KLH-EC-01 – APPLICATION FOR ETHICS COMMITTEE OPINION ON THE CONDUCT OF A CLINICAL TRIAL IN THE CZECH REPUBLIC – requirements governing the documentation to be submitted

This guideline is being published in order to harmonise the operation of ethics committees in terms of documentation to be submitted with the sponsor's/applicant's application for ethics committee opinion.
The effective date of the guideline is July 1 2009.

Abbreviations used in the text:
EC – ethics committee
MEC – ethics committee for multicentric clinical trials
LEC – local ethics committee
CT – clinical trial on medicinal products for human use
HF – healthcare facility
MP (IMPD) – medicinal product
TS – trial subject
KLH-.. – SÚKL guidelines for the sphere of clinical trials
GMO – genetically modified organisms

Guidance for applicants for ethics committee opinion on the conduct of a clinical trial of pharmaceuticals

The application for approval of an authorised/notified clinical trial shall be submitted by the applicant/sponsor:

a) In the case of a multicentric clinical trial:
In writing as well as in electronic format only to a single MEC. Concurrently, the sponsor/applicant shall submit the application in writing and in electronic format to all local ethics committees (hereinafter referred to as LEC) at the planned trial sites where the clinical trial is to be conducted and shall inform the LECs on the MEC to which the application for opinion on the CT has been submitted. The sponsor/applicant shall inform the concerned MEC about all other sites and LECs where the application has been submitted (*or will be submitted)*.

b) **In the case of a monocentric clinical trial:**
In writing as well as in electronic format only to the LEC established in the relevant healthcare facility (hereinafter referred to as "HF"). Sites without their own LEC shall apply for the opinion with the geographically closest EC or MEC.

Overview of documents to be submitted together with the European application form to ethics committees with the specification of documents which have to be submitted with the application to the MEC and which to the LEC (section K of the European application form)

Document	**Required by MEC**	**No. of copies**	**Required by LEC**	**No. of copies**
EudraCT confirmation	**NO**		**NO**	
Cover letter in the Czech language	**YES**	**1**	**YES**	**1**
European application form for clinical trial authorisation/notification in writing	**YES**	**1**	**YES**	**1**

Disk with the EudraCT application form in XML format	**NO**		**NO**	
Protocol with all of its current amendments (see KLH-8)	**YES**	*	**YES**	**1**
Investigator's Brochure – preclinical and clinical data - see KLH-9	**YES**	*	**YES**	**1**
Case Report Forms	**NO**		**NO**	
IMPD	**NO**		**NO**	
Summary of the product characteristics (SmPC), if part of the submitted documentation	**YES**	**1**	**YES**	**1**
List of control authorities with which the application has been lodged and information about decisions (e.g. the State Office for Nuclear Safety, Czech Ministry of Health, etc.)	**YES**	**1**	**NO**	
A copy of SÚKL ´s opinion, if available	**NO**		**NO**	
If the applicant is not the sponsor, the authorisation empowering the applicant to act on behalf of the sponsor	**NO**		**NO**	
A copy of the authorisation to use or release genetically modified organisms (if applicable and available)	**NO**		**NO**	
Informed Consent Form in the Czech language with its amendments, if applicable	**YES**	*	**YES**	**1**
Patient Information Sheet in the Czech language	**YES**	*	**YES**	**1**
Subject recruitment scheme (where the investigator selects prospective TS from his/her patients, it shall be sufficient to note this in the cover letter)	**YES**	**1**	**YES**	**1**
Protocol summary in the Czech language – Annex 2 refers	**YES**	*	**YES**	**1**
An overview of all active clinical trials on the same tested IMP	**NO**		**NO**	
Peer review of the clinical trial, if available	**NO**		**NO**	
An ethical assessment performed by the principal investigator or by the coordinating investigator	**NO**		**NO**	
Viral safety study	**NO**		**NO**	
Sample labelling in the national language	**NO**		**NO**	
Relevant authorisations issued for the trial or products of	**NO**		**NO**	

special nature (if available), such as GMOs, radiopharmaceuticals				
TSE certificate, if applicable	**NO**		**NO**	
GMP status declaration for active substances of biological origin	**NO**		**NO**	
A copy of marketing authorisation pursuant to Article 13.1 of the Directive, specifying the scope of this authorisation, if the IMP is manufactured in the EU and has not been authorised in any of the EU Member States	**NO**		**NO**	
Declaration of the qualified person of the importer from third countries confirming that the manufacturing site complies with EU GMP requirements (where applicable)	**NO**		**NO**	
A copy of manufacturing authorisation for importers from the third countries pursuant to Article 13.1 of the Directive. Manufacturing authorisation shall be required for importers from the third countries.	**NO**		**NO**	
A representative certificate of analysis for the tested product	**NO**		**NO**	
Sites where the CT is to take place (including the full name and title of the investigator, full address + contact details)	**YES**	**1**	**YES**	**1**
CV of the coordinating investigator in a participating Member State for multicentric CTs	**YES**	**1**	**YES**	**1**
CV of the investigator responsible for the conduct of the CT in individual sites (principal investigator)	**YES**	**1**	**---**	**---**
CVs of all investigators conducting the CT in the concerned site	**----**	**-----**	**YES**	**1**
Information about auxiliary staff, including qualifications	**----**	**----**	**YES**	**1**
Information on the contact person referred to in Article 3.4 of the Directive (to be provided in the Patient Information)	**YES**	**1**	**YES**	**1**
Provision of insurance or compensation for injury or death due to participation in the CT – **	**YES**	**1**	**YES**	**1**
Liability insurance concluded for the investigator	**YES**	**1**	**YES**	**1**
Liability insurance concluded for the sponsor	**YES**	**1**	**YES**	**1**

Compensation for the investigator	**YES**	**1**	**YES**	**1**
Compensation for CT subjects	**YES**	**1**	**YES**	**1**
Draft agreement between the sponsor and trial sites	**YES**	**1**	**YES**	**1**
Certificate of agreement between the sponsor and investigator, unless provided in the protocol	**NO**		**NO**	
Draft agreement between the investigators and trial sites	**NO**		**NO**	
EC clinical trial questionnaire in the Czech language	**YES**	**1**	**YES**	**1**
If you apply with the EC for an approval of a site in another healthcare facility than that where the EC has been established, the following documents have to be submitted: 1. registration of non-state healthcare facility 2. declaration of adequate resources of the site with respect to the CT 3. a document evidencing the qualifications of investigators	**YES**	**1**	**YES**	**1**

* - The number of required copies shall be specified by the concerned ethics committee

** - the ethics committee shall specify whether the insurance contract or certificate or draft contract is required

Additional information and explanations:

1. **Cover letter** – this has to be submitted with each application, always in the Czech language and providing the following information:

a) whether the applicant applies for a MEC or LEC opinion;

b) where an application to a LEC is concerned, the specification of the MEC which assesses the CT;

c) where an application to the MEC is concerned, a list of all sites and concerned LECs, including addresses;

d) invoicing details (company name, address, Company Registration Number (IČ), VAT Reg. Number (DIČ), etc.);

e) a list of all submitted documents, including the date of issue of the document and revision number of the document, where it has been revised;

f) the contact person for the Czech Republic, including contact details.

If the applicant asks for a confirmation of receipt of the submitted documents, the cover letter shall be submitted in two copies, so that it is possible to note the proper receipt of the documents by the EC on one of them.

2. Pursuant to Section 53, paragraph 1) of Act No 378/2007 Coll., on Pharmaceuticals and on Amendments to Some Related Acts (the Act on Pharmaceuticals), the ethics committee shall be entitled to request **the reimbursement of costs** incurred in association with the issue of the opinion. The applicant shall be obliged to submit the invoicing details upon the submission of the application, the reimbursement of costs shall be required by means of an invoice sent after the assessment of the

application is completed. The amounts of reimbursements of costs are provided on the websites of the ethics committees or shall be provided to applicants upon request by the ethics committee or by its establishing entity.

3. The applicant shall submit the same version of the **Protocol Summary in the Czech language** as to SÚKL + the **Ethics committee questionnaire** in the Czech language – ***Annex 1***

4. Where an application for **site assessment** is concerned (for a LEC or MEC in the position of a LEC or MEC assessing, at the same time, also the site) the following shall be submitted: **CVs of investigators** (of the principal investigator as well as co-investigators) in the concerned site and a **list of staff** specifying their positions and scope of activities to be performed thereby within the framework of the clinical trial in question (ideally in tabular format). Where a private/non-state healthcare facility is concerned, the applicant shall, furthermore, submit a copy of the HF registration. Where a state healthcare facility is concerned, the applicant shall submit the approval of the hospital management and management of the workplace where the study is to be conducted.

5. The applicant shall submit all **recruitment and information materials** to be used in the concerned clinical trial, including questionnaires for trial subjects or instructions for use of medicinal products or used medical devices in the Czech language – if they are to be used.

6. **Insurance –** the applicant shall submit a copy of the insurance contract or draft insurance contract – to be specified by the concerned ethics committee.

7**. Trial subject compensation –** the information on the amount of compensations for trial subjects and other specifications shall be provided by the sponsor/applicant in the CT questionnaire (Annex 1 refers).

8**. Information on renumeration or compensation for the investigators –** together with the application, the sponsor shall submit **a written information on the amount of remuneration for the investigator** (as referred to in Section 5, paragraph 3 (c) of Decree No 226/2008 Coll.)

Both LEC and MEC shall issue their opinions on the clinical trial within 60 days of receipt of the complete application, unless a type of study for which the Act stipulates other timelines is concerned (gene therapy, somatic cell therapy, incl. xenogenic cell therapy or involving genetically modified organisms). Within the period when the application is being assessed for the purposes of issuance of the opinion, the EC may once send a request for information to supplement the data submitted by the applicant. The timeline established for the issuance of the opinion shall be suspended until the additional data are delivered to the EC. Following the submission of the documentation, the applicant may not amend the documents; this would be considered as a new submission unless the provision of documents requested by the EC is concerned. The EC shall have this power with respect to all types of assessments. Where the EC declines the conduct of the CT, the applicant shall be obliged to re-submit the application to the same EC to which the initial application for assessment has been submitted.

Grant projects

If a grant project complies with the statutory requirements for clinical trials, the applicant shall submit to the EC the same documentation which has been submitted thereby to the State Institute for Drug Control for assessment, and the same obligations as those of other sponsors shall be applicable thereto – see above for the requirements.

Methodological notes

General recommendations regarding Patient Information Sheet and Informed Consent Form

- do not use foreign terminology;
- perform proofreading – from scientific, linguistic and psychological (ethical) aspects;
- explain abbreviations;
- explain procedures and assessments to be performed;
- patient information should be presented briefly and clearly;
- restrict the number of pages, especially in the case of CTs involving trial subjects suffering from severe conditions;
- comply with the terminology established by Czech or European legislation (e.g. names: ethics committee, State Institute for Drug Control and foreign control authorities);
- where placebo is used, mention the likelihood of being assigned to the placebo group and properly explain why placebo has to be used and what does it mean;
- where biological material sampling is involved, explain the research for which the sample will serve, the site where the taken sample is to be processed, method of sample anonymisation or encryption, sample storage period, and if a future use of the sample is considered, an explanation of the purpose for which is to be used and how long the sample is to be stored;
- the section on insurance should, for example, mention that the clinical trial has been covered by insurance in compliance with the Czech legislation;
- the section on potential injuries should state that the trial subject has the right to claim compensation for damages as per the effective legislation, if he or she suffers an injury due to his or her participation in the clinical trial. Explain that if the trial subject thinks that he or she has suffered an injury due to his or her participation in the study he or she should contact the investigator who will provide contact with the CT sponsor.