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: Patient-centric blood sample collection to enable decentralised clinical trials and improve access to healthcare

Expected impacts to be achieved by this topic

Collecting venous blood samples for diagnostic purposes has been the cornerstone for informing patient care and a key element of clinical trials. Ordering a blood draw has become almost a reflex for clinicians and drug developers, however venipuncture is still the traditional way to collect blood. Venipuncture can be painful and requires individuals to see their healthcare provider or visit a clinic. This results in a burden on patients, doctors, healthcare systems, payers, and the pharmaceutical industry. A particularly high burden may be imposed on vulnerable populations such as children and elderly individuals, as it may lead to increased exposure to disease during a pandemic, or to anaemia (e.g. in oncology). Furthermore, the current procedure is too inflexible to allow for ongoing monitoring for treatment, progression, or intervention in decentralised clinical trials and clinical practice [1]. There is a great need for the acceptance and implementation of patient-centric (as opposed to clinic-centric) sampling approaches.

The generation of an infrastructure and logistics for at-home collection of small-volume (less than 500 µl) blood samples ('microsampling') as an alternative to venipuncture for routine central lab analysis will contribute to the following impacts:

- It will deliver a much-improved experience to our patients by decreasing the burden on patients (in particular vulnerable populations) and optimising patient care in Europe.
- It will improve decentralised clinical trials, trials at home, and inclusion trials.
- It will facilitate monitoring for prevention, treatment, and surveillance.

Expected outcomes

The results of the project generated by this topic will enable innovations in healthcare delivery and research by generating the infrastructure and logistics for blood collection at home, that is simple, minimally invasive, less painful, convenient, and feasible.

Importantly, the project will also provide new insights and enrich information related to the research questions by creating an unprecedented data set that will enable multiple secondary research options for years to come. Notably:

1. It will create insights into the public acceptability for microsampling home: are patients comfortable with a new kind of medical technology? What training is necessary?
2. Are we able to advance the transition of care from the hospital to the home? Does the care quality improve?
3. How do we utilise the higher frequency of data, including its integration with electronic medical records and using advanced analytics methodology?
4. Do doctors' practices and decisions change with the increased frequency of biomarker data, and does it lead to better outcomes for the patient?

While integrating existing components for microsample collection and central lab analysis, quality standards for the new infrastructure and logistics will be rigorously and transparently validated and established in Europe and harmonised with parallel ongoing efforts in the USA. The harmonisation will critically enhance the implementation of microsampling in global clinical trials of new therapeutics. The validation and establishment of microsampling at home by patients and/or their caregivers will be undertaken in ways that are acceptable for patients and their caregivers, health care professionals, regulatory agencies, policy makers, Health Technology Assessment (HTA) experts, payers, and advocacy groups.

Scope

The overall aim of the project generated from this topic is to create and validate the infrastructure and logistics for blood collection by the patient and/or caregiver at home as a healthcare tool and an alternative to the current gold standard venous blood for routine clinical assays. This project will employ only commercially available CE-marked microsampling devices, according to their intended use. The development of new devices for blood sampling or of new clinical assays / analytes is not the focus of this project, and no new clinical assays will be evaluated. Similarly, given their current maturity, home sample analysis is out of scope.

Training materials, customised for patients and caregivers as well as for medical personnel will be developed, ensuring the acceptability of the new approach to these groups. Interactions with regulatory authorities, the European Medicines Agency (EMA), local European agencies as well as regulatory agencies from non-EU European countries and the US Food and Drug Administration (FDA) will be sought to advance the regulatory acceptability of the logistics model and harmonisation across the EU, other non-EU European countries and the US. Further, key stakeholders (e.g. policy makers, HTA experts, payers, patient advocacy groups) will be encouraged to implement the infrastructure and logistics throughout Europe. Lastly, the best ways to integrate, transmit, and analyse (including AI) the data generated will be explored. Results will be shared broadly through peer-reviewed publications or other mechanisms.

To be noted – home blood microsampling has been used in geographically restricted pilot projects [2]. With the project generated from this topic, it is expected to generalise them, and leverage the learnings from the pilot projects, to enable broad adoption. Importantly, it is known that patients greatly appreciated this experience compared to the traditional blood sampling methods currently in use.

Applicants should in their proposal address the following:

1. **Demonstration of concordance between patient-centric microsampling techniques and venipuncture**

This requires delivery of a framework across Europe for establishing concordance between capillary blood as collected by microsampling devices outside of traditional collection setting by the patient and/or caregiver, versus the gold standard venous blood, for routine clinical assays.

- To generate an umbrella / master protocol that is acceptable for regulatory authorities in Europe and other non EU-European countries, and can be easily adopted for future applications (e.g. in additional patient populations, countries, by any vendor or organisation). To assure patient-centricity, feedback on the umbrella protocol by patient representatives and caregivers will be sought.

The umbrella / master protocol must include:

- sites in at least 3 EU member states, and may include additional sites in third countries associated to Horizon Europe or other European countries; at least one of the countries must be in Eastern Europe[1];
- **at least** two different types (e.g., finger stick, upper arm capillary) of commercially available CE-marked microsampling devices;
- routine clinical assays: i.e. blood chemistry, liver and lipid panels;
- collection of at least 50 % of microsamples by the patient and/or the caretaker; the other 50 % may be taken by hospital or nursing personnel (including remote or traveling nurses);
- collection of least 50 % of microsamples at home; the project may include collections in other locations (e.g. hospitals, general practitioners, specialists' offices) for concordance testing and establishing microsampling of capillary blood versus venous blood for routine assays.

- To design, adapt, and translate patient-facing materials, obtain ethics board approvals, obtain competent/regulatory authority approvals, recruit healthy human volunteers and expand to a patient population which should be agreed upon in a project committee, collect biological samples and conduct bioanalysis according to the study protocol.
- To investigate potential errors related to the mishandling of samples and design ways to mitigate them, as well as the potentially harmful downstream effects for the individual.
- To conduct concordance analyses according to existing regulatory guidance for routine clinical assays [3], and define sample quality criteria (if applicable).

2. Validation of the logistics of sample collection and shipping, standardising central lab analysis.

This requires identification of an optimum workflow for device ordering, fulfilment, shipping, at-home collection and return to central labs and a seamless integration of microsampling into current central lab processes, accessioning, analysis and reporting.

- To select at least two different types of CE-marked microsampling devices, and identify and audit device vendors with ordering (portal) and fulfilment capabilities; to work with device vendors on ordering devices.
- To define appropriate shippers/processing/temperature based on the devices and assay requirements, and confirm requisition requirements.
- To identify strategic partners in terms of logistical expertise, e.g. global couriers.
- To identify countries to test devices in and confirm regulatory requirements for self-collections or collections by caretaker and shipping of devices.
- To define the support need for the use of devices and training participants on devices; to identify telehealth partners e.g. for identification verification.

[1] Due to the ongoing conflict in Ukraine, the participation of legal entities from Russia or Belarus in Horizon Europe and IHI JU projects is prohibited. https://research-and-innovation.ec.europa.eu/strategy/strategy-2020-2024/europe-world/international-cooperation/russia_en#:~:text=Russian%20researchers%20and%20organisations%20are,various%20EU%20and%20Russian%20funding

- To identify the best ways to integrate the new data with existing electronic medical records and medical decision frameworks.

- To investigate the 'green dimension' of logistics: microsampling has the potential to reduce the green footprint of office visits and transportation required (fuel, costs, carbon emissions).

- To confirm the accessioning process needed, reporting requirements, and data management model.

  If possible, to assess the cost savings obtained with microsampling methods as compared to gathering blood in the hospital.

3. **Education and medical & patient acceptability**

- To deliver training materials for patients, caregivers and clinical trial sites, taking into account the variety of patients' and caregivers' ages, abilities, etc., and ensuring smooth behind-the-scenes shipment logistics and support.

- To develop guidelines for compiling training materials to meet expectations from different training recipients, such as clinical sites, patients, caregivers, telehealth and home health providers, leveraging previous feedback collected from users (patients, caregivers, principal investigators (PIs) and medical personnel), including to develop training by telehealth.

- To develop a plan to collect patient, caregiver and medical personnel (site staff, PIs, trial coordinator) experience and feedback:

  - to develop a well-designed questionnaire that will be used either electronically or in paper format, develop tool(s) to collect feedback and store the information, pilot the use, refine the questionnaire and data base as needed;

  - to implement the questionnaire to collect feedback from different groups (patients and caregivers, medical personnel, regulators, device manufactures);

  - to maintain a database of information collected and perform data analysis to obtain patient acceptability scores;

  - to get insights into research questions related to the implementation of microsampling which are described in 'Expected outcomes' (see above).

- To publish survey results to validate the training and feedback with other patient advocacy groups.

4. **Regulatory acceptability and implementation in clinical practice in the EU, other non-EU European countries and the US**

- To prepare an overview of the regulatory landscape of microsampling at home per country in the EU, third countries associated to Horizon Europe, and other European countries, and to conduct an in-depth exploration in those countries that might be suitable for the microsampling logistics modelling.

- To establish an early and continuous dialogue with the European Medicine Agency (EMA) Innovation Task Force, in addition to local regulatory agencies of the EU, and relevant authorities of other non-EU European countries and the FDA:

  - to assess acceptability with regulators and seek prospective input on the umbrella / master protocol, choice of countries and approach to validating the logistics;

- to discuss the best strategy/timing for qualification and/or integration of project outputs into regulatory practices, prepare relevant documents (e.g. briefing books, EMA guidance document) to share project results, request scientific and qualification advice, and seek a harmonisation with the regulatory agencies from other non-EU European countries and the FDA, which is key to global clinical trials of new therapeutics.

- To interact with policy makers, HTA experts, payers, and advocacy groups to facilitate the implementation of project results in clinical practice throughout the EU, and other non-EU European countries and the US.

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

A joint concerted initiative is required to create a practical implementation path in Europe for patient-centric blood samples in decentralised clinical trials, trials at home, and inclusion trials.

It is essential that industry partners from different sectors, e.g. the pharmaceutical industry, medical device manufactures, *in vitro* diagnostic companies, exchange knowledge and experience and contribute complementary infrastructures. Moreover, collaboration is required with clinical centres that are experienced in conducting decentralised trials, and with academia and SMEs that are experienced in methods and devices for microsampling and data collection and analysis. The engagement of patients, caregivers, and health care professionals is required to ensure the incorporation of the user experience into the novel infrastructure and logistics for patient-centric blood microsample collection at home. Lastly, the involvement of regulators, policy makers, payers, and HTA experts will facilitate the acceptance of the microsampling logistics model.

It is crucially important to develop a harmonised approach that is both acceptable and accessible to all stakeholders in the healthcare systems to ensure implementation across Europe, and this can be best assured under a public-private partnership.

Pre-identified industry consortium and contributing partners

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:

Eli Lilly (‘Lead’), Pfizer, MSD, Bayer, Novartis, Gilead, Astra Zeneca, Servier, GSK, Becton Dickinson, Labcorp, Q2labs solutions, Roche.

In addition, the following contributing partners will participate to the IHI project: JLL, Miebach Consulting.

In the spirit of partnership, and to reflect how IHI 2-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 stage 2, 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 is up to EUR 4 412 556.

- The indicative in-kind and financial contribution from industry partners is EUR 3 493 000.

- The indicative in-kind contribution from IHI JU contributing partners is EUR 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 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.

Indicative duration of the action

The indicative duration of the action is 42 months.

This duration is indicative only. At stage 2, the consortium selected at stage 1 and the predefined industry consortium and contributing partners may jointly agree on a different duration when submitting the full proposal.

Contribution of the pre-identified industry consortium and contributing partners

The industry consortium and contributing partners expect to contribute to the IHI project by providing the following expertise and assets:

- Grant administration:
  - To provide legal administration.
- Clinical trial and medical expertise:
  - To design the protocol of the umbrella / master study.
- Technologies:
  - Analytical techniques and sample analysis.
  - Microsampling techniques and provision of 1 device for the collection of capillary blood of the finger stick
  - Relevant samples might be provided.
- Logistics:
  - To identify and audit device vendors, logistics and telehealth partners.
  - To define acceptable sample quality, collection compliance tests, and shipment requirements ensuring appropriate sample bioanalysis given collection (including at-home collection) and shipment.
  - To confirm accessioning processes needed, reporting requirements, and the data management model.
- Training materials:
  - Expertise in defining needed support for use of devices, providing guidance in feedback collection and guiding principles for developing training materials for patients, caregivers and healthcare professionals.

    - To facilitate user group, technical and compliance Key Opinion Leader (KOL) panel discussions.

- Integration of requirements of regulatory authorities, HTA, payers, policy makers, and advocacy groups:
    - To prepare an overview of the regulatory landscape of microsampling at home in Europe.
    - To interact with regulatory authorities, HTA, payers, policy makers and advocacy groups to facilitate acceptability of the microsampling logistics modelling and its implementation throughout the EU and harmonization with efforts in other non EU-European countries and the USA.

Furthermore, the industry consortium will help with data flow, data management, operational support for clinical sites, project management, data and knowledge management, and the communication and dissemination of results. It will also provide contributions to joint meetings and steering committees, networking, exploitation and sustainability.

Applicant consortium

The stage 1 applicant consortium is expected, in the submitted short proposal, to address the scope and deliver on the expected outcomes of the topic, taking into account the expected contribution from the pre-identified industry consortium and contributing partners.

The applicant consortium is expected to address all the research objectives and make key contributions to the defined deliverables in synergy with the industry consortium. The focus of this project is not on development of novel devices or assays, but on integration of existing innovative technologies to establish the infrastructure and logistics for patient-centric blood microsample collection at home in Europe.

Applicant consortia should bring together partners with relevant expertise such as patients and patient representatives, patient-centric organisations, healthcare professionals, clinical trial centres with experience in decentralised trials, research organisations, and health technology developers. SMEs are encouraged to join the consortium, in particular those with expertise in various methods and devices that enable microsampling. Moreover, the participation is encouraged of SMEs which have expertise in interaction with patient groups, collecting user experience data and prioritising patient care needs, and the development of training materials for patients, caregivers and healthcare professionals. For facilitating acceptability and implementation of the microsampling logistics model across Europe, input from other relevant stakeholders, in particular regulatory agencies, payers, HTA bodies and advocacy groups would be necessary.

Applicants should clearly outline their approach for data capture, storage and sharing within the consortium as well as sharing results through peer-reviewed publications or other mechanisms. They must ensure that the relevant results and data repositories will be sustainable after the end of the project and made public.

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

- Grant administration:
    - To provide financial administration, submission of deliverables, periodic reports etc.
- Project management:
    - To coordinate internal communication and meetings, general oversight and management of communication, exploitation and dissemination activities, risk management.
    - To provide and maintain an IT infrastructure, to develop and implement an efficient data governance and management strategy of the joint consortium according to adequate standards and deliver the “Data Management Plan”.

    - To coordinate networking, joint activities and synergies with other European initiatives, or other relevant groups (e.g. patient-centric organisations, advocacy groups).

    - To develop a strategy for the exploitation and sustainability of project results and outcomes and deliver the “Exploitation and Sustainability Plan”.

- Umbrella / master study:

    - To obtain the necessary authority approvals, develop participant / patient facing materials, provide recruitment of participants / patients and conduct the umbrella / master study including the collection of biological samples.

- Technologies:

    - To analyse samples according to the protocol.

    - To perform statistical evaluations of concordance according to existing regulatory guidance for routine clinical assays.

    - To provide microsampling techniques and at least 1 device for the collection of capillary blood of the upper arm.

- Logistics:

    - To develop logistical capability around implementing new technologies for microsampling, work with device vendors on ordering devices, develop protocols for the testing of microsampling devices, act as investigative sites to test devices including Institutional Review Boards (IRB), consents etc., and train participants on devices.

- Training materials:

    - To engage and activate patients, caregivers, clinicians, and hospitals and obtain feedback on the support needed, develop questionnaires to collect their experience, perform data analysis, assess acceptability and concerns, and develop and refine training materials for different recipients.

- Interactions with regulatory authorities, HTA bodies, payers, policy makers, and advocacy groups:

    - To contribute to the regulatory landscape for microsampling at home in the EU and in other non-EU European countries.

    - In conjunction with industry, to discuss with regulatory authorities, HTA bodies, payers, policy makers, and advocacy groups the acceptability and implementation of the microsampling logistics modelling in the EU and harmonisation with efforts in other non-EU European countries and the US.

    - To prepare relevant documents of the approach and the results being generated by the project (e.g. briefing books, EMA guidance document).

At stage 2, the consortium selected at stage 1 and the predefined industry consortium and contributing partners 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 stage 1.

Dissemination and exploitation obligations

The specific obligations described in the Conditions of the calls and calls management rules under “Specific conditions on availability, accessibility and affordability” do not apply.

References

[1] Fantana AL, Cella GM, Benson CT, Kvedar JC, The Future of Drug Trials Is Better Data and Continuous Monitoring, Harvard Business Review, 2019 https://hbr.org/2019/05/the-future-of-drug-trials-is-better-data-and-continuous-monitoring.

[2] Wickremsinhe ER, Fantana AL, et al. Standard Venipuncture Versus a Capillary Blood Collection Device for the Prospective Determination of Abnormal Liver Chemistry. JALM 2022 (accepted for publication).

[3] CLSI. Measurement Procedure Comparison and Bias Estimation Using Patient Samples. CLSI guideline EP09c, Wayne, PA: Clinical and Laboratory Standards Institute; 2018.