Real World Data Overview

RWD Audit Readiness

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On behalf of Transcelerate Audit Readiness Workstream

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TransCelerate is a not-for-profit entity created to foster collaboration.

Our mission is to improve the health of people around the world by accelerating and simplifying the research and development of innovative new therapies.

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Real World Data Overview

Real World Data (RWD) Related Initiatives at TransCelerate

Health Authority Engagement*

Leveraging RWE use cases as a discussion mechanism with Health Authorities, develop a reliable, streamlined, & scalable approach for interactions with Heath Authorities to clarify regulatory requirements on RWE use to supplement or replace clinical trials.

Today's Focus

Audit Readiness*

Engage with Health Authority & Data Service Providers to develop documentation that supports quality management (QA, QC, and audit) for RWD sources, resulting in an "Audit Readiness Considerations" tool targeting data relevance and reliability

Pragmatic Clinical Trials

Identify the current requirements and regulatory guidance that could be applied to PCTs and identify where guidance gaps are causing sponsor-specific challenges for pragmatic clinical trial conduct

Rapid Signal Assessment Using RWD

Evaluate current practice and identify novel practice opportunities in using rapid non-protocolized RWD analyses to complement Safety Signal Assessment practice opportunities.

Clinical Trial Data Sharing

Control Arm substitution & complementary use of historical data as part of trial design & evidence package

Vulcan FHIR Accelerator**

A multi-stakeholder collaboration aligning clinical care and clinical research data at the point of collection to support the bidirectional flow of data through the development of the HL7® FHIR standard.

* Initiatives part of this overview presentation
**TransCelerate is an active member of Vulcan which operates under HL7.

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Real World Data
Audit Readiness Initiative Overview

TransCelerate's RWD Audit Readiness Initiative

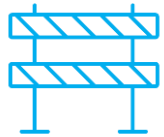
Focus

Operationalize the thought leadership stemming from **Duke Margolis/FDA** and many others on the use of RWD in regulatory decision-making.

The team will leverage Health Authority and Data/Service Provider interactions to **develop documentation that supports quality management (QA, QC, and audit) for RWD sources**, resulting in an **"Audit Readiness Tool"** targeting data relevance and reliability.

Desired Outcomes

Build Trust



Reduce Barriers

Demonstrate Fit-for-Purpose Use

*The **Audit Readiness Considerations** will help operationalize best practices in order to aid quality management oversight of RWD, including inspection readiness, in a manner suitable for regulatory decision making.*

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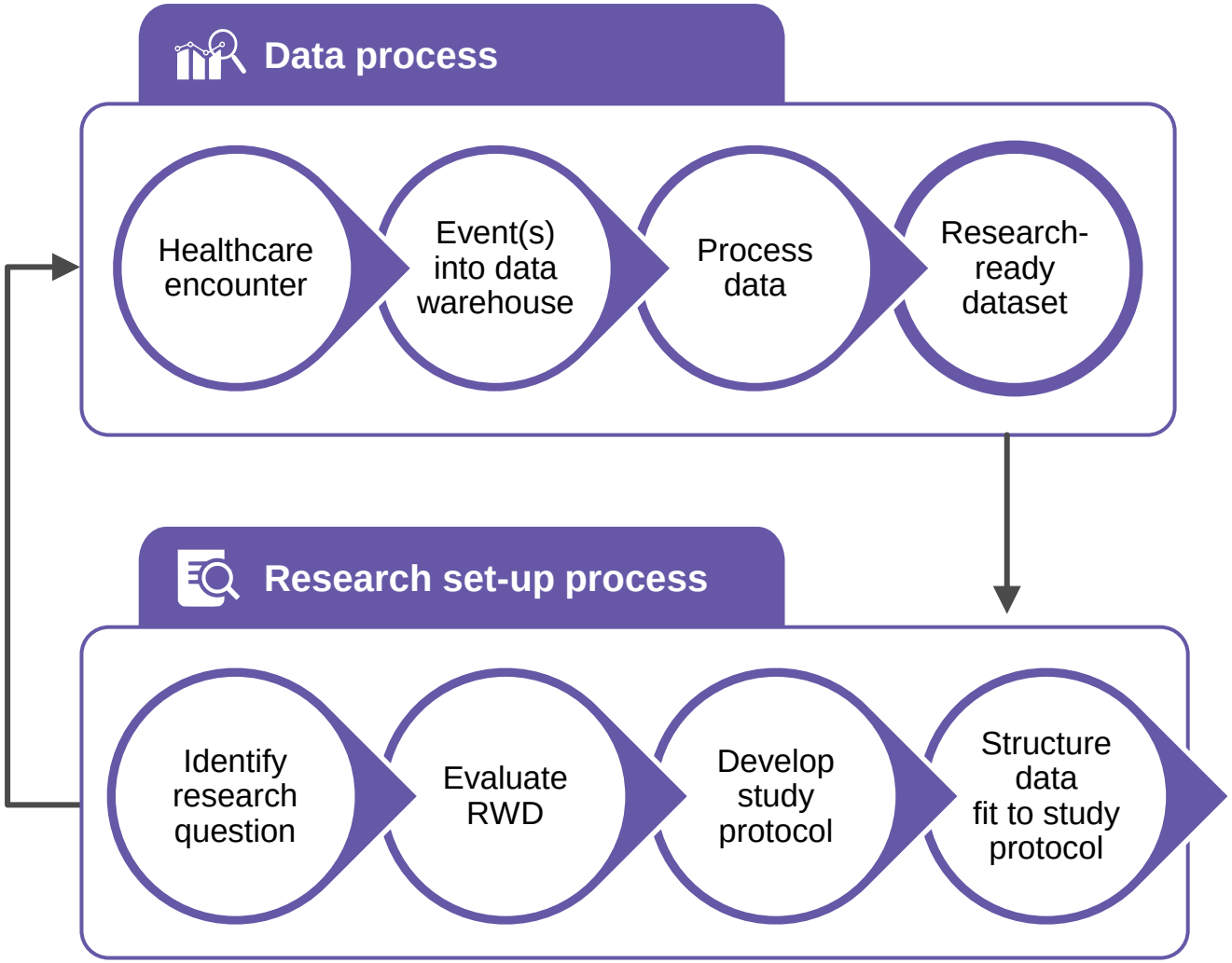
Scope of RWD Audit Readiness Initiative



- Focus (in purple) **relevance** and **reliability** of RWD given the scientific question (i.e., up to but not including performing analytics)
- Rationale: Numerous other initiatives focused on the research analytics & submission process

Research analytics and submission process

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RWD Audit Readiness: Data/Service Provider Survey Background

Survey Intention

Help answer the question: **'what is feasible to include in an 'Audit Readiness Tool' targeting data relevance and reliability?'** that could increase HAs confidence in using RWD for regulatory decision making*.

Survey Population

Data/Service Providers such as: Market Suppliers | EMRs / EHRs | Clinical Disease Registries | Qualified Clinical Data Registry Companies

Survey Sections

Organization Information | Point of View of Organizations | Representativeness | Accrual | Completeness | Accuracy | Provenance | Documentation | Audit Readiness Checklist

**Please note: The survey does not seek any specific documentation or examples of documentation, rather the goal is to assess what types of documentation would be available to share with clients/health authorities that could increase the health authorities' confidence in using RWD for regulatory decision-making.*

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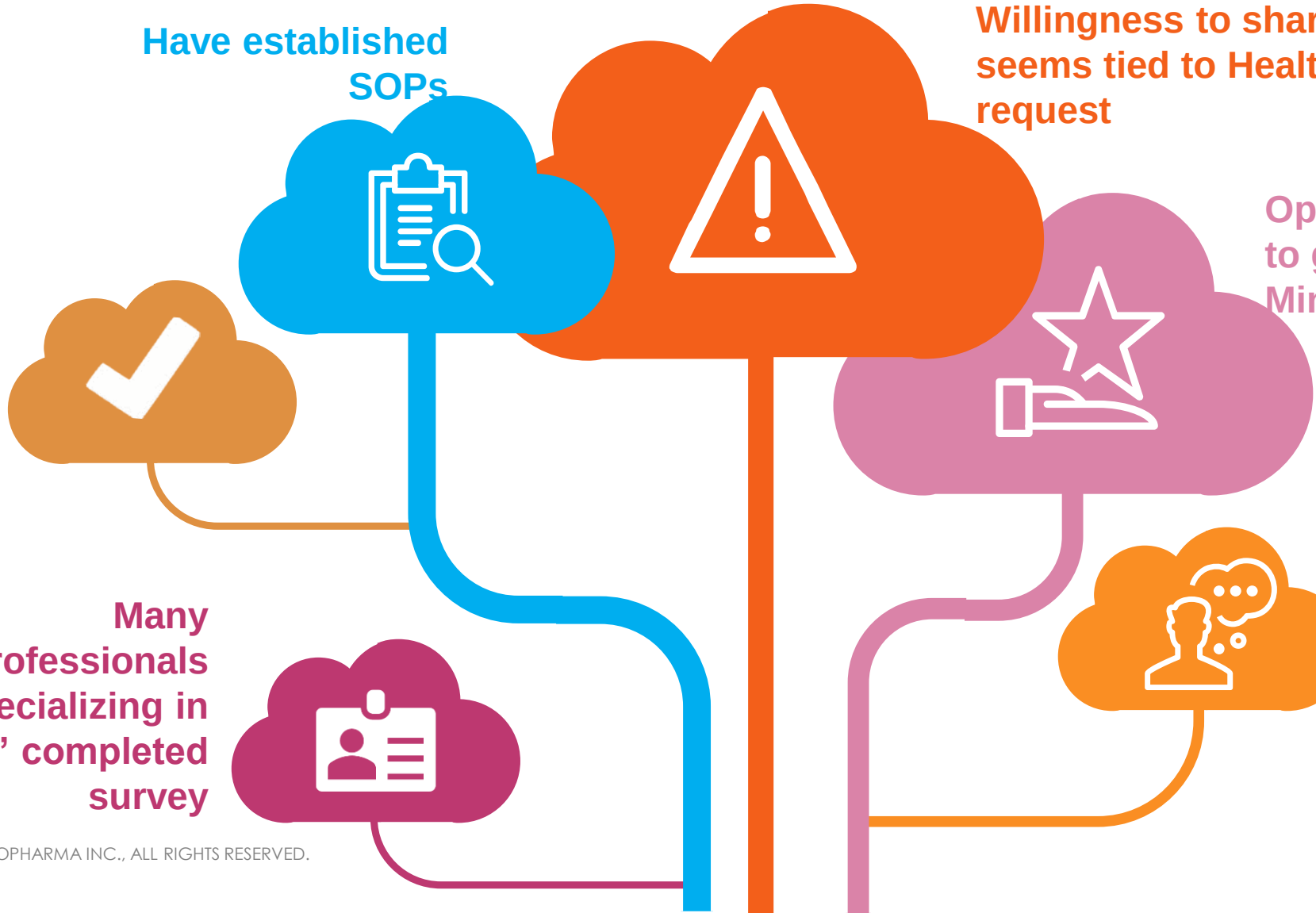
Survey Insights from Data/Service Providers



Have established SOPs

Willingness to share information seems tied to Health Authority request

Expect moderate to high impact to DSP operations based on release of Health Authority RWD/E Guidance documents

Openness to measures to gain efficiency (Cf., Minerva meta-data)

Many professionals specializing in 'Quality' completed survey

Lower overall participation in survey than anticipated

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RWD Audit Readiness Initiative

Focus

Operationalize the thought leadership stemming from **Duke Margolis/FDA** and many others on the use of RWD in regulatory decision-making.
The team will leverage Health Authority and Data/Service Provider interactions to **identify potential documentation that supports quality management (QA, QC, and audit) for RWD sources**, resulting in an **"Audit Readiness Tool"** targeting data relevance and reliability.

Deliverable

*'Draft RWD Audit Readiness Considerations'**

What is it? *This tool will help operationalize best practices to aid quality management oversight of RWD, including inspection readiness, in a manner suitable for regulatory decision making.*

Benefits:

- *A practical and usable approach to assess RWD sources as suitable and "fit-for-purpose" for the generation of RWE that could be used by health authorities, sponsors, and data service providers*
- *May assist researchers interested in using RWD for regulatory submissions. The overall goal of this list of considerations, when used in conjunction with published guidance documents from regulatory agencies and other groups of experts, is to help provide insights into what factors and circumstances may affect a Health Authority's willingness to accept and use RWD as a basis for regulatory decision-making in the drug approval process.*

*TransCelerate released this document as a draft for public review/comment. Deliverable is still in progress.

RWD Audit Readiness Initiative: Landscape Assessment Insights Framework

DRAFT

Data Relevance

Data Reliability

	RELEVANCE	ACCRUAL	PROVENANCE	COMPLETENESS	ACCURACY
Definition	Robust and representative of the population of interest, and the data elements available for analysis address scientific/ regulatory questions when valid and appropriate analytic methods are applied (PICOTS)	Process by which data are collected/aggregated and patients are included in a study (including record prompts for entry/exit from dataset, operational definitions, and inclusion/exclusion criteria)	Origin(s) of data, sometimes including a chronological record of data custodians and transformations (sometimes referred to as 'data lineage' or 'data traceability').	Presence of all needed and expected elements for a given percentage of data points of an individual variable	Whether data values stored for an object are correct values and stored in consistent and unambiguous form
Documentation	Protocol; Final study report (FSR), Meta-data catalog	Protocol; Statistical analysis plan (SAP); Data mgmt. plan (DMP); Standard operating procedures (SOPs) Meta-data catalog	Protocol; SAP; DMP; SOPs, Meta-data catalog	Customized report for key variables; DMP; SOPs; FSR, Meta-data catalog	Customized report for key variables; DMP; SOPs; FSR, Meta-data catalog
Gaps	No widely accepted approach for validation	No widely accepted approach (level of detail) or most appropriate place to document	No widely accepted approach (level of detail, structured vs. unstructured) or most appropriate place to document	None evident	Unclear: Validation or verification

Validation Process

* Insights gathered from targeted literature review, including the following sources: Daniel et al. Characterizing RWD Quality and Relevancy for Regulatory Purposes. Oct 2018; Franklin et al. Evaluating the use of nonrandomized real-world data analyses for regulatory decision making. Clin Pharmacol Ther 2019;105:867; Kahn et al. A Harmonized Data Quality Assessment Terminology and Framework for the Secondary Use of Electronic Health Record Data. Egems 2016;4:1244; Mahendraratnam et al. Determining Real-World Data's Fitness for Use and the Role of Reliability. Sep 2019; US FDA. Framework for FDA's Real-World Evidence Program. Dec 2018; Data Quality Framework for EU medicine regulation. October 2022; EMA Technical workshop on real-world metadata for regulatory purposes. September 2021

Draft RWD Audit Readiness Considerations* Example

PROVENANCE	Purpose
Describe the source dataset metadata and audit trail system for each original data source: - Was data collection done as a matter of routine practice or is the data captured as part of a 'bespoke' program or process? - What type of system does the data originate from (e.g., EHR, administrative data, registry, primary data collection, chart review, etc.)? - What information was collected, how was information coded/recorded, who performed collection or how (e.g., digital health tech)? - Were there changes to data collection over time? - Are the audit trails/metadata complete? i.e., do they fulfill the minimum ALCOA+ criteria? - Are the audit trails/metadata viewable/accessible? - Can the information be changed?	Shows how, why, when and by whom data may have been changed or updated and is thought to be a fundamental element of proving reliability.

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Draft RWD Audit Readiness Considerations* Website

TOOLS TO CONSIDER WHEN ENGAGING HEALTH AUTHORITIES

CONSIDERATIONS FOR DATA RELEVANCE AND RELIABILITY

CONSIDERATIONS FOR DATA RELEVANCE AND RELIABILITY

The RWD Audit Readiness Initiative drafted a functional list of key considerations of RWD quality that can assist researchers interested in using RWD for regulatory submissions. The overall goal of this list of considerations, when used in conjunction with published guidance documents from regulatory agencies and other groups of experts, is to help provide insights into what factors and circumstances may affect a Health Authority's willingness to accept and use RWD as a basis for regulatory decision-making in the drug approval process.

Preview the draft RWD Audit Readiness Considerations Document*.

Public review period closed February 17, 2023. Should you have any questions please contact feedback@transceleratebiopharmainc.com and put RWD Audit Readiness in the subject line.

**TransCelerate released this document as a draft. Deliverable is still in progress.*

https://www.transceleratebiopharmainc.com/assets/real-world-data-solutions/#audit-readiness

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THANK YOU

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