Insight Guide

Mapping Feasibility Criteria Across 46 Real-World Evidence Guidelines, Gap Analysis, and IQVIA's Mitigation Strategies

SUMMER DRUMMOND, DNP, MSN, RN, CCRC, CCRP, Associate Director, Data Access & Feasibility, Epidemiology and Database Studies, Real World Solution, IQVIA

JULIEN HEIDT, MS, Scientific Strategy Lead, Center for Advanced Evidence Generation and Applied AI Science, Real World Solutions, IQVIA

DONY PATEL, Ph.D., Senior Director Epidemiology and Database Studies, IQVIA

Executive Summary

Database studies can be an efficient, cost effective, and ethical way to research a condition or therapeutic using data captured in the real-world to generate evidence on safety and effectiveness. Researchers can gain approval to analyze retrospective health data, or to plan for future analyses of prospective data. A feasibility assessment can be completed prior to or in tandem with protocol development to evaluate the key study specific variables, data access logistics, and sample size of patient cohorts to inform a non-biased selection of fit-for-purpose data sources for a protocol design.

Regulators and payers are placing increased importance on the transparent reporting of feasibility criteria and selection of data sources for real-world evidence (RWE) studies.[1–7] Contemporary Practice and Considerations for Real-World Data Source Identification and Feasibility Assessment, developed in 2022 as a part of an International Society for Pharmacoepidemiology (ISPE)-funded initiative, aimed to assess differences in 14 published guidance documents and variability in practice related to identifying and evaluating real-world data (RWD) sources for studies with regulatory purpose.[8] To build on the insights from the original assessment, IQVIA aimed to identify and map guidelines released after its development, and ultimately included 32 additional publications. To elucidate the overlap in recommendations and feasibility criteria across the guidelines, a review, mapping, gap analysis, and summary of IQVIA's strategies to mitigate gaps is presented.

Mapping of key feasibility assessment criteria against relevant regulatory guidance

Between 2017 and 2024, regulators and other organizations published 46 important guidance documents to provide researchers information on RWE study conduct. These included, but were not limited to, the Food and Drug Administration (USA), European Medical Agency (Europe), Medicines and Healthcare products Regulatory Agency (UK), National Medical Products Administration (China), Pharmaceuticals and Medical Devices Agency (Japan), International Council for Harmonisation (ICH), and the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP).

This approach builds upon the original assessment completed in 2022[8], and maps key feasibility assessment criteria against relevant regulatory guidance available through July 2024. In addition to the extended period to collect important releases, this updated mapping includes additional national guidance from Australia, Brazil, and Canada; international guidance from ICH and some notable frameworks by subject matter experts. The inclusion of additional publications provides a more complete view of the landscape and further illustrates trends across geographies and stakeholders. Feasibility criteria were minimally adjusted, and all guidelines reviewed and mapped. IQVIA has global, regional, and local RWE expertise and leveraged this when reviewing each publication, assigning two subject matter experts per guideline, with additional reviewers added in the event of discrepant findings. It is important to note that the mapping indicated whether the feasibility criterion was mentioned in the document and does not specify depth of detail provided, to avoid a subjective assessment.

Mapping identified critical gaps and recommendations

In total, 46 RWD guidance documents were identified and mapped against 14 RWD feasibility assessment criteria developed from ISPE survey results in the original publication, and slightly adapted for the purposes of this effort (Tables 1 and 2). Newly released guidelines include key criteria to complete feasibility assessment studies more consistently for identification of fit-for-purpose data sources but challenges with implementation of feasibility dimensions remain due to a lack of operational detail.

Table 1: Available guidance by geography

GEOGRAPHY	AVAILABLE GUIDANCE
Australia (TGA, MI-CRE)	3
Brazil (Anvisa)	1
Canada (CADTH)	2
China (CDE, NMPA, CMDE)	9
Europa (EMA, ENCePP)	7
International (ICH)	2
Japan (PMDA)	4
United Kingdom (MHRA, NICE)	3
United States (FDA)	5
Other Frameworks	10

See table 2 on the following page for details.

Out of the 46 guidelines mapped, 45 (97.8%) are missing >1 of the key feasibility assessment criteria. The 11th Revision of the ENCePP Guide on Methodological Standards in Pharmacoepidemiology published in 2023 is the sole document mentioning all 14 (a notable change from the 10th Revision published in 2022 which only included 6 criteria).[9,10] Guidance documents from ICH and TransCelerate as well as regulators in Australia, China, Europe, and United Kingdom mention 13 of the 14 feasibility criteria that were considered relevant to feasibility of data sources.[2,3,5,11–13] Additionally, MHRA, NMPA, FDA, and MINERVA guidelines include 12 criteria[6,14,15,] while other NMPA, EMA, FDA and two non-affiliated documents included 11 criteria.[14,16–19] However, more than half of the guidance documents are missing ≥4 criteria (27/46 [58.7%]) and almost one third (14/46 [30.4%]) are missing ≥7 of the criteria.

The percentage of at least 1 mention for each of the 14 feasibility criteria across 46 guidelines was: study elements (97.8%), reliability (87.0%), relevance (84.8%), validity (80.4%), sample size and bias/limitations (78.3%), provenance (73.9%), coverage, linkage, and governance (58.7%), data dictionary/definitions (54.3%), local ethical requirements (52.2%), data lag/timelines (41.3%), and cost (17.4%).

Table 2: Mapping of guidance documents to key factors for data source suitability

Zoom in to view

GUIDELINE/FRAMEWORK					DESIGN FEATURES			DATA QUALITY				DATA LOGISTICS						
GEOGRAPHY	TITLE	REGULATOR/AUTHOR	DATE PUBLISHED	LINK TO GUIDANCE	STUDY ELEMENTS (OUTCOMES, EXPOSURES, COVARIATES, ETC.)	SAMPLE SIZE	DATA BIAS, LIMITATIONS	DATA RELEVANCY	DATA RELIABILITY	DATA VALIDITY	DATA COVERAGE	DATA DICTIONARY/ DEFINITIONS	DATA LINKAGE	DATA GOVERNANCE, COLLABORATION	DATA SOURCE ETHICAL CONSIDERATIONS	DATA PROVENANCE/ COLLECTION METHODS	DATA ACCESS/ LAG TIMELINES	DATA COST
					Please enter Y (Yes) if the term/concept is present in the guideline (the extent to which it is discussed, is not relevant to this assessment)													
Australia	Real World evidence and patient reported outcomes in the regulatory context	Australian Government Department of Health, Therapeutic Goods Association (TGA)	Nov 2021	RWE and PROs	Y	Y	Y	Y										
	Optimising the availability and use of Real World data and Real World evidence to support health technology assessment in Australia	Commissioned by Australian Government, Department of Health and Aged Care. Authored by NHMRC Medicines Intelligence Centre of Research Excellence (MI-CRE)	25 Mar 2024	Australia RWD & RWE	Y	Y	Y	Y	Y	Y	Y		Y	Y	Y	Y	Y	Y
	Real World evidence regulatory considerations for medical devices	Australian Government, Department of Health and Aged Care	Apr 2024	Australia RWE Regulatory	Y	Y	Y	Y	Y	Y	Y			Y		Y		
Brazil	Guia de boas práticas para estudos de dados do mundo real (best practice guide for Real-World studies)	Agência Nacional de Vigilância Sanitária (Anvisa)	26 Sep 2023	Brazil Anvisa Regulatory	Y	Y	Y	Y	Y	Y		Y		Y	Y	Y		
Canada	Elements of Real World Data/ Evidence quality throughout the prescription drug product life cycle	Government of Canada	04 Mar 2020	Canada RWD/E Quality	Y	Y	Y	Y	Y	Y			Y		Y	Y		
	Guidance for reporting Real-World evidence	Canada's Drug and Health Technology Agency (CADTH) and Health Canada	May 2023	CADTH Guidance for RWE	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y				Y
China	Guidelines for Real-World evidence supporting drug development and review	National Medical Products Administration (NMPA)	Jan 2020	NMPA Guidelines	Y	Y	Y	Y	Y			Y	Y	Y	Y	Y	Y	
	Technical guidelines for Real-World studies to support drug development and review for children	NMPA	Sep 2020	NMPA Guidelines	Y													
	Guideline for clinical evaluation of medical devices using Real-World data	NMPA	Nov 2020	NMPA Guidelines for clinical evaluation	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y		
	Technical guidelines for the use of Real-World data in clinical evaluation of medical devices (trial version)	Center For Medical Device Evaluation (CMDE), NMPA	Nov 2020	Technical guidelines	Y	Y	Y	Y	Y	Y	Y							
	Guiding principles of Real-World data used to generate Real-World evidence	NMPA	Apr 2021	NMPA RWD	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
	Guidelines for drug Real-World research design and protocol framework (draft for comments) — DRAFT	CDE, NMPA	DRAFT – 07 Jul 2022	Guidelines for RW Study	Y	Y	Y	Y	Y			Y		Y	Y			
	Guidelines for communication of Real-World evidence supporting drug registration applications	CDE, NMPA	Feb 2023	CDE Guidelines	Y	Y	Y	Y	Y	Y	Y			Y	Y	Y		
	Guidelines for the application of Real-World data based on disease registries — DRAFT	CDE, NMPA	DRAFT – Nov 2023	CDE Guidelines for the Application of RWE based	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
	Guidelines for regulatory review of Real-World study designs and statistical analyses for medical devices	CMDE, NMPA	Jan 2024	CMDE Guidelines for Regulatory Review	Y	Y	Y	Y	Y	Y	Y	Y	Y		Y	Y	Y	
Europe	Guideline on good pharmacovigilance practices (GVP) Module VIII — Post-authorization safety studies (Rev 3)	European Medicines Agency (EMA)	13 Oct 2017	GVP Module VIII	Y	Y	Y	Y		Y			Y			Y		
	Guideline on registry-based studies	EMA	16 Sep 2021	EMA Guideline	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
	10th Revision of the ENCePP guide on methodological standards in pharmacoepidemiology	ENCePP	01 Jul 2022	*Not available	Y			Y	Y					Y	Y	Y		
	Good practice guide for the use of the metadata catalogue of Real-World data sources — DRAFT	EMA	DRAFT – 16 Nov 2022	EMA Good Practice Guide	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y		Y		
	11th revision of the ENCePP guide on methodological standards in pharmacoepidemiology	ENCePP	13 Jul 2023	ENCePP v11 Guide	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
	Data quality framework for EU medicines regulation	EMA	30 Oct 2023	EMA Data Quality				Y	Y	Y	Y	Y				Y	Y	
	Reflection paper on use of real-world data in non-interventional studies to generate real-world evidence — DRAFT	EMA	DRAFT – 15 Apr 2024	EMA RWD	Y	Y	Y	Y	Y	Y	Y		Y	Y				
International	Pursuing opportunities for harmonisation in using Real-World data to generate Real-world evidence, with a focus on effectiveness of medicines	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)	May 2024	Harmonization in Using RWD	Y			Y	Y	Y	Y	Y		Y				
	General principles on plan, design and analysis of pharmacoepidemiological studies that utilize Real-World data for safety assessment of medicines M14 — DRAFT	ICH	DRAFT – 21 May 2024	ICH M14 Draft Guidance	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
Japan	Basic principles on the use of medical information databases in post-marketing pharmacovigilance	PMDA	09 Jun 2017	PMDA Medical	Y	Y	Y	Y	Y	Y								
	Points to consider for ensuring data reliability on post marketing database study for drugs	Pharmaceuticals and Medical Device Agency (PMDA)	21 Feb 2018	PMDA Ensuring Data	Y	Y	Y	Y	Y	Y						Y		
	Instructions for protocols of the Post-Marketing Database Study	PMDA	30 Jan 2023	PMDA Instructions	Y	Y	Y	Y	Y	Y								
	Proceeding with consideration of the formulation of implementation plan for Post-Marketing surveillance of Pharmaceuticals	PMDA	18 Jul 2024	PMDA Proceeding	Y													
United Kingdom	MHRA guidance on the use of Real-World data in clinical studies to support regulatory decisions	MHRA	16 Dec 2021	MHRA guidance	Y	Y	Y	Y	Y	Y	Y		Y	Y	Y	Y	Y	
	NICE Real-World evidence framework	National Institute for Health and Care Excellence (NICE) — Recommended by Medicines and Healthcare products Regulatory Agency (MHRA)	23 Jun 2022	NICE real-world	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
	DataSAT assessment template	NICE — Recommended by MHRA	23 Jun 2022	NICE Tools and Resources	Y	Y		Y	Y	Y	Y	Y	Y	Y		Y		
United States	Considerations for the use of Real-World data and Real-World evidence to support regulatory decision-making for drug and biological Products	U.S. Food and Drug Administration (FDA)	Aug 2023	FDA RWD & RWE	Y			Y	Y							Y		
	Real-World data: Assessing registries to support regulatory decision-making for drug and biological Products	FDA	Dec 2023	FDA RWD: Assessing	Y		Y	Y	Y	Y	Y	Y	Y	Y	Y	Y		
	Use of Real-World evidence to support regulatory decision-making for medical devices — DRAFT	FDA	DRAFT – 19 Dec 2023	Use of Real-World	Y	Y	Y	Y	Y	Y	Y	Y	Y		Y	Y	Y	
	Real-World evidence: Considerations regarding non-interventional studies for drug and biological products — DRAFT	FDA	DRAFT – Mar 2024	Real-World Evidence	Y	Y	Y	Y	Y						Y	Y		
	Real-World data: Assessing electronic health records and medical claims data to support regulatory decision-making for drug and biological Products; guidance for industry; availability	FDA	Jul 2024	Real-World Data	Y	Y	Y	Y	Y	Y	Y		Y			Y		
Other Frameworks	Determining Real-World Data's fitness for use and the role of reliability	Duke Margolis Center for Health policy	26 Sep 2019	RWD Fitness	Y		Y	Y	Y	Y		Y	Y			Y		
	ADVANCE database characterisation and fit for purpose assessment for multi-country studies on the coverage, benefits and risks of pertussis vaccinations	Sturkenboom et al.	12 Feb 2020	Global Studies	Y	Y			Y		Y	Y	Y	Y	Y	Y		Y
	Considerations when evaluating Real-World Data quality in the context of fitness for purpose	Reynolds et al.	6 May 2020	RWD Quality: Fitness	Y		Y		Y	Y		Y	Y	Y	Y	Y	Y	Y
	Evaluating the feasibility of electronic health records and claims data sources for specific research purposes	Ritchey & Girman	07 May 2020	Feasibility of EHR	Y	Y	Y	Y	Y	Y	Y		Y					
	Suitability of databases in the Asia-Pacific for collaborative monitoring of vaccine safety	Duszynski et al.	23 Mar 2021	APAC Databases	Y	Y			Y	Y	Y		Y	Y	Y	Y	Y	Y
	The structured process to identify Fit-For-Purpose Data: A Data Feasibility Assessment Framework (SPIFD)	Gatto et al.	30 Oct 2021	SPIFD	Y	Y		Y	Y	Y						Y	Y	Y
	MINERVA: Metadata for data discoverability and study replicability in observational studies	Gini et al.	10 Jan 2022	MINERVA Framework	Y	Y	Y	Y		Y	Y	Y	Y	Y	Y	Y	Y	
	A structured process to identify Fit-for-Purpose study design and data to generate valid and transparent Real-World evidence for regulatory uses (SPIFD 2)	Gatto et al.	17 Mar 2023	SPIFD 2	Y	Y	Y		Y	Y		Y					Y	Y
	Assuring audit and inspection readiness — considerations for the use of RWD and RWE in regulatory decision-making	TransCelerate BioPharma	Dec 2023	Transcelerate Audit	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	
	Describing diversity of real world data sources in pharmacoepidemiologic studies: The DIVERSE scoping review	Gini et al.	09 May 2024	DIVERSE Framework	Y		Y			Y		Y		Y		Y	Y	

*ENCePP removed the 10th Revision from online forums. On 07 Nov 24 the ENCePP Secretariat stated that the "latest revision of the guide supersedes previous editions, which is why it is no longer available"

Key findings, recommendations, and strategy

Feasibility criteria mapping identified six gaps across reviewed guidelines which included: presence of feasibility assessment guidance, operational methods for feasibility evaluations, stages/steps for feasibility assessment conduct, multi-country/data source evaluations, templates for disseminating feasibility results, and data controller quality management requirements.

To substantiate the gaps, eligibility criteria were applied to the 46 RWE guidelines reviewed (included for recency [2021–2024] and excluded if not published by a health authority or in English), with 17 guidelines selected for further analysis. Of these, 15 (88.2%) did not provide templates for disseminating feasibility results, 14 (82.4%) did not mention stages or steps required for the feasibility assessment, 13 (76.5%) lacked operational methods to conduct the feasibility assessment, 12 (70.6%) were missing guidance on conducting feasibility assessments for multi-country and/or multi-data source studies, 8 (47.1%) did not provide requirements for data controllers related to transparent reporting of source-level quality management systems and data quality processes, and 6 (35.3%) did not mention feasibility assessments at all. All 17 guidelines had > 1 gap, 13 (76.5%) had > 3 gaps, and 6 (35.3%) had all 5 gaps.

Recommendations and IQVIA's strategies for mitigating these gaps are provided below.

1. Improved consistency of guidance for RWD "fit-for-purpose" assessment criteria was noted, however, gaps remain

ICH released the M14 glossary of RWD definitions but more clarity on the requirements for each feasibility criteria would be beneficial.[11] For instance, ICH cited FDA guidance for the definition of reliability describing this as "data accuracy, completeness, provenance, and traceability", whereas EMA guidance describes reliability as "accuracy, precision, plausibility, and traceability", with extensiveness defined separately, encompassing completeness and coverage sub dimensions.[1,11,31]

Recommendation

Guidelines aim to align on feasibility criteria and data quality sub dimensions, including adopting similar conceptual and operational definitions for each element, in future guidelines published.

IQVIA's strategy

Feasibility assessment checklists, table shells, and templates have been drafted utilizing each regulator's (e.g., EMA, MHRA, FDA, etc.) feasibility criteria, considering prior feasibility assessment and protocol submission feedback from said regulators, generating variable assessment based on study objectives and endpoints, and considering target trial emulation methods (47). This provides a fit-for-purpose approach utilizing the intended regulators recommendations, terms, criteria, and definitions.

2. Description of feasibility evaluation methods is warranted

Guidance documents mention important feasibility criteria (the 'what') but do not provide techniques to assess these criteria prior to protocol approval and data extraction (the 'how'). In the absence of a regulator aligned approach on the 'how,' experience and expertise in dialoguing with regulators around feasibility and RWD source selection are critical.

Recommendation

Guidelines aim to provide examples of feasibility assessment methods for each feasibility element. It is also important for guidelines to acknowledge that feasibility assessments are often completed prior to data access, and will include assessment of data sources that are not selected for the study protocol, so qualitative measures for data reliability assessments should be included in the methods for evaluation recommended (in addition to the traditional quantitative measures that can be completed after contracting and regulatory steps are completed and access to data is gained for selected data sources).

IQVIA's strategy

IQVIA has designed robust and tested strategies for data landscaping and fit-for-purpose feasibility assessments to operationalize regulatory recommendations. IQVIA's evaluation methods are continuously updated based on new guidance published and frequent regulator interaction and feedback tracked.

3. Aligned strategy across guidelines to conduct a 2-stage feasibility process for data source selection is warranted

According to recent guidance from ICH, "Feasibility assessments should be structured in at least two phases: An initial scan to determine whether data are available, likely sufficient, and to narrow down data source options; and a subsequent, more comprehensive feasibility assessment of the candidate data sources".[11] This approach can address regulator requests to select data sources without bias and provide risk management for sponsors. However, most guidelines published to date do not address these important steps.

Recommendation

Guidelines aim to highlight the importance of data source landscaping, as well as to provide methods for shortlisting data sources when preparing for a feasibility assessment, in future publications.

IQVIA's strategy

IQVIA has developed a two-stage feasibility process, providing a study specific data source screening tool and process to shortlist data sources in Stage 1, and a robust feasibility assessment for the potentially fit-for-purpose data sources in Stage 2. This approach has allowed IQVIA to address regulator feedback from protocol synopsis submissions by sponsors and proactively prevent regulators from requesting additional data source selection techniques and tools, to prevent data source limitations and bias.

4. Guidance on feasibility criteria for multi-country and/or multi-data source RWD studies is still lacking

We see ever increasing need to employ multi-RWD studies or RWD network studies to meet evidence needs. We note there are new considerations added to the updated ENCePP, ICH, FDA, and EMA guidance; however, a greater level of detail surrounding evaluation of coherence and common data model implications during a feasibility assessment would be valuable for this study approach.[1,9,11,31,32]

Recommendation

Guidelines aim to define feasibility assessment elements and corresponding methods for multi-country and/or multi-data source RWD studies in future publications.

IQVIA's strategy

Harmonising multiple data sources across multiple countries to deliver standardised outputs and aligned quality standards is complex. IQVIA leverages learnings, processes, and data models from related study experiences and common data model expertise (e.g., utilizing EMA DARWIN, ODHSI/OMOP, study specific CDM design, etc.). Additionally, IQVIA includes specialised global, regional, and local teams that collaborate and manage data partnerships across health care systems, claims datasets, National Registers, and disease specific registries to reduce the risk and effort for study sponsors.

5. Need for a standardized format to disseminate feasibility findings

Because regulators recommend that feasibility assessment results are included in RWE protocols, the minimum requirements for the content of this summary should not be left for researchers to define.

Recommendation

Regulators aim to provide exemplary feasibility assessment result tables in protocol templates and guidelines. For instance, an amendment to Good Pharmacovigilance Practices (GVPs) provision of protocol and reporting templates in GVP Module VIII to include exemplary feasibility assessment results tables, would be helpful.[30]

IQVIA's strategy

IQVIA has developed summary tables for protocol submissions, to disseminate data source screening and feasibility assessment results. These are tailored to the study design taking into account recently published guidance and the latest feedback from RWE protocol submissions, to proactively address regulator expectations

6. Specific requirements for data holders including transparent reporting of quality management systems and processes for their collected, stored, and transferred data, would be beneficial

Some guidance documents provide helpful considerations on quality checks required to assess RWD robustness, but there are still many ambiguous areas in terms of responsibilities of the data holders. For instance, in relation to utilizing quality management systems (QMS) set up for their primary data collection studies this may not be fully applicable to conduct of secondary data studies where many elements are not needed or require significant adaption.

Recommendation

Guidelines aim to include recommendations for the data holders, specifically notating that transparency of quality measures and procedures utilized during data collection, maintenance, and transfer, is important for a RWD feasibility assessment and ultimately data source selection.

IQVIA's strategy

IQVIA has integrated QMS and data qualiy related questions for the data holders into feasibility questionnaires, to obtain this valuable information during the feasibility assessment. This allows IQVIA to speak to the quality and data management processes the data holders use for their data, outside of the study specific quality management plan.

Opportunity to improve available resources

Existing guidelines are widely utilized by researchers; nonetheless, these documents often fail to align on methods for assessing the feasibility of RWD studies and identifying fit-for-purpose RWD sources. Regulators recognize that RWE guidelines are essential, and related publications are becoming more prevalent, as evidenced by the number of guidelines mapped for this exercise. Nonetheless, there are opportunities to improve the resources available to researchers who are considering leveraging RWD sources. IQVIA's recommendations reflect review of 46 guidelines published between June 2017 to July 2024, which demonstrate a need for aligned feasibility criteria and definitions for each element, methodology for assessments, acknowledging the importance of the two-stage feasibility approach, inclusion of feasibility considerations for multi-country and multi-data source studies, introduction of regulator facing templates to disseminate findings, and provision of QMS recommendations for the data holders.

To read *Contemporary Practice and Considerations for Real-World Data Source Identification and Feasibility Assessment* (referred to on page 2), please go to: https://onlinelibrary.wiley.com/doi/10.1002/pds.5862

Acknowledgements

The authors would like to express gratitude to Deborah Layton PhD (Director at PEPI Consultancy Limited [Dr Layton has received funds from Ariello, Annexon Biosciences, and AstraZeneca]), Pierre Engel PharmD PhD (Global Head of Data Access and Feasibility at IQVIA), Leanne Li MBA MPH (Senior Principal for Real-World Strategy and Innovations at IQVIA), Chinenye Ugoji Ph.D. MPH BPharm (Principal for Real World Strategy & Innovation, IQVIA), and Finlay MacDougall BA (Head of EMEA Real-World Networks and Partnerships, IQVIA) for peer review prior to publication.

We would also like to thank the following subject matter experts at IQVIA for contributing to review and mapping of regulatory guidelines: Marta Viana Ph.D. (Clinical Planning Analyst), Angela Yin Ph.D. (Head of Real-World Evidence, Greater China), Yigong Zhou MSc (Senior Consultant), Long Pang MPH, (Engagement Manager), Jing Li MSc (Associate Principal), and Sophia Fleming MSc (Senior Consultant).

References

1. U.S. Food and Drug Administration. Real-world data: Assessing electronic health records and medical claims data to support regulatory decision-making for drug and biological products [Internet]. 2024 [cited 2024 Sep 29]. Available from: https://www.fda.gov/media/152503/download
2. National Medical Products Administration. NMPA: Attachment: “Guiding Principles of Real World Data Used to Generate Real World Evidence (Trial).” 2021 Apr; Available from: https://redica.com/wp-content/uploads/NMPA_-Attachment_-_Guiding-Principles-of-Real-World-Data-Used-to-Generate-Real-World-Evidence-Trial_.pdf
3. NHMRC Medicines Intelligence Centre of Research Excellence (MI-CRE). Optimising the availability and use of real world data and real world evidence to support health technology assessment in Australia [Internet]. 2024. Available from: https://www.health.gov.au/sites/default/files/2024-07/hta-policy-and-methods-review-optimising-the-availability-and-use-of-real-world-data-and-real-world-evidence-to-support-health-technology-assessment.pdf
4. CADTH. Guidance for Reporting Real-World Evidence [Internet]. Canada´s Drug and Health Technology Agency; 2023. Available from: https://www.cadth.ca/sites/default/files/RWE/MG0020/MG0020-RWE-Guidance-Report-Secured.pdf
5. European Medicines Agency. Guideline on registry-based studies. 2021.
6. Medicines & Healthcare products Regulatory Agency. GOV.UK. 2021 [cited 2024 Sep 29]. MHRA guidance on the use of real-world data in clinical studies to support regulatory decisions. Available from: https://www.gov.uk/government/publications/mhra-guidance-on-the-use-of-real-world-data-in-clinical-studies-to-support-regulatory-decisions/mhra-guidance-on-the-use-of-real-world-data-in-clinical-studies-to-support-regulatory-decisions
7. PMDA. Points to Consider for Ensuring the Reliability in Utilization of Registry Data for Applications [Internet]. Pharmaceuticals and Medical Devices Agency; 21Feb2018. Available from: chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.pmda.go.jp/files/000240811.pdf
8. Patel D, Guleria S, Titievsky L, Flaherty S, Everage N, Korjagina M, et al. Contemporary Practice and Considerations for Real-World Data Source Identification and Feasibility Assessment. Pharmacoepidemiol Drug Saf [Internet]. 2024 Aug 30 [cited 2024 Sep 29]; Available from: https://onlinelibrary.wiley.com/doi/10.1002/pds.5862
9. The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP). Guide on Methodological Standards in Pharmacoepidemiology. Revision 11 [Internet]. 2023 [cited 2024 Feb 1]. Available from: https://encepp.europa.eu/encepp-toolkit/methodological-guide_en
10. The European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP). Guide on Methodological Standards in Pharmacoepidemiology (Revision 10) [Internet]. EMA/95098/2010; Available from: https://www.encepp.eu/standards_and_guidances/methodologicalGuide.shtml

11. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use. ICH_M14_Step3_DraftGuideline_2024_0521.pdf [Internet]. 2024 [cited 2024 Sep 5]. Available from: https://database.ich.org/sites/default/files/ICH_M14_Step3_DraftGuideline_2024_0521.pdf

12. TransCelerate BioPharma. Assuring-Audit-and-Inspection-Readiness-Considerations-for-the-use-of-RWD-and-RWE-in-Regulatory-Decision-Making_12.11.23.pdf [Internet]. 2023 [cited 2024 Sep 29]. Available from: https://www.transceleratebiopharmainc.com/wp-content/uploads/2023/12/Assuring-Audit-and-Inspection-Readiness-Considerations-for-the-use-of-RWD-and-RWE-in-Regulatory-Decision-Making_12.11.23.pdf

13. NICE. NICE real-world evidence framework, corporate document [ECD9] [Internet]. National Institute for Health and Care Excellence; 2022. Available from: https://www.nice.org.uk/corporate/ecd9/resources/nice-realworld-evidence-framework-pdf-1124020816837

14. U.S. Food & Drug Administration. Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices (draft for comments). 2023 Dec 19; Available from: https://www.fda.gov/media/174819/download

15. Gini et al.,. MINERVA_GoodPracticeGuide_10Jan2022.pdf [Internet]. [cited 2024 Nov 16]. Available from: https://catalogues.ema.europa.eu/sites/default/files/document_files/MINERVA_GoodPracticeGuide_10Jan2022.pdf

16. European Medicines Agency. good-practice-guide-use-metadata-catalogue-real-world-data-sources_en.pdf [Internet]. 2022 [cited 2024 Sep 29]. Available from: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/good-practice-guide-use-metadata-catalogue-real-world-data-sources_en.pdf

17. National Medical Products Administration (NMPA). Notice of the National Medical Products Administration on the issuance of the Guiding Principles (Trial) for Real-World Evidence Supported Drug Development and Review (No. 1 of 2020) [Internet]. 2020 [cited 2024 Nov 16]. Available from: https://www.nmpa.gov.cn/directory/web/nmpa/xxgk/ggtg/ypggtg/ypqtggtg/20200107151901190.html

18. Reynolds MW, Bourke A, Dreyer NA. Considerations when evaluating real-world data quality in the context of fitness for purpose. Pharmacoepidemiol Drug Saf. 2020 Oct;29(10):1316–8.

19. Duszynski KM, Stark JH, Cohet C, Huang WT, Shin JY, Lai ECC, et al. Suitability of databases in the Asia-Pacific for collaborative monitoring of vaccine safety. Pharmacoepidemiol Drug Saf. 2021;30(7):843–57.

20. Australia Government Department of Health Therapeutic Goods Administration. Real world evidence and patient reported outcomes in the regulatory context. 2021; Available from: https://www.tga.gov.au/sites/default/files/real-world-evidence-and-patient-reported-outcomes-in-the-regulatory-context.pdf

21. Australia Government Department of Health Therapeutic Goods Administration. Real World Evidence Regulatory considerations for Medical Devices. 2024 Apr; Available from: https://www.tga.gov.au/sites/default/files/2024-04/real-world-evidence-guidance.pdf

22. Agência Nacional de Vigilância Sanitária (Anvisa). Guia de boas práticas para estudos de dados do mundo real (Best Practice Guide for Real-World Studies) [Internet]. 26Sep2023. Available from: chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.gov.br/anvisa/pt-br/assuntos/noticias-anvisa/2023/anvisa-publica-guia-de-evidencias-de-mundo-real-e-anuncia-grupo-de-trabalho-para-outubro/Guian64_2023_versao1.pdf

23. Canada H. Elements of real world data/evidence quality throughout the prescription drug product life cycle [Internet]. 2020 [cited 2024 Sep 30]. Available from: https://www.canada.ca/en/services/health/publications/drugs-health-products/real-world-data-evidence-drug-lifecycle-report.html

24. National Medical Products Administration (NMPA). Guideline for clinical evaluation of medical devices using real-world data [Internet]. 2020. Available from: https://www.nmpa.gov.cn/xxgk/ggtg/ylqxggtg/ylqxqtggtg/20201126090030150.html

25. NMPA, Center For Medical Device Evaluation (CMDE). Technical guidelines for the use of real-world data in clinical evaluation of medical devices (trial version [Internet]. 2020. Available from: https://www.nmpa.gov.cn/directory/web/nmpa/xxgk/zhcjd/zhcjdylqx/20201130144911110.html

26. CDE, NMPA. Guidelines for Drug Real-World Research Design and Protocol Framework (Draft for Comments) (draft for comments) [Internet]. 2022. Available from: https://www.cde.org.cn/main/news/viewInfoCommon/ea778658adc3d1ae3ffe3f1cc0522e5e

27. CDE, NMPA. Guidelines for Communication of Real-World Evidence Supporting Drug Registration Applications [Internet]. 2023. Available from: https://www.cde.org.cn/main/news/viewInfoCommon/8b59a85b13019b5084675edc912004f1

28. CDE, NMPA. Guidelines for the Application of Real-World Data based on Disease Registries (draft for comments) [Internet]. 2023. Available from: https://www.cde.org.cn/main/news/viewInfoCommon/01181ec42968738d304ff02511a21293

29. CMDE, NMPA. Guidelines for Regulatory Review of Real-World Study Designs and Statistical Analyses for Medical Devices [Internet]. 2024. Available from: https://www.cmde.org.cn/flfg/zdyz/zdyzwbk/20240118102128166.html

30. European Medicines Agency. Guideline on good pharmacovigilance practices (GVP) - Module VIII - Post-authorisation safety studies (Revision 3) [Internet]. 2017 [cited 2022 Oct 21]. Available from: https://www.ema.europa.eu/en/human-regulatory/post-authorisation/pharmacovigilance/good-pharmacovigilance-practices#final-gvp-modules-section

31. Data Analytics and Methods Task Force. European Medicines Agency. 2023 [cited 2024 Jul 16]. data-quality-framework-eu-medicines-regulation_en.pdf. Available from: https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/data-quality-framework-eu-medicines-regulation_en.pdf

32. European Medicines Agency. reflection-paper-use-real-world-data-non-interventional-studies-generate-real-world-evidence_en.pdf [Internet]. 2024 [cited 2024 Sep 29]. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-use-real-world-data-non-interventional-studies-generate-real-world-evidence_en.pdf

33. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). ICH_Reflection Paper_RWE_2024_0521_EndorsedbyICHAssembly_2024_0604.pdf [Internet]. 2024 [cited 2024 Oct 1]. Available from: https://admin.ich.org/sites/default/files/2024-06/ICH_Reflection%20Paper_RWE_2024_0521_EndorsedbyICHAssembly_2024_0604.pdf

34. PMDA. Basic Principles on the Use of Medical Information Databases in Post-marketing Pharmacovigilance [Internet]. 2017. Available from: https://www.pmda.go.jp/files/000250561.pdf

35. PMDA. Instructions for Protocols of the Post-Marketing Database Study [Internet]. 2023. Available from: https://www.pmda.go.jp/files/000222302.pdf

36. PMDA. Proceeding with Consideration of the Formulation of Implementation Plan for Post-Marketing Surveillance of Pharmaceuticals [Internet]. 2024. Available from: https://www.mhlw.go.jp/web/t_doc?dataId=00tc8649&dataType=1&pageNo=1

37. National Institute for Health and Care Excellence (NICE). Tools and resources | NICE real-world evidence framework | Guidance | NICE [Internet]. NICE; 2022 [cited 2024 Nov 21]. Available from: https://www.nice.org.uk/corporate/ecd9/resources

38. U.S. Food and Drug Administration (FDA). Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products [Internet]. 2023. Available from: https://www.fda.gov/media/171667/download

39. Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research, and oncology Center of Excellence. U.S. Food and Drug Administration. 2023. Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/real-world-data-assessing-registries-support-regulatory-decision-making-drug-and-biological-products

40. U.S. Food and Drug Administration (FDA). Real-World Evidence: Considerations Regarding Non-Interventional Studies for Drug and Biological Products (draft for comments) [Internet]. 2024. Available from: https://www.fda.gov/media/177128/download

41. Duke Margolis Center for Health policy. Determining Real-World Data's Fitness for Use and the Role of Reliability [Internet]. 2019. Available from: https://healthpolicy.duke.edu/sites/default/files/2019-11/rwd_reliability.pdf

42. Sturkenboom M, Braeye T, van der Aa L, Danieli G, Dodd C, Duarte-Salles T, et al. ADVANCE database characterisation and fit for purpose assessment for multi-country studies on the coverage, benefits and risks of pertussis vaccinations. Vaccine. 2020 Dec 22;38:B8–21.

43. Ritchey ME, Girman CJ. Evaluating the Feasibility of Electronic Health Records and Claims Data Sources for Specific Research Purposes. Ther Innov Regul Sci. 2020 Nov 1;54(6):1296–302.

44. Gatto NM, Campbell UB, Rubinstein E, Jaksa A, Mattox P, Mo J, et al. The Structured Process to Identify Fit-For-Purpose Data: A Data Feasibility Assessment Framework. Clin Pharmacol Ther. 2022 Jan;111(1):122–34.

45. Gatto NM, Vititoe SE, Rubinstein E, Reynolds RF, Campbell UB. A Structured Process to Identify Fit-for-Purpose Study Design and Data to Generate Valid and Transparent Real-World Evidence for Regulatory Uses. Clin Pharmacol Ther. 2023 Jun;113(6):1235–9.

46. Gini R, Pajouheshnia R, Gardarsdottir H, Bennett D, Li L, Gulea C, et al. Describing diversity of real world data sources in pharmacoepidemiologic studies: The DIVERSE scoping review. Pharmacoepidemiol Drug Saf. 2024;33(5):e5787.

47. Arnold K, Antunes L, Coles B, Lee H. Application of the target trial emulation framework to external comparator studies. Front Drug Saf Regul [Internet]. 2024 Apr 11 [cited 2024 Apr 30];4. Available from: https://www.frontiersin.org/articles/10.3389/fdsfr.2024.1380568

CONTACT US

iqvia.com