Common Protocol Template (CPT) Frequently Asked Questions

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DISCLAIMER REGARDING THE CPT

This document is a common protocol template. It contains sections marked as common text or text that may be used across protocols with little to no editing if the user chooses to do so. The use of this template is at the discretion of the user. Recommendations for modifications in future releases of the common protocol template can be submitted at any time and will be reviewed on a routine basis.

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Common Protocol Template (CPT) Frequently Asked Questions

1 Rationale for Using the CPT

1.1. Q: ‘CPT ‘black text’ is strongly recommended to be used. Why is the workstream recommending that sponsors not deviate from the common text?

A: CPT ‘black text’ was developed based on regulatory requirements, ICH, and TransCelerate member company templates. The team feels that this represents ‘fit for purpose’ text, and that consistent wording and terminology in key sections found in the majority of protocols (e.g. AE, withdrawal criteria, LFT monitoring) will help build consensus with regulators/IRBs/sites on minimum requirements for these sections. One of the major goals of this project is to make life easier for sites by minimizing confusion (by the Site, IRB or Regulatory Agency) caused by similar statements being worded differently throughout a protocol or in protocols from different companies. Those potential benefits will be diminished the more the template is altered. Adoption without significant deviation by sponsors will allow stakeholders to derive maximum benefit, e.g. facilitation of use of the protocol by study site staff to simplify start up and execution, and faster review time by health authorities. In the end, each sponsor must decide for itself how to best use the template to meet its needs, including whether and how much to alter proposed common content.

1.2. Q: In the Implementation ToolKit, there is a slide with a comment from FDA “If you have standards without traceability, then you aren’t really Clinical Data Interchange Standards Consortium (CDISC) compliant”. Please explain what this statement means for ‘traceability’. It is not clear from this statement what ‘traceability’ is being referred to.

A: The concept of traceability refers to incorporating data standards (e.g. CDISC) from end to end – e.g. in the Protocol, in the eCRF/data collection tool, in the database, in the Clinical Study Report, and in the electronic datasets. We believe the FDA was saying that true standards compliance requires data collected pursuant to the standards to be traceable from end to end. This is a long-term objective for the TransCelerate Common Protocol Template – to create a machine-readable template containing such standards, which can then feed the downstream processes and systems.
2 Stakeholder Input to CPT Development

1.3. Q: 'Is there any documentation around the decisions made about specific content, headers, etc.?
   A: Decisions about specific content, headers, etc. were made based on a review of ICH-GCP guidelines and relevant regulations, and a review and comparison of anonymized sample protocol templates in use at the TransCelerate member companies.

1.4. Q: What is the timing of the input from regulators (e.g. FDA, European Medicines Agency [EMA]) and Institutional Review Boards (IRBs) on the CPT?
   A: Input from regulators is ongoing. Input from FDA/NIH has been incorporated into the May 2017 release. Input from one central IRB was received during July 2015.
   
   Input from local IRBs will be assessed on an ongoing basis as protocols are developed by TransCelerate member companies using the template.

1.5. Q: Have the regulations in the EU-CTA (Clinical Trial Application) Annex 1: Section D-Protocol, been included in the CPT?
   A: The latest version of the EU Regulations (EU 536/2014) was used during the drafting of the CPT and all the requirements of Annex 1, Section D have been included along with the contraceptive requirements of the Clinical Trial Facilitation Group (CTFG) supporting this. ICH E6 and the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) checklist were also incorporated where information was not present in other documents.

1.6. Q: Liver Chemistry Stopping Criteria Algorithms: Were these algorithms reviewed by a Medical Reviewer?
   A: Stopping Criteria were developed by the team and medical review was included in the development. The criteria were also reviewed by Western Institutional Review Board (WIRB), and that review included a medical review.

1.7. Q: Can you please provide the rationale/explanation for the reason for the change in terminology from Study Drug to Study Treatment in early CPT releases, and to Study Intervention with the May 2017 CPT release?
   A: The term ‘study treatment’ allowed for use for investigational product, devices, vaccines, comparators, multiple drug regimens. The term ‘study drug’ may be limited to interventional compounds, and therefore was not chosen to be used in the CPT. Based on alignment discussions with FDA/NIH, the term ‘study intervention’ was
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selected to enable use of a template across the broadest range of clinical study types.

1.8. Q: Was the CPT content checked to conform to EU regulation 536/2014?
A: The latest EU regulations, including 536/2014, were used to create the CPT, however, nothing in the template should be construed as providing legal advice and all individuals and organizations using this template bear responsibility for complying with the applicable laws and regulations for the relevant jurisdiction.

3 Alignment of CPT and National Institutes of Health (NIH)-Food and Drug Administration (FDA) Protocol Template Content

3.1 Q: If the CPT and the NIH-FDA Protocol Template are aligned, why are there still two templates?
A: The NIH is made up of 27 different components called Institutes and Centers. Each has its own specific research agenda. The NIH supports and funds this research. The NIH-FDA Protocol Template is focused on the investigator trials requesting funding from the NIH. The CPT focuses on all trial types and is available for use by any sponsor and trial type.

3.2 Q: Can you explain how the CPT and the NIH-FDA Protocol Template are aligned?
A: The Level 1 and 2 headings have been aligned; i.e., the section numbers and section titles are the same. Where there was a need to have a custom Level 2 heading, these were placed at the end of a section in order to maintain consistency in numbering. For example, the NIH template includes Section 8.4 Reporting of Unexpected Problems to address a requirement for NIH-funded studies.

3.3 Q: What are the differences between the CPT and the NIH-FDA Protocol Template?
A: There are differences in three key areas:

• **Audience**: The NIH-FDA Protocol Template is aimed at NIH investigator funded and run trials. The CPT focuses on all trial types, global or single-country, and is available for use by any sponsor. Harmonizing structures across both templates will benefit
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many common stakeholders.

- **Headings:** Level 3 headings and below vary between the templates. In some sections there are level 2 headings specific to only one template, in which case they were put at the end of the section to retain the same section numbers for the aligned headings.

- **Content:** The topics are aligned between the two templates, however the content was generated separately. There are variations in suggested content, example text, and instructional text.

4 Template Content

4.1 Q: Can a tabular format be used for the common core text to represent the text information in a different manner than text sentence structure?

A: A tabular format is used in some areas particularly appendices for a more clear and concise presentation of the information. This could be considered for other sections as the template is further developed. A mechanism for feedback and suggestions for template improvements is available to those implementing the template.

4.2 Q: Is there any documentation around text types, font sizes, colors, etc. that have been used in the CPT?

A: This is available in a separate Implementation Toolkit element entitled "CPT_ImplTK-Text-Color-Guide."

4.3 Q: Has there been any discussion on how best to handle protocol amendments? Are there any plans to incorporate amendments into the protocol template or do you see these as separate documents?

A: Release 3 (June 2016) of the CPT included new sections for Document History, Overall Rationale for the Amendment, and a Summary of Key Changes table, as well as amendment authoring instructions (including naming and numbering conventions). Appendix 10 has also been added to provide a place to document the cumulative Protocol Amendment History. There is no standalone Protocol Amendment template.

4.4 Q: Is the order of the assessments meant to be fixed as they are currently presented in the Schedule of Activities (SoA)?

A: No. The order presented in template is a suggestion, and can be altered as appropriate for the trial and sponsor preferences.
4.5 Q: Expectation for the Clinical Study Report (CSR) of using “participant” in the protocol: Is it expected that the term participant will be used in the Tables/Figures/Listings (TFLs) and the CSR text, or companies doing mapping of participant to subject, etc.?
A: “Participant” was chosen by the CPT team as a best practice and in consideration of input from various stakeholders and including patient advocacy perspectives. Use of this term in the protocol or any other document, and consistency across documents, is at the discretion of the sponsor. Sponsors may choose to define or map the terminology used within the documents to ensure clarity and to demonstrate compliance with applicable laws and regulations or internal policies and procedures.

4.6 Q: Where should Number of Sites and Geographic location be put in the synopsis and protocol body text (for example, x sites in US; all sites in Japan, etc.) Study Design section does not include guidance for number of sites.
A: Sponsors may choose to add this information in a section as deemed appropriate for the needs of the trial. Inclusion of this information in the protocol may also drive amendments if the information changes during the trial.

4.7 Q: EU needs short title in addition to full title – should this be specifically designated on the title page?
A: In early releases of the CPT, there was no designated location for short title. Based on additional input, a short title field was added to the Title Page as part of Release 3 (June 2016).

4.8 Q: In the Synopsis, should safety assessments only be included if they are primary or secondary endpoints?
A: Yes. The synopsis is designed to include the primary and key secondary objectives and endpoints. Any safety assessments listed in the synopsis should fall into these categories.

4.9 Q: Where would the clinical hypothesis be presented/discussed?
A: In early releases of the CPT, there was no defined section for hypotheses. Sponsors were free to add this information in a section as deemed appropriate for the needs of the trial. Based on additional input, a section was added (9.1 Statistical Hypotheses) as part of the May 2017 CPT release.
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4.10 Q: In Section 9.2 (as of May 2017 CPT release, and Section 5.2 in earlier CPT releases) is “evaluable” participants really key language to be retained?

A: The term "evaluable" was chosen by the CPT team as a best practice and in consideration of input from various stakeholders. Use of this term in the protocol is at the discretion of the sponsor.

4.11 Q: How is numbering as relates to eligibility criteria to be handled if eligibility criteria are either added or removed in an amendment?

A: Sponsors should handle this as deemed appropriate for the needs of the trial.

4.12 Q: Can the APPENDICES be deleted if not applicable, or does the word ‘Not Applicable’ need to be inserted to retain the sequence/order of the Appendices numbering?

A: The decision about whether to modify, delete or add appendices rests with the individual Sponsor. Appendices provide additional information that can be accessed when needed (e.g., abbreviations, company specific content). Individual Appendices are to be omitted if not applicable. This is a different expectation than applies to the body of the document, where Level 1 and 2 section headings should be marked “Not Applicable” if appropriate.

4.13 Q: Section 6.2 Preparation/ Handling/ Storage/ Accountability (as of May 2017 CPT release, and Section 7.5 in earlier CPT releases) includes Common text that refers to a “Study Reference Manual”. Our company does not use a Study Reference Manual, or other type of protocol-accompanying manual. Therefore, this bullet is NOT Applicable. Should the reference be deleted or marked “not applicable”? Can company-specific instructions be included in a separate Level 3 section?

A: The decision about whether to delete or retain content rests with the individual Sponsor. Level 3 headings and content may be added if appropriate to meet company-specific needs.

4.14 Q: Does the CPT Template include a Document History page (or table), that lists the original protocol, administrative letters, global Amendments and revised protocols? In our company Protocol Template, this document history is a table that follows the cover/title page of the Protocol. Included in the table are ‘Document’, ‘Date of Issue’ (of the documents) and ‘Summary of the change’.

A: In early releases of the CPT, sponsors could choose to insert a Document History page after the title/cover page of CPT and before Section 1. Based on additional input, a Document History table was added as part of the Protocol Amendment Summary of Changes Table included in Release 3 (June 2016).
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4.15 Q: Can a study schematic also be included in the Section 4. Study Design? Study Schematic is included in the CPT Section 1. Protocol Summary - 1.2 Schema.

A: The TransCelerate Common Protocol Template (CPT) workstream recommends that the study schematic be included in only one location to minimize the potential for confusion. For example, include in Section 1.2 Schema, and reference the reader to this from Section 4 (e.g. "See Section 1.2 for schema.")

4.16 Q: Section Title: Scientific Rationale for Study Design. Why does the CPT have two different sections for Rationale (Section 2.1 Study Rationale and Section 4.2 Scientific Rationale for Study Design) and also Section 4.3 Justification for Dose? What is the purpose of splitting these sections up?

A: The intent of Section 2.1 Study Rationale is to present a 2-3 sentence high level reason for the trial. Examples: “This trial is being conducted to study the interaction of <experimental intervention> with <other intervention>, as many participants who will receive <experimental intervention> are anticipated to also be receiving <other intervention>.”

“This is the initial Phase III trial in those participants with <diagnosis> who are also expected to be receiving <other intervention>.”

By contrast, Section 4.2 Scientific Rationale for Study Design is intended to present the reason for the specific design elements/features of the trial. Features may include duration of intervention, choice of comparator, or justification of placebo use.

Section 4.3 Justification for Dose is a separate section to highlight dose selection rationale, and to ensure that this information was included in the protocol as specified in ICH-GCP.

4.17 Q: Can sponsors use Level 4 headings?

A: Yes

4.18 Q: In Section 10. Supporting Documentation and Operational Consideration – 10.1.7 Data Quality Assurance (Appendix 3 – Study Governance in earlier CPT releases) would it be possible to add the underlined wording below? This would help clarify the situation and what the expectations are and would be in line with our current guidance which is we would never tell a site to destroy their records. We would only ever say they no longer need them. Hence if a site contacted us during the retention period about destroying records, we would say No and if they contacted us after the retention period we would tell the site we no longer require the records.

“Records and documents, including signed informed consent forms (ICFs), pertaining to the conduct of this study must be retained by the investigator for [XX] years after
study completion unless local regulations or institutional policies require a longer retention period. No records may be destroyed during the retention period without the written approval of the Sponsor. No records may be transferred to another location or party without written notification to the Sponsor."

A: The additional wording was added to the CPT as part of Release 3 (June 2016).

4.19 Q: Why is the Sponsor signature line on the title page?
   A: Placement of the Sponsor signature line on the title page facilitates easy confirmation of signature.

4.20 Q: Where is the Investigator to sign the protocol, or is there an alternative plan to collect the Investigator signature?
   A: Sponsors can create their own signature page.

4.21 Q: What is the source of the definitions for Adverse Event severity? These do not match CDISC Controlled Terminology definitions.
   A: The definition of severity was taken from several blank, anonymized templates, provided by member companies to the TransCelerate Common Protocol Template team during the development of the CPT. The definition used in the CPT is also aligned with other FDA guidance such as that found at: link: http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Vaccines/ucm091977.pdf and also with the NIH-FDA Protocol Template recently released: (http://osp.od.nih.gov/sites/default/files/Protocol_Template_05Feb2016_508.pdf) If a sponsor wishes to use other definitions, there is flexibility to do so.

5 Template Technology

5.1 Q: Was testing performed on the CPT? Is that documentation available?
   A: Yes. Documentation of End User Testing is available including the test steps performed, user attestation of completion, a summary of findings, and actions taken. It was decided that End User Testing was sufficient for the tool based on the fact that this template is an intermediary to arrive at a final document.

5.2 Q: When will functionality be included for identification of KEY endpoints?
   A: As of CPT Release 3 (June 2016), the Tech Enabled Edition of the CPT has included functionality to duplicate objectives and endpoints that are entered in Section 3 so that they also appear in Section 1.1 Synopsis. This functionality can be used to
differentiate which objectives and endpoints are considered “key” (e.g. Primary and Secondary Objectives/Endpoints).

5.3 Q: What is the compatibility of the Tech-Enabled version?
A: The Tech Enabled CPT is for windows-based use and not compatible with Apple iOS.

6 Implementation of the CPT by the Sponsor

6.1 Q: Is the use of the CPT limited to TransCelerate member companies?
A: No. Beginning with Release 2 (December 2015), the template releases have been posted to the TransCelerate website, making it available for download and use by any interested party.

6.2 Q: Can sponsors alter the content of the CPT to their liking? Can we use some sections of the CPT and not others?
A: TransCelerate initiatives are voluntary, meaning that sponsors, including TransCelerate member companies, decide whether and how they will use deliverables like the CPT. Many of the benefits of the project (reduced study start up time, faster review and approval by regulators, improved data accuracy) largely depend on template consistency. To achieve maximum benefits, the workstream strongly recommends all Level 1 and 2 Headers should be left intact, and if no content is needed for a section, that section is to be marked as Not Applicable.

6.3 Q: Is the expectation that a company would use the template for all its protocols or perhaps just for certain types of studies?
A: Maximum benefit will be realized to all stakeholders (e.g. sponsors, investigators, IRBs, regulators, participants) when more sponsors use the template for more and more types of protocols. However, all implementation is voluntary, and sponsors can choose their own strategies for implementation.

6.4 Q: Why is there no flexibility in the headers?
A: The intent is that all Level 1 and 2 Headers should be left intact, so that the template structure remains consistent. If they are not applicable, you can mark them N/A. The Investigators, study staff and IRB will be able to locate the same information in the same place and meaning the same thing.
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6.5 Q: Is it possible for the team to see a demo? Will there be special software required to implement?

A: No special software will be needed. The template utilizes functionality native in MSWord versions 2010, 2013, and 2016. The architecture is such that companies can add customized libraries and incorporate into other systems. The Implementation Toolkit being released with the template will include videos within the Guidance for Use to demo functionality of the template as well as “how to” documentation geared both to users and technical representatives.

6.6 Q: Is there a mechanism for Companies working to adopt the TransCelerate CPT structure (Level 1 and 2 Headers) and/or the core content to know that the content is aligned with the content in their current templates?

A: There is a Mapping Table Exercise that can be performed to ensure alignment between your company protocol template and the TransCelerate CPT. The headings and subheadings are compared to identify where content is now located. In addition, the content can be compared to identify any gaps, which will trigger the need to determine if there is another mechanism in place within your organization to capture this information (e.g., Monitoring Guidelines, Clinical Trial Agreements, Standard Operating Procedures) or if and how the gap needs to be addressed.

6.7 Q: How is the Technology Enabled Edition provided and what support/training is available for companies to help with implementation?

A: Installation instructions are included and guide the user through installing add-ins and templates in the appropriate locations.

6.8 Q: Will there be additional guidance for authors provided with the CPT or will it be a standalone document?

A: Instructional Text (guidance for authors) has been embedded into the CPT and will be visible as red italicized text in the Basic Word Edition or as a guidance pane in the Technology Enabled Edition. An Implementation Toolkit is also provided to assist with training/awareness.

6.9 Q: What do I do if I don’t have a compatible version of MSWord or if I am using an Apple computer?

A: For those who do not have a compatible version of MSWord, or for those who wish to review the template without installing the technical components, a Basic Word Edition is also provided. While this edition does not have the technology enhancements, it contains the content in a cleanly formatted document. Instructional text is in line with protocol content and visible as red text when the paragraph marks are enabled.
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6.10 Q: Is the CPT intended for use only for interventional protocols, and not intended to be used for non-interventional protocols?

A: As there are typically many differences in protocol content between interventional and non-interventional, the TransCelerate CPT team suggests that the template be used only for interventional trials.

7 Implementation of the CPT at the Site

7.1 Q: Is there a mechanism for Investigators, and also Institutional Review Boards (IRBs) to know that the TransCelerate CPT structure (Level 1 and 2 Headers) and/or the core content was used in the protocol that a Sponsor submits to them?

A: There is no standard approach to communicating that a sponsor protocol was created using the TransCelerate CPT. It is suggested that this could be included in "cover letter" communications to relevant stakeholders when the protocol is provided to them. Example: "This protocol was created using the TransCelerate Common Protocol Template (CPT) <insert elements actually used - headers, headers and core content>.

8 Metrics

8.1 Q: What are the TransCelerate CPT Workstream's metrics for success around CPT implementation (e.g., faster study start up times, etc.)? How will these be measured and reported?

A: The approach to potential metrics is currently under discussion.

9 Updates to the CPT

9.1 Q: What are the expectations for future releases of the CPT? Will there be major changes? How can users provide feedback and what will happen to this? Based on concerns about adjusting internal technical components to fit the protocol, major future changes will be challenging to implement. How often will there be new releases available?

A: A governance model is currently under development to ensure that the template can evolve (e.g., based on changes in regulation, feedback from key stakeholders such as sites, regulators, and sponsors) but also to ensure it evolves in a controlled manner which facilitates consistency across use. The current proposal under consideration is that the template would be updated yearly once in business continuity (i.e., maintenance) mode. The frequency of update may be greater and
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will be influenced by the feedback received. Feedback, including suggestions for future releases, may be submitted via the TransCelerate website http://www.transceleratebiopharmainc.com/.

9.2 Q: As further therapeutic area data standards are developed, how and when will these be included in the Common Protocol Template? Which indications will be addressed in new libraries?

A: A number of factors are being considered in planning additional therapeutic area libraries, including existence of data standards, and volume of activity for the indication. Development of additional libraries is targeted to be completed in 2018, including Cardiovascular Safety, Devices, and Vaccines.

9.3 Q: Are there any recommendations how to handle the summary of changes for a protocol amendment?

A: Release 3 (June 2016) of the CPT included new sections for Document History, Overall Rationale for the Amendment, and a Summary of Key Changes table, as well as amendment authoring instructions (including naming and numbering conventions). Appendix 10 has also been added to provide a place to document the cumulative Protocol Amendment History. There is no standalone Protocol Amendment template.