The EFGCP Report on
The Procedure for the Ethical Review of Protocols
for Clinical Research Projects in Europe
(Update: April 2012)

Luxemburg

Question 1: What laws or regulations apply to an application for conducting a clinical trial in Luxemburg?

- The 2001 Clinical Trial Directive is nationally transposed by the Règlement grand-ducal du 30 mai 2005 relatif à l'application de bonnes pratiques cliniques dans la conduite d'essais cliniques de médicaments a usage humain.

However, other national legal texts are important in the context of clinical trials and other types of studies which involve human experimentation:

- Loi du 28 aout 1998 sur les établissements hospitaliers and in particular the article 25, which states that no trial, study or experimentation can be done on a human being with the aim of furthering knowledge in the fields of biological and medical sciences if the project has not firstly been submitted to the approval of a research ethics committee.

- Code de déontologie médicale (2005), and in particular the 5th Chapter (articles 69, 70, 71, 72) on human experimentation, which states that no study protocol, whether it is done in a hospital context or not must have been authorized. The trial can only start after the delivery of a positive opinion from the research ethics committee and after the implicit or explicit approval of the health Minister, in agreement with the legal and regulatory requirements which are to be applied in the matter.

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?

In Luxemburg, there is only one national research ethics committee, called Comité National d'Ethique de Recherche (CNER). However its composition, which includes experts specialised in the medical and pharmacology fields, allows the committee to be able to give an opinion on projects which are submitted to its attention. When an
external expert is needed for a specific study, he/she will be asked to attend the CNER meeting to give his/her opinion and insight on the study documentation received.

**Question 3:** What is the process for achieving clinical trial authorisation from the competent authority in Luxemburg?

Submission of a file containing:

- Confirmation of EudraCT number.
- Clinical Trial Application form.
- List of competent authorities in the EU to which an authorisation request has already been submitted for the study.
- Copy of the CNER opinion if it is already available when the file is submitted to the CA.
- Study protocol with all the previous amendments (and their dates) if applicable.
- Peer review of the trial if available.
- Patient information sheet and informed consent form in French and German.
- Investigator brochure with all information regarding the safety and pharmaceutical quality of the product.
- IMPD or simplified IMPD for the known products.
- SmPC for the products which have already received a market authorization within the EU.
- A list of all ongoing clinical trials with the same experimental product.
- A copy of the manufacturing authorisation following the article 13 of the 2001 EU Directive.
- A recent curriculum vitae of the principal investigator.
- Other documents specifically demanded for a study by the Division de la Pharmacie et des Médicaments (Competent Authority in Luxembourg).

**Question 4:** What is the process for obtaining ethical review of a clinical trial protocol by a competent (research) ethics committee in Luxemburg?

- Synthetic descriptive sheet, downloadable on the CNER website.
- Study protocol as well as all amendments with their respective dates.
- Patient information sheet and informed consent form in French and German. If the study involves genetic material analysis, the informed consent form must be divided into two parts, so that the participants can sign once to consent to the main study and a second time if they want to participate in the genetic study. In the case where patients' personal data would need to be stored, the storage length would need to be given in the informed consent form / information sheet.
- Subject recruitment procedures.
- Investigator brochure with all information concerning the safety and pharmaceutical quality of the product.
- Information concerning the financial aspects of the study, as well as the financial contract signed by the sponsor and the principal investigator.
- Insurance certificate.
- A recent curriculum vitae of the principal investigator.
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- Patient questionnaires.
- Other documents specifically demanded for a study by the CNER.
- Electronic version of the documents (on CD-Rom, by email or on a USB key).

**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, there is only one REC in Luxembourg, the National Research Ethics Committee (Comité National d'Ethique de Recherche, CNER) which provides a single opinion which is valid for all the country's investigational sites.

**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?

www.cner.lu

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

The National Research Ethics Committee (CNER) sends the competent authority (Division de la Pharmacie et des Médicaments at the Health Ministry) a copy of the single opinion letters sent to the investigators for each new study and each amendment which have been reviewed by the CNER.

**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?

They can be submitted in parallel.

**Question 9:** How many (research) ethics committees are there in Luxembourg?

Only one, the National Research Ethics Committee (Comité National d'Ethique de Recherche, CNER).

**Question 10:** How are RECs funded in Luxembourg? Do they charge fees? If yes, what is their scale of fees?

The functioning and logistics CNER is partly financed by public funds it receives from the Ministry of Health, and, since January 2010, partly through submission fees which are applied when studies are submitted for ethical review. Scale of fees: information available on the website www.cner.lu.
**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 national coordinating investigator or the principal investigator.

**Question 12:** How is a “single opinion” achieved for multi-site studies?

The CNER, which is the only REC to which the documents have to be submitted, delivers a single opinion which is valid for all Luxemburgish investigational sites.

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

Eleven members.

**Question 14:** How many members constitute a quorum?

Six members.

**Question 15:** How are REC members appointed?

By Ministerial decree from the Health Minister.

**Question 16:** How is the independence of members ensured?

The CNER is a non-governmental, independent body. If there are possible conflicts of interest, the concerned members are not allowed to take part in the deliberations and to vote for the submitted study.

**Question 17:** How are conflicts of interest of REC members avoided?

See Question 16.

**Question 18:** What backgrounds and/or qualifications of members are actively sought?

The largest possible range of qualifications in scientific fields and representatives from the civil society (philosophy, law…), including patient representatives.

**Question 19:** How do RECs obtain specialist expertise?

When no member of the CNER has the necessary expertise to evaluate a given study, external experts are called upon to participate in the discussion during the CNER meeting.
**Question 20:** What are the training requirements for members of RECs?

1. Have a substantial personal experience in research.
2. Familiarise oneself with the local and international regulations concerning clinical research.
3. Participate in seminars/conferences where ethical problems are discussed.

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

Every year, a day of training is organised by the CNER and other partner institutions about clinical research, the ethical aspects of research and the standard procedures in biomedical research.

**Question 22:** What are the timelines for the assessment of single- and multi-site studies?

Sixty days after the date of receipt of the dossiers.

**Question 23:** How are substantial amendments submitted during the review process dealt with?

They are submitted in thirteen copies (with highlighted track changes) to the CNER, which sends its single opinion to the national coordinating investigator within 35 days after the receipt of the dossiers.

**Question 24:** How does a REC assess the suitability of investigators and of sites?

Personal interviews of investigators during the CNER meeting, and on the basis of CVs.

**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?

For each study, the sponsor has to provide the CNER with a copy of the contract signed between the principal investigator and the sponsor. Very often, the sponsor also provides a budget sheet for the study.

**Question 26:** How are the requirements for (research) ethics committees to review the compensation arrangements for study subjects handled?

See Question 25.
**Question 27:** Is there an ongoing quality assurance process (e.g. audits, inspections, internal SOP) for (research) ethics committees in Luxembourg?

The CNER single opinion for each study is sent to the Minister of Health (which transmits it to the competent authority).

**Question 28:** Is there an appeal mechanism?

Yes, the 1998 law states that the investigator can appeal to the Minister of Health.

**Question 29:** How do RECs deal with SUSAR reports and Annual Safety Reports?

The SUSARs and ASRs are sent to each member for review, and mark their agreement with the continuation of the studies, either directly (email or phone notification), or through implicit consent.

**Question 30:** How are ‘substantial amendments’ defined?

The CNER applies the definition given in the 2001 Directive on Clinical Trials.

**Question 31:** What are the indemnity insurance requirements for research projects?

The participant is insured for everything relating to the study procedures, and does not need to prove that the damage was related to his/her participation in the study.

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

In case of a formal complaint towards the CNER, the Luxemburgish government will cover the legal costs incurred.

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

From the subject's legal representative.

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

They ask to receive regular safety reports, annual reports 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?

Through a regular monitoring performed by the CNER secretariat.

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

Yes.

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

No, but it is not formally forbidden.

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

Yes, the investigators are asked to attend the CNER meetings to present their study.

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

No.

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

Yes (urgent matters, follow-up, amendments).

**Question 41:** Do (research) ethics committees ever appoint subcommittees for any specific purpose?

Until now there has not been an opportunity to do so, but the law allows it.

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

No.

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

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

N/A.

**Question 45:** With regard to Clinical Trial Insurance, do research ethics committees in Luxemburg work to a set template of requirements?

No.

**Question 46:** If the answer to Q45 is ‘yes’, how are these requirements
   a) Decided upon?
   b) Cross referenced to statutory requirements?
   c) Updated?

N/A.

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