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Chapter 6.

Clinical study reports

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Introduction

The clinical study report describes the results of a single human study and thus represents the most fundamental building block in a drug product's argument for use in humans. The results of all human trials conducted by a drug or biologics company must be recorded in some type of report, although the type of reporting may vary. This chapter describes a clinical study report as defined by the International Conference on Harmonisation (ICH) in the E3 Guideline [1], which is the type of report used for most clinical studies conducted in the three major geographic regions (Europe, Japan, and the United States) and is referred to as a "full" clinical study report in this chapter.

This chapter also describes two alternatives to the full clinical study report. The Food and Drug Administration (FDA) in the United States has provisions for two additional report types: an abbreviated report, and a synopsis [2]. Table 1 presents a description of each of these report types. A full ICH E3 clinical study report is a labor- and time-intensive task and is intended to fully support both safety and effectiveness for product labeling; however, many product development programs include clinical studies that for several reasons (eg, inadequate enrollment, poor study design, bias in the data resulting from lack of control of confounders, or noncompliance with Good Clinical Practices) do not meaningfully contribute. The purpose of FDA's provisions for abbreviated reports and synopses is to reduce needless work on a full report.

The decision to submit an abbreviated report or a synopsis instead of a full report is generally the responsibility of regulatory affairs, and is often the result of negotiations with FDA.

Table 1. Clinical study report types for submission in the United States

Report type	Description
Full study reports	Complete ICH E3 reports are submitted for all clinical and human pharmacology investigations that contribute to the evaluation of effectiveness for the proposed indication, or that otherwise support information included in labeling.
Abbreviated reports	Submitted for studies that are not intended to contribute to the evaluation of product effectiveness or provide definitive information on clinical pharmacology, but about which the reviewer needs sufficient information to determine that the study results do not, in fact, cast doubt on the effectiveness claims or the description of the clinical pharmacology. Abbreviated reports should contain all the safety information included in a full report.
Synopses	Submitted for studies that are not relevant to evaluation of product effectiveness or clinical pharmacology, but that provide information the reviewer needs to evaluate the safety data from the study. Complete safety information from a study submitted in synopsis format should be included in the Integrated Summary of Safety (ISS) [21 CFR 314.50(d)(5)(vi)(a)] for drug products and for biologic products where an ISS is included in the application. For biologic product applications not containing an ISS, the safety information for studies submitted in synopsis format should be appended to the synopsis.

Full clinical study reports

Full clinical study reports should be written using the ICH E3 Guideline for Industry, Structure and Content of Clinical Study Reports [1] and in close collaboration with a multidisciplinary team that minimally includes medical, statistical, and regulatory expertise. Careful and thoughtful interpretation of statistical data, within the framework of clinical medicine, and with the objective of supporting the drug's indication statement, is the goal for a study report.

The ICH E3 Guideline provides solid advice for content, but contains a table of contents that has been misconstrued as a directive from the ICH Working Group as an outline that must be followed exactly, with potential for disaster for anyone who dares to deviate. The rumors suggesting such rigidity in this guideline have caused a fair amount of angst in the industry, as efforts to force every product into the same outline have resulted in some rather obscure pairings of headings and content. These odd combinations of heading and content only serve to confuse health authority reviewers as they attempt to locate information.

The working group for this guideline never intended this interpretation of the table of contents and, in fact, vigorously defends the right to modify the outline to best characterize a product. Adherence to the general organization as suggested in the first and second headings has been found to be useful, however, as reference to these numbers is becoming easily recognizable in the industry. This chapter describes writing a clinical study report in terms of these first- and second-level section