

Guidance Snapshot

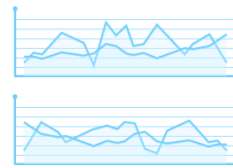
E19 A Selective Approach to Safety Data Collection in Specific Late-Stage Pre-Approval or Post-Approval Clinical Trials

Guidance for Industry



What is Recommended in This Guidance?

This guidance is intended to provide internationally harmonized guidance on the use of selective safety data collection, SSDC, that may be applied in specific pre-approval or post-approval late-stage clinical trials.



Why Is This Guidance Important?

By tailoring the method and streamlining the approach to safety data collection, it may be possible to carry out clinical trials with greater efficiency. This may facilitate the conduct of large-scale efficacy and safety clinical trials with large numbers of participants and long-term follow-up. In all circumstances in which the use of SSDC is considered, it is important that the welfare of every trial participant is safeguarded. This document describes circumstances in which it may be appropriate to reduce the collection of safety data in late-stage pre-approval and post-approval clinical trials, e.g., long term outcome trials, when appropriate and with agreement from regulatory authorities.

What is SSDC?

SSDC refers to the reduced collection of certain types of data in a clinical trial after thorough consideration of factors that would justify such an approach. Throughout the course of medicinal product development sponsors collect extensive safety-related data that may include vital signs and other physical examination data, laboratory data, and all adverse events. In specific phase 3 or post-approval clinical trials, if the safety profile of a drug is well-understood and documented, collection of comprehensive safety data may provide only limited additional knowledge of clinical importance. In such circumstances, a more selective approach to safety data collection may be adequate.



How Was This Guidance Developed?

The final guidance was prepared under the auspices of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). As a Founding Regulatory Member of ICH, FDA plays a major role in the development of each of the ICH guidelines, which FDA then adopts and issues as guidance for industry. Regulatory harmonization represents a process where regulatory authorities align technical requirements for the development and marketing of pharmaceutical products. Harmonization of regulatory requirements has many benefits such as ensuring favorable marketing conditions to support early access to medicinal products, promoting competition and efficiency, and reducing unnecessary duplication of clinical testing.

What is ICH?

The ICH is an international nonprofit association that brings regulatory authorities and pharmaceutical industry together to harmonize scientific and technical aspects of drug registration. ICH's mission is to achieve greater harmonization to ensure that safe, effective, and high-quality medicines are developed and registered in the most resource-efficient manner. This work is accomplished through the development of internationally harmonized Guidelines in the areas of Safety, Efficacy, Quality, and Multidisciplinary topics. International harmonization leads to improved efficiency in the regulatory review process, reduced time to get a product to the market, reduced patient burden through prevention of unnecessary duplication of clinical trials and post market clinical evaluations, and reduction of unnecessary animal testing without compromising safety and effectiveness.

General Principles for SSDC

Ensuring Safety of Trial Participants: Safety monitoring in clinical trials serves to protect participant wellbeing and gather safety information about the investigational medicinal product. This approach does not affect the responsibilities of investigators, as health care professionals, to monitor trial participants and ensure they are treated according to prevailing standards of care.

Factors Influencing the Decision for SSDC: Several factors can contribute to the conclusion that the safety profile of a drug is sufficiently characterized to justify SSDC in a proposed clinical trial, including the regulatory status of the drug, mechanistic factors, clinical safety database, similarity of the planned clinical trial to previous trials, clinical pharmacology, non-clinical data, and post-authorization data.

Baseline Data Considerations: Use of a SSDC approach does not change considerations for baseline data collection determined by the clinical trial objectives. Baseline data are essential to ensure that prospective trial participants are eligible for trial enrolment. Baseline data are also needed for assessment of efficacy and safety in certain subgroups.

Data That Should Generally Be Collected: The following list includes the data elements that should generally be collected: serious adverse events, important medical events, medication error/overdose, adverse event that led to study drug discontinuation, pregnancy and lactation exposure and outcomes, and adverse events of special interest, including laboratory abnormalities, identified in the protocol as critical to safety evaluations.

Data That May Be Appropriate for Selective Collection: When SSDC is justified, it may be acceptable to limit collection of certain data: nonserious adverse events, certain laboratory monitoring, physical examinations and vital sign data, and changes in concomitant therapies (after baseline use is documented).

Benefit-Risk Considerations for SSDC: It should be recognized that the contribution of non-serious adverse events to the benefit-risk profile of a drug may differ depending on the indication of use and patient characteristics (e.g., age, cardiovascular risk factors). These factors should be considered when accepting the comparability of patient populations and the applicability of SSDC.

Early Consultation with Regulatory Authorities: Clinical trials must be conducted in accordance with local and regional laws and regulatory requirements. Sponsors considering SSDC should gain prospective agreement with regulatory authorities.

Situations Where Selective Safety Data Collection May Be Considered:

After careful consideration and a determination that the safety profile of a drug is sufficiently characterized, SSDC may be appropriate for situations, such as:

- Clinical trials to support a new indication of an approved drug where the two populations are similar.
- Clinical trials intended to expand the label information of an approved drug with additional endpoints in the same patient population.
- Safety trials designed to further investigate potential safety concerns focusing on specific parameters when the safety profile has been well characterized.
- Clinical trials designed to provide additional evidence of efficacy, where the safety profile of the drug has been well characterized.

Implementation of SSDC

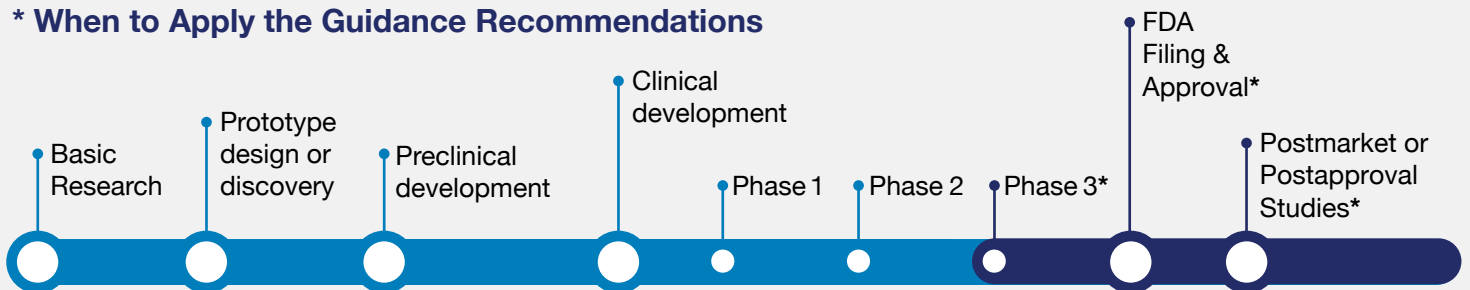
The SSDC approach should be carefully planned and clearly described within the relevant clinical trial documents (e.g., protocol; monitoring plan; statistical analysis plan), with reference to this guidance. The implementation methods are meant to be flexible with respect to the particular types of data for which collection can be reduced, as well as the monitoring intervals for these data. Regardless of the method chosen, it is essential to ensure patient safety and adherence to local and regional laws and regulations. When safety findings are presented, the approaches should be described in the appropriate document(s), e.g., ICH E2F; ICH guidances for industry E3 Structure and Content of Clinical Study Reports (July 1996) and M4 Common Technical Document (October 2017).

Practical Considerations for SSDC

A sponsor considering SSDC should consider impacts to patients, trial conduct, data analysis, and interpretation. Although these approaches can improve efficiency, there are disadvantages. The use of SSDC may present complexities for data analysis, presentation, and summarization. Some questions that may arise retrospectively cannot be explored if the data were never collected, e.g., issues with respect to concomitant medications, laboratory parameters, blood pressure. The feasibility of SSDC approaches and plans for implementation should be discussed with regulatory authorities in advance, and agreement should be reached.

Drug Development Timeline

* When to Apply the Guidance Recommendations



Recommendations from E19 apply to late-stage (Phase 3) pre-approval or post-approval clinical trials



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Hear highlights straight from FDA staff

Speaker: Mary Thanh Hai, MD, Deputy Director for Clinical Science, Office of New Drugs, Center for Drug Evaluation and Research



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