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

Question 23

How are substantial amendments submitted during the review process dealt with?
Austria

The process depends on the time of receipt of the amendment. If received in time, the amendment will be dealt with in the respective convened meeting of the EC and will be considered during the decision making. In case of receipt after the respective meeting the decision will be made based on the documents available at the meeting and the amendment will be dealt with separately.

Belgium

By the investigator to the research ethics committee; for a multicentre trial only to the single opinion committee.

Bulgaria

Substantial amendments are forwarded to the expert that makes the assessment and the amendment is approved within the initial approval decision.

Croatia

Substantial amendments are subject to the same principles of review as a new study.

Cyprus

As per the provisions of the Operational Guidelines for the Establishment of Ethics Committees in reviewing Biomedical Research involving Human Subjects (Κ.Δ.Π. 175/2005), any amendments of the study protocol that are likely to influence the rights, the safety and/or the prosperity of the individuals participating in the study or the general conduct of the study must be notified to the Cyprus National Bioethics Committee, immediately, and in any case before their implementation in the research protocol procedures. The principal investigator has to use the Form EEBK 10 to submit an application to the Ethics Committee for approval of suggested changes to the protocol of a study. The Review Bioethics Committee will issue its decision in the timelines set above and notify the principal investigator.

Czech Republic

They are considered by the REC within 35 days, a fee having been paid (see 10).

Denmark

If submitted separately they are assessed accordingly.
Estonia

They are submitted with a summary of the amendment and are discussed at the next regular EC meeting.

Finland


France

In the same way as the original protocol.

Germany

Submission of substantial amendments during the review process is usually not accepted – in line with the practice of the competent authorities. However, sometimes it would reduce the work of the REC and the competent authority, therefore sometimes a requesting phone call is advisable.

Greece

They are reviewed within 35 days, in accordance with the legislation (see 1).

Hungary

The same procedure applies to all protocol amendments. Their submission follows the route of the original submission.

Iceland

All amendments are reviewed and approved by the ethics committee (as well as by the IMCA in the case of clinical trials). Substantial amendments can be made to a study which has been approved by the Committees. Amendments shall be decided upon within 35 days from submission to the NBC.

Ireland

Substantial amendments to IMPs should be notified in writing, using the European Commission notice of amendment form, to the single recognised ethics committee that originally reviewed the submission, together with the appropriate fee. The ethics committee has 35 days from receipt of the notice of amendment to give an opinion. Where an unfavourable opinion is given on a substantial amendment, the sponsor may submit a modified amendment on which the ethics committee has 14 days to give an opinion.
Italy

The substantial amendments are submitted by the sponsor according to the same procedure followed to obtain the initial approval of the clinical trial. In the case of a single site trial the Ethics Committee releases its opinion by 35 days from the receipt of substantial amendments application.

In the case of a multi-centre trial the Ethics Committee of the coordinating site releases its opinion by 20 days from the receipt of the application and the Ethics Committees of the collaborating sites may accept or refuse this opinion by 15 days from its receipt.

Latvia

They are submitted to the ethics committee and to the SAM. The Ethics Committee shall provide an opinion and the State Agency of Medicine shall take a decision not later than 30 days after receipt of an amendment.

Lithuania

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.

Luxemburg

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.

Malta

The Regulations apply and the HEC has a maximum of 35 days from the receipt of a valid application to issue an opinion.

Netherlands

These require a new decision from the METC, but the chairman may be mandated to review the amendment without the involvement of the full committee.

Norway

They are fully reviewed by the Committee.

Poland

These are dealt with within the periods allowed for the clock to stop.
Portugal

The evaluation is made on a case by case basis. If the amendment has an impact in the patient’s recruitment process, the time frame for evaluation is a further 60 days. If this is not the case the amendment is evaluated within 35 days.

When an unfavourable opinion is given to the clinical trial protocol the amendment consequently obtains the same decision.

Romania

The substantial amendments are submitted by correspondence during the review process. NECCT has to communicate to the applicant the reception and the approval (or not) of the amendments.

Russia

They are handled separately in accordance with a specific SOP.

Serbia

The sponsor or CRO submits any request for substantial amendments approval, with documentation, to the CA.

Slovakia

Substantial amendments have to be reviewed within 35 days.

Slovenia

They are subject to the same principles of review as a new study.

Spain

Substantial amendments are validated in 10 days and assessed within 35 days, in accordance with the regulations.

Sweden

They are handled separately and charged accordingly. If not too late in the review process, they may actually be considered in the vetting of the original application.

Switzerland

Within the ordinary REC sessions.
Turkey

If, after the commencement of a clinical trial, the need arises to make any of the amendments described in the Guideline for Good Clinical Practice, such amendment(s) will be notified to the ethics committee concerned, to be approved by the sponsor, and to the relevant general directorate. Should the amendments be found acceptable, the ethics committee will approve them within fifteen days, and the general directorate concerned within thirty days, to the extent they find the amendments acceptable.

United Kingdom

Substantial amendments are notified to the REC using the Notice of Substantial Amendment form within the Integrated Research Application System. The main REC has 35 days from receipt of a valid notice of amendment to give an opinion. Amendments may be reviewed either at a meeting of the full Committee with at least 7 members, or more normally by a sub-committee either at a face-to-face or telephone meeting or in correspondence. Review in sub-committee must include the Chair or a vice-chair together with at least one other member. Reviews by telephone meeting or in correspondence are minuted in the same way as face-to-face meetings.

Where an unfavourable opinion is given on a substantial amendment, the Regulations allow the sponsor to submit a modified amendment. The ethics committee has 14 days to give an opinion on a modified amendment. If the opinion remains unfavourable, there is no formal appeal mechanism but a further modified amendment may be submitted.

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