The EFGCP Report on
The Procedure for the Ethical Review of Protocols
for Clinical Research Projects in Europe
(Update: April 2011)

Slovenia

**Question 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.

**Question 2:** Which government, legal or authoritative body or bodies is or are responsible for the establishment and/or accreditation of (research) ethics committees for IMPs, and for 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](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.

**Question 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](http://www.jazmp.si).

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

**Question 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](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.

**Question 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](http://www.mf.uni-lj.si/kme-nmec).

**Question 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](http://www.mf.uni-lj.si/kme-nmec).
**Question 7:** Is there a procedural interaction between the national or local competent authority and the (research) ethics committee during the approval process?

Not regularly.

**Question 8:** Does the application to the REC and to the competent authority have to be submitted in parallel, or, if not, in which order?

The application can be submitted in parallel.

**Question 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.

**Question 10:** How are RECs 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.

**Question 11:** Who is responsible for submitting the request for ethical review to the competent (research) ethics committee for single-site and for multi-site clinical trials?

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

**Question 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.

**Question 13:** How many members serve on a REC?

Thirteen.
Question 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.

Question 15: How are REC members appointed?

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

Question 16: How is the independence of members ensured?

There are no specific measures.

Question 17: How are conflicts of interest of REC 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.

Question 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.

Question 19: How do RECs 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.

Question 20: What are the training requirements for members of RECs?

None.

Question 21: What training programmes are available for REC members in Slovenia?

None.
**Question 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.

**Question 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.

**Question 24:** How does a REC 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.

**Question 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.

**Question 26:** How are the requirements for (research) 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.

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

No.
**Question 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.

**Question 29: How do RECs 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.

**Question 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.).

**Question 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.

**Question 32: What are the indemnity insurance requirements for (research) ethics committee members themselves?**

None are in existence.
**Question 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.

**Question 34:** How do RECs assess the progress and outcome of research projects that they have approved?

By interim and final reports.

**Question 35:** How does the REC 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.

**Question 36:** Do national regulations in Slovenia allow research on healthy volunteer children (subjects under 16)?

Information not available.

**Question 37:** Do national regulations in Slovenia allow payment, (other than expenses), to children taking part in research?

Information not available.

**Question 38:** Do RECs invite or allow a) applicants or b) observers to attend committee meetings?

Information not available.

**Question 39:** Are the minutes of (research) ethics committee meetings made public?

Information not available.

**Question 40:** Is there any scope for Chairman’s actions in between meetings?

Information not available.
**Question 41:** Do (research) ethics committees ever appoint subcommittees for any specific purpose?

Information not available.

**Question 42:** Is there a national policy on the registration of clinical trials before they start?

Information not available.

**Question 43:** If the answer to Question 42 is ‘yes’, do (research) ethics committees have any role to play in reviewing such registration?

Information not available.

**Question 44:** If the answer to Question 42 is ‘yes’, is this register of clinical trials made available to the public?

Information not available.

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