Final Concept Paper

Establishment of a new ICH guideline on "General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines"

23 March 2022

Endorsed by the Management Committee on 5 April 2022

Type of Harmonisation Action Proposed

Establishment of a new harmonized guideline entitled "General principles on plan, design, and analysis of pharmacoepidemiological studies that utilize real-world data for safety assessment of medicines." For this guideline, medicines refers to drugs, vaccines and other biologics.

This guideline will focus on non-interventional pharmacoepidemiological studies using Real-World Data (RWD). Studies with treatment assignment are excluded, including randomized clinical trials or single arm clinical trials. However, the basic principles presented in this guideline may be applicable to these studies when real-world data elements are included.

Statement of the Perceived Problem:

While the number of pharmacoepidemiological studies utilizing RWD in a regulatory context have increased globally, currently, there are no ICH guidelines that focus on how to generate fit-for-purpose Real-World Evidence (RWE). Although many regions (e.g., Canada, China, EU, Japan, and US) have published guidelines related to general principles of planning and designing such studies, mainly for the purpose of drug, vaccine and other biologic safety assessment, a lack of harmonisation in this area can cause challenges for sponsors and regulators.

Issues to be Resolved:

The proposed guideline will outline general considerations and recommendations for use of RWD for drug, vaccine and other biologic product safety assessments, including defining the research question, data source selection/generation, study design, definitions of target populations, exposure and outcome(s), covariates, data source fit-for-purpose evaluation, sources of and methods to address confounding and bias, analytic approaches, and format and content of reporting.

Background to the Proposal:

The Pharmacoepidemiology Discussion Group (PEpiDG) reached a consensus that the establishment of an ICH guideline on the general principles of planning, designing and analysis of pharmacoepidemiological studies that use RWD in the context of drug safety assessment is the highest

priority for promoting an internationally harmonised approach on the use of such studies for regulatory purpose. This is because: 1) there are sufficient regulatory use cases accumulated on this topic; and 2) the guideline will cover fundamental issues and overarching principles which will support other important topic areas with the potential for harmonization, such as aspects of "protocol and report format" and "methodology".

Guidelines on the proposed topic are currently available, among others, in EC, Europe; FDA, United States; Health Canada, Canada; MHLW/PMDA, Japan and NMPA, China.

EC, Europe:

- The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) Guide on Methodological Standards in Pharmacoepidemiology (Revision 9, July 2021)
- Guideline on good pharmacovigilance practices (GVP) Module VIII – Post-authorisation safety studies (Rev. 3 October 2017)
- Guideline on registry-based studies (September 2020)

FDA, United States:

- Best Practices for Conducting and Reporting Pharmacoepidemiologic Safety Studies Using Electronic Healthcare Data (May 2013)
- Considerations for the Use of Real-World Data and Real-World Evidence To Support Regulatory Decision-Making for Drug and Biological Products (Draft Guidance, December 2021)
- Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products Guidance for Industry (Draft Guidance, November 2021)
- Data Standards for Drug and Biological Product Submissions Containing Real-World Data (Draft Guidance, October 2021)
- Real-World Data: Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision-Making for Drug and Biological Products (Draft Guidance, September 2021)
- Framework for FDA's Real-World Evidence Program (December 2018)

Health Canada, Canada

- Elements of Real-World Data/Evidence Quality throughout the Prescription Drug Product Life Cycle (Updated March 2019)

MHLW/PMDA, Japan

- Guidelines for the Conduct of Pharmacoepidemiological Studies in Drug Safety Assessment with Medical Information Databases (March 2014)
- Basic Principles on the Use of Medical Information Databases in Post-marketing Pharmacovigilance (June 2017)

NMPA, China

- Guideline on Using Real-World Evidence to Support Drug Development and Review (January 2020)
- Guideline on Real-World Study to Support Pediatric Drug Development and Review (August 2020)
- Guideline on Real-World Data Used to Generate Real-World Evidence (April 2021)

The working group will focus on harmonization of regulatory guidelines but will consider non-regulatory guidelines in the development of the M14 guideline.

Type of Expert Working Group Recommended:

The Expert Working Group (EWG) will include regulators and industry representatives with innovative thinking, adequate expertise and experience in technical and regulatory issues relating to pharmacoepidemiology utilizing RWD for drug, vaccine and other biologic safety assessment.

Regulatory, industry, and observer experts with experience and expertise relating to the use of RWD for studying the safety of drugs, vaccines and other biologics are needed for the development of these guidelines. The core disciplines include: pharmacovigilance, epidemiology, biostatistics, data curation and management, and ethics.

Timing:

The anticipated time to complete the establishment of the guideline will be 2-3 years (by January 2025).