ISPOR EU 2024

Comparing and contrasting RWE guidance: what researchers need to know considering the global picture

19 November 2023
Barcelona, Spain

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Our session

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Disclosures

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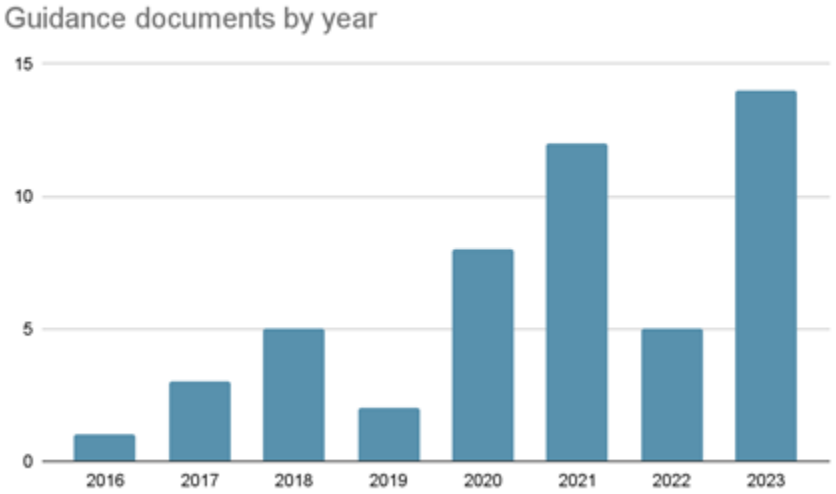
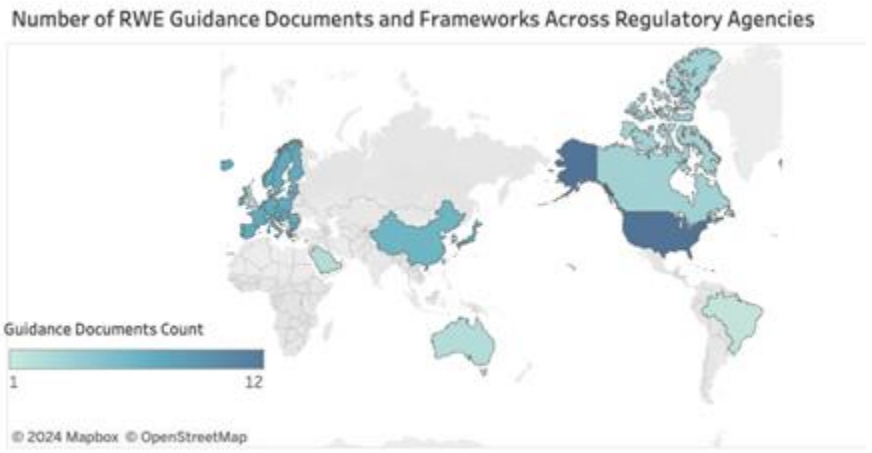
Agenda

RWE guidance landscape, e.g., data quality	Ulka
What researchers should consider in designing RWD studies: Regulatory perspective	Patrice
What researchers should consider in designing RWD studies: HTA perspective	Pall
How industry operationalizes guidance	Solange
Discussion	
Is harmonization necessary?	All
What are the potential steps to harmonization?	

Increase in published RWD/RWE guidance



Source: IHI and IDERHA's Report on Global Regulatory Best Practices which did a scoping review of the published and grey literature that outlined RWD/E policies or provided context to policies.



Source: Duke Margolis Dashboard for regulatory guidance: https://healthpolicy.duke.edu/projects/international-harmonization-real-world-evidence-standards-dashboard

Calls for global harmonization of RWD/RWE guidance

Harmonization is important for many stakeholders. For example:

- Industry - Meeting different decision-makers' requirements is resource intensive and poses challenges to efficiency
- HTA bodies/payers - A lack of harmonization between regulatory and HTA body/payer requirements can limit evidence relevant for decision-making and delay patient access

Example of groups focused on harmonization

Figure 2. Efforts from international organizations on harmonizing global real-world evidence (RWE) regulatory environment. CIOMS = Council for International Organizations of Medical Science; ICH = International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use; ICMRA = International Coalition of Medicines Regulatory Authorities; ISPOR = Professional Society for Health Economics and Outcomes Research; RWD = real-world data.

Source: Burns, L. et al. RWE for regulatory decision-making: guidance from around the world. 2022 Clinical Therapeutics, 44(3).

Variability in how data quality is addressed

Key findings related to "Data Quality" assessment of published guidance documents:

- Agreement that data quality is fundamental for RW studies
- "Reliability" and "relevance" and/or related elements are key quality parameters with several related components defined, such as accuracy, timeliness, and representativeness.
- There is no clear consensus on how researchers should demonstrate data quality

Source: IDERHA, Report on Global Regulatory Best Practices Analysis: A scoping review of HTA and Regulatory RWD/E policy documents https://www.iderha.org/sites/iderha/files/2024-05/D6.2%20Report%20on%20Global%20Regulatory%20Best%20Practices%20Analysis_v2.0.pdf

Agency	Discussion of data quality
EMA	Data quality is defined as fitness for purpose for the users' needs in relation to health research, policy making, and regulation and that the data reflects the reality, which they aim to represent Components of data quality include: ● Extensiveness ● Coherence ● Timeliness ● Relevance ● Reliability The Data Quality Framework restricts its scope to aspects of data quality related to regulatory decision-making
FDA	The evaluation of data quality pertains to the data lifecycle: ● Characterizing the data with respect to completeness, conformance, and plausibility of data values ● Documenting the QA/QC plan that includes transformation processes ● Defining a set of procedures for ensuring integrity of the data For registries, documentation of data collection and management procedures must be comprehensive

Sources: FDA Guidance: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision-Making for Drug and Biological Products; EMA Data Quality Framework for EU medicines regulation

Agency	Discussion of data quality
NICE (UK)	Described as a dimension of "data suitability": completeness and accuracy DataSAT: tool researchers can use to document data quality
HAS (France)	Focused on representativeness and minimized missingness of the data Cites several additional guidance documents published by others that researchers should reference for data quality
IQWiG (Germany)	Focused on registry data only, due to limitations of claims and EHRs Mandatory criteria for data quality: ● Detailed registry description ● Exact definition / operationalization of variables ● Current data plan / coding manual ● Training on data collection and recording ● Clearly defined inclusion and exclusion criteria for registry patients ● SOP system for data collection ● Accuracy checks ● Documentation trail ● Scientific independence ● Sustainable financing

Sources: NICE RWE Framework, HAS's RWE studies for medical products and devices, IQWiG's routine practice data for benefit assessments

Examples of potential benefits of harmonizing data quality guidance

- Universal taxonomy and terminology to ensure clear communication and facilitate adherence to agency standards
    - Consensus on “above-study” vs. “below-study” data characteristics would help clarify ownership roles

- Universally operationalized transparency standards to ensure preparedness to provide complete documentation, especially for “above-study” characteristics - for example:
    - Registry protocol, case report forms, investigator training materials
    - Methods and findings for linkage validation
    - Data management plan, including query issuance and resolution

Beyond data quality

Areas of alignment

- Preference for RCTs and justification needed for RW studies
- Transparency in study design and conduct
- Full detailed, pre-specified protocol and protocol registration
- Tailored analytical strategies to account for bias and confounding
- Ethics (e.g., patient privacy)

Potential areas for harmonization

- Terminology
- Appropriate analytical approaches
- Transportability / transferability and appropriate approaches to using data outside the jurisdiction