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DISCLAIMER REGARDING THE COMMON SAP TEMPLATE This document is a Common Statistical Analysis Plan template. It contains sections marked as common text or text that may be used across SAPs 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 SAP can be submitted at any time and will be reviewed on a routine basis. These materials are provided 'AS IS' WITHOUT WARRANTY OF ANY KIND, EITHER EXPRESSED OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, THE IMPLIED WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR NON-INFRINGEMENT. TransCelerate and its members do not accept any responsibility for any loss of any kind including loss of revenue, business, anticipated savings or profits, loss of goodwill or data, or for any indirect consequential loss whatsoever to any person using these materials or acting or refraining from action as a result of the information contained in these materials. Any party using these materials bears sole and complete responsibility for ensuring that the materials, whether modified or not, are suitable for the particular use and are accurate, current, commercially reasonable under the circumstances, and comply with all applicable laws and regulations. Nothing in this template should be construed to represent or warrant that persons using this template have complied with all applicable laws and regulations. All individuals and organizations using this template bear responsibility for complying with the applicable laws and regulations for the relevant jurisdiction.

Legally approved Nov-2018
Common Statistical Analysis Plan (SAP) Frequently Asked Questions

1 Stakeholder Input to Common SAP Template Development

1.1. 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 SAP templates in use at some TransCelerate member companies.

2 Template Content

2.1. Q: Can authors modify the Level 1 and 2 headings?
   A: Yes, however, it’s important to note that Level 1 and 2 headings are designed to be consistent with the Common Protocol Template (CPT), which in turn is consistent with the FDA/NIH template. Keeping Level 1 and 2 headers consistent also makes it easier for users to navigate the document and facilitates content reuse. Modifying these headers will diminish the efficiencies that can be achieved through use of the template.

2.2. Q: Has the Common SAP template been communicated with regulatory agencies?
   A: The Common SAP is aimed to be consistent with the Common Protocol Template statistics section, which has been revised based on FDA review of CPT version 2, and taking into consideration of the ICH EWG E9 (R1) draft guidance on estimands. Feedback on the Common SAP, from users and from regulatory agencies, will be incorporated into later versions.

2.3. Q: does TransCelerate has recommendation on the timing of initial version of SAP and the final version of the SAP?
   A: TransCelerate initiatives are voluntary, meaning that Sponsors, including TransCelerate member companies, decide whether and how they will use deliverables like the Common SAP. Timing of the SAP depends of the procedures and/or processes of adopters or the Common SAP Template.

2.4. Q: Is this template for study SAP applicable for integrated summaries for safety or efficacy (ISS/ISE)?
   A: The template has been developed for Phase 1 through 4 clinical trials, Sponsors can decide if they want to use it for other purposes.
2.5. Q: Could you clarify the differences between: “endpoints”, “variable”, “clinical variables”, and “parameters”?  
A: “Endpoints” and “variables” are used interchangeably, and “parameters” are other derived variables not defined as endpoints, but need to be pre-specified in either the protocol or SAP. Examples include but are not limited to: immunogenicity, biomarkers, pharmacokinetic/pharmacodynamic/population pharmacokinetics parameters, health care utilization variables and health technology assessment related variables.

2.6. Q: which section should the summary of compliance be included?  
A: We recommend it is included in the Appendix or any other relevant document created by the Sponsor to supplement the SAP.

2.7. Q: Can we use two tables, one for efficacy and one for safety, to implement the estimand framework?  
A: Yes. The grouping currently in the template is just an example. The Sponsor that decides to adopt the template can modify as required.

2.8. Q: Should the format of the output (for example, p-value format with number of significant digits) be included in Section 5.1, General Consideration?  
A: The use of this template is at the discretion of the user. This template is not comprehensive of all content that could be included in an analysis plan, adopting Sponsors can decide how and where to include additional information.

2.9. Q: Why does the Common SAP template always use "consider" when making recommendation to guidances that seems mandatory?  
A: TransCelerate initiatives are voluntary, meaning that Sponsors, including TransCelerate member companies, decide whether and how they will use deliverables like the Common SAP. Accordingly, TransCelerate does not mandate content; instead it leaves it to the Sponsor to decide on the content.

2.10. Q: What are the differences between "sensitivity analyses" and "supplementary analyses"?  
A: Sensitivity analyses target the same estimand but using different methods; supplementary analyses target a different estimand.

2.11. Q: section 5.4.1 title has "key/confirmatory secondary endpoint(s)". Does this mean that either the companies can choose either one?  
A: Yes.

2.12. Q: Why is Section 5.4.1 labelled as "key/confirmatory secondary endpoint(s)"? In its (draft) multiple endpoint guidance from last year, FDA is very clear in discouraging the use of the term "key secondary endpoints". Instead, any objective that supports
label claims and extensions should be denoted as "secondary" and be considered for multiplicity adjustment (i.e. strong FWER control)?

A: The Sponsor can adjust the heading as they see appropriate.

2.13. Q: Should the tertiary/exploratory endpoints analyses that are not intended for regulatory purposes be excluded from the SAP?

A: It is up to the Sponsor to decide whether the exploratory endpoints analyses are important enough to be included in the SAP. The SAP is intended to cover analyses required for the clinical study report.

2.14. Q: Why is the title for Section 5.6 "(Other) Safety Analyses"?

A: This section is intended to include safety analyses that are not already included in Section 5.3 - 5.5.

2.15. Q: Why aren't the commonly required analyses of Laboratory Data and Vital Signs in their designated sections?

A: When the trial includes laboratory data and/or vital signs, these can be included in the respective sections, primary, secondary, or safety analysis as is specified in the protocol.

2.16. Q: Why isn't there a designated section for Patient Reported Outcomes (PRO)/Clinical Outcomes Assessment (COA)?

A: These data can be included in primary endpoints analyses, secondary endpoints analyses, or exploratory endpoints analyses section as specified in the protocol.

2.17. 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.

2.18. 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 different from the body of the document, where Level 1 and 2 section headings should be marked “Not Applicable” if appropriate.
3 Implementation of the Common SAP template by the Sponsor

3.1. Q: Is the use of the Common SAP template limited to TransCelerate member companies?

A: No, the word version release is posted on the TransCelerate website, making it available for download and use by any interested party. The Technology-Enabled Edition will initially only be available to member companies.

3.2. Q: Can Sponsors alter the content of the Common SAP template to their liking? Can we use some sections and not others?

A: Yes. TransCelerate initiatives are voluntary, meaning that Sponsors, including TransCelerate member companies, decide whether and how they will use deliverables like the Common SAP. 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 work stream strongly recommends all Level 1 and 2 Headers be left intact, and if no content is needed for a section, that section is marked as “Not Applicable”.

3.3. Q: Is the expectation that a company would use the template for all its SAPs 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 SAPs. However, all implementation is voluntary, and Sponsors can choose their own strategies for implementation.

3.4. 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 “Not Applicable”. The regulators, Investigators, study staff and IRB will be able to locate the same information in the same place and it will mean the same thing.

3.5. 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.

3.6. Q: Is there a mechanism for companies working to adopt the TransCelerate Common SAP structure (Level 1 and 2 Headers) and/or the core content to know if the content is aligned with that in their current template?

A: There is a Mapping Table Exercise that can be used to check alignment between your company’s SAP template and the TransCelerate proposal. 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.

3.7. Q: Will there be additional guidance for authors provided with the Common SAP template or will it be a standalone document?
   A: Instructional Text (guidance for authors) has been embedded into the document and will be visible as red hidden text. An Implementation Toolkit is also provided to assist with training/awareness.

3.8. Q: What do I do if I do not 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 SAPs content and visible as red text when the paragraph marks are enabled.

4 Updates to the Common SAP

4.1. Q: What are the expectations for future releases of the Common SAP? 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 SAPs, major future changes will be challenging to implement. How often will there be new releases available?
   A: A governance model is in place 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 frequency of update may be greater and will be influenced by the feedback received. Feedback, including suggestions for future releases, may be submitted via the TransCelerate website http://www.transceleratebiopharmainc.com/.

4.2. Q: Are there any recommendations how to handle the summary of changes for a SAP amendment?
   A: The SAP template includes a Version History section, which contains a version history summary table and provides guidance on how to handle SAP amendments.