2022年7月7日
第45回ICH即時報告会

M14 WG

General principles on planning and designing pharmacoepidemiological studies that utilize real-world data for safety assessment of a medicine

医薬品の安全性評価のためにリアルワールドデータを活用する
薬剤疫学調査の計画及びデザインに関する一般原則（仮題）

独立行政法人医薬品医療機器総合機構　医療情報活用部
梶山　和浩

本日の内容

M14

■ 背景

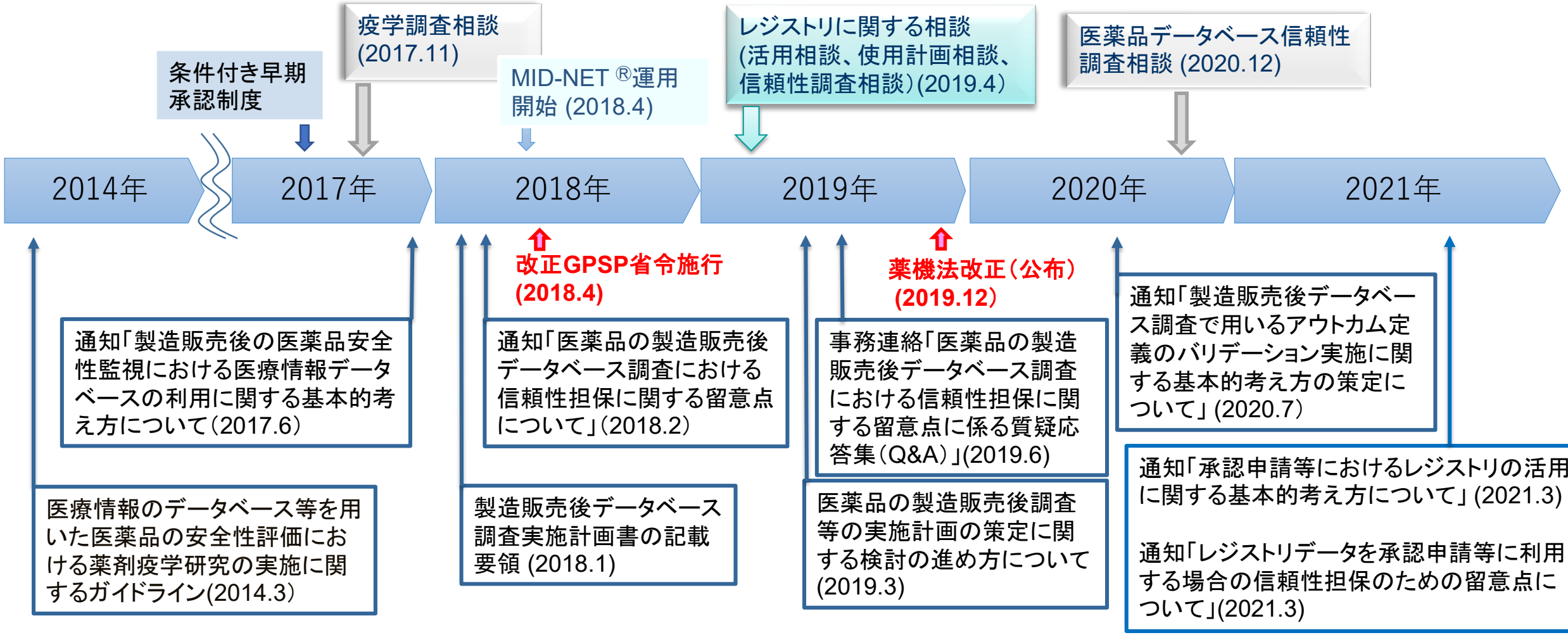
- 医薬品開発へのRWDの活用に向けた国内の状況
- ICHにおけるRWDの活用に関するこれまでの活動

■ M14：医薬品の安全性評価のためにリアルワールドデータを活用する薬剤疫学調査の計画及びデザインに関する一般原則（仮題）

- Concept Paper
- Business Plan

■ おわりに

医薬品開発へのＲＷＤの活用に向けた国内の状況



RWDより得られた結果の国際的な受け入れ可能性の向上に向けて、薬事申請に利用する際の技術的・科学的な要件について国際的な議論が必要

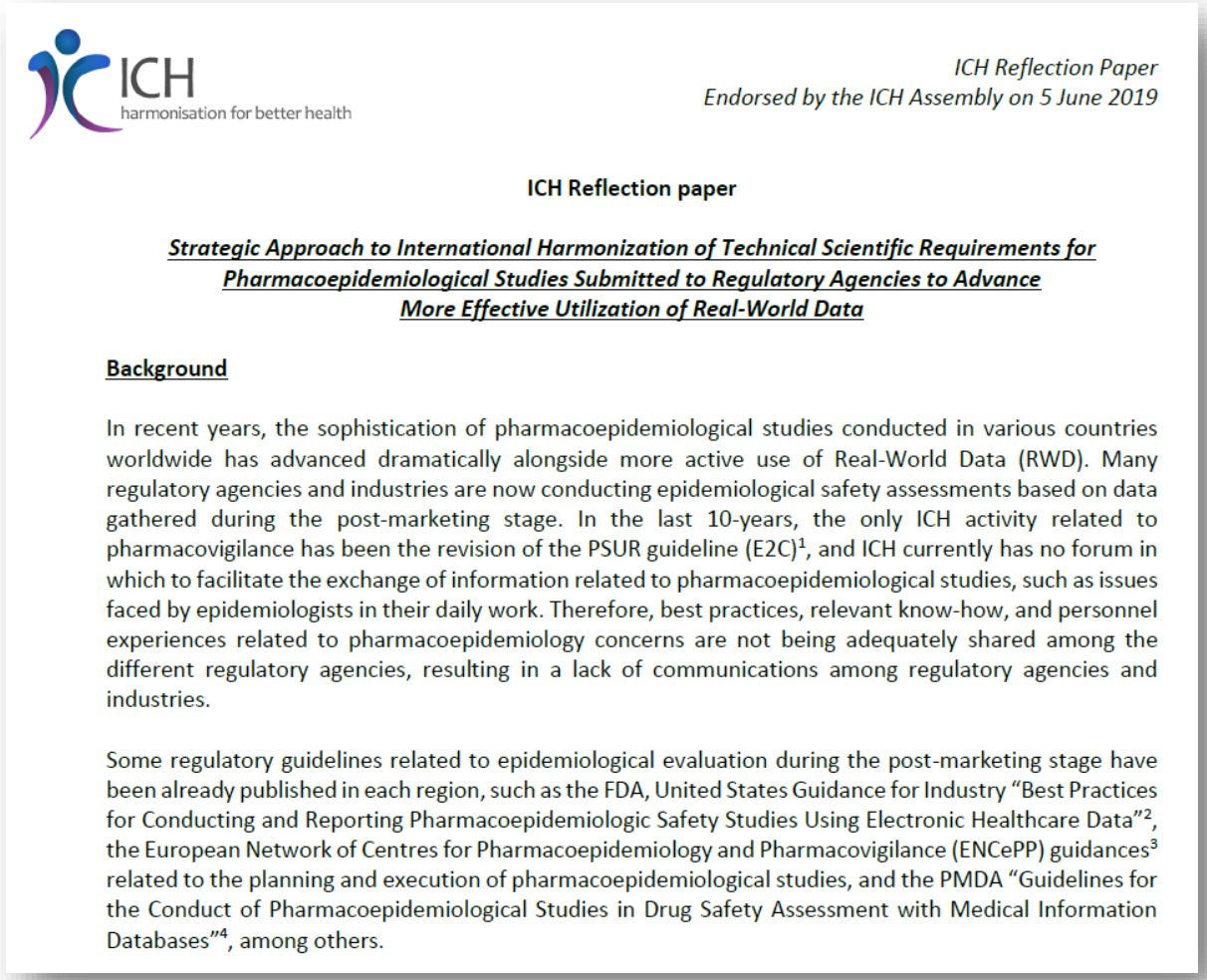
ICHにおけるRWDの活用に関するこれまでの活動（１／３）

M14

2019年　6月　Reflection paperの採択

■ 提案の目的

- 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.



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ICH Reflection Paper
Endorsed by the ICH Assembly on 5 June 2019

ICH Reflection paper

Strategic Approach to International Harmonization of Technical Scientific Requirements for Pharmacoepidemiological Studies Submitted to Regulatory Agencies to Advance More Effective Utilization of Real-World Data

Background

In recent years, the sophistication of pharmacoepidemiological studies conducted in various countries worldwide has advanced dramatically alongside more active use of Real-World Data (RWD). Many regulatory agencies and industries are now conducting epidemiological safety assessments based on data gathered during the post-marketing stage. In the last 10-years, the only ICH activity related to pharmacovigilance has been the revision of the PSUR guideline (E2C)[1], and ICH currently has no forum in which to facilitate the exchange of information related to pharmacoepidemiological studies, such as issues faced by epidemiologists in their daily work. Therefore, best practices, relevant know-how, and personnel experiences related to pharmacoepidemiology concerns are not being adequately shared among the different regulatory agencies, resulting in a lack of communications among regulatory agencies and industries.

Some regulatory guidelines related to epidemiological evaluation during the post-marketing stage have been already published in each region, such as the FDA, United States Guidance for Industry "Best Practices for Conducting and Reporting Pharmacoepidemiologic Safety Studies Using Electronic Healthcare Data"[2], the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) guidances[3] related to the planning and execution of pharmacoepidemiological studies, and the PMDA "Guidelines for the Conduct of Pharmacoepidemiological Studies in Drug Safety Assessment with Medical Information Databases"[4], among others.

https://admin.ich.org/sites/default/files/2019-08/ICH_ReflectionPaper_Pharmacoepidemiology_2019_0605.pdf

ICHにおけるRWDの活用に関するこれまでの活動（２／３）

2019年9月　Pharmacoepidemiology Discussion Group (PEpiDG)活動開始

■ 目的

- 薬剤疫学的調査に関する技術的・科学的な要件の調和に向けた検討

■ 検討の流れ

1. 各地域で作成されているRWDの活用に関するガイドラインの作成状況を調査
2. 既存のガイドラインの内容を比較し、国際的な調和が可能なトピックの検討・優先順位付け
3. ICHで作成することが望ましいガイドラインの提案

2020年12月　新規ガイドラインのConcept Paper OutlineをMCに提案

“General principles on planning and designing pharmacoepidemiological studies that utilize real-world data for safety assessment of a medicine”

Concept Paper Outlineにおける提案の概要

- The proposed guideline will **outline recommendations on general considerations when utilizing RWD for drug safety assessments**, such as: data source selection, study design, definitions of target populations, exposure and outcome(s), and analytic approaches.
- The guideline will promote faster access of patients to new drugs by giving **more confidence for pharmacovigilance activity with RWD** and **accelerating rapid accumulation of safety data** in an internationally harmonized way in real world setting.
- It also promotes **sharing post-marketing safety information among different regulatory agencies**, leading to better decision making.

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

ICHにおけるRWDの活用に関するこれまでの活動（３／３）

2021年12月　M14 Informal Working Group 活動開始

■ 目的

- PEpiDGより提案されたConcept Paper Outlineに基づき、ICHが作成すべきガイドラインの具体的な方針を示すConcept Paper及びBusiness Planの作成。

■ 活動の概要

- 定期的にWEB会議を開催し、各文書の最終化に向けた議論を実施。

2022年3月　Concept Paper及びBussiness PlanをMCに提案

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Dated 16 May 2022

ICH ASSEMBLY ATHENS HYBRID MEETING

AGENDA

Tuesday 24 May and Wednesday 25 May 2022

Athens, Greece

Tuesday 24 May 2022 – 09h00 to 17h00 Athens time

6.14 M14 EWG: General principles on planning and designing pharmacoepidemiological studies that utilize real-world data for safety assessment of a medicine (Rapporteur: Mr. Moeny – FDA, United States; Regulatory Chair: Dr. Kajiyama – MHLW/PMDA, Japan)

The M14 informal WG was established in December 2021.

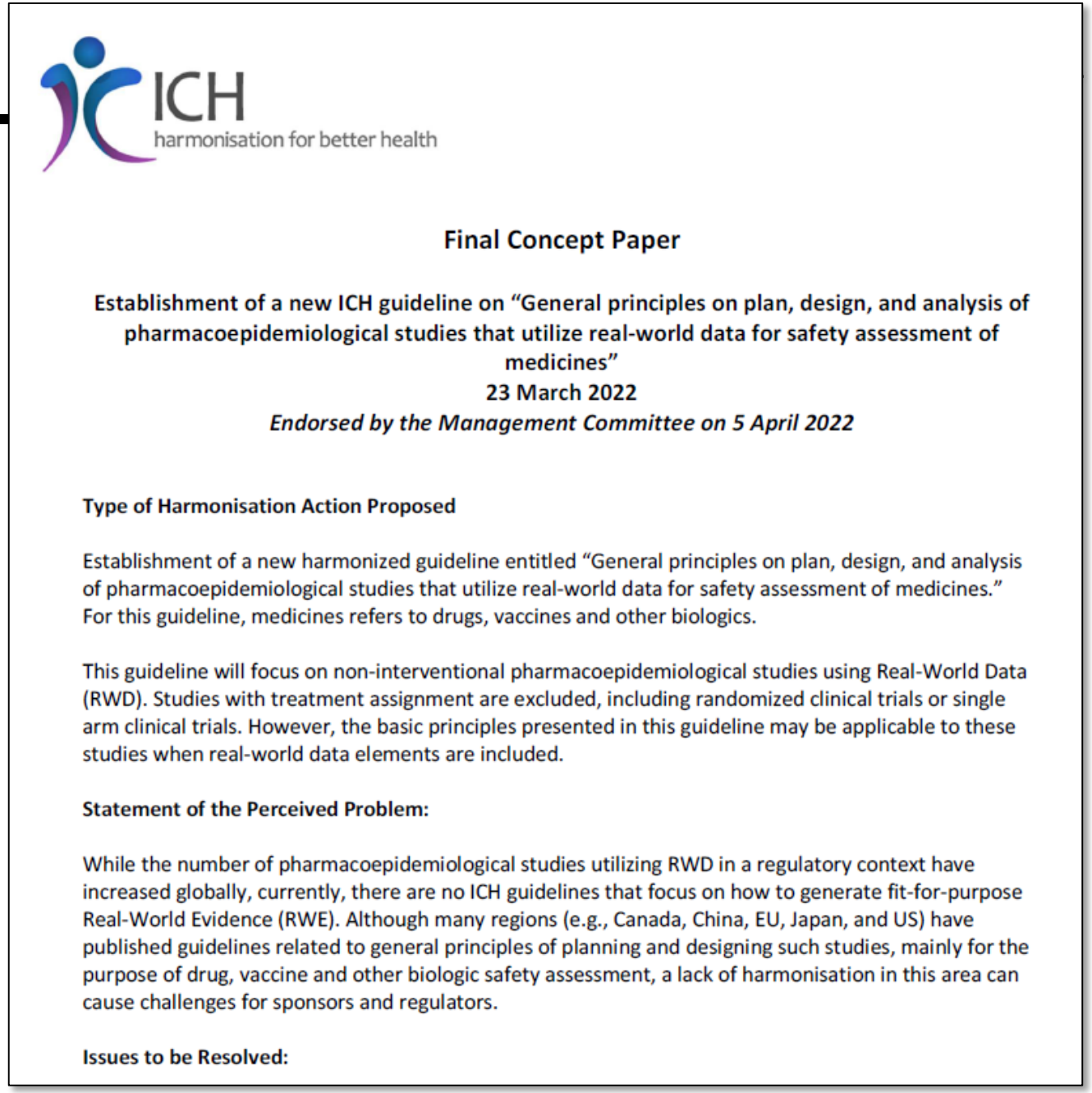
The Concept Paper and the Business Plan were approved by the MC in April 2022, and the M14 formal EWG established.

https://admin.ich.org/sites/default/files/2022-05/ICH44_Assembly_Agenda_Meeting_2022_0516.pdf

M14 Concept Paper

■ Type of Harmonisation Action Proposed

- 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.
- The basic principles presented in this guideline may be applicable to these studies when real-world data elements are included.



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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:

https://database.ich.org/sites/default/files/M14_ConceptPaper_2022_0405.pdf

M14 Concept Paper

■ 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, 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.

■ Timing

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

M14 Concept Paper

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)

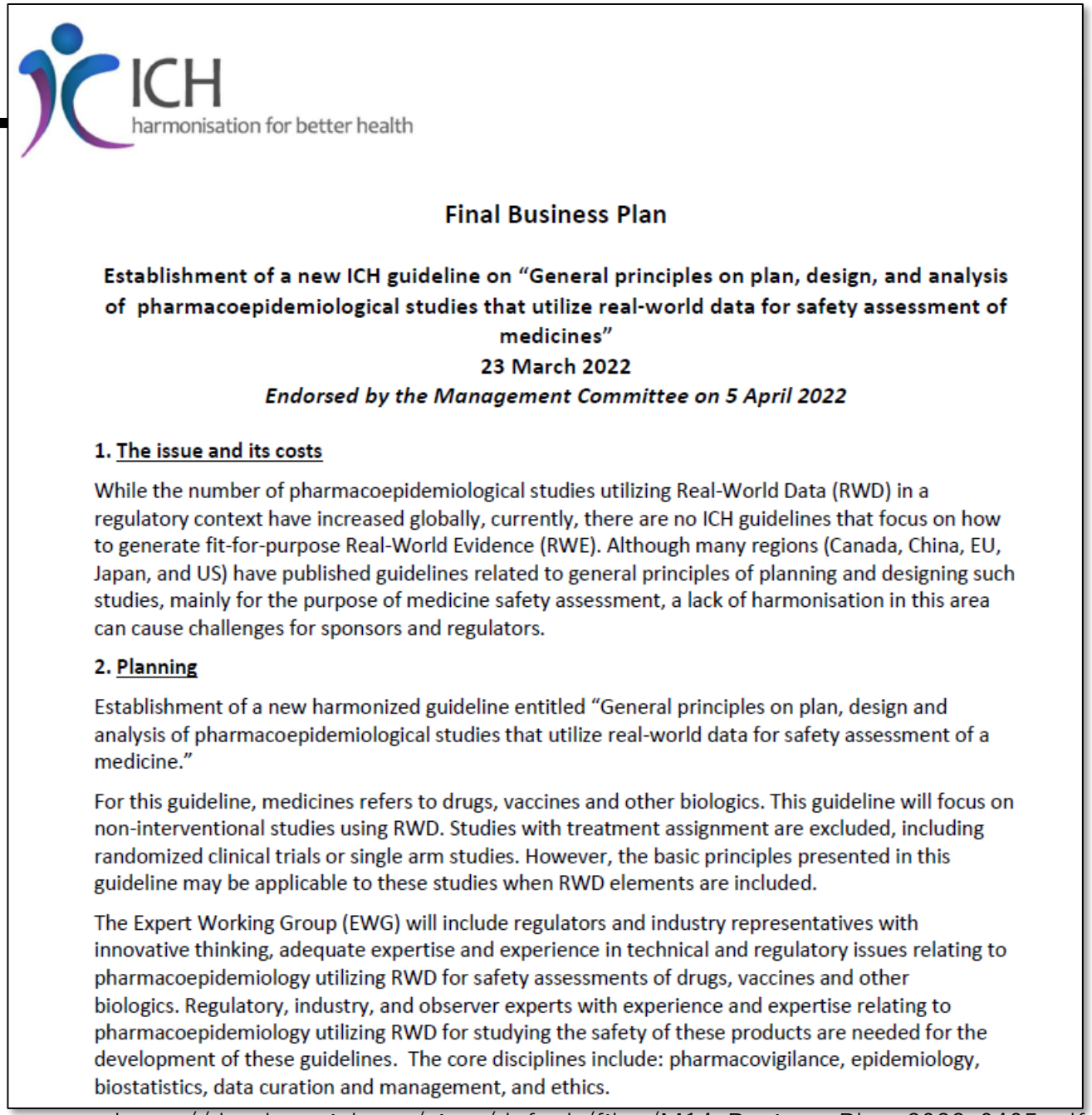
NMPA, China

- 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)

M14 Business Plan

■ The impacts of the project

- Fundamental issues and overarching principles of following topics will be addressed in this guidance.
  - ➢ Definitions and associated requirements
  - ➢ Format and content of regulatory filings and reporting of study materials and results
  - ➢ Data source generation and/or selection, and fit for purpose requirements
  - ➢ Outcome identification by study design and data type
  - ➢ Selection of proper methods
  - ➢ Safety reporting requirements, in line with regional regulatory frameworks



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Final Business Plan

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

1. The issue and its costs

While the number of pharmacoepidemiological studies utilizing Real-World Data (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 (Canada, China, EU, Japan, and US) have published guidelines related to general principles of planning and designing such studies, mainly for the purpose of medicine safety assessment, a lack of harmonisation in this area can cause challenges for sponsors and regulators.

2. Planning

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 a medicine."

For this guideline, medicines refers to drugs, vaccines and other biologics. This guideline will focus on non-interventional studies using RWD. Studies with treatment assignment are excluded, including randomized clinical trials or single arm studies. However, the basic principles presented in this guideline may be applicable to these studies when RWD elements are included.

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

https://database.ich.org/sites/default/files/M14_BusinessPlan_2022_0405.pdf

M14 Expert WG :

General principles on planning and designing pharmacoepidemiological studies that utilize real-world data for safety assessment of a medicine

医薬品の安全性評価のためにリアルワールドデータを活用する
薬剤疫学調査の計画及びデザインに関する一般原則（仮題）

M14 Expert WG

■ 目的

- Concept Paper及びBusiness Planに基づくICHガイドラインの作成

■ 参加団体

ANVISA, Brazil	BIO
CDSCO, India	EC, Europe
EFPIA	FDA, United States (Rapporteur)
Global Self-Care Federation	Health Canada, Canada
IFPMA	IGBA
JPMA	MFDS, Republic of Korea
MHLW/PMDA, Japan (Regulatory Chair)	NMPA, China
PhRMA	SFDA, Saudi Arabia
TFDA, Chinese Taipei	WHO

M14 Expert WG

■ ガイドライン策定に向けた作業の流れ

M14 informal WGの発足

↓ Final Concept Paperの作成

↓ Business Planの作成

↓

☞ **M14 formal EWGの発足**

↓ Work Planの作成

↓ Step 1：Consensus Building

↓ Step 2a：Consensus on the Technical Document

2b：Endorsement of the ICH Draft Guideline

↓ Step 3：Public Regulatory Consultation and Discussion

↓ Step 4：Adoption of the ICH Harmonized Guideline

Step 5： Implementation

おわりに

- 安全性評価にRWDを活用する取り組みは、日本を含む複数の地域において既に開始されており、その結果は規制当局への提出資料として用いられるなど、安全対策措置の検討に利用されている。

- M14の活動を通じて、安全性評価にRWDを活用する際の国際的な基準が確立することで、調査結果について多地域における受け入れ可能性が高まり、RWDを活用した迅速かつ効率的な安全対策措置の検討・実施が実現できる。

- M14においてRWD活用時の原則を安全性評価の観点から検討し、国際的な共通理解を得ることで、RWDを有効性評価へ活用する場合においても、効率的に国際的な議論が実施できるものと期待している。