should be disclosed to the NMEC; there should be no suspicion of any improper pressure or inducement, neither financial nor any other.

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

No.

28. Is there an appeal mechanism?

An applicant may file an appeal against the NMEC's decision. This must be considered at the next session of the NMEC. The second rejection (if the applicant fails to comply with the NMEC's advice) is final. A further appeal may be submitted to the responsible body of the Council of Europe; the NMEC is obliged to reconsider its decision in the light of the opinion of the latter.

An applicant who has received a negative opinion by one of the local research ethics committees may file an appeal to the NMEC. The decision reached by the NMEC is binding.

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

Prompt reporting of suspected unexpected serious adverse events/reactions (SUSARs) to the NMEC is required when it may be considered by the sponsor/CRO or the responsible investigator that the risk to the participants could exceed the anticipated or acceptable level, or that the originally estimated risk / benefit ratio is changed unfavourably. This also includes cases of unexpectedly frequent occurrence of the anticipated SAEs. Regarding other SAEs, quarterly, semi-annual or annual safety reports accompanied with a comment by the sponsor/CRO or the clinically responsible principal investigator are sufficient. The reports to the NMEC can be sent by e-mail to tone.zakelj@kclj.si as PDF files attached to the main message giving all the necessary study identifying data.

30. How are 'substantial amendments' defined?

The Bylaw on Clinical Trials defines the substantial amendment as set out by Directive 2001/20/EC: "*Changes which are likely to have an impact on the safety of the trial subjects or to change the interpretation of the scientific documents in support of the conduct of the trial*" (e.g. change of dosage, number, and mode of investigation(s), of the planned statistical analysis etc.).

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

A copy of a valid insurance policy is required as a constituent part of application for a clinical trial.

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

None in existence.

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

The interests of vulnerable subjects are safeguarded according to the provisions of the Oviedo Convention and other legally binding documents as well as recommendations.

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

By interim and final 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?

The NMEC has no means or power to ensure reception of these documents. However, it is felt that the policy of sponsors, following international regulations and recommendations regarding monitoring of studies, should suffice.

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