Initial Considerations for a Real-World Data Quality and Relevance Package for Regulatory or Health Technology Assessment Submissions

Cynthia J Girman[1], Christina Mack[2], Dana Y Teltsch[3], Morgan A. Marks[4], Grazyna Lieberman[5], Rachel Leahy[1,6] and Christopher Atzinger[7]

[1]CERobs Consulting, Mills River, NC USA; [2]IQVIA, Durham, NC USA; [3]Takeda, Cambridge, MA USA; [4]Moderna, Cambridge, MA USA; [5]Retired; [6]Paradigm Bioscience, LLC, Annapolis, MD USA; [7]Astellas, Northbrook, IL USA

Abstract ID: 136798
Poster: RWD44
May 6, 3:30-6:30

Introduction

Real world evidence (RWE) from medical claims and EHR reflect routine clinical practice and have been used to study safety of marketed products for decades. In recent years, regulators have issued guidance documents for data relevance and data quality on the use of real-world data (RWD) for regulatory decision-making.[1-5]

The TransCelerate RWD Audit Readiness initiative was started in 2020[6] to operationalize the thought leadership stemming from Duke-Margolis/FDA and others on the use of RWD/RWE in regulatory decision-making for product effectiveness.[6] In 2023, TransCelerate released related considerations for the evaluation of RWD sources.[6]

While this work provides a useful roadmap, additional detail is needed to create a full picture of what a successful real-world data submission package might look like. An outline and framework for a submission package would bring clarity to sponsors and data providers, making the TransCelerate considerations more tangible and actionable.

Objective

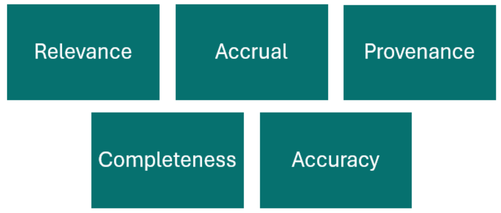
To use TransCelerate's Audit and inspection Readiness Consideration summaries to develop documentation on data quality and relevance intended for regulators.

Methods

We convened a working group of leaders from the International Society of Pharmacoepidemiology (ISPE), International Society of Pharmaceutical Outcomes Research (ISPOR) and TransCelerate to craft a more tangible view of what should be included in submissions to justify relevance and data quality of sources considered and selected to implement RWE protocols. Recognizing that clarity could be helpful on the content and level of detail for a regulatory data package addressing data quality and relevancy, our working group met to discuss potentially helpful tactical guidance from TransCelerate Considerations for Audit Readiness as foundation. Using the TransCelerate Considerations Report for Audit and Inspection readiness of RWD/RWE,[8] we carefully reviewed the considerations under each conceptual pillar.

(See Figure 1: relevance, accrual, provenance, completeness, and accuracy). We also utilized the FDA guidance documents on RWE to create an annotated Table of Contents and a dynamic framework for submission packages.

Figure 1. TransCelerate's five conceptual pillars for audit and inspection readiness[6]



Results

Table 1 below describes some of the high-level headings for a regulatory package Table of Contents (TOC). Additional details and annotated TOC will be forthcoming in publication.

Table 1: High-Level Table of Contents for Documentation on Data Quality and Reliability

I. Research Question (PICOTS: Population, Intervention, Comparator, Outcome(s), Setting)

II. Selection of Data Source - Feasibility Assessments

1. Feasibility assessments- data sources assessed, results from all feasibility evaluations
   - A Selection or exclusion of data sources
   - B. Relevancy
   - C. Accuracy, Provenance and Completeness
   - D. Longitudinality
   - E. Audit trails

III. Selected Database: Data collection procedures, Error checking and Curation

1. Describe the data source(s)
2. Structured Data Collection and Completeness

IV. Analytic

1. Missing Data Handling
2. Modification to data at analytic stage
3. Important intercurrent events
4. Selection of patients
5. Population

V. Provenance

1. Data custodians used over lifecycle of data collection process
2. Source dataset metadata and audit trail for each original data source
3. Data Privacy and De-identification

Table 2 depicts a sample RWE data package submission form that can be used as a tool for collecting and presenting the necessary information for regulatory decision-making. This form is designed to be adaptable based on the specific needs of the research question and expanded to provide information on additional data sources relevant to the study.

Table 2 : Contents for RWE Data Package- EXCERPTS ONLY

I. Relevancy and Fit-for-purpose		
	Research Question: _____ To assess *<safety/effectiveness>* of *<intervention>* *<compared to comparator>* on *<outcome> in patients with <population>*... Population: _____ Intervention: _____ Comparator: _____ Outcome: _____ Setting (in- or out-patient): _____	Regulatory Context: Is study supporting: ☐ Product approval ☐ New indication ☐ Labeling expansion ☐ General effectiveness ☐ Safety
II. Feasibility of Data Sources In General + Link to Feasibility Report		
At Database Level	**Data Source 1:** ☐ EHR ☐ Claims ☐ Registry ☐ Other ☐ Single, or ☐ Multiple health systems Context of data collection: ☐ Patient care ☐ Billing ☐ Research study Coding system(s) (e.g., ICD-10): _____ Can data capture: Indicated population? ☐Y ☐N ☐U Outcome? ☐Y ☐N ☐U Exposure? ☐Y ☐N ☐U Documentation (if available): ETL procedures SOP Error/range checking Plausibility checks <*etc.*>	*Insert column for each additional relevant data source*

////////// <SOME DATA OMITTED FOR POSTER> //////////

These sections omitted from Table 2 due to pending publication:

III. Feasibility for Specific Study
IV. Missing Data
V. Handling of Unstructured Data
VI. Validation of Study Elements
VII. Data Handling in Analysis
VIII. Risk of de-identification

Conclusions

RWE is only recently being used for decision-making; hence, little precedence exists to help sponsors understand regulatory expectations. A submission package template should help researchers generate the necessary documentation to justify the evaluation and selection of RWD sources for addressing a specific research question and regulatory/HTA decision and ensure that pertinent information is included. It can also be useful as an aid to help data providers understand the level of documentation needed. Creating a submission package is likely to be a multi-step process involving multiple groups. This TOC supports efficient gathering of the information required from these multiple groups to allow creation of a complete package submission for regulatory decision-making.

Our TOC and framework table is based substantially on the TransCelerate work, which in turn built on the draft guidance RWE documents issued by the U.S. FDA between 2018 and 2023 as well as similar documents provided by the EMA and professional organizations such as Duke-Margolis. The framework we present is not intended to be prescriptive but rather to provide clarity on the potential documentation that could be helpful to health authorities reviewing RWE submissions for decision-making. The specific details of the framework would change based on the data issues for a specific study and regulatory decision.

References

1. Berger ML, Daniel G, Frank K, hernandez A, McClellan M. A Framework for Regulatory Use of Real-World Evidence. Published online September 13, 2017. A Framework for Regulatory Use of Real-World Evidence
2. Daniel G, Silcox C, Bryan J et al. White paper: characterizing RWD quality and relevancy for regulatory purposes. https://healthpolicy.duke.edu/sites/default/files/2020-03/characterizing_rwd.pdf
3. U.S. Food & Drug Administration. Considerations for the use of real-world evidence to support regulatory decision-making for drug and biological products: Guidance for Industry. https://www.fda.gov/media/171667/download
4. U.S. Food & Drug Administration. Real-world data: Assessing electronic health records and medical claims data to support regulatory decision-making for drug and biological products: Guidance for Industry. https://www.fda.gov/media/152503/download
5. Real-world evidence framework to support EU regulatory decision-making Report on the experience gained with regulator-led studies from September 2021 to February 2023. https://www.ema.europa.eu/system/files/documents/report/real-world-evidence-framework-support-eu-regulatory-decision-making-report-experience-gained_en.pdf
6. Assuring audit and inspection readiness – Considerations for the use of RWD and RWE in regulatory decision-making. 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

Acknowledgments and Contact Information

This study received no funding. The authors thank Molly Aldridge of CERobs LLC for assistance with the poster.

Contact: Cynthia J Girman, DrPH, FISPE; Email: cindy.girman@cerobs.com