ePRO: Cross-Trial Libraries, Standards and Best-Practice Gains

About this document

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Related documents: *Data Handling and Change of eCOA data.*

1 Aspects for consideration

There are two key aspects regarding ePRO, instrument validity and trial application IRB/EC submissions that are important to consider when discussing cross-trial libraries, standards and best-practice gains.

1.1 Validation

We are (in most cases) operating with so called "validated instruments". In most cases, this is a paper questionnaire which has been validated to give an accepted and consistent "measure" across countries/cultures. If these are in any way altered or deployed in a different way than what has been validated, this alteration must then also be validated to ensure the instrument validity is kept and that the result can be used. Most instrument providers have a defined process for validating an electronic implementation, and many also provide a validated electronic version.

> *"Requirements for a final, validated system is separate from requirements for submission to national authorities/ ECs / IRBs"*

1.2 Submission requirements

Since the instrument is used by patients, national authorities/ECs/IRBs require information to be included in the submitted material. Whilst the instrument validation and technical validation must be completed *before* the ePRO solution can be released and used, this work does not need to be fully completed before submission to national authorities/ECs/IRBs. These are two separate requirements.

There are generally four levels of requirements for what must be included in the submission for different national authorities/ECs/IRBs:

a) The exact same screens in the local language that the patient will see including log-on screens (system framework), edit-check-questions etc., plus any reference guide or other relevant material.

b) Screens with the same content/questions as that the patients will see: a generic screen is acceptable. It doesn't have to be on the exact device the patient will end up using, so a different screen-size, font, colours etc., is fine. Many instrument providers provide these as part of the licensed "package".

Phone +45 52 19 31 99 |Mail: info@triticom.com

TriTiCon | Sandvejen 30 | DK 2665, Vallensbæk Strand | Denmark

c) A description of the method (normally in the protocol) and a paper "original", in English or in the local language, of the actual questions (not requiring the system framework).

d) A clear reference in the protocol to the instrument that is going to be used.

NB: The joint industry and regulatory consortium C-path recommends accepting description of approach and paper-original only (alternative c above).

2 Current practices

2.1 The standard process

Most ePRO vendors work on a trial-by-trial default process. Each trial is built more or less from scratch before going through the instrument and technical validation process, and finally through translation verification. It is only then that submission material, in the form of final screen dumps, is created.

Furthermore, the default process/preference is to run all languages/translations in one batch, meaning that first the “original building language” (normally US English) is available (but only after both instrument and technical validation is completed). Subsequently, all other languages are run in one batch, but only when all translations and translation verifications, plus submission material generation, is complete.

Even if the eCOA data you collect would be fully unique to each trial (which of course it’s not), there is a large part of the setup you can fully standardize across any trial

2.2 How can we improve the process?

By being more agile we can significantly decrease the dependency on the full system set-up to generate screens and translations for submissions, and thereby be more adaptive to meet timelines whilst still complying with requirements. Obviously, this requires an associated process to support and control requirements and submission deliverables, and it will not come without trade-offs in terms of managing the process “in pieces” instead of “one big batch”. However, this is fully manageable, and differences in requirements for different submissions is something we do anyway.

The advantages of working in this way:

a) It will allow for increased re-use of material and decreased redundant work, by creating simple libraries of submission material. Such libraries can (depending on vendor capabilities and technology) be separated into a) a "screen-dump library" with (pdf) material for submissions, and b) a technical library with pre-built components.

b) There are a series of specifications and documents (parts) that can be defined once and for all (standard/best practice) and re-used across trial to drive efficiency and consistency (outside of the “plug-in” difference of the instrument and protocol design). This includes, though is not limited to:

- How to handle re-screenings and re-scheduled visits
- Screen-“flow”, dynamics and checks
- Handling of mandatory/non-mandatory questions

- Training approach and training slides/videos and other material
- Data handling conversions, query categorizations and approvals
- Vendor technical components and test scripts
- Sponsor test-scripts
- Compliance definitions and reports
- Data delivery formats and methods

2.3 Summary

With comparatively long specification, build, translation and validation timelines combined with requirements to include patient facing material in regulatory submissions, eCOA often ends up in the critical path to study start. By disconnecting the ePRO system finalization from the generation of submission material and managing them as the two separate entities they really are, we can de-couple this dependency and decrease the risk of delays or even shorten start-up timelines.

EC: Ethics Committee

IRB: Institutional Review Board

eCOA: Electronic Clinical Outcome Assessment

C-path: The Critical Path Institute is an independent, non-profit organization dedicated to bringing together experts from regulatory agencies, industry, and academia to collaborate and improve the medical product development process.

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