ANNEX II

APPLICATION DOSSIER FOR SUBSTANTIAL MODIFICATION

A.INTRODUCTION AND GENERAL PRINCIPLES

1. Where a substantial modification concerns more than one clinical trial of the same sponsor and the same investigational medicinal product, the sponsor may make a single request for authorisation of the substantial modification. The cover letter shall contain a list of all clinical trials to which the application for substantial modification relates, with the EU trial numbers and respective modification code numbers of each of those clinical trials.

2. The application shall be signed by the sponsor or a representative of the sponsor. This signature shall confirm that the sponsor is satisfied that:

(a) the information provided is complete;

(b) the attached documents contain an accurate account of the information available; and

(c) the clinical trial will be conducted in accordance with the amended documentation.

B. COVER LETTER

3. A cover letter with the following information:

(a) in its subject line, the EU trial number with the title of the clinical trial and the substantial modification code number which allows unique identification of the substantial modification, and which shall be used consistently throughout the application dossier;

(b) identification of the applicant;

(c) identification of the substantial modification (the sponsor's substantial modification code number and date), whereby the modification may refer to several changes in the protocol or scientific supporting documents;

(d) a highlighted indication of any special issues relating to the modification and an indication as to where the relevant information or text is located in the original application dossier;

(e) identification of any information not contained in the modification application form that might impact on the risk to subjects; and

(f) where applicable, a list of all clinical trials which are substantially modified, with EU trial numbers and respective modification code numbers.

C. MODIFICATION APPLICATION FORM

4. The modification application form, duly completed.

D. DESCRIPTION OF THE MODIFICATION

5. The modification shall be presented and described as follows:

(a) an extract from the documents to be amended showing previous and new wording in track changes, as well as an extract showing only the new wording, and a explanation of the changes; and

(b) notwithstanding point (a), if the changes are so widespread or far-reaching that they justify an entirely new version of the document, a new version of the entire document (in such cases, an additional table lists the amendments to the documents, whereby identical changes can be grouped).

6. The new version of the document shall be identified by the date and an updated version number.

E. SUPPORTING INFORMATION

7. Where applicable, additional supporting information shall at least include:

(a) summaries of data;

(b) an updated overall risk/benefit assessment;

(c) possible consequences for subjects already included in the clinical trial;

(d) possible consequences for the evaluation of the results;

(e) documents which relate to any changes to the information provided to subjects or their legally designated representatives, the informed consent procedure, informed consent forms, information sheets, or to letters of invitation; and

(f) a justification for the changes sought in the application for a substantial modification.

F. UPDATE OF EU APPLICATION FORM

8. If a substantial modification involves changes to entries on the EU application form referred to in Annex I, a revised version of that form shall be submitted. The fields affected by the substantial modification shall be highlighted in the revised form.

G. PROOF OF PAYMENT OF FEE (INFORMATION PER MEMBER STATE CONCERNED)

9. Proof of payment shall be submitted, if applicable.

Changes to legislation:
There are currently no known outstanding effects for the Regulation (EU) No 536/2014 of the European Parliament and of the Council, ANNEX II.