Transition Trials

Which documents have to be provided for part II in case of "transition trials"?

In accordance with questions 5 and 6 of the "Guidance for the Transition of clinical trials from the Clinical Trials Directive to the Clinical Trials Regulation", 19. July 2023 the sponsor is requested to submit the latest authorised versions of the subjects' information sheet(s) and the informed consent as a minimum set for Part II. No additional part II documents are required for validation for the transitioning application. Thus, additional document should not be uploaded. Additional documents would not be part of the validation. No other documents should be submitted. Be reminded that during the transitioning application no changes to already approved documents, trial sites, investigators etc. are allowed.

Only the clinical trial sites which are active need to be included in application form. For any previously approved and not yet deregistered trial site that is not being transitioned, the sponsor should clarify in the cover letter that this site shall be deregistered.

Unless stated otherwise in the cover letter and CTIS, trial sites will be deemed to proceed under CTR with only their principal investigator (“Prüfer”) and not the former deputy (“Stellvertreter” named in the site suitability form) as investigator.

For further details we refer to the Guidance mentioned above.

Interner Vermerk: Im Rahmen der Validierung sollte geprüft werden, ob die vorgelegten Dokumente den letzten genehmigten Fassungen entsprechen (Versionsbezeichnung und Versionsdatum). Eine inhaltliche Prüfung erfolgt weder zu den Dokumenten zu Teil I, noch zu Teil II. Sollte dennoch ausnahmsweise offenbar werden, dass die klinische Prüfung mit den **Prinzipien der CTR** nicht vereinbar ist, ist nach der Transition zu erwägen, in Abstimmung mit den Bundesoberbehörden eine Corrective Measure einzuleiten.

Im AR II würde in dem Falle, dass über Unterlagen über das Minimumset hinaus eingereicht würden, folgender Hinweis erfolgen: “In accordance with the guidance ("Guidance for the Transition of clinical trials from the Clinical Trials Directive to the Clinical Trials Regulation", 19 July 2023) the validation did include the subjects' information sheet(s) and the informed consent form(s) and the application form concerning the named trial sites and investigators, only.”

What needs to be considered concerning part II in the event of a subsequent substantial modification after the clinical trial has been transferred to the CTIS as a transition trial?

With the first substantial modification of part II, the sponsor should complete **all** elements related to Part II of the dossier (i. e. all documents required for part II according to Annex I CTR). E. g., for all named investigators the CV, FDF and training certificates have to be uploaded.

In transitioned trials, no formal evidence (“update” certificate) is required to show that investigators previously approved under CTD have been trained up to the standards of CTR. According to ICH E6 5.6.1 it is the sponsor’s responsibility to ensure that investigators are qualified to properly conduct the trial under CTR. In general, the CVs, FDF and certificates approved under CTD do not have to be updated. The site suitability statement does not have to be updated retrospectively. Please note that formal evidence on regulatory training including training on CTR (cf. https://www.akek.de/curriculare-fortbildungen/) is required for any new investigators added after transition.

In the course of a substantial modification application, the sponsor should clearly state in the cover letter or by way of a “Summary of Changes”-document:

- which documents in part II are only being supplemented and have not changed since their approval under CTD, and
- which documents in part II have been amended since their approval under CTD and are now being submitted for approval as part of the substantial modification application.
- If during the SM documents are replaced by new versions, it is sufficient to provide the new version.

The sponsor should provide a document with a list of the trial sites including the names of investigators. Any changes to trial sites and/or investigators that are being submitted for approval as part of the substantial modification application should be highlighted.

Interner Vermerk: Nach Question 8 der Guidance brauchen Dokumente, die wegen des Fortschreitens der klinischen Prüfung nicht mehr eingesetzt werden, nicht nachgeliefert zu werden. („The upload of new template documents for procedures in the trial already completed, e.g. if recruitment of trial participants has ended, is not required.")