Lithuania

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

The Law on Ethics of Biomedical Research of 11 May 2000 covers the conduct of all biomedical research studies, including clinical drug trials.

The Law on Pharmacy of 22 June 2006 specifically deals with specific issues of clinical trials on medicinal products.

**The following bylaws are applicable for the conduct of clinical trials on medicinal products:**

5. The Decree No. V-14 of the Chairman of the Lithuanian Bioethics Committee on the Requirements for the Biomedical Research Protocol, Patient Information Sheet and Informed Consent Form and for the CV of Investigator, dated: 5 November 2010.

**The regulations that specifically cover clinical trials are:**

3. The Decree No. V-11 of the Chairman of the Lithuanian Bioethics Committee on the Documents Required by the Lithuanian Bioethics Committee to be Presented by the Sponsor of Biomedical Research and (or) by the Principal Investigator in Order to be Authorized to Conduct a Clinical Trial on Medicinal Products, and on the Procedure on the Submission of the Documents to be presented to the Lithuanian Bioethics Committee, dated: 30 June 2004.

**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?

The Lithuanian Bioethics Committee (LBEC) is the main institution responsible for bioethics policy in Lithuania and it is also responsible (among other functions) for the ethical review of multi-site biomedical research projects (including clinical trials on IMP), issuing the single opinion for the country. The LBEC is established by and is accountable to the Ministry of Health. According to the Law on Ethics of Biomedical Research, Regional Biomedical Research Ethics Committees are established at the universities where medical studies of three levels take place. Currently there are two Regional Biomedical Research Ethics committees in Lithuania: in Kaunas region (based at Kaunas Medical University) and in Vilnius region (based at Medical faculty of Vilnius University).

The activities of the Regional Biomedical Research Ethics committees are monitored by the LBEC.

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

The sponsor must apply for clinical trial authorization to the State Medicines Control Agency (SMCA), which is the competent authority for Lithuania. More information about the procedure can be found at [http://www.vvkt.lt/index.php?3327723903](http://www.vvkt.lt/index.php?3327723903).
Question 4: What is the process for obtaining ethical review of a clinical trial protocol by a competent (research) ethics committee in Lithuania?

The sponsor or the principal investigator must apply to the LBEC for obtaining ethical review of a clinical trial protocol. In this case, the LBEC shall get the opinion of the regional biomedical research ethics committee(s) of the region(s) where research will be carried out. The examination of the clinical trial shall be undertaken by Kaunas Regional Biomedical Research Ethics Committee if it is planned to be conducted in Alytus, Kaunas, Klaipeda, Marijampole, Taurage and Telsiai district regions and/or by Vilnius Regional Biomedical Research Ethics Committee if it is planned to be conducted in Vilnius, Utena, Panevezys and Siauliai district regions.

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, for multi-site applications (the LBEC).

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?


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

The competent authority (The State Medicines Control Agency) requires obtaining an opinion from the LBEC before considering the application at the meeting of experts of the State Medicines Control Agency.

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 applications may be submitted either sequentially (in either order) or in parallel. In both cases the competent authority (The State Medicines Control Agency) must receive an opinion from the LBEC before making the decision to issue approval for the research project.
**Question 9: How many (research) ethics committees are there in Lithuania?**

There are three EC in Lithuania responsible for the ethical review of biomedical research projects: the LBEC, the Biomedical Research Ethics Committee based in Vilnius and the Regional Biomedical Research Ethics Committee based in Kaunas.

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

Ethics committees are funded from the state budget in Lithuania. Following the Law on Pharmacy (Article 18, Paragraph 6), a state fee shall be paid for examining and issuing a favourable opinion to conduct a clinical trial on medicinal products. The state fee shall be paid to an account of Vilnius District State Tax Inspectorate. According to the Decree of the Government of the Republic of Lithuania, the state fee ranges from approximately 2000 to 3000 LTL depending on the number of research ethics committees involved.

**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?**

A person legally authorised to act on behalf of sponsor submits the request. This might be a principal investigator, representative of CRO or representative of the sponsor.

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

Please see the answer to question 2.

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

The Group of Experts on Biomedical Research of the LBEC as well as Regional Biomedical Research Ethics committees are composed of 9 members.

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

Two-thirds of the appointed members.

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

The members of the Group of Experts on Biomedical Research of the LBEC (9 members) are elected by the members of the Lithuanian Bioethics Committee, and approved by the director of the LBEC. Following Article 14 of the Law on Ethics of Biomedical research, the composition of a Regional Biomedical Research Ethics Committee shall be approved by the rector of a founding university upon agreement of the Ministry of Health. Regional biomedical research ethics committees shall consist of 9 members:
1. Two representatives of the biomedical science holding a scientific degree and two representatives of social or humanitarian sciences holding a scientific degree shall be appointed by a university.

2. Three health care specialists from the health care establishments functioning in that region and one specialist of the field of social or humanitarian sciences shall be appointed by the Ministry of Health.

3. One member shall be appointed by patients’ organisations.

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

The measures to safeguard against a lack of independence of Regional Biomedical Research Ethics committee decision making include the following:

Regional Biomedical Research Ethics committees are governmental institutions, financed from the state budget so they are financially independent from commercial entities and applying researches.

The formation and activities of the regional biomedical research ethics committees as well as the Lithuanian Bioethics Committee are legally regulated. These structural and procedural safeguards guarantee Regional Biomedical Research Ethics committee independence from governmental agencies.

Independence of the Regional Biomedical Research Ethics committee members is further ensured because:

1. All essential decisions concerning ethical review of a research protocol are based on the collective decision of the Regional Biomedical Research Ethics committee members.

2. All members of the Regional Biomedical Research Ethics committee must sign the Statement of Impartiality.

3. Experts, who may have any interest in particular decisions or are in way involved with the applying researcher(s) are obliged not to participate in the decision making process of the Regional Biomedical Research Ethics committee regarding that protocol.

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

See question 16 above.

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

Regional Biomedical Research Ethics Committees are composed of the specialists representing biomedical and social sciences as well as humanities, part of them holding a scientific degree. No specific backgrounds or qualifications are required for the member appointed by patients’ organization. Similar principles of representation are followed in the process of composing the Group of Experts on Biomedical Research of the LBEC.
The EFGCP Report on
The Procedure for the Ethical Review of Protocols for Clinical Research Projects in Europe
(Update: April 2012)

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

The LBEC and the Regional Biomedical Research Ethics committees have the right to request that (an) independent expert(s) present(s) conclusions on the biomedical research to be carried out.

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

None are laid down.

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

National and international discussions, seminars and conferences on research ethics organised by different institutions (e.g. Universities, LBEC, etc.) several times a year might be considered as the main training activities for EC members.

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

In both cases no more than 60 days from receiving a valid application for the clinical trials on IMP (with exception of trials involving medical products for gene therapy or somatic cell therapy or medical products containing genetically modified organisms).

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

Substantial amendments are reviewed by the LBEC. The decision to issue approval for a substantial amendment is discussed and approved in a meeting of the committee or by the director of the committee.

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

The assessment of suitability of investigators and sites is based on the review of the presented documents (e.g. CVs of the investigators, licences of health care institutions, as well as other relevant documents).

**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?

Each principal investigator must fill in an Ethical Assessment of Clinical Trial on Medicinal Product form, which includes a request to present the information about the sources of funding, financial interest of investigators (the amount foreseen in the contract) and possible conflicts of interest as well as the financial interest of the trial site. The agreements between sponsor and principal investigator and/or trial site shall
also be presented to the EC. The form of Ethical Assessment of Clinical Trial on Medicinal Products is available online at http://bioetika.sam.lt/index.php?-463543156.

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

Compensation for study subjects is regulated by a Health Care Ministry decree on the Procedure for the Estimation and Covering of Expenses Incurred by Research Subjects.

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

There is no formal quality assurance process system of Regional Biomedical Research Ethics committees in Lithuania. However, the establishment of Regional Biomedical Research Ethics committees, their activities and monitoring procedures are legally regulated. The LBEC is accountable to the Ministry of Health and the Committee annually reports to the Ministry of Health about its own activities, including ethical review of biomedical research.

By law, the LBEC must monitor the activities of Regional Biomedical Research Ethics committee(s).

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

The decisions of the Regional Biomedical Research Ethics committee can be appealed to the LBEC; the decisions of the LBEC can be appealed to the court.

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

The detailed guidelines for the SUSAR reporting to the investigators and the EC in Lithuania are regulated by the Decree No. 435 of the Ministry of Health on the Procedure for Issuing Favourable Opinion to Conduct Clinical Trial on Medicinal Product, Approval for Clinical Trial on Medicinal Product, Conducting and Controlling Clinical Trials. The following reports have to be submitted to the Lithuanian Bioethics Committee:

1. Fatal or life-threatening suspected unexpected serious adverse reactions (SUSARs) that occurred in the concerned trial in Lithuania should be reported in CIOMS form no later than within 7 calendar days and follow-up information - within additional 8 days.
2. Other SUSARs (not fatal and not life-threatening) that occurred in the concerned trial in Lithuania should be reported in CIOMS form within 15 days.
3. All SUSARs that occurred in other Member States and, where applicable, from third countries, should be periodically reported at least every 6 months as a line listing and summary table.
4. Other fatal & life threatening SAEs/SARs (only related) that occurred in the concerned trial in Lithuania should be reported no later than within 7 calendar days and follow-up within additional 8 days.

5. Other safety reports that could essentially change the assessment of the risk/benefit ratio should be reported no later than 15 days.

6. Annual safety report of all SUSARs in the concerned trial should be submitted as a line listing and summary table.

The reports are reviewed by the secretariat members and by appropriate experts if needed.

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

According to the Decree No. 435 of the Ministry of Health on the Procedure for Issuing Favourable Opinion to Conduct Clinical Trial on Medicinal Product, Approval for Clinical Trial on Medicinal Product, Conducting and Controlling Clinical Trials, amendments to the trial are regarded as substantial where they are likely to have a significant impact on the safety or physical or mental integrity of the subjects; the scientific value of the trial; the conduct or management of the trial or the quality or safety of any IMP used in the trial.

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

The civil liability of the sponsor and the principal investigator of biomedical research must be covered by the third party insurance (against research-related damage under Compulsory Third Party Insurance Contracts of the Principal Investigator and the Sponsor of Biomedical Research) provided by insurance companies having an authorization to provide this type of insurance.

The Regulations of Insurance are detailed in the Rules of Compulsory Civil Liability Insurance for the Principal Investigator and the Sponsor.

According to Article 20 of the Rules of Compulsory Civil Liability Insurance for the Principal Investigator and the Sponsor, the insured sum is established by the agreement of the insurer and the policyholder, but can be no less than 100,000 Lt (€29000) for damages which were inflicted during or occurred because of the subject’s participation in the research.

According to Article 6.251 of the Civil Code, the damage incurred must be compensated in full, except in cases when limited liability is established by laws or a contract; according to the Article 6.252, it shall be prohibited to exclude or limit civil liability for impairment of health, deprivation of life or non-pecuniary damage caused to another.
**Question 32:** What are the indemnity insurance requirements for (research) ethics committee members themselves?

Liability of Regional Biomedical Research Ethics committee(s) and the LBEC are not specified in the law.

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

According to the Article 5 of the Law on Ethics of Biomedical Research the following subjects are regarded as vulnerable:

1. Persons with mental disorders, but capable of giving their consent to participate in biomedical research.
3. Students, where their participation in biomedical research is related to their studies.
4. Persons in nursing homes.
5. Soldiers in the active military service.
6. Personnel of health care institutions where biomedical research is being conducted who are subordinate to the investigator.

According to the Article 7 of the Law on Ethics of Biomedical Research (“Protection of Vulnerable Persons”) if the subject is a minor, consent to undertake a biomedical research shall be given by both parents or by the legally acceptable representatives of the minor and the children's rights protection agency of a district or a city. If the parents of a minor are separated, consent of one of the parents or of the legally acceptable representative and of the district or city children’s rights protection agency must be obtained. The consent of a person who has a mental disorder but may give his free and informed consent to take part in a biomedical research must be attested by two witnesses and the head of a health care establishment where a biomedical research is being conducted. Approval of the Medical Ethics Commission must also be obtained. The procedure of forming the Medical Ethics Commission and conducting its activities are laid down in the model regulations of the Medical Ethics Commission of a health care establishment approved by the Ministry of Health.

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

According to the Decree No. 435 of the Ministry of Health on the Procedure for Issuing Favourable Opinion to Conduct Clinical Trial on Medicinal Product, Approval for Clinical Trial on Medicinal Product, Conducting and Controlling Clinical Trials, the sponsor or its legal representative shall submit the Annual Safety Report and the Summary of the Final Report of a research project to the LBEC who will review them.
**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?

According to the Decree No. 435 of the Ministry of Health on the Procedure for Issuing Favourable Opinion to Conduct Clinical Trial on Medicinal Product, Approval for Clinical Trial on Medicinal Product, Conducting and Controlling Clinical Trials it is the responsibility of the sponsor to ensure that annual safety reports are submitted.

For further information please refer to the website of the LBEC: http://bioetika.sam.lt/index.php?-428692189.

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

According to the provisions of Article 5 of the Law on Biomedical Research, children (subjects under 18) are included into a group of vulnerable subjects. One of the specific requirements for the clinical trials on vulnerable subjects (Article 7 of the above mentioned law) is that biomedical research involving vulnerable subjects shall be permitted only where the results of the biomedical research may be of direct benefit to the health of these subjects. Therefore, it might be concluded that national regulations will not allow research on healthy volunteer children (subjects under 16) in Lithuania.

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

As it is stated in the Decree No. 435 of the Ministry of Health on the Procedure for Issuing Favourable Opinion to Conduct Clinical Trial on Medicinal Product, Approval for Clinical Trial on Medicinal Product, Conducting and Controlling Clinical Trials the clinical trial on minors may be undertaken only if no incentives or financial inducements are given except compensation. According to this provision, Lithuanian regulations do not allow payments other than expenses to children taking part in research.

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

The applicants (legal representatives of the sponsor) or principal investigators may be invited to attend the EC meeting when their biomedical research project is discussed. EC members may also invite external experts for the problematic questions to be discussed.

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

The minutes of the ethics committee meetings are not public. However, according to the Decree No. V-405 of the Ministry of Health on the Procedure for Keeping a Record of Biomedical Research, Collecting, Storage and Providing Information on Biomedical Research, dated: 6 May 2010, the list of clinical trials approved by the LBEC is made
publicly available by providing the following information: the title of clinical trial, protocol number, trial site(s) in Lithuania, trial phase, sponsor and legal representative of the sponsor, date of issue and number of approval (favourable opinion) of the LBEC.

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

The chairman of the regional research ethics committee:

- Prepares, convenes, and chairs regular and extraordinary Regional Biomedical Research Ethics committee meetings.
- Represents the Regional Biomedical Research Ethics committee before the appointing authority and to the public.
- Elaborates the plans of Regional Biomedical Research Ethics committee meetings and other activities.
- Ensures timely response to applications.
- Signs official Regional Biomedical Research Ethics committee documents.
- Coordinates, leads, and oversees the work and various activities of the Regional Biomedical Research Ethics committee and of its secretariat.

As the scope of functions of the LBEC in the field of research ethics is not limited to the review of biomedical research projects, the director of the LBEC (who acts as a Chairman of the Group of Experts on Biomedical Research) is also responsible for designing and approving model document forms and operating procedures, monitoring of Regional Biomedical Research Ethics committees activities, dealing with SUSARs, annual safety reports and substantial amendments, as well as the organization of other LBEC activities.

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

The LBEC as well as Regional Biomedical Research Ethics committees do not appoint subcommittees for specific purposes.

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

Clinical trial shall be registered on the European Clinical Trials Database (EudraCT Database). There are no other specific national requirements for the registration of clinical trials before they start.

**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 Lithuania work to a set template of requirements?

No. The insurance requirements for the biomedical research (including clinical trials) are set by the Rules of Compulsory Civil Liability Insurance for the Principal Investigator and the Sponsor approved by the Ministry of Health (The Decree No. 745 of the Ministry of Health on the Rules of Compulsory Civil Liability Insurance for the Principal Investigator and the Sponsor, dated: 20 December 2000).

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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