

Regulatory Requirements for Clinical Trials Conduct in the Czech Republic

This document provides applicants for clinical trials approval in the Czech Republic with information on substantial regulatory requirements. The information provided match requirements as of 2008. The document is published at <http://vpatras.blogspot.com>

GENERAL INFORMATION

REGULATORY AUTHORITIES (or Competent Authority (CA))

State Institute for Drug Control – Clinical Trials and Pharmacovigilance Branch
(Státní ústav pro kontrolu léčiv, Sekce klinického hodnocení a farmakovigilence)
www.sukl.cz

Czech Ministry of Health
(Ministerstvo zdravotnictví)
<http://www.mzcr.cz/>

Products containing radiopharmaceuticals
State Office for Nuclear Safety
(Státní úřad pro jadernou bezpečnost)
<http://www.sujb.cz/>

Products containing GMOs
Ministry of Environment
(Ministerství životního prostředí)
<http://www.env.cz/>

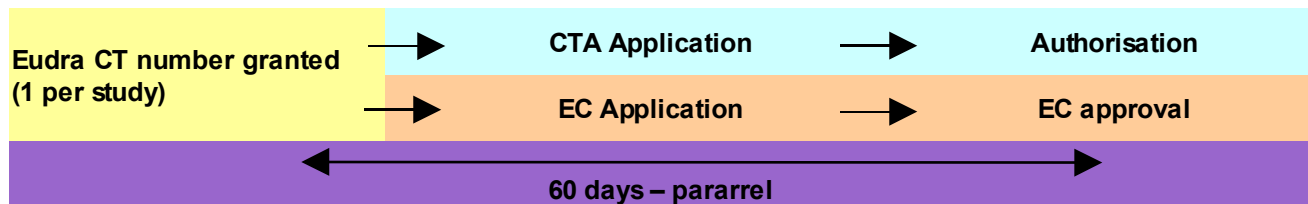
OTHER RELEVANT BODIES

- Central Ethics Body: Ethics Committee of Ministry of Health (Etická komise Ministerstva zdravotnictví)
- Industry Bodies:
 - ACRO Czech Republic (Association of CROs) <http://www.acro-cz.cz/index.php>,
 - Association of Innovative Pharmaceutical Industries <http://www.aifp.cz/cz/index.php>

LIST OF RELEVANT LEGISLATION

Law No. 79/1997 on Medical Products and its amendments,
Regulation No. 228/2008 on Good Clinical Praxis and Clinical Trials

CTA FLOW CHART



BEFORE THE STUDY (submissions - all phases)

REGULATORY AUTHORITIES

Documents required:

Reference: SUKL regulations KLH 19 (Documentation required for an approval of a clinical trial on a human pharmaceutical) and KLH 20 (Application for approval/notification of a clinical trial)

<http://www.sukl.cz/download/en08/klh/klh19a.rtf> (KLH 19)

<http://www.sukl.cz/download/en08/klh/klh20a.rtf> (KLH 20)

- EudraCT number
- Electronic EudraCT number application
- Cover letter (Czech or English language)
- Clinical Trial Application (CTA) – The EU standard application form (filled in Czech or English language)
- Protocol
- Investigator's Brochure
- Case Report Forms (CRF)
- IMPD
- SPC for registered medicines
- List of authorities where the application has been submitted and their decision
- Copy of Ethics Committee decision (if already issued)
- Approval of GMO use or release (if applicable)
- Power of attorney if applicant is not sponsor
- Informed consent in Czech language
- Patient information in Czech language
- Protocol synopsis in Czech language
- List of all ongoing trials with the same IMP,
- Viral safety assessment
- Approvals for preparations with special substances (such as radiopharmaceuticals, GMO) if applicable
- TSE certificate if applicable

- GMP declaration for substances of biological origin
- Copy of manufacturing approval
- Declaration of certified person of importer from third countries that manufacturing site comply with GMP requirements (if applicable)
- Manufacturing permit for importers from third countries (if applicable)
- Analytical certificate for IMPD, list of study centers, information on contact person

Procedure:

60 days approval time, 90 days for gene therapy and products containing GMOs, unlimited approval time for xenogenic cell therapy – clockstop if additional documents are required. Sponsor shall report beginning of the trial (start of recruiting) in 60 days to SUKL.

ETHICS COMMITTEE

CENTRAL ETHICS COMMITTEE (MULTICENTRIC ETHICS COMMITTEE)

Documents required:

- Clinical Trial Application (CTA) – The EU standard application form (filled in Czech or English language)
- Protocol
- SIS/IC
- Recruitment plan including advertising
- Investigator brochure and available safety data
- Information on payments to subjects and possible compensation
- Investigator CV or other documents confirming his/her experience
- EC can require further relevant documents

Procedure:

All EC submissions can be made as parallel to CA submissions. There is single opinion for multicentric studies (MEC - Multicentric Ethics Committees). Sponsor can address any EC, which should have relationship toward investigation site, to act as MEC. MEC review all aspects of the study except of investigator qualification and site suitability.

Multicentric EC decision is issued within 45 days after application submission. Local EC stage follows. Only investigator qualifications and site suitability are subject to evaluation of local EC, which shall (in multicentric studies) express its position within 15 days after multicentric EC decision and report it to SUKL, sponsor and multicentric EC. Total time for EC decision (multicentric and local

together) is 60 days. This period can be extended in case of gene therapy products or products containing GMOs. The period is unlimited for xenogenic cell therapy. Stopclock applies if further information is required. Ethics committee should check course of the trial approved at least once a year.

LOCAL ETHICS COMMITTEE

Documents required:

The same as in case of central ethics committee

Procedure:

Competence of local ethics committees are investigator qualification and site suitability as described above. Also studies with only one site require opinion of ethics committee having multicentric designation.

DURING THE STUDY (amendments – all phases)

REGULATORY AUTHORITIES

Sponsor have to notify all substantial amendments which include:

- The safety or physical or mental integrity of the subjects
- The scientific value of the trial
- The conduct or management of the trial
- The quality (including composition, manufacturing process) or safety of any IMP used in the trial

And all changes which include changes in number of enrolled subjects, dosage and administration, trial duration, inclusion and exclusion criteria, methods of data processing, procedures of samples collection.

Documents required:

- The EU standard form for notification of amendment (filled in Czech or English)
- EudraCT number
- Amended documents
- Proof of payment

Procedure

The sponsor may implement a substantial amendment when the CA has raised no grounds for non-acceptance. Amendment may be implemented after 35 days from the receipt of a valid notification of amendment if the CA has not raised grounds for non-acceptance.

CENTRAL AND LOCAL ETHICS COMMITTEES

Substantial amendments have to be submitted for EC review. Requirements as in the case of RA.

Documents required

- Amended documents
- Covering letter

Procedure:

The sponsor may implement a substantial amendment when the EC opinion is favourable. EC should provide opinion within 35 days.

THE END OF THE STUDY (all phases)

End of study reporting

- In the case of a premature termination, expedited reporting is required to CA/EC/Hospital and sponsor. Applicant is required to present explanation of premature termination. Period to report premature termination of the study to CA is 15 days.
- The sponsor/CRO reports to CA termination of trial within 90 days. Final reports must be submitted to CA in both premature and planned termination of the study
- Within 1 year after termination, the sponsor submits a annual study and annual safety report to the CA and the EC.

OTHER REQUIREMENTS

INVESTIGATIONAL MEDICINAL PRODUCT

Labelling

Labelling must include following information:

- All informations must be presented in Czech language, information in other languages can also be included
- Name, address, telephone number of sponsor, investigation site, or investigator
- Pharmaceutical form, administration route, dose quantity, name/identifier and strength/efficacy in open label studies
- Batch number and/or code for identification of content and adjusting operations
- Reference code enabling study identification, place of study, investigator and sponsor if not stated elsewhere

- Instructions for use (can refer to PIL or other instruction document for subjects or person administering the medicinal product)
- Label “For research use only” or similar
- Storage conditions
- Usable life in month/year format legible and unambiguous
- Label “Keep out of reach of children” this apply only if subjects take the medicine to their homes
- Symbols and pictograms can be included in order to make content more clear
- In the case of supplementary prolongation of usability, an additional label with the new expiry date or the date of re-test and the batch description is to fix on the box and, if used on the outer envelope. The new label may cover the prior date, but not the batch description. The new label may be applied by a certified person only.

Manufacturing

If product used in the trial is not registered in the Czech Republic one of following documents shall be submitted:

- Certificate on good manufacturing practice
- Manufacturing licence issued by CA of the country
- Written declaration of person responsible for quality assurance acting on behalf of sponsor on manufacturer compliance with good manufacturing practice requirements - this can only be used as provisional measure, sponsor should require CA on inspection (in order to receive GCP certificate)

http://www.sukl.cz/_download/cs08pokynform/klh/klh12.rtf (in Czech language only)

Import License

No import license is necessary if the IP is manufactured in an EEA state

If the IP is manufactured in a Non-EAA state

- A qualified person is responsible for batch analysis
- GMP certificate of a competent authority of the country

SAFETY

- SUSARs – expedited reporting - 7+8 = 15 days
- Line listings – submitted quarterly to ECs with covering letter, should be sent with a cover letter containing an assessment of the safety status, information on whether safety measures are necessary and if so a listing of what measures to be taken and the justification
- Annual safety report, new findings from scientific literature must be included
- Investigator`s brochure must be updated accordingly at least once a year

http://www.sukl.cz/_download/en08/klh/klh21a.rtf

INSURANCE / INDEMNITY

According to the Czech law sponsor is obligated to arrange liability insurance for the subjects of assessment to cover damages to health. Also both sponsor and investigator must be insured. There is no defined amount for insurance coverage.

FEES

Regulatory approval

	Sum in Czech crowns	Sum in Euros
Clinical Trial Application	67300	2760
Extension of approved clinical trial	15800	650
Protocol amendment	15800	650
Ethics committee fee (multicentric trial)	Approx. 40000	1400

http://www.sukl.cz/uploads/Poplatky_a_sazebnik/ust29v2_an.doc

Ethics approval

Each EC has its own fee policy

MISCELLANEOUS

Documents to be submitted in Czech language:

Protocol synopsis, informed consent, patient information

SIS/IC requirements

- Information on purpose of clinical trial
- The subject is to be informed that the subject may discontinue participation at any time without penalty or loss of benefits
- Potential risks and benefits of treatment, other treatment options
- Guarantee and explanation of data protection
- Information on rights and duties of the patient in regard of the trial

Data protection

Czech law no. 101/2000 on personal data protection applies.