RWE FRAMEWORK

Select **all relevant options**

START

What is your research objective?

- ☐ To inform **internal** decision-making
  - ☐ Business strategy
  - ☐ Go/No go
  - ☐ Indication selection
  - ☐ Clinical trial planning
- ☐ To inform **external** decision-making
  - ☐ Patients
  - ☐ Providers
  - ☐ Regulatory agencies
  - ☐ Payers

- ☐ To study the therapeutic area
- ☐ To study product/demonstrate product value

At study initiation, will the product be approved in the indication?

- N → Ph II-III → Clinical Trial or Expanded Access: Interventional
- Y → Ph IV

Will study be conducted in routine practice, i.e. intervention /altering of routine practice will not be necessary?

- N → Clinical Trial or Expanded Access: Interventional
- Y → RWE study

Consult Clinical Research Team

If conducted in routine practice setting, consult RWE Team as well

Follow ICH GCP/GVP/LLR and regulatory requests

Consult RWE Team

What are the outcomes of interest?

- ☐ Epidemiology
- ☐ Disease burden
- ☐ Patient experience
- ☐ Treatment pathway/patterns
- ☐ Adherence/switching
- ☐ Off-label use
- ☐ Safety
- ☐ Effectiveness
- ☐ Patient-reported outcomes
- ☐ Clinician-reported outcomes
- ☐ Observer-reported outcomes
- ☐ Resource use
- ☐ Costs

Study endpoints: _____ _____

Are the data of interest recorded in routine practice?

Consider

- ☐ Secondary data analysis (use an existing dataset)
- ☐ Hybrid
- ☐ Primary data collection (collect/create a new dataset)

Can patient population be identified in existing datasets?

- N → Consider primary/hybrid data collection
- Y → **Are required data variables captured in existing datasets?**
  - N → Consider primary/hybrid data collection
  - Y → Select database/ methodology

Is randomisation necessary?

- N → Select study type/ methodology
- Y → RWE: interventional

RWE: non-interventional/observational (retrospective only)

- ☐ Case control ☐ Cohort ☐ Cross-sectional
- ☐ Electronic health/medical records
- ☐ Patient portal data
- ☐ Administrative data
- ☐ Payer claims data (primarily US)
- ☐ Lab test results databases
- ☐ National registries
- ☐ Consumer/employee/social data

RWE: non-interventional/observational (retrospective or prospective)

- ☐ Case control ☐ Cohort ☐ Cross-sectional
- ☐ Registry
- ☐ Other prospective observational study
- ☐ Chart review/abstraction
- ☐ Digital health
- ☐ Survey
- ☐ Focus group
- ☐ Interview

Level of Complexity / Resources Required

RWE: interventional

- ☐ Pragmatic trial

Follow GPP/GVP/LLR and regulatory requests

Follow ICH GCP/ GVP/LLR and regulatory requests

PROCEED WITH STUDY DESIGN/PROTOCOL IN CONSULTATION WITH RWE TEAM

COVANCE

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INSTRUCTIONS:

- This flow diagram is a tool to aid initial planning for and design of an RWE study. It contains two main sections, each with several steps, as follows.

Define Objectives and Endpoint(s)

- Tick the relevant objectives to determine the aim of the research, for example, to inform indication selection by studying unmet need in multiple therapeutic areas or to meet EMA requirements by collecting long term safety data on the product.
- Determine if the planned study is an RWE study or a clinical trial.
- If RWE, tick all relevant boxes to identify the key outcomes of interest, and determine your study endpoints, for example, EQ-5D score, hospital length of stay, time to switch, occurrence of treatment-related adverse event.

Determine Study Design

- Determine whether the planned study should rely on primary data collection, analysis of existing secondary data, or a combination of both (hybrid).
- Determine whether the RWE study is a non-interventional/observational study or a pragmatic trial.
- Determine the study design; for example, for non-interventional/observational studies, these include case-control, cohort, and cross-sectional designs, based on whether the studies are comparative or not, and whether they capture data over time or at a specific time point.

KEY TERMS AND DEFINITIONS:

- **ICH:** International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.
- **GCP:** Good Clinical Practice.
- **GVP:** Good Pharmacovigilance Practices.
- **LLR:** Local Legal Requirements.
- **Effectiveness:** The extent to which a health care intervention provides a degree of beneficial effect compared to alternative interventions under conditions of routine clinical practice.*
- **Hybrid:** An approach involving primary data collection supplemented with secondary data analysis (for example, registry study that links patient data with claims data).
- **Non-interventional/observational:** A study in which health care intervention is not decided by trial protocol, but within the conditions of routine clinical practice.*
- **Case-control:** A study that compares exposure among two groups: individuals who have experienced a specific outcome (cases) and individuals with similar characteristics who have not experienced the outcome (controls).*
- **Cohort:** A study in a group of individuals from a source population who are classified by a defining characteristic and followed over a period of time to determine the occurrence of a specific outcome.*
- **Cross-sectional:** A study that examines the relationship between exposure status and an outcome for a defined population at a single point in time.*
- **Pragmatic Trial:** A randomised study that compares health interventions and outcomes among a diverse population under the conditions of routine clinical practice. A pragmatic trial is designed to measure the effectiveness of an intervention.*
- **Registry:** A database that results from the collection of longitudinal, observational data among a defined patient cohort or cohorts (eg, those with a specific condition or undergoing a specific health care intervention).*
- **GPP:** Good Pharmacoepidemiology Practice.

CHECKLIST BEFORE PROCEEDING WITH RWE STUDY:

- ☐ Justify timeline
- ☐ Budget is available and signed off
- ☐ Data exists and is contracted/available
- ☐ Protocol review committee approval

RESOURCES:

The PICO framework: Used to frame a clinical or healthcare-related question, the PICO acronym stands for Population, Intervention, Comparison, Outcome. https://www.ncbi.nlm. nih.gov/pubmedhealth/PMHT0029906/

Loudon K et al. The PRECIS-2 tool: designing trials that are fit for purpose. *BMJ* 2015;350:h2147.

ABPI. Demonstrating value with real world data: a practical guide. http://www.abpi.org.uk/about- us/resources/publications-library/real-world-data. Published May 2011.

Berger M et al. Good practices for real-world data studies of treatment and/or comparative effectiveness: recommendations from the joint ISPOR-ISPE special task force on real-world evidence in health care decision making. *Value Health* 2017;20:1003–8.

Motheral B et al. A checklist for retrospective database studies—report of the ISPOR task force on retrospective databases. *Value Health* 2003;6(2):90–7.

B.R.I.D.G.E. TO_DATA Interactive Map. https:// www.bridgetodata.org/map.

Get Real (www.imi-getreal.eu)

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*Definition adapted from the RWE Glossary compiled by the Innovative Medicines Initiative GetReal Consortium.
Goettsch W, Makady A, and the IMI GetReal Consortium. Glossary of Definitions of Common Terms. http://www.imi- getreal.eu/Publications/Deliverables-and-reports. Updated June 2016.

Resources required