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 3: Clinical validation of biomarkers for diagnosis, monitoring disease progression and treatment response

Expected outcomes

Actions under this topic must contribute to all the following expected outcomes:

- Access for healthcare professionals to novel, robust and fit for purpose biomarkers[1] with linked technologies enabling their use in clinical setting and progress towards validation. Biomarkers and linked technologies may be for diagnosis, monitoring disease progression, selecting the optimal therapeutic treatments, or assessing treatment response.
- Availability for researchers of robust and fit-for-purpose biomarkers with linked technologies enabling their clinical use for diagnosing disease, disease monitoring, or monitoring treatment response. This will enable researchers to develop safer and more effective personalised treatments tailored to the individual's characteristics and the stage of their disease. Alternatively, availability for researchers of key technology (e.g. companion diagnostics) that could be essential for the safe and appropriate use and selection of a corresponding drug or biological product or its development.
- Availability for regulators of robust evidence on the suitability of selected biomarkers and their linked technologies to enable regulatory acceptance for a specific use.

Scope

Biomarker-driven approaches for diagnosis, monitoring disease progression and assessing treatment response have immense potential to help us progress precision medicine. Despite intense research, few biomarkers are subject to rigorous testing in clinical settings and shown to be fit for purpose (clinically validated). In addition, while there are several novel biomarkers that have shown significant promise for a number of use cases, often the technology to make them accessible for clinical use is not mature enough, which hampers their validation for use. Thus, technology development or improvements to existing technologies may be required to progress these biomarkers to clinical validation. For example, there are many novel and highly innovative technologies in development (e.g. imaging, artificial intelligence (AI), omics markers, phage-based diagnostics in multiple formats among others) and their further development and validation would be a necessary element for validating their detected biomarkers in the clinic.

Furthermore, different healthcare actors (e.g. academics, clinicians, patients, health technology developers and regulators) may have different definitions and expectations on the utilities of

[1] See definition as in the IHI JU Strategic Research and Innovation Agenda (Glossary): BIOMARKERS are biological characteristics, which can be molecular, anatomic, physiologic, or biochemical. These characteristics can be measured and evaluated objectively. They act as indicators of a normal or a pathogenic biological process. They allow the assessment of the pharmacological response to a therapeutic intervention. A biomarker shows a specific physical trait or a measurable biologically-produced change in the body that is linked to a disease or a particular health condition. A biomarker may be used to assess or detect a specific disease as early as possible (diagnostic biomarker), the risk of developing a disease (susceptibility/risk biomarker), the evolution of a disease (prognostic biomarker) – but it can also predict response to a given treatment including potential toxicity (predictive biomarker).

biomarkers, and there is a need for an aligned methodological framework for scaling up the clinical validation of candidate biomarkers.

To address this challenge, this topic aims:

- to progress candidate biomarkers towards clinical validation and, when relevant, to regulatory acceptance;
  and/or
- to progress towards clinical validation innovative technologies necessary for making biomarker(s) accessible for clinical use. In proposals focusing uniquely on these technologies, applicants should justify how such progress will enable the validation of the biomarker(s) for use in a clinical context.

Projects funded under this topic should:

- Assemble a cross-sectoral public-private partnership to align and develop a methodological framework and roadmap for progressing selected candidate biomarker(s) and/or linked technologies enabling the clinical use of the biomarker(s) (or a combination thereof) to rigorous clinical validation.
- Provide a justification and clearly demonstrate why the proposal area responds to an unmet public health need[2].
- Progress biomarker(s) and/or technologies towards clinical and analytical validation in one or more of these areas: diagnosing disease, early treatment path selection, monitoring disease progression, or treatment response assessment :
  - All types of biomarkers including digital, combinations of biomarkers and multimodal biomarkers are in scope. Proposals addressing biomarker(s) intended for specific populations such as the elderly or children are very welcome.
  - The candidate biomarkers can be combined with existing biomarkers for more personalised decision making.
  - All types of technologies for progressing biomarkers to a stage closer to clinical validation, including innovative and novel approaches, are in scope. Some examples could be technologies for the effective collection, preparation, measurement and analysis of samples and biomarkers, or diagnostic equipment, methods, or systems.
  - In their proposal, applicants must clearly identify the candidate biomarker(s) and/or linked technology(ies) and the proposed application in research and development (R&D) and/or clinical practice.
  - Applicants should provide in their proposal sufficient preliminary evidence, including relevant methodology(ies) and high-quality data to demonstrate that the biomarker(s) and/or technology(ies) can be progressed towards clinical validation and, when relevant, to regulatory acceptance.
- As relevant, applicants must ensure effective collection, preparation, measurement, and analysis of biomarker samples to allow validation in the clinical setting.
- Build on existing solutions to develop a collaborative platform to integrate, analyse and share data (historical and generated de novo) gathered for the validation of biomarker(s) and/or linked

[2] See definition in Art 125.1 of the Council Regulation (EU) 2021/2085 establishing the Joint Undertakings under Horizon Europe: “An unmet public health need shall be defined as a need currently not addressed by the health care systems for availability or accessibility reasons, for example where there is no satisfactory method of diagnosis, prevention or treatment for a given health condition or if people’s access to health care is limited because of cost, distance to health facilities or waiting times.”

technologies during the project, as well as to support future biomarker validation beyond the project duration. Applicants should plan to ensure the future scalability and sustainability of the platform and future data sharing and ensure adherence to FAIR (findable, accessible, interoperable, reusable) principles.

- Develop a regulatory strategy and interaction plan for evidence generation to support the regulatory qualification of the biomarker/s and/or technologies and engage with regulators in a timely manner (e.g. national competent authorities, European Medicines Agency (EMA) Innovation Task Force, qualification advice). Applicants should reserve resources to support these interactions.
- Elaborate a plan for interacting with all the relevant actors in the learning healthcare system (for example clinicians, academic researchers, healthcare professionals, health technology developers, policy makers, and others as relevant) to align on utilities of the candidate biomarker(s) and/or technologies for clinical use and guide the roadmap.
- Disseminate the results of the project to ensure uptake by relevant stakeholders, including healthcare systems and technology developers.
- Applicants should also reserve resources to synergise with other relevant initiatives, including other projects funded under this topic and those funded under IHI Call 3 topic 1[3] as relevant.

Expected impacts to be achieved by this topic

Actions under this topic are expected to achieve the following impacts:

- New clinically-validated biomarker-driven approaches are available that lead, as relevant, to more precise and effective diagnosis, leaner diagnosis-to-treatment pathways, better treatment path selection, or improved follow-up and treatment response assessment and monitoring.
- A significant reduction in the diagnostic or therapeutic burden for patients (and caregivers) for example by favouring non- or minimally-invasive approaches.
- Validated tools and approaches supporting evidence-based health and care decisions addressing both the needs of patients and of healthcare systems.
- An increase in the competitiveness of European health industries.

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

The clinical validation of biomarkers and the development of their linked technologies is a challenging process. To meet the topic objectives, a collaboration across several industry sectors (including pharmaceutical and medical technology industries) combined with other relevant stakeholders in the healthcare ecosystem is necessary. The IHI framework is the ideal enabler for gathering the necessary significant cross-sectoral expertise , and fostering collaborative open innovation, including from patients, clinicians, statisticians, healthcare professionals, biomarker specialists, machine learning experts, scientists, experts in regulatory affairs, small and medium-sized enterprises (SMEs), pharmaceutical and medical technology industries among others.

Indicative budget

Applicant consortia will be competing for the maximum financial contribution from IHI up to EUR 45 000 000.

[3] https://www.ihi.europa.eu/apply-funding/ihi-call-3

IHI estimates that an IHI financial contribution of EUR 15 000 000 would allow a proposal to address these outcomes appropriately. Nonetheless, this does not preclude submission and selection of a proposal requesting different amounts.

Applicant consortia must ensure that at least 45 % of the action's eligible costs and costs for the action-related additional activities are provided by in-kind contributions to operational activities ('IKOP'), financial contributions ('FC's), or in-kind contributions to additional activities ('IKAA'). While 45 % is the threshold for eligibility, applicant consortia are strongly advised to aim for 50 % to provide a margin e.g. for unforeseen changes during the project lifetime.
IKOP and FCs may be contributed by the constituent and affiliated entities of both the private members and the contributing partners. IKAA may be contributed by constituent and affiliated entities of the private members only. Contributing partners and their affiliated entities cannot contribute IKAA. See the call conditions in the annual Work Programme for further information (also in the document ''call text" published on the IHI website).

Indicative duration of the actions

Applicants should propose a project duration that matches the project's activities and expected outcomes and impacts.

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" apply.