

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: Inclusive clinical studies for equitable access to clinical research in Europe

Expected impacts to be achieved by this topic

The following impacts are expected:

- Awareness and understanding of what diversity, under-represented and underserved communities look like in geographies across Europe, including barriers and gaps to recruitment and retention in different types of clinical research, such as clinical studies¹ on medical products, clinical investigations for medical devices, and performance studies in *in vitro* diagnostics (IVDs), cohorts, and registries.
- Enhanced representativeness of underserved populations in clinical studies across Europe, through the building of a patient-centric, sustainable infrastructure that improves the recruitment and retention of these patients.
- Increased study data reliability and genetic diversity by including different demographic groups, thereby enhancing patient trust in the evidence generated. More patients benefit from increased access to improved innovative health technologies including medicinal products and medical devices that meet the specific needs and profiles of all patient populations.
- Promoting the implementation of new tools, solutions, approaches, or process models that will reduce the burden of clinical studies and facilitate and increase diverse patient populations' access to clinical studies.
- Contribution to the Accelerating Clinical Trials in the EU² (ACT-EU) objectives to proactively deliver inclusive patient-oriented medicines development and delivery across populations.

Expected outcomes

The research and innovation (R&I) action (project) to be supported under this topic should aim to deliver results that contribute to all of the following expected outcomes.

- Researchers, including industry stakeholders, clinical investigators and healthcare providers, strengthen the understanding, through use cases, of the impact of study design/protocols and study conduct on patient recruitment/retention that will help future clinical studies. These stakeholders will also benefit from gaining clarity on what clinical study diversity means in Europe, especially considering the emerging guidance from the US Food and Drug Administration (FDA) on clinical trial diversity in the US.

¹ Clinical study EC definition as per Horizon Europe information on clinical studies template: Clinical study covers clinical studies/trials/investigations/cohorts and means, any systematic prospective or retrospective collection and analysis of health data obtained from individual patients or healthy persons in order to address scientific questions related to the understanding, prevention, diagnosis, monitoring or treatment of a disease, mental illness, or physical condition. It includes but it is not limited to clinical studies as defined by Regulation 536/2014 (on medicinal products), clinical investigation and clinical evaluation as defined by Regulation 2017/745 (on medical devices), performance study and performance evaluation as defined by Regulation 2017/746 (on *in vitro* diagnostic medical devices).

² https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/accelerating-clinical-trials-eu-act-eu-delivering-eu-clinical-trials-transformation-initiative_en.pdf

- Patients will benefit from a sustainable, easy-to-use digital platform, built with input from patients and/or patient support organisations, enabling more underserved patients to identify clinical studies that they are eligible for. Investigators/sites would be able to locate patients for ongoing clinical studies. This will benefit both recruitment and retention of underserved patients as it will act as a match-making portal that will be accessible to all sponsors (including academics/investigator-initiated trials, industry, etc.), and provide patient support to enable patients to allay their concerns in a timely manner, increasing their knowledge/education and building trust toward clinical research
- Researchers, including industry stakeholders, sponsors, clinical investigators, clinical research organisations, healthcare providers and patients/caregivers benefit from a toolbox of new approaches, tools, solutions and best practice approaches to facilitate and increase patient recruitment and retention, to better design and conduct clinical studies including adaptive designs, registry studies and decentralised studies with a particular focus on under-represented and underserved patient populations in Europe. Taking account of regulatory requirements, this will lead to more effective clinical studies with an increased recruitment/retention of diverse patient populations that is supported by a community-informed approach.
- Increasing population representativeness also better reflects real-world patients and helps the generalisability of the study findings, leading to better innovations. This is a positive outcome for all patients (not just underserved patients). Targeted under-represented and underserved patient populations have increased trust in clinical studies, which helps to overcome recruitment, participation, and retention challenges through educational programmes, public outreach, and community outreach/engagement.
- Clinical investigators, clinical sites and existing clinical networks benefit from cultural competency and educational training to better engage with diverse populations. New investigators from underserved communities will benefit from inclusion in clinical studies.
- The pool of clinical sites with access to diverse clinical research staff that can facilitate the education, recruitment, and retention of diverse populations in clinical studies is broadened.
- Community-based sites and organisations are better engaged to provide input on the conduct of clinical studies and to promote diversity in patient populations through inclusive enrolment practices.
- Regulators, health technology assessment bodies and payers benefit from better information on health technologies including medicinal products, medical devices benefit-risk profile across the patient populations for use in clinical practices.
- Data standards established in agreement with regulators. Standardisation of data standards for demographic descriptors across sponsors such as race, ethnicity, gender, sex, and other selected diverse factors for the defined underserved and under-represented populations are essential for consistent reporting and valid demographic measurement.

Scope

Patient recruitment and retention remains a leading challenge in the efficient completion of clinical studies, including studies on medicinal products, medical devices, or IVDs. Furthermore, despite advancement of enrolment practices designed to better reflect the population most likely to use the health technologies in clinical practice, there is still only limited diversity within recruited patient populations. The under-representation of diverse populations (due for instance to their race and ethnicity, gender, age, socio-economic status, geographical location) creates knowledge gaps about the risks and benefits of health technologies for these specific populations.

This topic aims to develop a multi-faceted, intersectional approach to overcome the multifactorial barriers associated with the recruitment and retention of underserved patient populations in clinical studies and to contribute to transforming the way clinical studies are conducted in Europe.

To fulfil this aim, the following activities around the defined themes should be addressed.

Landscape

- Agree a definition of “underserved” populations in Europe with regulators, that includes populations facing socio-economic, systemic, or cultural barriers that prevent equitable access to clinical studies. This may be broader than populations currently defined in the demographics that sponsors collect, such as age, sex, gender, race, and ethnicity. This could include rural populations, refugees, homeless, illiterate, disabled people, and those belonging to minority populations.
- Estimate the current participation of diverse study populations in clinical studies differentiated by success in recruitment and retention; identify and evaluate the factors that contribute to and limit existing initiatives to increase diversity of recruitment and retention in clinical studies.
- Define and develop country-, social- and culture- specific understanding of factors driving under-representation and underserved populations in Europe. Shape the development of guidance on how to reach and retain underserved populations in clinical studies in different settings and countries, and how to collect data in a GDPR³-compliant fashion across Europe.
- Establish a sustainable patient-centric digital platform (open to all sponsors) connecting the patients, patient support organisations, sponsors, and investigators at different sites (including in community settings, hospitals, primary physicians, etc). To ensure patient engagement, the platform should use lay language and make use of existing resources such as ClinicalTrials.gov information; patient support information developed by patient organisations, or Clinical Trials Information System (CTIS). This is important to ensure that the patient/community engagement activities undertaken lead to patients being directed to use the platform, leading to an improvement in participation of diverse patients. The needs of underserved populations with access barriers to digital platforms or language barriers should be considered.
- Define the governance structure and maintenance/ownership of the platform. The active involvement of underserved patients / patient representatives is expected in the planning and development of the platform, as well as governance activities.
- Understand the interface between international, regional, and local approaches from a patient-centricity perspective (while the strategies may need to be developed and implemented locally, they will be part of multi-regional/multi-country clinical studies conducted by sponsors).

³ General Data Protection Regulation

Protocol design and clinical operations

- Establish criteria for measuring 'representativeness', i.e. patients enrolled in the trial represent the prevalence of the disease in different sub-populations. For example:
 - Representation: age, sex, gender, race, ethnicity (measured against prevalence).
 - Inclusion: socioeconomic status, rural vs. urban access, sexual orientation, disability, payer status (private vs public), pregnancy/lactation status, etc.
- Identify and assess existing tools and solutions for patient recruitment and retention that could be used for recruitment and retention of a diverse population from a European perspective. Develop a set of suitable tools, solutions, and strategies applicable for different types of clinical studies, including studies with medicinal products, medical devices, or IVDs.
- Identify and review aspects of study design such as narrow eligibility criteria, methodological approaches, logistical and other patient-related factors that could limit broader patient and communities' engagement, taking account of regulatory requirements; define recommendations for best practices.
- Explore and validate approaches that improve access, participation, recruitment, and retention of diverse patient populations, including innovative technology solutions, clinical research methodologies (e.g., adaptive, home based/hybrid), leveraging real world data sources etc.

Community engagement

- Raise awareness, develop educational activities and inclusive toolkits to increase knowledge and trust of target populations towards clinical studies to overcome recruitment, participation, retention challenges and to enable early patient engagement.
- Develop targeted activities to foster community engagement and build trust with patients.
- Establish connections between different stakeholders in the community e.g. researchers, industry stakeholders, patients, caregivers, investigators, and healthcare providers.

Investigators / clinical sites

- Build new site capabilities and develop training activities to increase the number of community-based sites and expand the pool of investigators, including investigators from under-represented communities and naïve investigators, to set them up in geographies where the infrastructure is missing.
- Create the necessary support mechanisms and define specialised training e.g. cultural competency training, naïve investigator training, etc. through existing clinical networks, medical institutions, patient organisations and community-based organisations. Existing resources such as Clinical Trials Transformation Initiative (CTTI), or other projects such as IMI (Innovative Medicines Initiative) projects connect4children (c4c) and EUPATI can be leveraged.

To ensure the applicability of the solutions/tools/recommendations, the applicants should test them in pilot use cases, which will be determined during the project based on the availability of cases from sponsor companies and in discussion with the consortium, in one or more disease areas of choice. The proposed disease areas should constitute an unmet public health need and a significant burden to patients, healthcare systems and society (e.g. breast cancer, prostate cancer, hypertension, lupus etc). Furthermore, the proposed areas should be representative to allow broad implementation across diverse disease areas, different cultural and geographical distributions, types of clinical research such as clinical studies on medical products, clinical investigations for medical devices, performance studies for IVDs, and studies testing non-pharmacological and rehabilitation interventions.

The purpose of the pilot use cases is to test tools and solutions for patient recruitment and retention, assess the functionality of the digital platform, and test the improvements brought by the digital platform on patient recruitment and retention. The focus will be on testing the robustness of the infrastructure to ensure the solutions put in place are “fit for purpose”. The testing could establish the viability of the solutions, for example:

- number of new sites added to the platform;
- number of under-represented investigators trained through this initiative;
- number of investigators that serve underserved patient populations;
- effectiveness of community engagement activities as judged by patient support organisations;
- effectiveness of recruitment and retention activities via the platform, as experienced by investigators and patients;
- analysis of number of users of the platform and the type of content accessed by users.

Applicants are expected to consider the potential regulatory impact of the results and as relevant develop a strategy/plan for generating appropriate evidence, and to engage with regulators in a timely manner (e.g., through the EMA Innovation Task Force, qualification advice).

In their proposals, applicants should leverage and build on existing tools & solutions and best practice experiences that have already been developed at national European and/or international level, including tools developed in IMI/IHI projects.

Why the expected outcomes can only be achieved by an IHI project

To achieve the transformation outlined above, a broad cross-sectoral collaboration is needed including healthcare professionals to give insights on their experience with the current technology utilisation and act as champions for the new developments, academic researchers, health economists, hospital management, public procurers, technology developers and vendors and patients, who will benefit from the solutions. Integrating data from multiple origins/sources requires the cooperation of data holders, both public and private, in a non-competitive, neutral setting like an IHI project. Improving clinical studies that address patients' needs is of paramount importance for the private and public sector. Recruitment, retention, and the insufficient participation of underserved patient populations in clinical studies are a challenge that the entire health industry faces, including large and small and medium-sized pharmaceutical and medical technology companies. Efforts to tackle those are riddled with complexities such as the geographical complexity (a solution appropriate in one country may be less appropriate in another). In addition, the multitude of healthcare partners in the health ecosystem hinders scalability of initiatives that can be put in place. Cultural barriers also exist that may result in the mistrust of under-represented and underserved patients towards clinical research.

An important paradigm change is needed to succeed in better including under-represented populations, requiring collaboration among stakeholders: patients, caregivers, academia, healthcare practitioners, clinical investigators, industry, sponsors, contract research organisations, regulators, health technology assessment bodies, payers, social scientists, and ethicists, etc. A cross-sectoral and multidisciplinary public-private approach is the only way to harness the insights from key stakeholders, consider all perspectives, and adjust the trajectory in real time. Increasing the recruitment and retention of underserved patient populations is a multistakeholder effort and the IHI provides the framework to bring together all sectors, and all involved in clinical research, including patients and caregivers to succeed in promoting more inclusive clinical studies.

Pre-identified industry consortium

The pre-identified industry consortium that will contribute to this cross-sectoral IHI project is composed of the following pharmaceutical and medical technology industry partners:

- Abbvie
- AstraZeneca
- Bristol Myers Squibb
- Eli Lilly
- GlaxoSmithKline
- Novartis (Lead)
- Novo Nordisk
- Pfizer
- Roche
- Sanofi
- Takeda

In addition, the following contributing partner will participate in the IHI project:

- JDRF

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

Indicative budget

The maximum financial contribution from IHI up to EUR 33 000 000.

The indicative in-kind contribution from industry partners is EUR 33 600 000.

The indicative in-kind and financial contribution from IHI JU contributing partner is EUR 250 000.

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 from those countries that are neither part of the EU nor associated to the Horizon Europe programme.

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

Indicative duration of the action

The indicative duration of the action is 72 months.

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

Contribution of the pre-identified industry consortium

The pre-identified industry consortium and contributing partner expect to contribute to the IHI project by providing the following expertise and assets:

- Expertise in legal, ethics and compliance, regulatory, diversity, equity and inclusion (DEI) in clinical research and clinical study design both at a local and regional level.
- At a minimum, three use cases (in selected disease areas) are expected to be used as “pilots” to test the infrastructure that will be established during the project. There could be additional comparator use cases depending on testing criteria. Industry contributions will be based on the ‘disease/indication’ and total number of participants interacting with the solutions/platform put in place through this project. The contributions could extend to costs incurred to recruit and retain included patients (in Europe) in the pilots, such as investigator fees, site coordinator fees, digital recruitment/social media costs, reimbursement of patient costs (transportation, etc), community engagement activities, patient retention activities, etc. Costs that do not relate to recruitment and retention activities will be excluded such as costs linked to safety and efficacy assessments, therapeutic ingredients, and supply chain costs.
- Contribution to the elaboration of educational programme and training materials building on existing materials. Sharing potential expertise or technologies that are beneficial for the broader community to help reduce the burden of participating in clinical research.
- Leverage synergies with existing IMI/IHI initiatives and TransCelerate collaborations across industry.
- Capability to enable the platform to be used widely (and adopted as a single solution) by a variety of stakeholders that are currently funded by the pharmaceutical industry to run clinical studies, e.g. contract research organisations (CROs), sites, patient support and advocacy organisations.

The allocation of the EUR 200 000 financial contribution will be decided by the full consortium at the second stage when preparing the full proposal.

Applicant consortium

The first stage applicant consortium is expected, in the submitted 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 and the contributing partner.

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

- Knowledge of the existing clinical studies and site databases in Europe.
- Project management expertise in running cross-sectorial projects.
- Partners with expertise in building a patient-centric digital platform that connects various health ecosystem stakeholders, for e.g. patients, patient support organisations, sites, CROs, sponsors, registries.
- Expertise in gathering patient insights for clinical studies – such as input to protocol design, user acceptance testing of the platform, etc.
- Partners who have strong relationships with patient representatives / patient organisations to ensure patient-centricity at all levels of the project.
- Partners with relevant expertise like healthcare professionals, community organisations, sites, CROs.

- Public health experts, social scientists, behavioural scientists, to help change behaviours and mindsets. Communication expertise to reach underserved communities. Patient advocacy experts that in particular work across multiple disease areas and countries in Europe.
- Knowledge on the regulatory aspects (including good clinical practice of drug and medical device development).
- Experience with consumer-directed communications and/or interactions and/or patient advocacy (social media reach and expertise in health sector communications preferred).
- Experience with localised epidemiology data (i.e. incidence/prevalence) overlaid by demographics and/or local ethnopharmacology.
- Expertise in delivering capability-building activities and cultural competency training to the sites.
- Experience in onboarding naïve investigator sites.

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