All information regarding future IHI Call topics is indicative and subject to change. Final information about future IHI Calls will be communicated after approval by the IHI Governing Board.

Topic 2: Development of evidence based practical guidance for sponsors on the use of real-world data / real-world evidence

Expected outcomes

- Industry, sponsors, and other stakeholders have access to structured, evidence-based and practical guidance and recommendations on the use of real-world data / real world evidence (RWD/RWE)[1] that could be followed to support the development, and regulatory, health technologies assessment (HTA), and payer decision-making of innovative medicines and health technologies with a focus on medicinal products, medical devices, and therapeutic products that combine a medicinal product with a medical device (drug-device combinations).
- Regulators, HTA bodies and payers will receive more structured and consistent RWD/RWE submissions to inform their decision making.

Scope

The use of real-world evidence to support decision making on the safety of medicinal products is already well established. More recently, RWE has also been used to complement evidence and support marketing authorisation, conformity assessments and HTA submissions. While high-level guidance on the use of RWD/RWE exists, the practical implementation is left up to individual sponsors. Currently, RWD/RWE submissions are usually custom-made to a specific use-case and require significant expertise and effort from the sponsor to prepare, and from the healthcare decision-maker to assess. Much knowledge exists within individual sponsors on these use-cases, but, to date, this has not been leveraged to develop practical guidance which could act as a baseline for future submissions.

To leverage the learning from individual use cases and facilitate the efficient use of RWD/RWE for regulatory, HTA, and payer submissions and to inform healthcare decision-making, structured, evidence-based, and practical guidance is needed.

To address this challenge, the action funded under this topic should:

- Map relevant RWD/RWE initiatives across Europe and their (expected) outcomes. Where relevant, build on, align, and complement these initiatives, including the European Medicines Agency's vision to establish the value of RWE across the spectrum of regulatory use cases by 2025[2].
- Identify the main challenges faced by industry, sponsors, non-commercial sponsors, health professionals, prescribers, and other stakeholders in the routine use of RWD/RWE for regulatory and HTA decision-making. This is to be done by also taking into account the differences in the regulatory frameworks of medicinal products and medical devices and how stakeholders' experiences, needs, and situations are reflected in these.
- In collaboration with the relevant stakeholders, identify, review, and evaluate existing methodologies, guidelines, and practices for the use of RWD/RWE in healthcare decision-making.

[1] Real World Data (RWD) are defined as "routinely collected data relating to a patient's health status or the delivery of health care from a variety of sources other than traditional clinical trials." Real-world evidence (RWE) is defined as the information derived from analysis of RWD. https://doi.org/10.1002/cpt.1426

[2] Arlett P. et al. Real-World Evidence in EU Medicines Regulation: Enabling Use and Establishing Value. Clinical Pharmacology & Therapeutics 2021 https://doi.org/10.1002/cpt.2479

- Focus on an in-depth study of a broad range of use cases where RWD/RWE has been previously assessed for decision-making for medicinal products, medical devices, and combinations. This should include an analysis of methods, designs, and defining variables that enable the grouping and thereafter the utilisation of RWD/RWE sources. Particular attention should be paid to the features that enable efficient assessments.
- Using the results of the study as a foundation, develop a draft of the practical guidance document and recommendations on the use of RWD/RWE to support submissions and decision-making processes, taking into consideration the specific needs of medicinal products and medical devices. Considerations on how RWD/RWE can be used within an ethical framework and respects EU values should be included. In addition, ensure that the guidance respects the EU data quality framework and the relevant RWD specialisation (which is currently under development).
- Test the draft guidance in several pilots to ensure validity and broad acceptability.
  The precise scope of these pilots should be selected by the full consortium during preparation of the full proposal and should address multiple contexts and areas that are not already being addressed, including but not limited to: chronic serious diseases, oncology, and auto-immune diseases. They should also cover clinical development and the regulatory, HTA, and payer assessment of medicinal products and medical devices including combinations.
- Based on the learnings from the pilots, finalise the practical guidance document and recommendations on the use of RWD/RWE to support clinical development, regulatory, HTA and payer submissions and inform decision-making processes.
- Broadly disseminate the guidance and recommendations to the stakeholder community. Create training plans to enable dissemination.

Applicants should develop a strategy and plan for generating appropriate evidence as well as for engaging and formally consulting with regulators, HTA agencies and payers in a timely manner, in particular on the draft guidance (e.g. through national competent authorities, the EMA Innovation Task Force, qualification advice).

In addition, while the project will focus on supporting the development of a recommendation for a structured, practical and evidence based guidance, the funded project is also expected to explore synergies with complementary initiatives to advance RWD/RWD in Europe such as the GetReal Institute, REDDIE, More-EUROPA, Oncovalue, Real4Reg, RWE4Decisions, TEHDAS, QUANTUM, CORE-MD, REALM[3] and projects under the ongoing call for proposals HORIZON-HLTH-2024-IND-06-08. It should also be aligned with the ambitions and guidelines set out for the European Health Data Space (EHDS)[4].

Expected impacts

The action under this topic is expected to achieve the following impacts:

- Improved access to innovations that meet the increasingly diverse needs of patients and those of the healthcare systems.
- Better informed decision-making at different levels of the healthcare system (authorities, organisations) using RWD/RWE that will in turn contribute to a better allocation of resources towards cost-effective innovations as well as representation of different patient populations and needs.
- Faster entry to the market of cost-effective medicinal products and devices (including combinations) developed by industry or public not-for-profit developers, which could translate to a positive effect on their R&I investments.

Why the expected outcomes can only be achieved by an IHI JU action

[3] www.getreal-institute.org, www.reddie-diabetes.eu, cordis.europa.eu/project/id/101095479, oncovalue.org, www.real4reg.eu, realm-ai.eu

[4] health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space_en

Translating current RWD/RWE standards into practical guidance that can be accepted and implemented by decision-makers is a significant challenge. The active involvement of many stakeholders working collaboratively in partnership is needed to ensure such guidance has broad applicability and adds value to the broader initiatives already underway. The diverse nature of these stakeholders, which includes patients, real world data custodians, academics, and SMEs with expertise in RWD, industry, regulators, HTA agencies, and payers, means that a public-private partnership is the ideal framework for such a collaboration.

Pre-identified industry consortium

The pre-identified industry consortium that will contribute to this cross-sectoral IHI JU project is composed of the following pharmaceutical and medical technology industry beneficiaries ('constituent or affiliated entities of private members'):

- Bristol Meyers Squibb
- Edwards Lifesciences
- GE HealthCare
- Medtronic
- Mölnlycke
- Novo Nordisk (Lead)
- Pfizer
- Sanofi
- Servier
- WL Gore

In the spirit of partnership, and to reflect how IHI JU two-stage call topics are built upon identified scientific priorities agreed together with a number of proposing industry beneficiaries (i.e. beneficiaries who are constituent or affiliated entities of a private member of IHI JU), it is envisaged that IHI JU proposals and actions may allocate a leading role within the consortium to an industry beneficiary. Within an applicant consortium discussing the full proposal to be submitted for stage 2, it is expected that one of the industry beneficiaries may become the project leader. Therefore, to facilitate the formation of the final consortium, all beneficiaries, affiliated entities, and associated partners are encouraged to discuss the weighting of responsibilities and priorities with regard to such leadership roles. Until the role is formalised by execution of the Grant Agreement, one of the proposing industry beneficiaries shall as project leader facilitate an efficient drafting and negotiation of project content and required agreements.

Indicative budget

- The maximum financial contribution from the IHI JU is up to EUR 13 300 000.
- The indicative in-kind and financial contribution from industry beneficiaries is EUR 13 300 000.

Due to the global nature of the participating industry partners, it is anticipated that some elements of the contributions will be in-kind contributions to operational activities (IKOP) from those countries that are neither part of the EU nor associated to the Horizon Europe programme.

The allocation of the EUR 200 000 financial contribution (FC) from industry beneficiaries will be decided by the full consortium at the second stage when preparing the full proposal.

The indicative in-kind contribution from industry beneficiaries may include in-kind contributions to additional activities (IKAA).

Indicative duration of the action

The indicative duration of the action is 60 months.

This duration is indicative only. At the second stage, the consortium selected at the first stage and the predefined industry consortium and contributing partner(s) may jointly agree on a different duration when submitting the full proposal.

Contribution of the pre-identified industry consortium

The pre-identified industry consortium expects to contribute to the IHI JU project by providing the following expertise and assets:

- industry expertise in real world evidence, clinical development, benefit risk evaluation, regulatory affairs, HTA, health economics and market access for medicinal products, medical devices, and combination products;
- previously assessed and utilised use cases that can be utilised to evaluate existing methodologies, encountered challenges, explored pathways and practices for the use of RWD/RWE in healthcare decision-making;
- leverage synergies with existing initiatives, including H2O, EHDEN, ConcePTION, IDERHA, REDDIE, REALM, Real4Reg, EHR2EDC, GetReal Institute, TransCelerate, Duke Margolis Real World Evidence Collaborative, CIOMS, RWE4Decisions, CORE-MD, REALM, projects under the ongoing call for proposals HORIZON-HLTH-2024-IND-06-08, TEHDAS, QUANTUM, and relevant EFPIA committees[5].

Applicant consortium

The first stage applicant consortium is expected, in the short proposal, to address the scope and deliver on the expected outcomes of the topic, considering the expected contribution from the pre-identified industry consortium.

This may require mobilising the following expertise and/or resources:

- comprehensive expertise in RWD/RWE including data science, standards & guidance;
- expertise in the access, linkage, and use of RWD and/or synthetic data to evaluate medicinal products, medical devices, and combinations;
- expertise in the technical, legal, and ethical requirements to access and use patient data in Europe;
- knowledge of medicinal product and/or medical device development regulations;
- expertise in interacting with regulatory authorities, national competent authorities, HTA bodies, notified bodies and payers;
- experience with consumer-directed communications and/or patient advocacy (social media reach and expertise in health sector communications);
- expertise in managing multi-stakeholder cross-sectoral projects;
- citizens and/or patient representatives;
- real-world data sources (healthcare providers, clinical sites, contract research organisations (CROs), vendors, national/regional databases);

[5] www.iderha.org, www.i-hd.eu/rd-and-collaborative-projects/ehr2edc, www.getreal-institute.org, www.transceleratebiopharmainc.com, https://healthpolicy.duke.edu/projects/real-world-evidence-collaborative, https://cioms.ch/

- previous use cases that can be used evaluate existing methodologies, guidelines, and practices for the use of RWD/RWE in healthcare decision making.

The applicant consortium is expected to enable effective collaboration with regulatory authorities, national competent authorities, HTA bodies, notified bodies and payers, and may consider, for instance, engaging them as consortium partners, or in an advisory capacity.

At the second stage, the public consortium selected at the first stage and the predefined industry consortium will form the full public-private consortium. The full consortium will develop the full proposal in partnership, including the overall structure of the work plan and the work packages, based upon the short proposal selected at the first stage.

Dissemination and exploitation obligations

The specific obligations described in the conditions of the calls and call management rules under ‘Specific conditions on availability, accessibility and affordability’ do not apply.