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

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Outline

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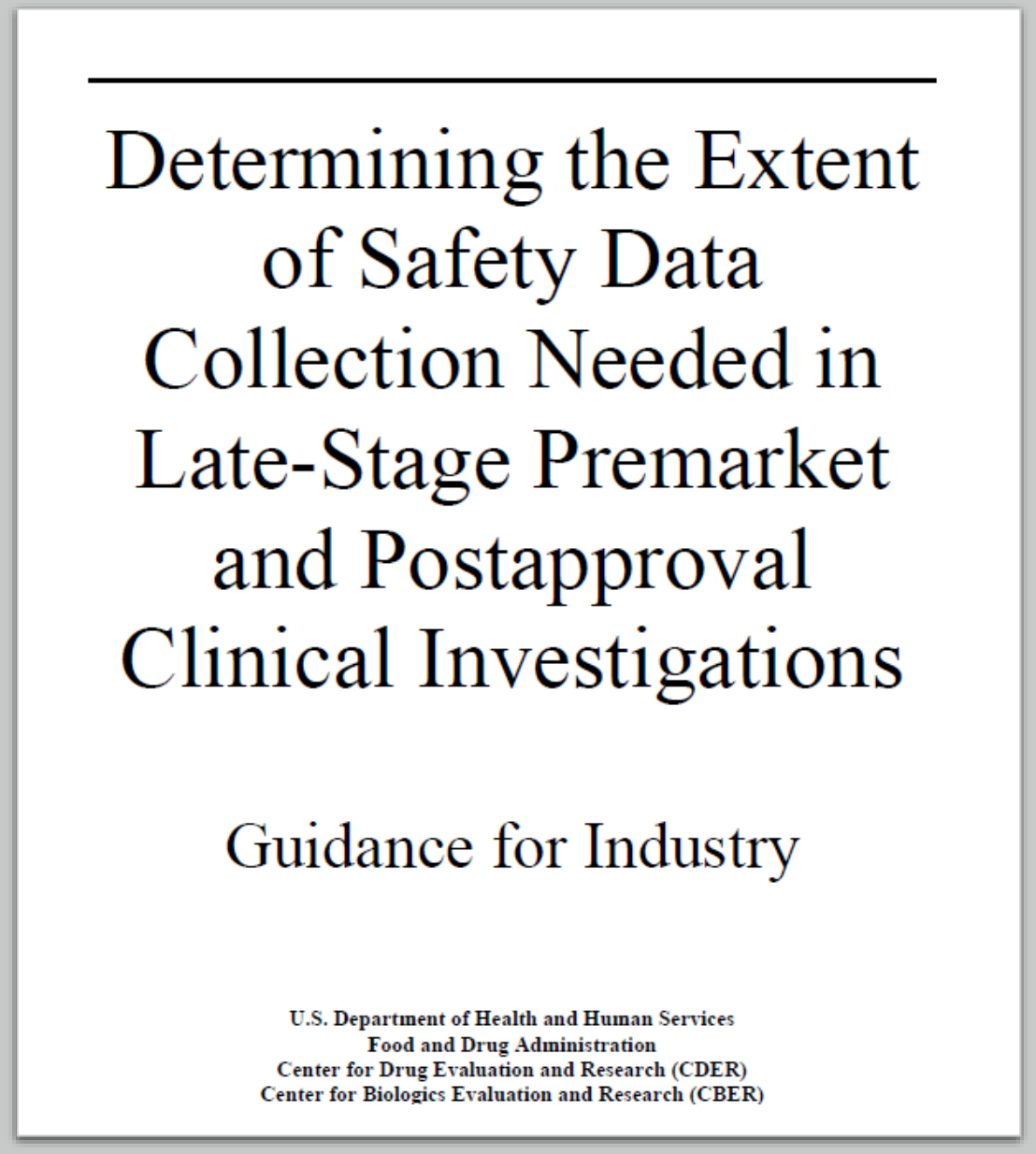
- Scope of E19
- Purpose of safety monitoring in clinical trials
- Factors contributing to establishing safety profile
- What is selective safety data collection
- Possible trial scenarios and methodologies for implementing E19
- Concluding remarks and next steps



Why was E19 proposed for development as an ICH Guideline?

- **Drug development is a global endeavor**
- **Alignment between regulators and industry essential to advance principles laid out in previously published guidance on this topic**

Objectives of E19

- **Provides recommendations regarding appropriate use of a selective approach to safety data collection in some late-stage pre- or post-marketing studies of drugs where the safety profile, with respect to commonly occurring adverse events, is well-understood and documented**
- **Tailoring the method of safety data collection may enable greater efficiency in the conduct of clinical trials. This may facilitate the conduct of large-scale efficacy and safety clinical trials with large numbers of participants and long-term follow-up**

Evolution of E19 (2017-2022)

- Montreal, Canada June 2017
  - Final concept paper endorsed by ICH Management Committee in July 2017
- Geneva, Switzerland November 2017
  - Refined objectives and scope – replaced targeted safety data collection with selective safety data collection
  - Group discussion/editing
- Kobe, Japan June 2018
  - Group discussion/editing
- Charlotte, North Carolina, US November 2018
  - Near final technical document
  - Goal for Step 1 finalization by 31 January 2019
  - EWG concurrence in February 2019
  - Draft guideline published for consultation 29 March 2019 through 29 September 2019 (Step 2b)
- Singapore, November 2019
  - EWG reviewed public comments and developed plan to address
- EWG held regular teleconferences from 2020-2022
- Step 4 reached of ICH Process on 27 September 2022

- **ICH E19 Guideline published 27 September 2022**
  https://database.ich.org/sites/default/files/ICH_E19_Guideline_Step4_2022_0826_0.pdf

- **FDA E19 Final Guidance issued 5 December 2022**
  https://www.fda.gov/media/163670/download

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Scope of E19

- Interventional clinical trials
- More often, post-approval trials
- In some circumstances, may be considered for pre-approval trials
- Not applicable to gene therapy or rare/orphan disease clinical trials
- Selective safety data collection (SSDC) following the principles of this guidance does not alter local/regional safety reporting requirements

Ensuring Safety of Trial Participants

Safety monitoring in a clinical trial serves two purposes:

- **To protect the safety and well-being of individual trial participants**
- **To obtain safety information to be used in the assessment of the risk profile of the investigational medicinal product**

When is the safety profile of a drug well-understood and documented?

Guidance lists several factors for consideration BUT not considered to be an exhaustive list or determinative

- **Regulatory status of drug (e.g., marketing status of drug)**
- **Mechanistic Factors (e.g., MOA including untoward effects, one of many in class or first-in-class)**
- **Clinical Safety Database (number and duration of exposure, dose, intensity of safety monitoring)**
- **Similarity of Planned Clinical Trial to Previous Trials (e.g., dosing regimen, patient population)**
- **Clinical Pharmacology (e.g., DDIs, ADME)**
- **Non-clinical Data (e.g., safety and pharmacologic effect well-characterized from animal studies)**
- **Post-authorization Data (extent and quality of post-marketing safety data)**

What is Selective Safety Data Collection (SSDC)?

SSDC in guideline refers to the recording of certain data on CRFs by investigators as well as reporting to sponsor for subsequent evaluation and submission to regulatory authorities.

Should generally expect that the following will be collected:

- **Serious adverse events (SAEs)**
- **Important medical events**
- **Medication error/overdose (intentional or unintentional)**
- **AEs leading to study drug discontinuation**
- **Pregnancy and lactation exposures and outcomes**
- **AESI, including laboratory abnormalities, identified in the protocol**

What is SSDC cont'd

When it has been determined and agreed to that SSDC may be appropriate for a clinical trial, collection of certain information may be limited or reduced in frequency of collection (need to be specified in protocol):

- **Non serious AEs**
- **Some laboratory monitoring***
- **Physical examination and vital sign data***
- **Concomitant meds***

If an SAE, AESI, important medical event, or an AE resulting in study drug or trial discontinuation occurs, sponsor may need to collect above information for the individual patient to characterize the particular event

***Expect that comprehensive baseline data have been collected for certain lab tests, con meds, and physical exam**

Situations Where SSDC May be Considered

- Approved drug seeking new indication in similar population to the one that is already approved
- Approved drug seeking to expand label to include additional endpoints in the same patient population
- Safety trial with objective to investigate specific safety concern
- Trial designed to provide additional evidence of efficacy when current available data support a well-characterized safety profile

Possible Approaches to Implementing SSDC in a Clinical Trial

- SSDC in everyone
- Comprehensive collection for a specific subset, SSDC in the rest
- Comprehensive collection in everyone initially, SSDC thereafter
- Comprehensive collection in a representative subset, SSDC for remainder of patients

Key Considerations Before Implementing SSDC

- **Is the safety profile of the drug well-characterized?**
- **Do the study objectives and design of the trial support SSDC?**
- **Has agreement been reached with regulatory agency on the protocol implementing SSDC?**

Conclusion

ICH E19 Guideline will have a significant impact on the feasibility and efficiency of clinical trials designed to yield important new medical knowledge and advance public health

Next Steps

- **Drug development is a global endeavor**
- **Alignment among regulators and industry essential to advance principles laid out in this recently finalized guideline**
- **Concerted effort needed to implement principles of E19**
- **Share experiences and lessons learned with implementation**

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