The EFGCP Report on
The Procedure for the Ethical Review of Protocols for
Clinical Research Projects in Europe and Beyond

Question 22

What are the timelines for the assessment of single- and multi-site studies?
Austria

The timelines for all applications for clinical trials with drugs which are submitted to the announced deadline are 35 days with one “clock stop” possible to ask for further information.

Clinical trials regarding gene therapy, somatic cell therapy including xenogene cell therapy as well as including all drugs with genetically altered organisms have a timeline of 90 days.

The timelines for clinical trials including medical devices are 60 days. All other trials have no regulation.

Belgium

15 calendar days for phase 1 studies, 28 days for other studies. One clock-stop for questions to the investigator is allowed. There are exceptions for protocols with GMO’s, biotech drugs, etc.

Bulgaria

The timeline for the ethics committee is 30 days. The timeline for the final competent authority authorization is 60 days.

Croatia

The Central EC is obliged to provide an opinion within 30 days. The exceptions are the drugs for gene therapy, treatment with somatic cells, including genetically modified organisms, for which the opinion has to be given within 90 days. This deadline can be extended for another 90 days if there is a need for consultation with experts or other committees. Time restrictions do not apply for xenogeneric drugs.

Cyprus

Timelines for bioethical assessments are the same for both single- and multi-site studies. Difference timelines apply for biomedical research and for clinical trials.

Biomedical Research:
According to the Operational Guidelines for the Establishment of Ethics Committees in reviewing Biomedical Research involving Human Subjects (Κ.Δ.Π. 175/2005), an ethics committee must announce its decision on the application within a period of 40 days after the submission of a complete study review application, by completing Form EEBK 04. The timetable that will be followed in cases where the Ethics Committee requests additional information or changes in documents submitted by the applicant will be determined by the Ethics Committee.
Clinical Trials on Medicinal Products of Human Use:
Regulation 14(4) of the Operational Guidelines on Medicinal Products for Human Use (Good Clinical Practice), K.Δ.Π. 452/2004, states that the Cyprus National Bioethics Committee has a timeline of 60 days from the time of receiving an application, to issue its decision and notifies the applicant and the Drugs Council.

According to the provisions of the legislation (Regulation 14 (3.6) of the Legislation on Medicinal Products for Human Use (Good Clinical Practice - K.Δ.Π. 452/2004) an extension of 30 days may be given in the case of trials involving medicinal products for gene therapy or somatic cell therapy or medicinal products containing genetically modified organisms.

**Czech Republic**

60 days for both.

**Denmark**

1. The committee shall decide on the approval of a project within 60 days of receiving a valid application, however, cf. subsections 2. and 3. below.

2. The time limit pursuant to subsection 1. above shall be extended by 30 days if the processing concerns an application for the approval of trials involving gene therapy or somatic cell therapy or medicinal products containing genetically modified organisms. The 90-day deadline shall be further extended by 90 days in case of consultation of public boards or commissions. No time limit shall apply to the authorisation period regarding the processing of an application for the approval of xenogenic cell therapy.

3. The committee may within the processing period of the application send one request for information supplementary to the information already supplied by the applicant. The time limit pursuant to subsections 1. and 2. above shall be suspended until receipt of such supplementary information.

**Estonia**

As a rule assessment will be completed within 60 days for biomedical research and 90 days for genetic research as the legislation requires, but when additional documents are needed or problems arise then correspondence with the applicant may last much longer.

**Finland**

Timelines are based on Directive 2001/20/EC.

**France**

Five weeks.
Germany

For mono-site trials it is 30 days for pharmaceutical drug trials, 60 days for medical device trials.

For multi-site trials (with pharmaceutical drugs or medical devices) it is 60 days after receipt of complete application documents.

For radiation research it is also 60 days. Other biomedical research projects do not have timelines for assessment.

However, for trials on somatic cell or gene therapy the timeline is 90 days. This can be extended by another 90 days if gaining external advice requires this.

For substantial amendments the timelines are 20 days for pharmaceutical drug trials, 30 days for medical device trials and 35 days for trials on somatic cell or gene therapy.

Greece

60 days, in accordance with the legislation (see 1 above) in both cases.

Hungary

No difference between multi and single site study assessment.

As for gene therapy, somatic cell therapy and GMO IMPs, the NIP’s process may last for 90 days, within which the KFEB has 72 days. In case of xenogenic cell therapy protocols, the deadline is 12 months (11 for the ethical approval).

Iceland

Multi-site studies are regarded as “a single” application in this context. According to Reg. 443/2004, the ethics committee has 60 days to assess clinical trials, barring special circumstances (see Art. 6). The NBC may make one request for additional data after it receives a valid application; the application process shall be suspended until the committee receives the data requested. Subjects brought to the NBC come preferably on the agenda of the next meeting, usually within 14 days. Approvals are issued within 50 days on the average - depending chiefly on the time applicants need for responding to remarks and requests for clarification, as applies.

Ireland

A recognised ethics committee must complete the single ethical review of any CTIMP within 60 days of receipt of a valid application. This includes the necessary site-specific assessments.
Italy

According to the Legislative Decree no. 211 of 24 June 2003, in the case of single site trials, the Ethics Committee has to notify its opinion to the sponsor, to the Italian Medicines Agency and to the competent Authority by 60 days from the receipt of the clinical trial application.

In the case of multi-sites trials, the single opinion has to be expressed by 30 days from the receipt of the application; the acceptance or refusal of it has to be notified by the Ethics Committees of the participating sites to the sponsor, to the other Ethics Committees, to the competent Authorities by 30 days from the receipt of the single opinion.

Latvia

30 days for ethics committees and 60 days for the State Agency for Medicines (SAM).

Lithuania

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).

Luxemburg

Sixty days after the date of receipt of the dossiers.

Malta

The HEC operates according to the Regulations and generally has a maximum of 60 days, plus one clock-stop to request supplementary information, from the receipt of a valid application.

Netherlands

The ethical review of research with medicinal products, whether single- or multi-site, must be completed within 60 days of receipt of a valid application. For specific studies (e.g., gene therapy) the time line is 90 days. The clock may stop once to request further information or clarification from the applicant.

Norway

The regulations state that the timeline, for single site and multi-site studies, is 60 days from the acknowledgement of the application. It is however more likely to be approximately 30 days.
Poland

The ethical review of any study, whether single- or multi-site, must be completed within 60 days. The clock may stop to request further information or clarification from the applicant.

In the case of multi-site studies, site-specific assessments (SSA) may take place in parallel with the main application so that the main REC has information about all the other sites within the 60 days. The timeline for SSAs is 14 days, but no response is deemed to be a positive response.

Portugal

The timelines are in line with what is defined in the national law (Lei 46/2004 de 19 de Agosto) and the 2001 EC directive.

Romania

Sixty days for both single- and multi-site studies.

Russia

Within 15 days after submission to the Ethics Committee under Federal Authority (not depending on the number of sites).

Serbia

60 days, if documentation is complete,

Slovakia

The timelines are provided for by law – 60 days, in accordance with the legislation.

Slovenia

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.

Spain

Timelines are 60 days in general, according to the regulations; 90 days for CT on cell or gene therapy or with GMO medicinal products. When a CEIC requests additional information, a clock stop is allowed. Conversely, there is no clock stop for the AEMPS.
Sweden

The only timeline, for single site and multi-site studies, is 60 days from the acknowledgement of the application. It is however in real life much faster, usually approximately 30 days for both EC and CA.

Switzerland

Initial review and feed-back to the investigator within 30 days after submission of the study documents to the REC.

Turkey

For ECs: Ethics committees will form their opinion and communicate it to the applicant within thirty days after the application date. Should additional information or clarifications become necessary during the ethics committee review, all of the requests will be communicated to the applicant in a single request. A second request will not be made to the applicant. The review process will be frozen until the required data and documents are submitted to the ethics committee.

For MoH: All drug clinical trials will be evaluated within not more than thirty days by the relevant general directorate.

United Kingdom

For most studies, ethical review must be completed within 60 days of receipt of a valid application. This applies both to single- and multi-site studies. The clock may stop once to request further information or clarification from the applicant.

A 90 day timeline applies to clinical trials of medicinal products for gene therapy, somatic cell therapy or containing a genetically modified organism or a tissue engineered product. Where a specialist group or committee is consulted on such a trial, the timeline may be extended to 180 days.

The operational aim of NRES is for RECs normally to give a final decision within 40 days where an application is reviewed at a full Committee meeting, or 14 days if reviewed by a sub-committee under procedures for Proportionate Review (see question 41).

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