Health Canada Santé Canada

Canada

ICH M14: General Principles on Plan, Design, and Analysis of Pharmacoepidemiological Studies that Utilize Real-World Data for Safety Assessment of Medicines

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M14 Use of real-world data for safety assessment of medicines

M14 EWG

General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines

This topic was endorsed by the ICH Assembly in June 2021.

Further to the ICH Management Committee's endorsement of the M14 Concept Paper and Business Plan in April 2022, the M14 EWG was established to work on the development of the harmonised ICH M14 Guideline on General Principles on Plan, Design, and Analysis of Pharmacoepidemiological Studies that Utilize Real-World Data for Safety Assessment of Medicines.

The guideline will focus on non-interventional pharmacoepidemiological studies using Real-World Data (RWD) and will include basic principles that may apply to these studies when real-world data elements are included.

Further information can be found in the M14 Concept Paper and Business Plan.

Rapporteur: Dr. David Moeny (FDA, United States)

Regulatory Chair: Dr. Kazuhiro Kajiyama (MHLW/PMDA, Japan)

Status: *Step 1*

Endorsed Documents

- M14 Concept Paper
- M14 Business Plan
- M14 Work Plan

WG list

LINK to ICH website

Background and History

Origins of ICH M14

- Proposal for a multidisciplinary guideline arose from the ICH Reflection Paper on Pharmacoepidemiological Studies

- Intended goals and impacts:
  - Harmonise the technical scientific requirements related to pharmacoepidemiology studies submitted to regulatory agencies.
  - Harmonisation in this area facilitates utilization of Real-World Data and promotes a globally-harmonised approach in post-marketing safety-related regulatory actions based on the most current scientific evidence

- Endorsed by the ICH Assembly June 2019

Pharmacoepidemiology Discussion Group (PEpiDG)

- Worked to harmonize the *technical scientific requirements* related to pharmacoepidemiological studies submitted to regulatory agencies

- Promote a globally-harmonized approach in post-marketing safety-related regulatory actions based on the most current scientific evidence

- Concept paper outline endorsed by the assembly in July 2021
  - Called for establishment of a new ICH guideline on “General principles on planning and designing pharmacoepidemiological studies that utilize real-world data for safety assessment of a medicine”

PEpiDG GAP Analysis

US-FDA : 1 | Swissmedic : 4 | EFPIA : 20 | SFDA : 1 | NMPA : 1 | Health Canada : 5 | PMDA : 7

The total number of guidelines submitted by 7 parties: 39

duplication

The unique number of guidelines submitted by 7 parties: 28

Exclusion criteria
Non-drug guideline: 1 (Deceive guideline)
Clinical Trial guideline : 1
Scientific article: 1 (bias analysis guideline)
ICH guideline: 1 (E2E)

The number of guidelines for GAP analysis: 24

Guidelines were categorized into 8 topics※ based on their contents

- **General** principles on study plan 9
- Methodology 8
- Protocol format 9
- Report format 4
- Regulatory purpose 9
- Glossary 4
- Validation 4
- Data reliability 9

※ Guidelines describing more than one topic are categorized in multiple relevant topics.

https://www.pmda.go.jp/files/000241195.pdf

PEpiDG Concept Paper

- Guideline to outline recommendations on considerations when utilizing RWD for drug safety assessments
  - Data source selection, design, definitions of target population, exposure, outcome, and analytic approach
- The guideline will promote faster access of patients to new drugs
  - Increase confidence for pharmacovigilance activity with RWD
  - Accelerating rapid accumulation of safety data
- Promote sharing of post-marketing safety information among different regulatory agencies, leading to better decision making

ICH M14 Expert Working Group (EWG)

- Informal working group formed November 2021
- Concept paper and business plan endorsed April 2022

<u>M14 EWG formalized May 2022:</u>

Draft Guideline

Draft Guideline Development

- Sub-“small group edits”: +/- weekly work in addition to biweekly EWG meetings
- Circulated for internal party review: June-August 2023
  - 615 comments and edits received
- Pre-ICPE F2F meeting of the EWG (informal): 24 August 2024
- Review of all member comments and edits: Completed January 2024

Contents

- Focus on post-approval non-interventional studies on drugs, vaccines and other biologics

- Studies with treatment assignment excluded
  - Principles may be applicable to these studies when RWD elements included

- Principles may be applicable to studies conducted for purposes other than safety evaluation, such as drug utilization and effectiveness studies

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Current Status and Next Steps

Current Status

- ICH parties reach consensus (ICH Step 2a): targeted April 2024

- Public consultation (ICH Step 2b): targeted for end of April 2024
  - 90 days in duration through the ICH website

Next Steps

Guideline establishment goal date:
January/February 2025

Step 5: Implementation	Planned May 2025
Step 4: Adoption of ICH Harmonized Guideline	Planned Jan/Feb 2024
Step 3: Regulatory Consultation and Discussion	Planned April 2024
Step 2a: ICH Parties Consensus Step 2b: Draft guideline adoption (Public Comment)	Planned April 2024
Step 1: Consensus Building- Technical Document	Planned March/April 2024

Thank you

Acknowledgements

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M14 EWG Members