Common CSR Template:

A Consistent Approach to Writing Compliant CSRs With Ease

AMWA Annual Meeting 2019
San Diego, CA
About Me

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- CSR & Lean Authoring SME
- TransCelerate CSR Workstream
Agenda

- Overview of TransCelerate (5 Minutes)
- Common Clinical Study Report (CSR) Template Development: Rationale and Benefits (10 Minutes)
- What Does the Template look like? (20 Minutes)
- Next Steps (10 Minutes)
Overview of TransCelerate
TransCelerate:

A Not-for-Profit Entity Created to Foster Collaboration

Our Shared Vision:
To improve the health of people around the world by accelerating and simplifying the research and development of innovative new therapies.
**Current State of TransCelerate**

**2012**
- TransCelerate Founded

**Today**
- **19** MEMBER COMPANIES
- **25+** INITIATIVES
- **1,000** people from Member Companies that design and develop TransCelerate solutions

**25+** CULTURE OF COLLABORATION
- With an effective and proven governance structure have increased the ease and desire to collaborate

**BREADTH & DEPTH**
- Over 30 solutions being delivered across 25+ initiatives, across 3 strategic priorities

**FACILITATING FUTURE PLATFORM TRIALS**
- 12+ initiatives deliver solutions that facilitate future platform trials

**Membership is available to biopharmaceutical research and development organizations that engage in innovative discovery, development and manufacturing of new medicines*.**

*to be eligible for membership, companies must meet specified eligibility criteria
External Collaborations: Critical to achieving future state

TransCelerate engages with, and secures feedback from a variety of partners which provide unique and important insights and perspectives.
Practical solutions to overcome inefficiencies in R&D

OUR MISSION:
Collaborate across the global biopharmaceutical R&D community to identify, prioritize, design and facilitate implementation of solutions designed to drive the efficient, effective and high-quality delivery of new medicines

HARMONIZE PROCESS AND SHARE INFORMATION
- Clinical Data Standards
- Common Protocol Template
- Common Statistical Analysis Plan Template
- Common Clinical Study Report Template
- Comparator Network
- DataCelerate™
- eSource
- Digital Data Flow*
- Investigator Registry
- Placebo Standard of Care
- Toxicology Data Sharing

IMPROVE THE PATIENT AND SITE EXPERIENCE
- Clinical Research Access and Information Exchange
- Clinical Research Awareness
- eConsent
- eLabels
- Patient Experience
- Patient Technology
- Site Qualification and Training
- Shared Investigator Platform

ENHANCE SPONSOR EFFICIENCIES & DRUG SAFETY
- Advancing Safety Analytics*
- Clinical Data Transparency
- Data Monitoring Committee*
- Intelligent Automation Opportunities in Pharmacovigilance*
- Interpretation of Pharmacovigilance Regulations
- Protocol Deviations*
- Quality Management System
- Risk-Based Monitoring
- Value of Safety Information Data Sources

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Common CSR Template Development: Rationale and Benefits
Problem

- CSR format & core content vary from sponsor to sponsor making review difficult for regulators
- CSRs have become more complex and lengthy driving up cost and time

Goal

- Develop a streamlined model CSR for efficient CSR writing & review
- Avoid redundancy
- Enable future state (eg, downstream automation)
Background: How was the template developed?

Collaboration
- Joint expertise of 15 member companies
- Broad adoption will drive greater efficiency for regulatory reviewers
- Continuous improvement
  - Stakeholders have the opportunity to suggest revisions

Participating Member Companies
Background: How was the template developed?

Based on well-known standards

- Content developed in adherence with ICH E3 and CORE
- Structure developed for readability

Guidance

ICH: E3: Structure and Content of Clinical Study Reports

Clarity and Openness in Reporting: E3-based
CSR Template Development: Guiding Principles

- **Compliant**: Content adheres to ICH E3 and CORE guidelines
- **Common**: Information always in the same place and means the same thing
- **Better**: Moves beyond incremental improvements and current limitations
- **Universal**: Provides value for all stakeholders; regulators are the first priority
- **Forward-thinking**: Human-readable & supports reuse for downstream automation
- **Efficient**: Lean with minimized redundancy
  - Content is significantly shorter allowing writer/reviewers to focus on study results
  - Refers to primary sources of information (e.g. Protocol, SAP) in appendices
  - Avoids duplication and possible contradiction; Less chance of error
CSR Template Development: General Approach

**Structure**
- New Table-of-Contents
- Common headings consistent w/ Common Protocol Template (CPT)
- Template for CSR body only
  - Appendices and TFLs follow company standards

**Content**
- Adheres to ICH E3 & CORE
- Common terminology consistent with CPT
- Streamlined
  - Focus on reporting data (no benefit/risk interpretation)
  - Avoid redundancy by referring to appended documents
CSR Template Development: The Model

Common CSR Backbone
- Common Level 1 Headings
- Common streamlined text
- Used across all phases & products
- Focus on reporting data

Guidance & Governance Model

Appendices & TFLs
- Apply Sponsor-specific standards

TransCelerate Implementation toolkit materials
- Governance while allowing company feedback

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CSR Template Development: Template Editions

**Basic WORD Edition**
- MSWord-based file
- Use as-is or modify
- Manually populate using instructions as a guide
- Initial Public Release: Dec 2018

**Technology-Enabled Edition**
- MSWord-based file with add-ins
- Automation to reuse content from the protocol
- Anticipated Public Release: Dec 2019
What does the template look like?
Summary of Key Decisions: Structure

Non-Data Driven Sections

- First 5 sections are unnumbered
  - No longer needed for navigation
- List of Abbreviations = 1st Use
- Headings updated for clarity & consistency with CPT
- Consistent terminology
  - Participant (vs subject, volunteer, or patient)
  - Study intervention (vs drug, device, vaccine)
  - Effectiveness for device & Efficacy for drugs
### Data Driven Sections

- **“Exposure”** under Study Participants (consistent with CORE)
- All **“Response”** results under single Level 1 heading
- Section 5 headings created for all endpoint types
  - Greater flexibility for universal use
  - Sections (including Summary) that are not relevant may be deleted
- **“Discussion”** removed
  - Focus on study outcomes
  - Interpretations in submission documents
  - Can include discussion points in conclusion if necessary (e.g., unexpected results)

### Summary of Key Decisions: Structure (cont.)

<table>
<thead>
<tr>
<th>4. Study Participants</th>
<th>4.1 Disposition of Participants</th>
<th>4.2 Protocol Deviations</th>
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<tbody>
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<td>4.3 Populations Analyzed</td>
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<td>4.4 Demographic and Other Baseline Characteristics</td>
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<td>4.5 Prior, Concomitant, [and/or] Post-intervention Therapy</td>
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<td>4.6 Exposure and Study Intervention Compliance</td>
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</table>

<table>
<thead>
<tr>
<th>5. Evaluation of Response to Study Intervention</th>
<th>5.1 Efficacy</th>
<th>5.2 Safety</th>
<th>5.3 Pharmacokinetics</th>
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<tbody>
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<thead>
<tr>
<th>5.4 Pharmacodynamics</th>
<th>5.5 Genetics</th>
<th>5.6 Biomarkers</th>
<th>5.7 Immunogenicity</th>
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<table>
<thead>
<tr>
<th>5.8 [Health Economics] OR [Medical Resource Utilization]</th>
<th>5.9 [Other]</th>
<th>5.10 Summary of Evaluation of Response to Study Intervention</th>
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</thead>
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<tr>
<th>6. Conclusions</th>
<th></th>
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</table>
### Cross-Reference Protocol

#### 3.3. Selection of Study Population

<table>
<thead>
<tr>
<th>3.3.1. Inclusion/Exclusion Criteria</th>
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<tbody>
<tr>
<td>Enrolled in this study were participants with [provide indication or population]. Detailed inclusion and exclusion criteria are provided in Appendix [X.X.X] Study Protocol.</td>
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</table>

<table>
<thead>
<tr>
<th>3.3.2. Removal of Participants From Intervention or Study</th>
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<tbody>
<tr>
<td>The specific criteria and procedures for early discontinuation from study intervention(s) or withdrawal from the study are described in Appendix [X.X.X] Study Protocol.</td>
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</table>

### Cross-Reference SAP

#### 3.7. Statistical Analysis

<table>
<thead>
<tr>
<th>3.7.1. Statistical Analysis Plan</th>
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<tbody>
<tr>
<td>The planned analyses, [comparisons, statistical tests] and determination of sample size are described in the final version of the SAP [Appendix [X.X.X] Statistical Methods] [and/or contained in the protocol [Appendix [X.X.X] Study Protocol].</td>
</tr>
</tbody>
</table>

### Cross-Reference Other Appendices

<table>
<thead>
<tr>
<th>3.2. - Investigators and Study Administrative Structure</th>
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<tbody>
<tr>
<td>Required information is to be provided in referenced appendices (e.g., include Sponsor and CRO contact information in the appendix that presents the list of investigators and other important study personnel). For a streamlined approach, suggest only providing text that directs the reviewer to the appropriate appendices. Do not include any personal protected information (PPI) or cpatented measurement) in this section.</td>
</tr>
</tbody>
</table>
Summary of Key Decisions: Content (cont.)

Reuse Content

- Manually or automatically (for tech-enable version) pull in content from the protocol

2. Study Objectives and [Estimands and/or] Endpoints

<table>
<thead>
<tr>
<th>Objectives</th>
<th>[Estimands/Endpoints]</th>
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<tbody>
<tr>
<td>Primary</td>
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<tr>
<td>Secondary</td>
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<tr>
<td>Tertiary/Exploratory</td>
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</table>

3. Investigational Plan

3.1. Overview of Study Design

The study design is depicted below in Figure 1. Additional details are available in Appendix [X.X.X] Study Protocol.

3.4. Study Intervention

3.4.1. Study Interventions Administered

The study intervention(s) are outlined in Table 1. The justification for the dose(s) selected is described in the justification for dose section of the protocol (Appendix [X.X.X] Study Protocol).
Suggested Content

3.5. Study Assessments and Procedures

3.5.1. Planned Measurements and Timing of Assessments

The specific [efficacy, immunogenicity, PK, PD, safety and/or other variables to be assessed] assessments, their schedule and measurement/collection methods are provided in the Schedule of Activities and described in the Procedures sections of the protocol (Appendix [X.X.X] Study Protocol). The collection and assessment of safety information during the study (evaluation, definitions, recording, and reporting of AEs, SAEs [ADEs, SADEs] and other reportable safety events) is detailed in the AE reporting section of the protocol (Appendix [X.X.X] Study Protocol).

3.5.2. Appropriateness of Measures

The [endpoints] used in this study (e.g., [efficacy, immunogenicity, PK, PD, safety and other endpoints], as applicable) were standard, generally reliable, and relevant to the objectives set forth in the protocol [Appendix [X.X.X] Study Protocol].

3.5.3. Additional Summary of Specific Assessments

- The investigator or his/her representative explained the nature of the study to the participant or his/her legally authorized representative and answered all questions regarding the study.
- Participants were informed that their participation was voluntary. Participants or their legally authorized representative were required to sign a statement of informed consent.
Summary of Key Decisions: Content (cont.)

Instructional Guidance

5.2. → Safety

5.2.1. → Adverse Events

5.2.1.1. → Brief Summary of Adverse Events

Briefly summarize the overall adverse event study results. Suggest a tabular format (e.g., insertion of the applicable summary table).

The incidence of all-TEAIs reported during the study was [similar or describe differences between groups] between the study intervention groups (Table 2).

Table 2. Summary of Adverse Events

5.2.1.2. → Analyses of All Adverse Events

Briefly describe the TEAIs by various categories as applicable, referencing supportive summary table(s). Subsections may be included as applicable, such as:

5.2.1.2.1. Frequency of AEs by Preferred Term
5.2.1.2.2. Frequency of AEs by System Organ Class
5.2.1.2.3. Frequency of AEs by Subgroups
5.2.1.2.4. Adverse Events by Severity
5.2.1.2.5. Treatment-related AEs

The presentation may be limited to selected thresholds for the study (e.g., those in at least 1% 5% of the treated group, or other thresholds appropriate to the study).

5.2.1.3. → Deaths

Briefly describe deaths occurring during the study, including the pre-treatment (Screening) period, post-intervention follow-up period and deaths that resulted from a process that began during the study. State if no events of death were reported in the study. If it is necessary to:

5.2.2. → Clinical Laboratory Evaluation

The laboratory evaluations described will depend on the observed results. Specific analyses performed, or known safety signals and should provide comparison between intervention groups. Subsections may be included as applicable, such as:

5.2.2.1. → Laboratory Values Over Time

Briefly describe laboratory values over time including topics such as:

- mean/median values, change from baseline, and range of values
- specific criteria used to identify clinically significant changes
- reference to appropriate summary table(s)

5.2.2.2. → Summary of Changes by Participant

Briefly describe the analysis of individual participant changes by study intervention group (e.g., “shift tables”). A reference to appropriate summary table(s) may be sufficient.

5.2.2.3. → Clinically Meaningful Laboratory Abnormalities

Briefly describe clinically meaningful changes (defined by the Sponsor) including topics such as:

- trends, relevance, and any likely relation of laboratory abnormality to the study intervention (e.g., dose/concentration, dechallenge effect)
- specific approach used to assess clinically meaningful abnormalities
- reference to appropriate summary table(s)

5.2.3. → Other Safety Evaluations

Briefly describe any clinically meaningful findings and their clinical relevance, referencing supportive summary table(s). Subsections may be inserted or deleted as applicable.
Next Steps
Intended to Prepare for the Future State

• A common CSR template structure with harmonized terminology

• Streamlined content and consistent structure enables identification of critical information for end users

• Facilitate automated reuse of content from protocol to CSR to ensure consistency and improve efficiency

• Enable efficient content reuse downstream of the CSR (e.g. disclosures)
Tech-enabled Template: Making documents intelligent

Starting Point

✓ Paper-based
✓ Manual process
✓ High customization
✓ Long cycle times
✓ Variable quality
✓ High costs
✓ Rework

Current State

✓ Flat structures
✓ Reuse via copy/paste
✓ Little or no Standards
✓ Cannot exploit information
  ✓ Reuse
  ✓ Downstream uses
✓ Variable quality & consistency

Future State

✓ Structured content across docs
✓ Standards driven
✓ Text mining, analytics
✓ AI to leverage knowledge from the content
✓ Regulatory agencies efficiencies
Your Next Steps: Implementation?

**Basic Word Edition**
- A document-based template and associated libraries for use across phases and study types
- Use as-is or modify current format template to reflect CPT content
  - ☑ Common Protocol Template; ☑ Common SAP; ☑ Common CSR

**Tech Enabled Edition (eTemplate)**
- An MS Word-based template with add-ins
- Automation to leverage “point and click” text
- Capture of protocol-level metadata to facilitate content reuse
  - ☑ eCPT; coming 2019: eSAP, eCSR

**Implementation Toolkit**
- Roadmap of activities to support implementation
- Materials tailored for various audiences
- Template evaluation tools and FAQs
  - ☑ Coming 2019: eSuite Implementation Toolkit

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**CPT Resources Available for Download**
http://www.transceleratebiopharmainc.com/assets/common-protocol-template

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Your Next Steps: Implementation?

The Implementation Materials are:
- High level roadmap of activities to support implementation
- Materials to communicate to various audiences
- Available to any company/sponsor who wants to implement

...are not:
- Detailed step-by-step workplan
- Activities that must be followed, including company-specific documentation

Are Highly Flexible

Are Not Mandatory

Guiding Principles
- Each company/sponsor is free to decide whether and in what manner to implement.
  » Note: changing certain CPT tools may reduce some of the efficiencies for sites/investigators/sponsors
- Materials are intended to help adoption in the most efficient way possible.
- Implementation components are generic and may need to be tailored before use.
  » Note: It is up to each company to define detailed steps for implementation in their organization.

http://www.transceleratebiopharmainc.com/assets/common-protocol-template
Conclusion: Common CSR Benefits Many Stakeholders

Near Term Benefits to Sponsors
- Reduction in redundant content
- Improved way of working
  - writing lean CSRs with cross-references when possible
- Improved efficiency and reduced cycle time for CSR & submission

Potential Future Benefits to Sponsors
- Availability of machine readable CSR with Content Reuse capability
- Automation of downstream processes and reuse of content for transparency

Near Term Benefits to Regulators
- CSRs are lean w/ less redundancy & cross-references used where possible
- Aligned with ICH E3, CORE, EU CTR and PDUFA VI
- Increased consistency between sponsors
- Easier to review

Potential Future Benefits to Regulators
- Increased ease of data interpretation
- Increased use of data standards enabling end-to-end use of metadata and traceability

Potential Future Benefits to Patients
- Faster access to study results through reuse of content for transparency

Sponsor
Regulator
Patient
Thank you