# A Real-World example of the journey to a RWD Playbook for Statistical Programmers

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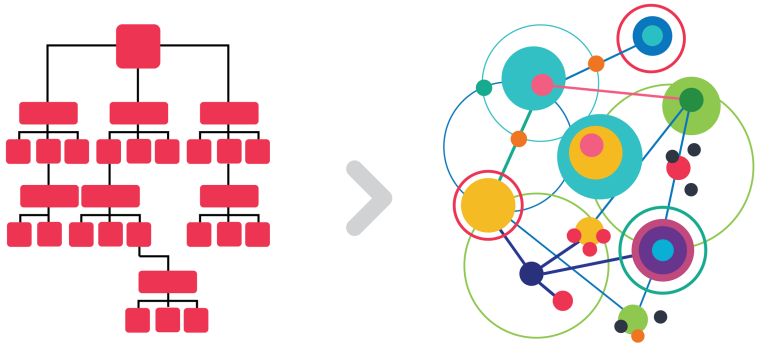
# Why a RWD Playbook?

Stating the obvious…

# Evolving Environment



- Development of legislation/guidelines/policy on the use of RWE in pharmaceutical regulatory activities is evolving
- Pharmaceutical organizations are evolving → specialized groups emerging to drive technological innovation
- Existing processes, systems in place for conventional Clinical Trials are not sufficient nor entirely relevant when we encounter RWD studies

When we have RWD studies to support REGULATORY submissions, where does that leave study teams and specifically…

Statistical Programmers?

# Statistical Programming Real-World Data (RWD) Playbook

The RWD Playbook provides colleagues in Janssen Statistical Programming and Analysis insights into the best practices and key considerations for RWD studies that are part of or have the potential to be included in regulatory submissions.

The RWD Playbook is aligned with the life-cycle of the study/project utilizing RWD/RWE and discusses roles & responsibilities and activities linked to data fitness, acquisition, standardization, analysis, and documentation … up to submission.

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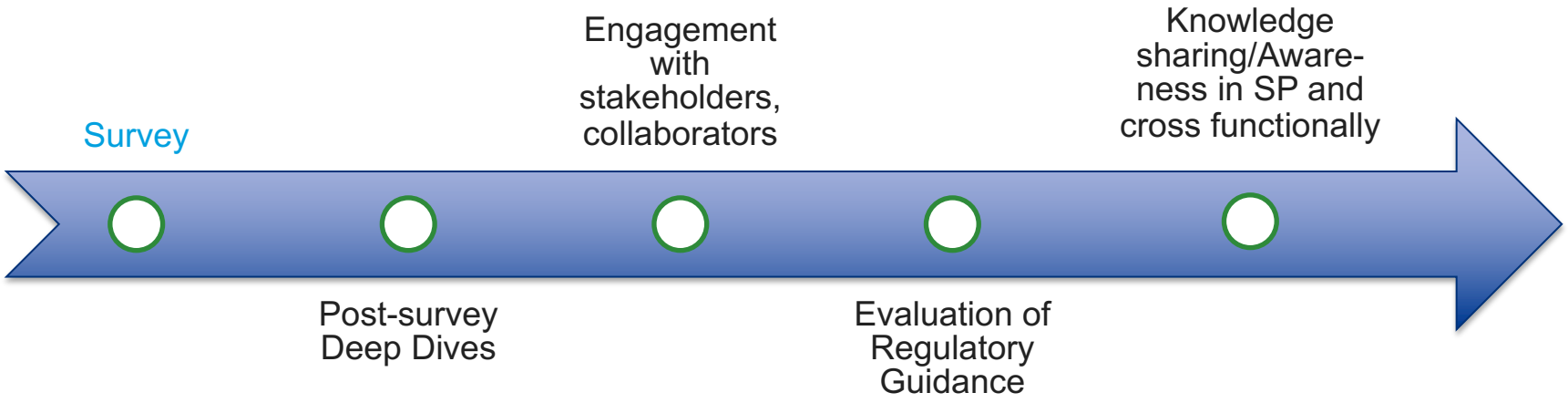
# Focus of RWD Playbook

## RWD Studies used for Regulatory Submissions

The purposes of the use of RWD as part of a regulatory submission / decision may include the following:

- To provide evidence in support of effectiveness or safety for a new product approval
- To provide evidence in of support labeling changes for an approved drug
- To be used as part of a post-marketing requirement to support a regulatory decision

# RWD Playbook Journey at Glance




**Ongoing effort to assimilate information (RWD Experts, HA guidance, Consortiums, PhUSE, White Papers, Working Groups, Real-world examples of RWD submissions, xPharma)**

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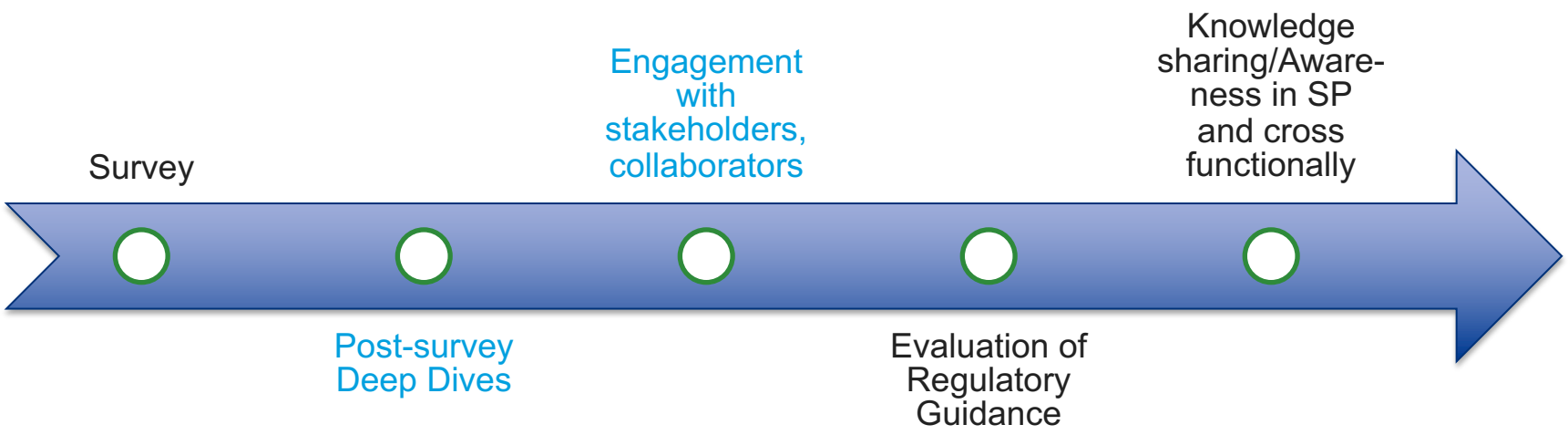
# Survey

## Exposed Opportunities:


- Early involvement in cross-functional / strategic discussions → diminished ability to provide functional input (e.g., into vendor contract discussions, data curation strategy) → less time to execute activities to meet submission timelines.
- Better clarity on roles and responsibilities (broader set of stakeholders with RWD projects)
- Clear strategy on data handling (privacy issues, how to select data, data cleaning, dealing with ambiguity, missingness, data transformation)
- Visibility on processes and platforms relating to data ingestion, transfer, anonymization and storage of source data
- Guidance on expectations of standards for RWD data

# RWD Playbook Journey at Glance

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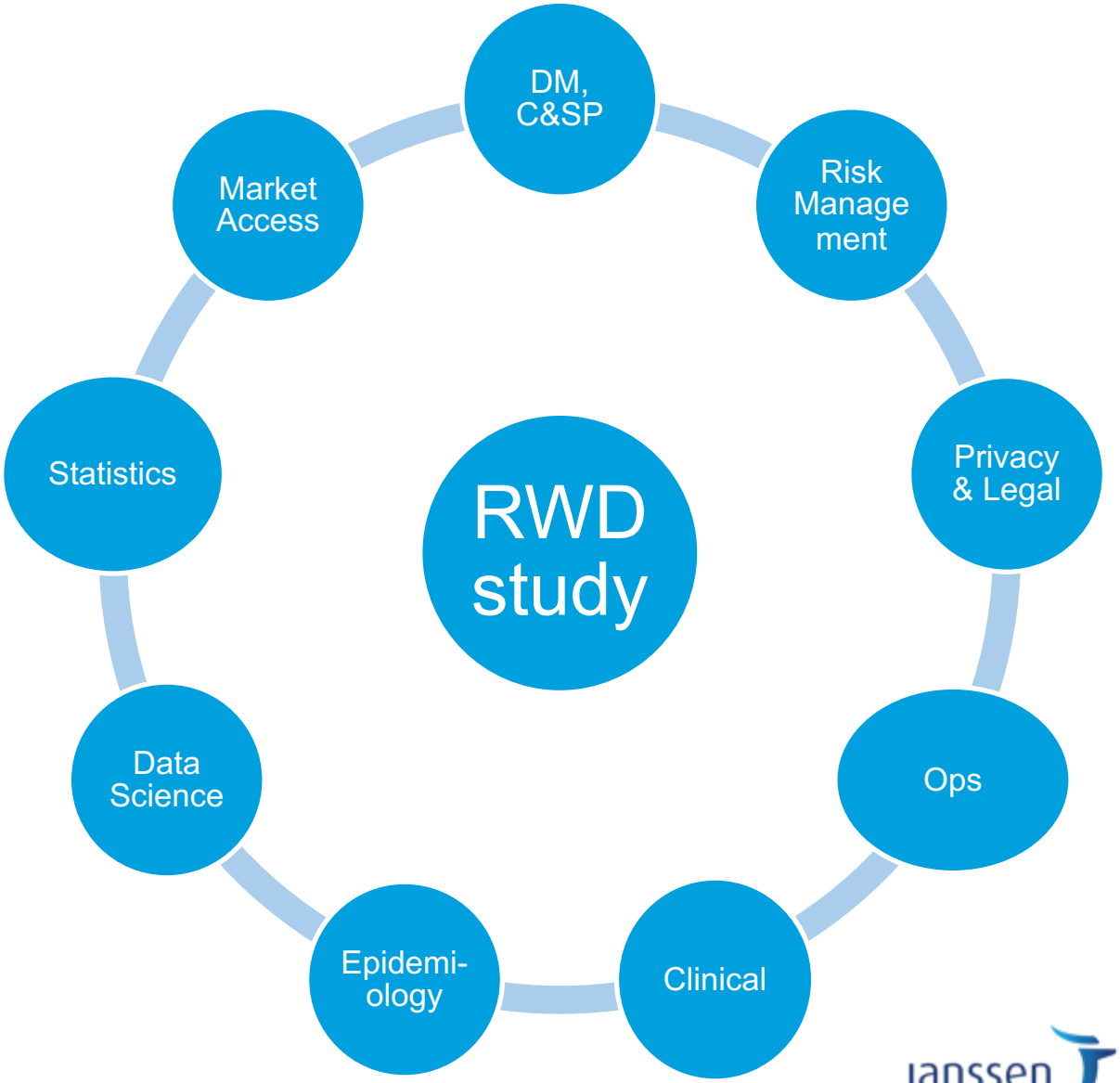
# RWD Study Stakeholders



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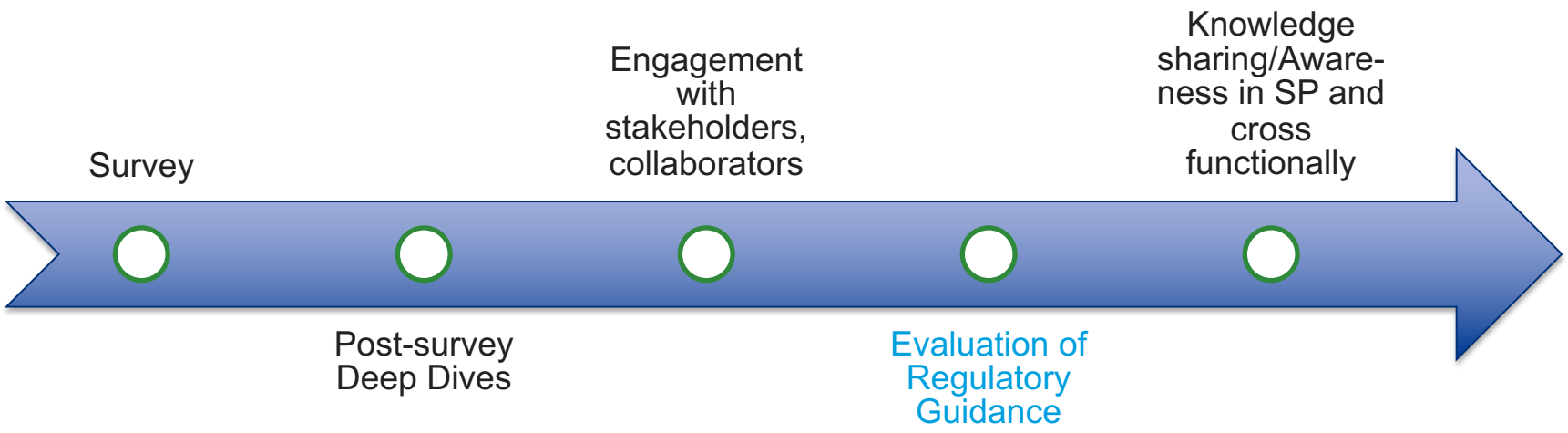


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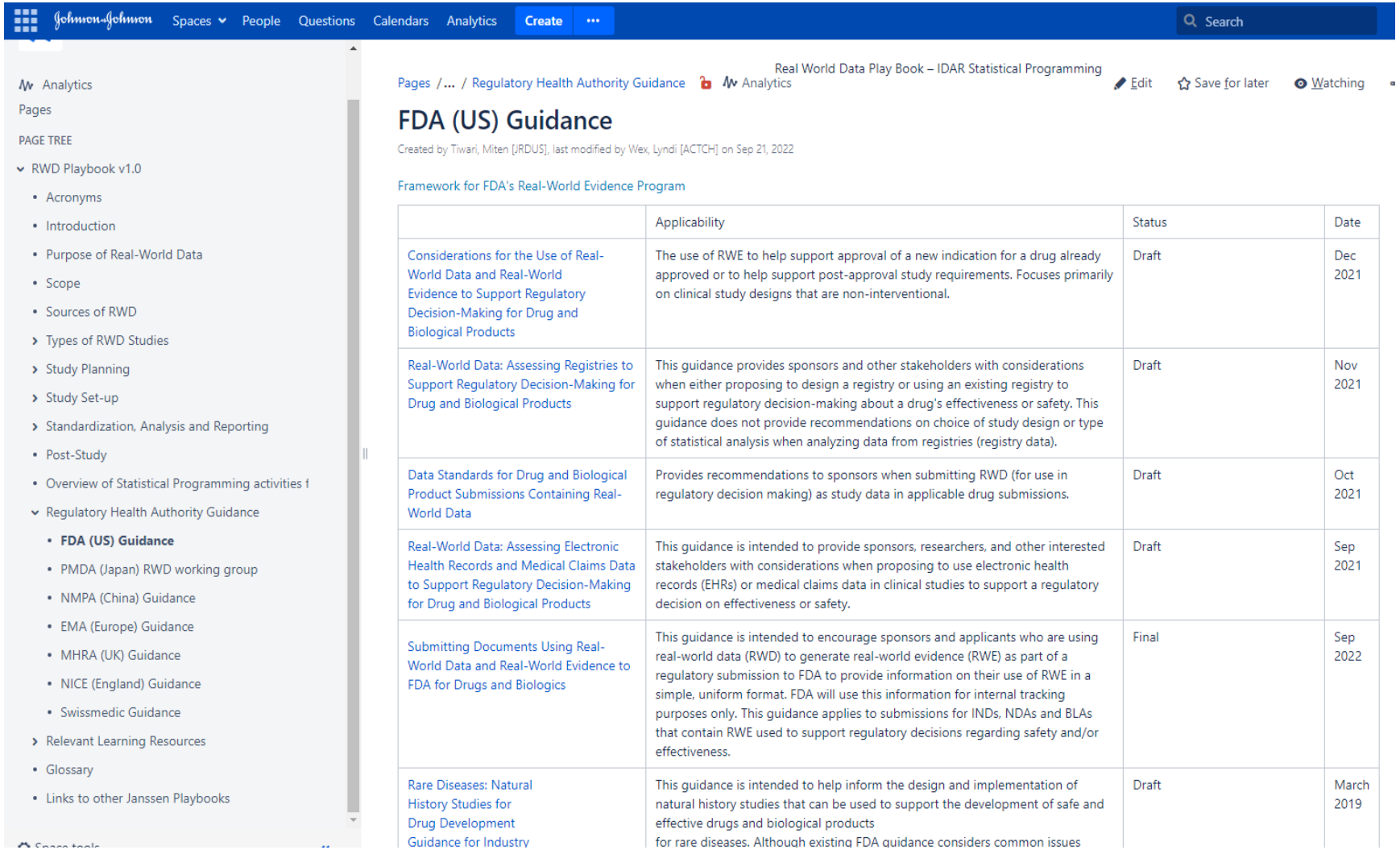
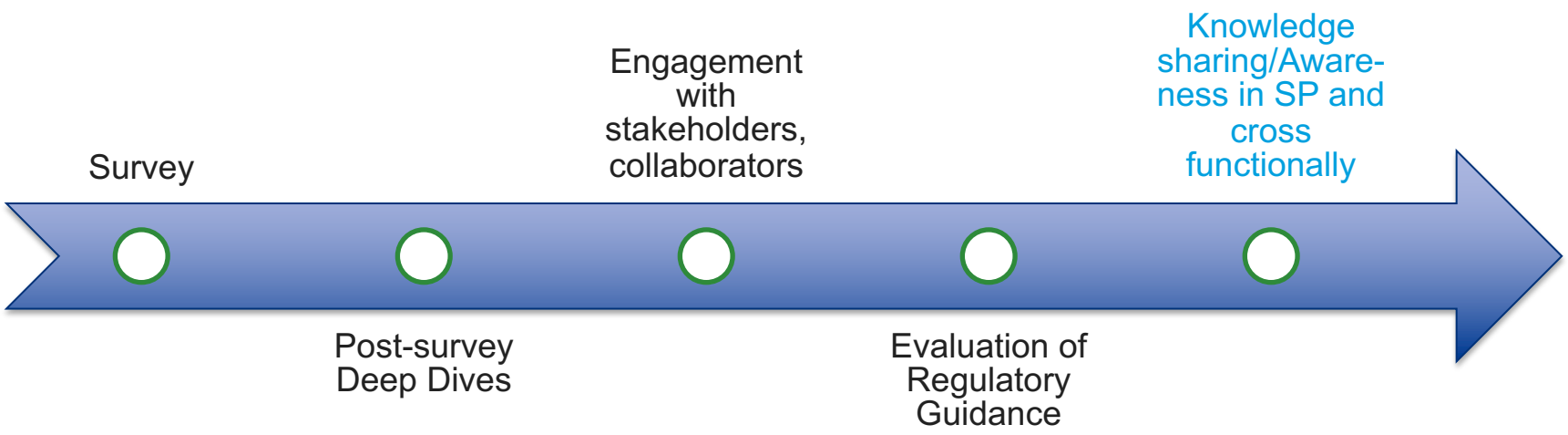
# Regulatory Guidance




| | Applicability | Status | Date |
|---|---|---|---|
| Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products | The use of RWE to help support approval of a new indication for a drug already approved or to help support post-approval study requirements. Focuses primarily on clinical study designs that are non-interventional. | Draft | Dec 2021 |
| Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products | This guidance provides sponsors and other stakeholders with considerations when either proposing to design a registry or using an existing registry to support regulatory decision-making about a drug's effectiveness or safety. This guidance does not provide recommendations on choice of study design or type of statistical analysis when analyzing data from registries (registry data). | Draft | Nov 2021 |
| Data Standards for Drug and Biological Product Submissions Containing Real-World Data | Provides recommendations to sponsors when submitting RWD (for use in regulatory decision making) as study data in applicable drug submissions. | Draft | Oct 2021 |
| Real-World Data: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision-Making for Drug and Biological Products | This guidance is intended to provide sponsors, researchers, and other interested stakeholders with considerations when proposing to use electronic health records (EHRs) or medical claims data in clinical studies to support a regulatory decision on effectiveness or safety. | Draft | Sep 2021 |
| Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drugs and Biologics | This guidance is intended to encourage sponsors and applicants who are using real-world data (RWD) to generate real-world evidence (RWE) as part of a regulatory submission to FDA to provide information on their use of RWE in a simple, uniform format. FDA will use this information for internal tracking purposes only. This guidance applies to submissions for INDs, NDAs and BLAs that contain RWE used to support regulatory decisions regarding safety and/or effectiveness. | Final | Sep 2022 |
| Rare Diseases: Natural History Studies for Drug Development Guidance for Industry | This guidance is intended to help inform the design and implementation of natural history studies that can be used to support the development of safe and effective drugs and biological products for rare diseases. Although existing FDA guidance considers common issues | Draft | March 2019 |

# RWD Playbook Journey at Glance

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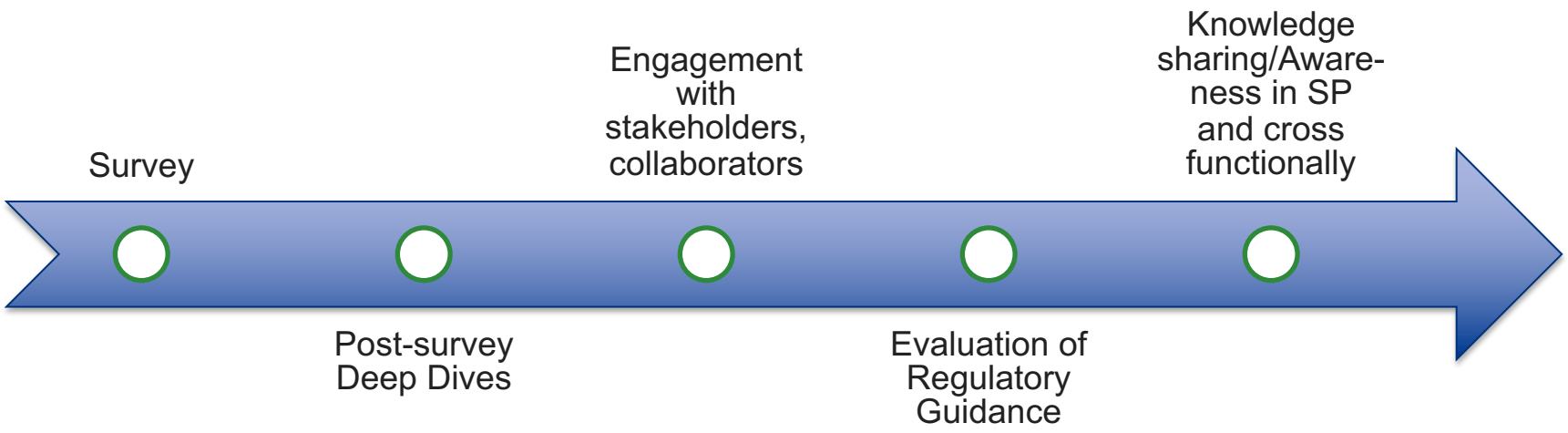


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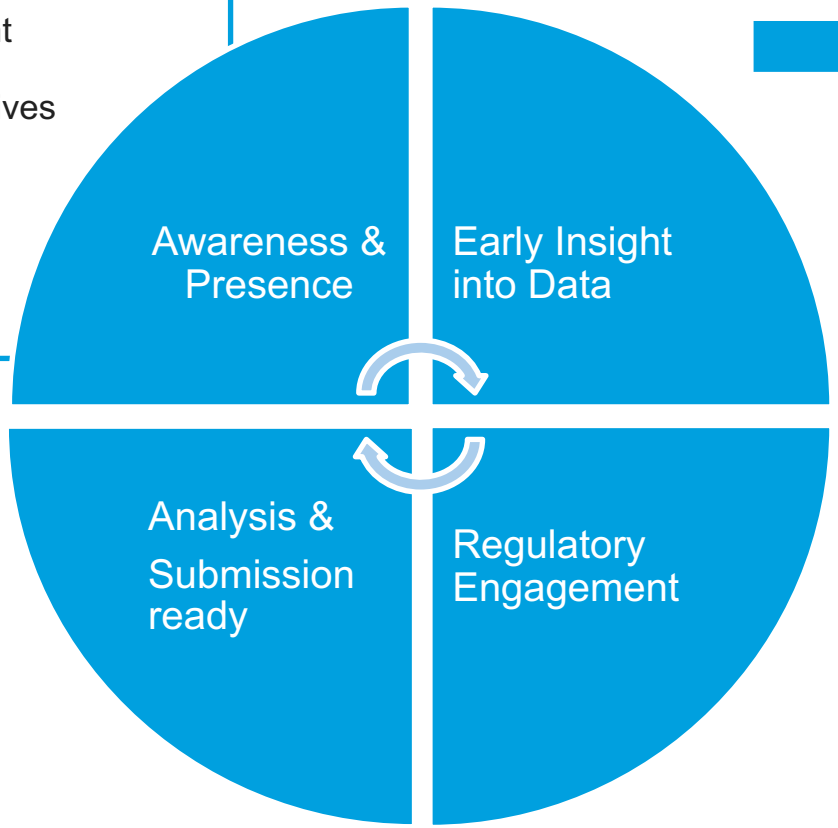
# RWD Playbook - Core Concepts

- Study Planning
- Early engagement
- Functional representatives
- RWDCT
- RACI
- Sourcing strategy




Clinical Questions; Protocol

Identify data sources

Get to know the data

Transformation and Ingestions

Analysis Ready & Submission Ready

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# RWD Council Team - RACI

*Table 5: Example Responsibility assignment matrix for RWD Council Team Members*

| Activity | Integrated Data Analytics Reporting (IDAR) | | | | | Non-IDAR Functions | | |
|---|---|---|---|---|---|---|---|---|
| | CDS | DT | DM | CP | SP&A | SDS | DS/Epi | CS |
| Responsible for identifying the RWD | | | I | I | I | R, A | R, A | R, A |
| Responsible for determining Data Relevancy | | I | I | I | C | R | R, A | R, A |
| Source Data Flows (including vendors, Data Transfer Agreements (DTAs), Business Partner Risk Assessment Process (BPRA)) | | | R, A | C | C | I | I | I |
| Data Acquisition and Coding | | | R, A | C | C | I | I | I |
| Assessment of Data Reliability | | | R | R | R | R, A | R, A | C |
| Database Releases | | | R, A | C | C | C | C | C |
| Creation of Mapping File | | | I | R, A | C | C | C | I |
| Creation of SDTMs | | | C | R, A | C | I | I | I |
| Creation of SAP | | | I | C | C | R, A | I | I |
| Creation of DPS | | | I | I | R, A | R | I | I |
| Creation of ADaMs | | | I | I | R, A | C | I | I |
| Data linkage from more than one Databases | | | I | C | R, A | R | R | R |
| Data Integrations | | | I | I | R, A | C | C | C |
| Standards used | | | I | R, A | R, A | R, A | R, A | I |
| Determination of waiver requirement for SDTMs | C | | I | R, A | R | C | I | I |
| Determination of waiver requirement for ADaMs | | | I | I | R, A | C | I | I |
| Privacy and Legal Considerations | | C | I | I | I | R, I | R, I | R, I |

R=Responsible, A=accountable, C=Consulted, I=Informed
CDS=Clinical Data Standards, DT=Data Transparency, DM=Data Management, CP=Clinical Programming, SP&A=Statistical Programming & Analysis, SDS=Statistics and Decision Sciences, DS=Data Sciences, Epi=Epidemiology, CS=Clinical Sciences

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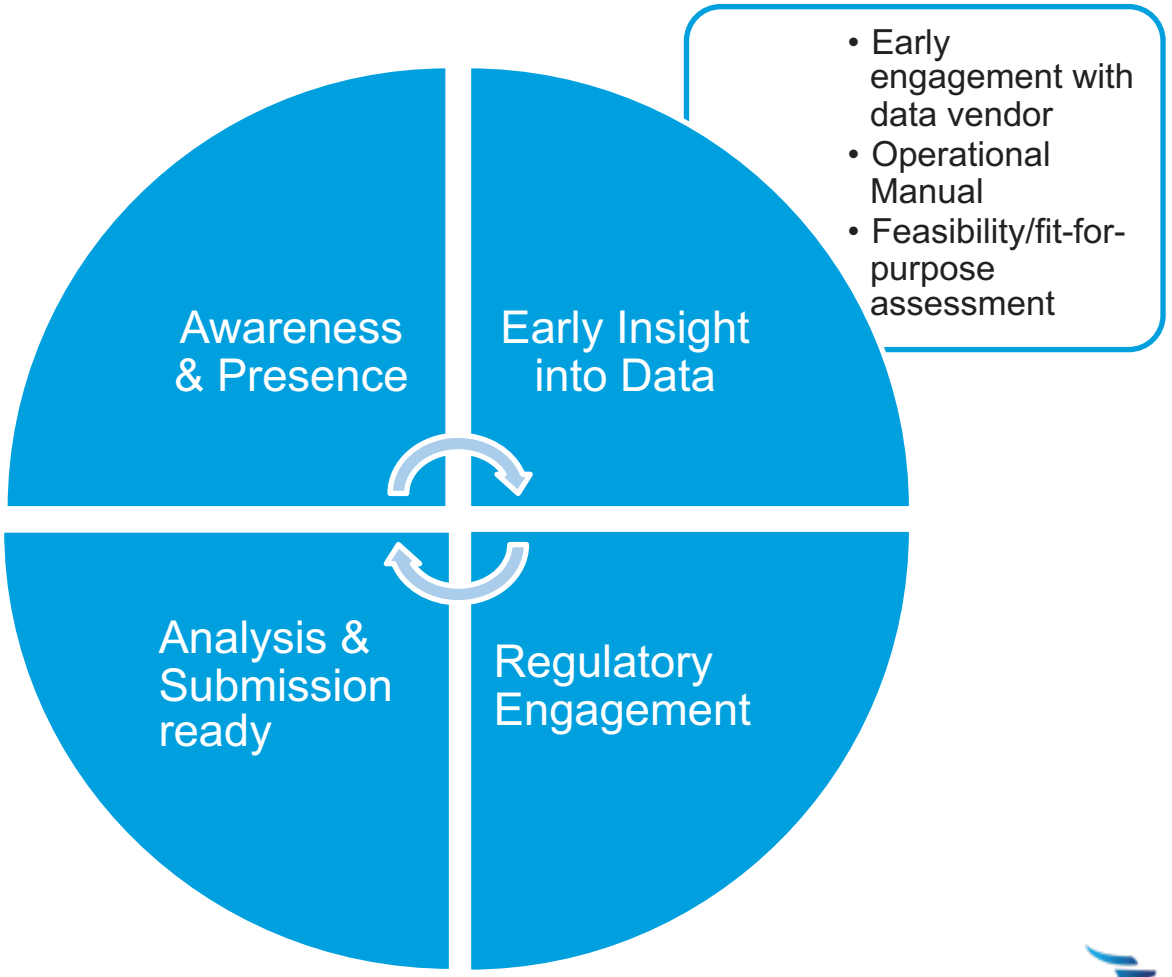


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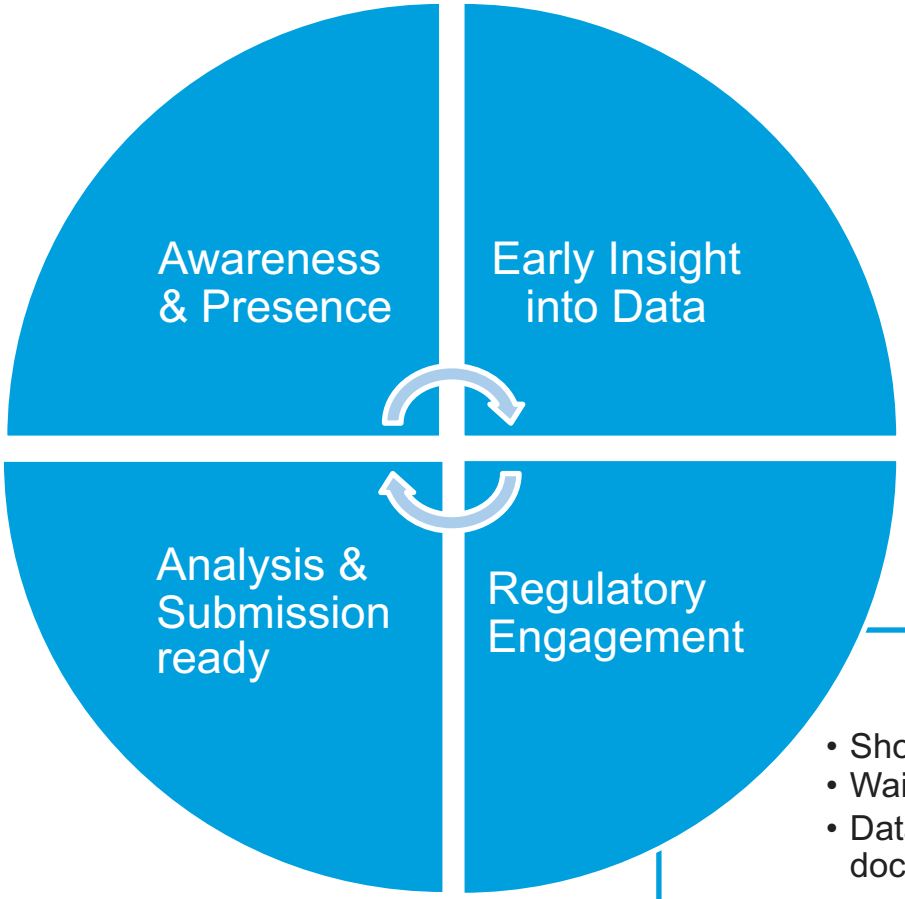
# RWD Playbook - Core Concepts




- Show “fit-for-use”
- Waiver for SDTM?
- Data model and documentation

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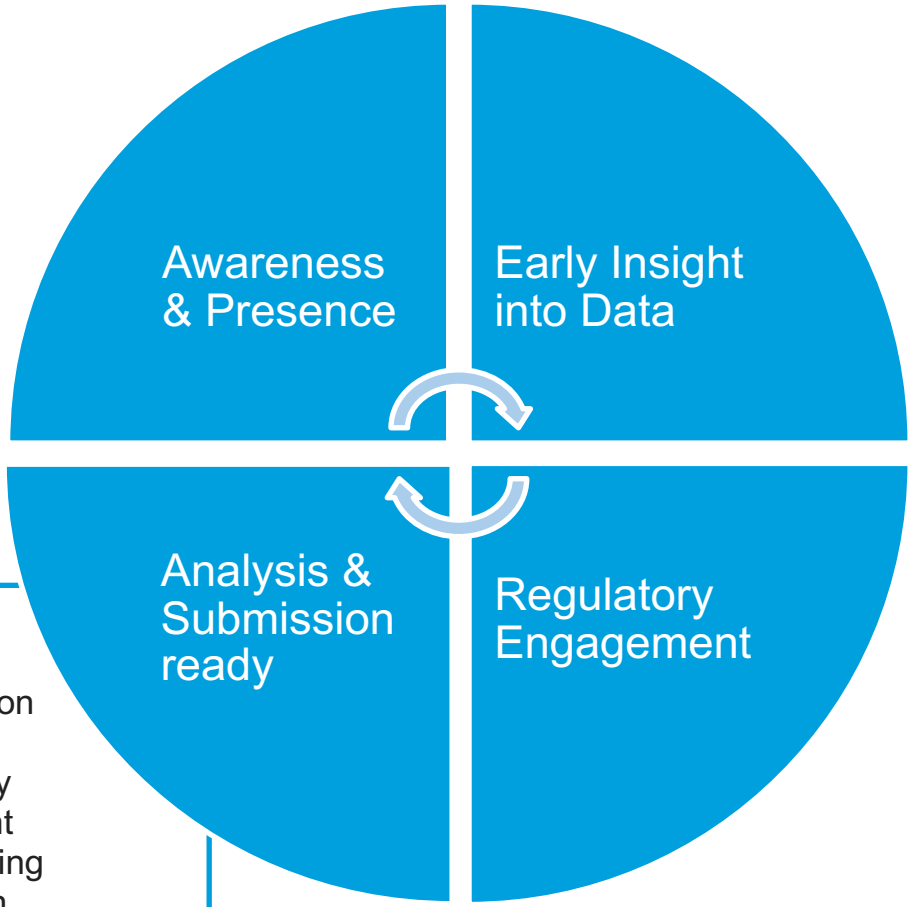
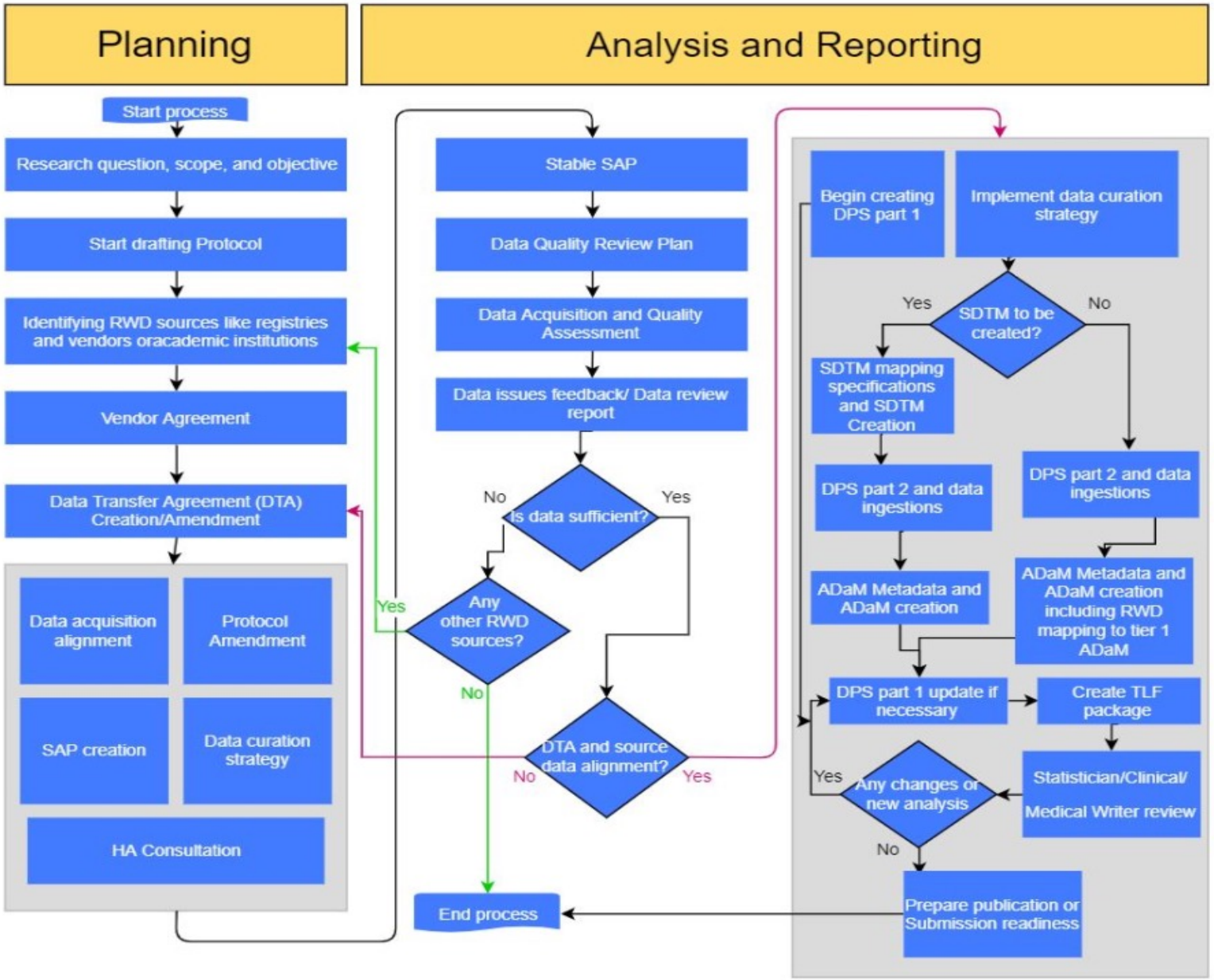
# RWD Playbook - Core Concepts




- Data curation strategy
- Data quality assessment
- Data mapping
- Submission considerations

# Process Flow

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# Best Practices

## Purpose of RWD:

***Best Practice:***
*Understand the purpose of the RWD study/project right from the start as this may impact the extent to which you implement the guidance contained herein.*

## Protocol:

***Best Practice:***
*Do not rely on other functions to identify issues and shortcomings in the Protocol, that have an impact on Statistical Programming activities - use your operational voice.*

# Overview of Statistical Programming Activities for RWD Projects

| Planning steps: | Set-up, Analysis & Reporting and Submission steps: |
| --- | --- |
| • Protocol Review<br>• Resource planning and allocation<br>• Support study planning/ RWDCT Meetings attendance<br>• Support contract or/ and data vendor agreement<br>• Support in assessment of data relevancy or/and reliability to ensure vendor takes action to address relevant topics in the draft Operational Manual<br>• Support RHA consultation (e.g., data models to be submitted)<br>• Evaluate the need for CDISC waiver/s and ensure this is communicated (to GRA) (if applicable)<br>• Make recommendations for the data curation strategy | • Protocol updates review (if applicable)<br>• SAP review<br>• Configuration of project environment in SPACE<br>• Finalize review of RWD Operational Manual from vendor<br>• Regular communication with data vendor<br>• Implement data curation strategy<br>• Data reliability checks and data issues communications<br>• Review data quality assessment plan<br>• Data quality assessment<br>• Support data quality assessment report<br>• Review of SDTM mapping file (if applicable)<br>• RBQR on selected SDTM elements<br>• Support/Create/Update DPS Part 1<br>• Create DPS Part 2 and ADaM metadata with data transformation rules incorporated<br>• ADaM, TLFs and e-sub package<br>• Support SDTM e-sub package QC (if applicable)? |

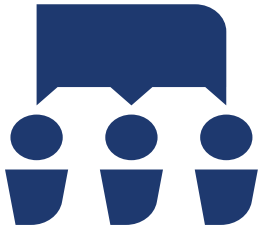
# In Summary

## Visibility

- Align on optimal approach for ensuring visibility on RWD studies planned.

  Data Science, SDS and functional representatives

**Missed Opportunities**



## Cross-Functional Council

- "Real-World Data Council"
- Forum for key stakeholders to formulate and align on strategy for feasibility analysis and data activities linked to acquisition, mapping, transforming, analyzing, reviewing, and submitting.

## RWD Study Tracker

- Cross functional collaboration with Data Science to understand triggers for current (RWD) study approaches
- Use outcome to help determine high level strategy.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