



Points to consider when developing a Clinical Study Report (CSR) for a clinical trial that has been disrupted due to unforeseen circumstances

Issued jointly by ACRO & TransCelerate BioPharma

About ACRO:

The [Association of Clinical Research Organizations](#) (ACRO) represents the world's leading clinical research and technology organizations. Our member companies provide a wide range of specialized services across the entire spectrum of development for new drugs, biologics, and medical devices, from pre-clinical, proof-of-concept and first-in-human studies through post-approval and pharmacovigilance research. ACRO member companies manage or otherwise support the majority of FDA-regulated clinical investigations worldwide. The member companies of ACRO advance clinical outsourcing to improve the quality, efficiency, and safety of biomedical research.

About TransCelerate:

[TransCelerate Biopharma Inc.](#) (TransCelerate) is a non-profit organization with a mission to collaborate across the global biopharmaceutical research and development community to identify, prioritize, design and facilitate implementation of solutions designed to drive the efficient, effective and high-quality delivery of new medicines.

Background on this Statement:

Both ACRO and TransCelerate member companies, as well as industry stakeholders generally, have faced unprecedented interruptions to clinical trials over the past three years. We have seen the COVID-19 global pandemic, geopolitical disruptions like the war in Ukraine, and natural disasters such as hurricanes and wildfires. These are some examples of the types of unforeseen disruptions that may have significant impacts on how a clinical trial is operationalized and how clinical trial data are collected and reported. These disruptions may have an impact on the participant and/or the study conduct. An agreement between trial sponsors and regulatory agencies on what mitigation strategies to expect and consistent reporting guidelines would be useful for those involved in preparing and reviewing Clinical Study Reports (CSRs).

Our Proposal:

ACRO and TransCelerate take the lessons learned from these unprecedented interruptions and propose that contract research organizations (CROs) and sponsors adjust how they develop CSRs for those clinical trials that have been impacted by any unforeseen disruption, whether it be a war, a pandemic or other public health emergency, or any geospatial disruption.

Currently, the International Council on Harmonisation (ICH) E3 [Guideline on the Structure and Content of Clinical Study Reports](#) and E3 [Structure and Content of Clinical Study Reports Q&A \(R1\)](#) documents are widely used across the industry. The [CSR template](#) developed by TransCelerate and the [CORE Reference resources](#) are also widely used. Our members generally have reported that most companies use these resources as a foundation and then tailor the structure of the CSR, creating their own individualized template. As a result, the way clinical trial disruptions are reported in a CSR varies from one company to another.

The review of data related to a significant disruption of trial conduct will be highly indication- and situation-specific, depending on whether the affected data relate to an efficacy endpoint, a safety signal, etc. In all protocols, there is planning for how missing data will be treated and how longitudinal data will be analyzed. Any changes to this planning in the protocol occasioned by a disruption should be noted in the CSR as outlined here.

- If a disruption occurred but it did not cause a major impact to the conduct of a clinical trial program, include a statement in the introduction explaining this.
- When there has been a disruption to the conduct of a clinical trial program, ACRO and TransCelerate propose that sponsors and CROs continue using the ICH-based CSR and report disruption-related information within each relevant section of the CSR. However, each scenario must be carefully evaluated as some disruption scenarios may be better described in a self-contained Summary of Impact document as an addendum or appendix, as described by TransCelerate's [CSR Considerations for Studies Disrupted by the COVID-19 Pandemic](#).
- In the cases when companies determine disruptions should be reported throughout various sections of the CSR, companies should work to improve the navigation of this content. ACRO and TransCelerate propose including a subsection in the introduction of a CSR that summarizes for the reader (or the regulatory [e.g., FDA] reviewer) the disruption at a high-level, including a tabular summary that includes links to all the subsections in the CSR where the disruption-related information is being reported. This list will act as a roadmap for reviewers.

An example of this is provided on the following page.

Example of Information to Include within the Introduction Section of a CSR:

7 Introduction

<company's standard text per ICH and/or template>

<if no major impact of a disruption, include a statement in introduction; if disruption was impactful and mitigations and impacts are reported throughout the CSR, propose adding a summary of impact subsection that includes a table linking to CSR sections that include disruption-related information. Alternatively, if a Summary of Impact document is included in the CSR appendices, include a statement and hyperlink to the location.>

7.1 Summary of Impact of <Disruption> on the Study

<high-level introductory description of the disruption and the landscape of the impacts relative to timing of the study> Details of the mitigations and impacts from this disruption are summarized throughout the CSR. Refer to [Table X](#) for a summary of applicable sections.

The intent is to include applicable sections with disruption-related information. Some sections may benefit from the use of disruption-specific subheading to support navigation and review of disruption content.

Table X Summary of Disruption-Related Content

Section	Title
Section 10.2.1 <i><include hyperlink to section></i>	<Disruption> Impact on Protocol Deviations

EXAMPLE OF A SECTION

10.2 Protocol Deviations

<company's standard text and table per ICH and/or template>

10.2.1 <Disruption> Impact on Protocol Deviations

<text and/or table summarizing participants with major/significant/important protocol deviations related to the disruption>

<overall statement of impact of disruption on protocol deviations>

<cross-reference to Appendix 16.2.x with the listing of subjects with disruption-related protocol deviations>