



# IHI 2<sup>nd</sup> Call for proposals



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## Introduction

The Innovative Health Initiative Joint Undertaking (IHI JU) is a partnership between the European Union and industry associations representing the sectors involved in healthcare, namely COCIR (medical imaging, radiotherapy, health ICT and electromedical industries); EFPIA, including Vaccines Europe (pharmaceutical industry and vaccine industry); EuropaBio (biotechnology industry); and MedTech Europe (medical technology industry).

IHI JU aims to pioneer a new, more integrated approach to health research and builds on the experience gained from the Innovative Medicine Initiative 2 Joint Undertaking (IMI2 JU).

IHI JU aims to translate health research and innovation into real benefits for patients and society, and ensure that Europe remains at the cutting edge of interdisciplinary, sustainable, patient-centric health research. Health research and care increasingly involve diverse sectors. By supporting projects that bring these sectors together, IHI JU will pave the way for a more integrated approach to health care, covering prevention, diagnosis, treatment, and disease management.

As current health challenges and threats are global, IHI JU should be open to participation by international academic, industrial and regulatory actors, in order to benefit from wider access to data and expertise, to respond to emerging health threats and to achieve the necessary societal impact, in particular improved health outcomes for Union citizens.

## Topics Overview

<p><b>IHI-2022-02-01</b></p> <p><b>Cardiovascular diseases - Improved prediction, prevention, diagnosis and monitoring</b></p>	<p>The maximum financial contribution from IHI JU is up to EUR 11 179 000.</p> <p>The indicative in-kind &lt;and financial&gt; contribution from industry partners is EUR 8 979 000.</p> <p>The indicative in-kind contribution &lt;and financial&gt; from IHI JU contributing partners is EUR 2 200 000.</p> <p>The indicative in-kind contribution from industry partners may include in-kind contributions to additional activities.</p>	<p>Research and Innovation Action (RIA)</p> <p>Two-stage submission and evaluation process.</p> <p>Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.</p>
<p><b>IHI-2022-02-02</b></p> <p><b>Setting up a harmonised methodology to promote uptake of early feasibility studies for clinical and innovation excellence in the European Union</b></p>	<p>The maximum financial contribution from IHI JU is up to EUR 10 750 000.</p> <p>The indicative in-kind &lt;and financial&gt; contribution from industry partners is EUR 10 750 000.</p> <p>The indicative in-kind contribution from industry partners may include in-kind contributions to additional activities.</p>	<p>Research and Innovation Action (RIA)</p> <p>Two-stage submission and evaluation process.</p> <p>Only the applicant consortium whose proposal is ranked first at the first stage is invited for the second stage.</p>

# Topic 1: Cardiovascular diseases - improved prediction, prevention, diagnosis, and monitoring

## Expected impacts to be achieved by this topic

Cardiovascular disease (CVD) remains one of the leading causes of death globally and, as such, has a major impact at a personal, societal, and economic scale. Over 60 million people in the EU live with CVDs, at an economic cost of EUR 210 billion annually.

CVD risk assessment is not fully implemented in many clinical practices across Europe<sup>1</sup>, and treatment of CVD is commonly practiced as with a “one size fits all” approach, meaning that all patients are treated with a standard medical regimen regardless of risk level. The prevalence of well-established CVD risk factors such as obesity, diabetes, and chronic kidney disease is rising, and combined with an ageing population in Europe, the urgency for a more personalised approach to cardiovascular risk assessment becomes evident.

The generation of a personalised risk-benefit approach, based on data derived from transcriptomic, proteomic and multimodality imaging studies, combined with data from electronic interventions via CE certified wearable devices, such as smartwatches or activity trackers, as well as routine clinical data from medical devices, will contribute to all of the following impacts:

- Accuracy of diagnosis and efficacy of treatment will increase thanks to an individualised sub-phenotype-risk approach which will allow for risk-focused targeted therapy.
- Patients will be empowered and encouraged to take control over their health by accessing an integrated overview, including biometric data derived from wearables, of their health information, which can also be used for a more informed dialogue with their healthcare provider(s).
- Early diagnosis of CVDs, combined with better understanding of the mechanisms involved, will lead to the development of more cost-effective strategies, and the identification of new care pathways.

## Expected outcomes

The results of the selected project will provide the basis for better primary and secondary prevention of CVD. The goal is to identify existing comprehensive CVD and heart failure (HF) patient datasets (with contextual parameters e.g., behavioural, socioeconomic, gender, ethnicity) and integrate them with data from diagnostic tools (e.g. wearables, imaging devices, bio samples / biopsies) and routine clinical practice. This will provide the basis for independently validated prediction models for improving the stratification of patients, and reveal insights to achieve earlier intervention. Additionally, the project will leverage developed algorithms to define and validate care pathways that tailor therapy towards individual patient needs and compare it to the “one-size-fits-all” approach.

<sup>1</sup> Rossello X, Dorresteyn JA, Janssen A, Lambrinou E, Scherrenberg M, Bonnefoy-Cudraz E, Cobain M, Piepoli MF, Visseren FL, Dendale P, This Paper Is A Co-Publication Between European Journal Of Preventive Cardiology European Heart Journal Acute Cardiovascular Care And European Journal Of Cardiovascular Nursing. Risk prediction tools in cardiovascular disease prevention: A report from the ESC Prevention of CVD Programme led by the European Association of Preventive Cardiology (EAPC) in collaboration with the Acute Cardiovascular Care Association (ACCA) and the Association of Cardiovascular Nursing and Allied Professions (ACNAP). Eur J Prev Cardiol. 2019 Sep;26(14):1534-1544. doi: 10.1177/2047487319846715. Epub 2019 Jun 24. PMID: 31234648.

This project is expected to achieve all of the following outcomes:

- Identification of relevant data sets, for instance derived from classical diagnostic screening; in-vitro diagnostics; 'multi-omic' platforms (comprising genomic, transcriptomic, proteomic and multimodality imaging data, most preferably with multiple timepoint assessments to ascertain the directionality and dynamics of relevant changes); continuous glucose monitoring (CGM) data, continuous electrocardiogram (ECG) data from wearables. In addition HF and activity data, wearable devices, digital health applications and routine clinical practice.
- Leverage data in currently available federated databases with 'open access' generated during, for example, IMI1/IMI2 projects in compliance with GDPR (General Data Protection Regulation), such as results/data/biomarkers/electronic health records provided by project participants, adding to the knowledge base.
- Demonstration of the utility of biomarker combinations including data from different modalities e.g., wearables, smart (acute or chronic) care setting devices, imaging/screening for the diseases and comorbidities.
- Based on existing biomarker combinations, determination of whether new biomarkers are needed for detecting patients at risk.
- Developed and/or evaluated artificial intelligence (AI) models that, using data from various sources, can identify patient subgroups who require and respond differently to the prevention and/or treatment of atherosclerotic cardiovascular disease (ASCVD) and HF in clinical practice.
- Identification of previously undiagnosed subgroups of ASCVD and HF patients, for instance people with insulin resistance, diabetes, and obesity, into clinically meaningful subgroups.
- Documentation and analysis of patient preferences regarding information, diagnosis and treatment of CVD, as well as requirements and preferences of individuals to share their data.
- Integration of patient data (e.g. via a federated database concept) to enable a holistic overview of specific patient groups to enable more effective and efficient disease management and execution of screening programmes and individual treatment tailoring.
- Inclusion of validated patient reported outcome and experience measure (PROMs and PREMs) data including biophysical, mental and psychosocial parameters with the aim of using it in a clinical setting. This may include, but is not limited to, measures on quality of life, sleep quality, physical activity, emotional stress, satisfaction with treatment, healthcare service experience.
- Leveraging developed algorithms/decision trees to define and validate care pathways that tailor therapy towards individual patient needs and compare them to the "one-size-fits-all" approach.
- Sustainability of relevant results and data repositories.
- Identification of incentives that reward positive health behaviour and motivate consistent and continuous data generation especially when health status has changed.
- Utilisation of the knowledge gained from the project to facilitate and guide better prevention, considering the patient perspective.
- Data collection in the patient population with type 1 diabetes that historically has been excluded from clinical trials. Identifying the highest-risk individuals (in the paediatric, adolescent and adult populations, among others) to aim for more intensive contemporary CVD risk lowering agents (such as

glucose, lipid and blood pressure lowering), and other, ideally personalised, cardioprotective adjunct therapies could help reduce the burden of CVD and contribute to improving outcomes in type 1 diabetes.

- Data collection in patient populations with other (genetically defined) predispositions to CVD and HF, that historically have been excluded from clinical trials. Identifying the highest-risk individuals could contribute to improving the outcomes in people with obesity, type 2 diabetes or (genetic) predisposition to CVD/HF.

## Scope

The overall aim of the project is to provide tools for the earlier diagnosis of atherosclerosis and heart failure as well as earlier identification of patients at risk. This includes biomarker or predictive algorithms to assess changes in risk and stratify patients according to individual responses to therapeutic intervention. Currently, patient data from various sources such as devices, intake forms, and diagnostic and exploratory tests are not integrated or monitored to give a complete understanding of the patient's disease state. Integration of these data sets, e.g. by a federated database, and its accessibility to healthcare providers and researchers will provide better understanding to help detect, monitor, and treat ASCVD and HF. The selected project should clearly outline their approach for data capture, storage and sharing, for instance data federation, or an open, centralised database architecture. The proposed data management strategy should be sustainable, seek synergies with other relevant projects, and align with the FAIR principles<sup>2</sup>. To fulfil this aim, the selected project should:

- 1 Increase our understanding of the initial hallmarks of disease, which will allow for a better identification of individuals at risk for ASCVD and HF at a young age, and the creation of a clinical risk profile based on a multi-omic approach (e.g. genetic markers, transcriptomics, proteomics, and in depth multimodality imaging data) in adolescents who have either genetic and/or enrichment of specific endpoint associated risk factors (obesity, chronic kidney disease, type 1 diabetes, type 2 diabetes, genetic preponderance for HF and increased atherosclerosis).
- 2 Generate and validate a risk model better than currently used risk engines such as SCORE, by evaluating whether and to which extent risk factors identified in large prospective CVD primary prevention cohorts are predictive in a secondary prevention setting. The data from surrogate markers such as imaging, electronic health records (EHR), and predictive markers (plasma based multi-omics), as well as data from wearables, will generate a more refined risk engine.
- 3 Outline the extent to which social, ethical, and regulatory implications can be considered and quantified in the new risk models and gauge the potential additive value of data generated by wearable devices in current healthcare systems. Outline the extent to which regional and legal issues have an impact, and what models and methodologies can be used to examine this. Moreover, as the risk-benefit of wearable derived data will be ascertained in individuals who are likely to be frontrunners in the adoption (i.e. people with type 1 diabetes and people with a (genetic) risk for premature atherosclerosis and/or HF), the project should include behavioural elements to be analysed to provide suggestions to increase adoption in other populations.
- 4 Model short- and long-term economic and public health morbidity and mortality benefit/risk assessments of therapeutic intervention in people at risk with the new risk models to prevent or delay onset of CVDs.
- 5 Develop a decision tool that will allow a physician to select the intervention to best address ASCVD and HF in an individual patient. The tool will provide a risk-benefit profile, helping the physician and the patient in a decision-making process, integrating also patient reported outcome and experience measure (PROMs and PREMs) data.
- 6 Explore possibilities for novel methods of clinical development and trial execution. Based on learnings about risk prediction and pathophysiological modelling, novel surrogate endpoints may be considered for a risk-based cardiovascular outcome trial approach. The project generated from this

<sup>2</sup> <https://www.go-fair.org/fair-principles/>

topic could provide an exploratory and interactive platform to discuss the validity of novel methods of evidence generation, such as the use of data from wearable devices. The project should pave the way to transform the rather static phase 3 clinical trial approach into a more agile (more inclusive/enriched patient population, faster, cost-effective etc.) and sustainable part of clinical development. Specifically, the project should engage in the Regulatory Science Research Needs initiative, launched by the European Medicines Agency (EMA), assessing the utility of real-world healthcare data to improve the quality of randomised controlled trial simulations (H2.3.3). During the COVID-19 pandemic, the world has experienced a transition to virtual and remote care as more and more patients connect with their health care teams online. This presents an enormous opportunity and benefits for patients. A pathway forward could be to through use of real-world evidence (RWE) data to address sex, ethnicity and race disparities in cardiovascular outcome trials and better promote CV management.

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

The data deemed useful in redefining and reclassifying the CVD risk profile are stored in a multitude of databases of clinical academic institutions (large cohorts of patients with multimodality imaging for example), research institutes (data about genetic risk markers; genome wide variation), large pharmaceutical companies (intervention studies with well documented parameters over time, in conjunction with plasma and genetic biobanks), medical device manufacturers (large numbers of datasets using the specific focus of the company e.g. device treatment data, proteomics data, specific novel biomarker tests), and healthcare wearables (large datasets on biometrics).

Concerted action is needed for sustainable data collection that explores new ways of leveraging existing 'open access' databases (see scope), and the subsequent analysis should be performed by the different stakeholders with a multitude of areas of expertise working in aggregated task forces. The subsequent question on whether and to which extent the data derived can and should be used in clinical care and/or clinical trials should be answered in close collaboration with payers, patients, and regulators.

Additionally, to change behaviours in a clinical practice setting where patients are empowered and encouraged to take control over their health and to secure a patient participatory research approach (e.g. through PROMs and PREMs), supported by interest organisations within the area of public health, a combined effort is needed under a public-private partnership that promotes the interchange of knowledge and experience. "Big cohort data" derived from medical care interactions, complemented by use of patient empowered information from biology, behaviour, social networks, geography, and the macroenvironment, should have the potential to yield real-world / real time answers to questions on the efficacy of treatments. Additionally, through a cross-sectorial collaboration focused on clinical research and public health, we can learn to recognise and appropriately address sex<sup>3</sup>, race and cultural biases and disparities in the healthcare delivery process of CVD management, whilst enabling novel ways to deliver people-centred, safe, effective, cost-effective, and affordable health solutions.

### **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:

Novo Nordisk ("Lead"), Becton Dickinson, Evotec, Fresenius, Huawei, Philips, Roche Diagnostics, AstraZeneca, Eli Lilly, Amgen

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

- JDRF

<sup>3</sup> Sex differences in quality indicator attainment for myocardial infarction: a nationwide cohort study | Heart (bmj.com)

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 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 up to EUR 11 179 000.
- The indicative in-kind contribution from industry partners is EUR 8 979 000.
- The indicative in-kind and financial contribution from IHI JU contributing partners is EUR 2 200 000.

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 48 months.

This duration is indicative only. At stage 2, the consortium selected at stage 1 and the predefined industry consortium and contributing partner 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 partner expect to contribute to the IHI project by providing the following expertise and assets:

- Data: data from clinical trials, biobank data, real world data, wearables and other smart devices, algorithms, identification of risk, sensor technology, telecommunication, data management/hospital information system, AI, mobile technology
- Expertise: medical expertise, bioinformatics, data science, public health, patient input, clinical and regulatory expertise, early identification from wearables
- Technology: such as wearable devices, mobile technology, telecommunication technology and other smart devices that will enable the recording of new data.
- The allocation of the EUR 2 000 000 financial contribution from JDRF will be decided by the full consortium at stage 2 when preparing the full proposal.

### **Applicant consortium**

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

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. Applicants must ensure that the relevant results and data repositories will be sustainable after the end of the project(s) and made public, in compliance with the guidelines on the European Health Data Space (EHDS)<sup>4</sup>. Potential spin offs from the project should be identified. The focus of this project is not target identification, but rather on leveraging currently available data for risk and outcome prediction tools, and subsequent prescription refinement. These are to be generated by artificial intelligence approaches, as brought in by the various project participants.

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

- Access to cohorts and databases of cardiovascular disease including data on people with atherosclerosis and heart failure.
- Access to cohorts of young adults and adults who have type 1 diabetes, type 2 diabetes, obesity or genetic preponderance for HF and increased atherosclerosis with early CVD risk markers such as inflammatory and mitochondrial biomarkers, aortic and cardiac structure and function, carotid atherosclerosis and arterial stiffness.
- Access to pre-existing clinical cohorts with as broad and detailed relevant phenotyping as possible and access to biobanked specimens for selected biomarker analysis wherever available (including documented informed consent), ideally including cohorts with, when relevant, different treatment approaches.
- Expertise in development of new biomarkers and genetic factors in type 1 and type 2 diabetes in CVD. Expertise in behavioural psychology models.
- Expertise in AI and software.
- Expertise in devices and digital health.
- Economic benefit-risk modelling should engage multidisciplinary teams of patient representatives, health care economists, and health care payers.
- Engagement with patient representatives and other interest organisations within the area of public health.

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<sup>5</sup> under “Specific conditions on availability, accessibility and affordability” do not apply.

<sup>4</sup> [https://ec.europa.eu/health/ehealth/dataspace\\_en](https://ec.europa.eu/health/ehealth/dataspace_en)

<sup>5</sup> See section 4.2.3.2 of this amended Work Programme

## Topic 2: Setting up a harmonised methodology to promote uptake of early feasibility studies for clinical and innovation excellence in the European Union

### Expected impacts to be achieved by this topic

By setting up a harmonised EU methodology to promote the uptake of early feasibility studies (EFS)<sup>6</sup>, this topic will improve patients' access to health technologies, including digital technologies, support technological innovation, and contribute to a smoother development process for these health technologies. As such it will contribute to all the following IHI scientific, technological and economic expected impacts:

- Improve quality of clinical evidence on health technology innovation generated through earlier clinical experience obtained in the development process from an EFS.
- Facilitate uptake of early feasibility studies in health technology development, including for digital technologies.
- Increase the attractiveness of conducting clinical research and trials for healthcare technologies in the EU, including for SMEs, spin-offs and start-ups.
- Enable faster translation of health technology innovation into practice with increased access to treatment for patients, especially those with medical conditions that have limited or no alternative therapeutic options.
- Better refined patient populations, their carers or patient representatives, and strengthened understanding of disease management and functional impairments, and treatment options.

### Expected outcomes

The research and innovation action to be supported under this topic is expected to deliver results including a methodology for EFS in the EU, to facilitate compliance with the relevant legislation applicable in the EU, and a stakeholder network. It will contribute to all of the following expected outcomes:

- Patients and/or their representatives are engaged and contribute from the start of the development process of innovative health technologies.
- EU-wide and national regulators, health technologies assessment (HTA) bodies and notified bodies benefit from novel and robust methodologies, gain early knowledge on innovations, and can better anticipate and plan conformity assessment processes.
- Researchers, healthcare professionals, medical societies, and hospitals:
  - contribute to the early generation of quality data;
  - strengthen our understanding of disease management and treatment options that could inform future medical guideline development;
  - provide input on innovation development;

<sup>6</sup> Early feasibility studies are specified in the Questions & Answers Guidance from the Medical Device Coordination Group of April 2021: [https://ec.europa.eu/health/system/files/2021-04/mdcg\\_2021-6\\_en\\_0.pdf](https://ec.europa.eu/health/system/files/2021-04/mdcg_2021-6_en_0.pdf)

- take part in the development of “hubs of clinical excellence”, thereby attracting investment into existing research and innovation as well as other areas (spin-off technologies).
- Health technology developers including those developing medical devices, drug-device combination products, imaging equipment and in-vitro diagnostics as well as SMEs, will have:
  - a controlled opportunity to assess their technologies and develop methods and best practices to support them in designing and conducting EFS when relevant.
  - early insights into the technology concept, patient characteristics and human factors that may impact technological performance, technology safety, future technological modifications or operator technique refinements.
  - a framework that will help to inform the subsequent development phase. In particular it will aid designing higher quality clinical studies while mitigating future patient risk, at the same time facilitating the conduct of future clinical investigations in broader patient populations.
- For SMEs, particularly, having access to a methodology and stakeholder network can facilitate the conduct of early feasibility studies. The availability of high-quality data early in the health technology development process would further support investment and development decisions.

## Scope

The incremental development of innovative / breakthrough health technologies takes a long time, during which an innovation will have to successfully go through a process of testing and evidence generation before it can be launched.

- As part of this process, early feasibility studies provide the opportunity to capture relevant additional information for the intended use from the real-world setting that would not be possible in non-clinical studies (i.e. bench testing and animal studies) at a very early stage. EFS can make it possible to optimise design and gain necessary information before running a large clinical investigation.

Even if it is legally possible to undertake EFS in the EU, such studies are not yet widely used. Indeed, most EFS are run today outside of the EU, and primarily in the United States<sup>7</sup>.

This means that the EU may be at risk of losing out on an important opportunity to attract clinical research and further investments in innovation development to the region.

- This topic seeks to develop and validate a methodology for EFS that is compliant with EU regulations, including a working methodology, easily accessible online, with information on how to undertake such studies, the process and requirements to follow and fulfil.
- It also aims to bring together the relevant stakeholders that could have an interest in EFS and to facilitate use-cases where technologies would run the newly developed EFS methodological framework in order to test it and recommend any adjustments to be made to the methodology.

The project would entail the following:

- **Research & analysis**, including a review of existing international, EU and national guidelines, standards and best practice experiences. This would also include a survey of potential current gaps,

<sup>7</sup> US National Library of Medicine, ClinicalTrials.gov. Out of the 300 EFS referenced, only 8 are conducted in Europe as per September 2020.

barriers and challenges to undertaking EFS in the EU, taking into account the interplay between the different relevant current and future EU regulations.

- **Development of an EU methodology for EFS**
  - The methodological framework would include:
    - i) definition and scope, including legal considerations;
    - ii) the place of EFS in the development pathway of health technologies and when there is an added value for EFS;
    - iii) the type of data required to conduct an EFS (technical data, preclinical data, number of patients, etc.);
    - iv) process evaluation, methods and tools, including statistical tools adapted to the analysis of EFS results, and tailored to the needs and specificities of different health technologies, including digital and mobile health technologies;
    - v) the contribution of EFS to making more patient-centred devices;
    - vi) the contribution of EFS to the development of training plans for healthcare professionals that would in turn improve the use of devices.
  - Recommendations for best practices, addressing also ethical aspects from the outset, and contractual elements.
  - Development of a sustainable, freely-accessible online portal, hosted and maintained by the consortium, which would act as a repository for the methodological framework and the best practices, and which would facilitate interactions between stakeholders with an interest in EFS.
- **Facilitate the creation of a sustainable stakeholder network at national and EU level**
  - The network would promote the conduct of EFS and continue to gather experience from subsequent studies where appropriate and relevant to inform the EU EFS methodology.
  - Target groups include patient organisations and representatives, healthcare professionals, research institutions and hospitals, health technology developers, including SMEs, regulators, and HTA bodies.
- **The selection of dedicated use-cases to inform, refine and validate the framework**
  - The purpose of selected use-case technologies will be to undertake an EFS in the EU, whilst applying the methodology developed by the selected project, in order to test the methodological framework and evaluate the benefits for the conformity assessment process and patient access.
  - Learnings acquired on the use-cases will be used to adapt and finalise the methodological framework, and, where necessary, the blueprints and templates.
  - During the project execution, the consortium will define specific criteria and processes to determine which use-cases can be selected. Indicators of success will be developed and defined within each pilot trial, to compare it to other trials, and used as potential stop criteria.

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

Experience from other regions outside the EU has shown<sup>8</sup> that enabling public-private collaboration and endorsing the need for more standardisation on EFS could support their uptake, thereby supporting patient access to novel technologies<sup>9</sup>.

As such, the topic seeks to contribute to a strengthened evidence-generation and cross-sectoral and multi-disciplinary innovation ecosystem by facilitating collaboration and early exchange and facilitating the creation of processes to conduct EFS.

To achieve these objectives, it is essential that different industry sectors come together to exchange knowledge and experience. Moreover, this cross-sectorial collaboration must be extended to academia, healthcare professionals, patients, research organisations, regulators, HTA bodies, and SMEs to ensure a harmonised understanding of the best practices and one comprehensive methodology for EFS.

IHI provides a unique opportunity to enable a unified approach towards promoting the uptake of EFS in order to ultimately strengthen clinical development excellence and the innovation attractiveness of the EU.

## Pre-identified industry consortium

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

Edwards Lifesciences AG (“Lead”), Medtronic, W.L. Gore & Associates, Philips Medical Systems B.V., Syntes, Abbott

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 up to EUR 10 750 000.
- The indicative in-kind and financial contribution from industry partners is EUR 10 750 000.

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

## Indicative duration of the action

<sup>8</sup> [MDIC-EFS-Blueprint-for-EFS-Success-2016.pdf](#); Holmes, D et al. (2018) [The 21st Century Cures Act and Early Feasibility Studies for Cardiovascular Devices: What Have We Learned, Where Do We Need to Go?](#) JACC: Cardiovascular Interventions, 11(21), 2220 – 2225

<sup>9</sup> David R. Holmes, Jr., MD, EFS Symposium: Implementation Strategies for Early Feasibility Studies TVT Chicago IL June 12-15, 2019, [EFS-Symposium-TVT-EFS-Symposium-Implementation-Strategies-for-Early-Feasibility-Studies.pdf \(mdic.org\)](#)

- The indicative duration of the action is 48 months.
- This duration is indicative only. At stage 2, the consortium selected at stage 1 and the predefined industry consortium may jointly agree on a different duration when submitting the full proposal. Where possible the duration of the project could be shortened in order to expedite the delivery of impacts in terms of clinical development excellence and the attractiveness of the EU for innovation.

### Contribution of the pre-identified industry consortium

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

- Legal, ethics & compliance, regulatory, R&D, and clinical expertise:
  - input to survey exercise, i.e. industry perspective on barriers to undertake EFS in EU;
  - dissemination of surveys to stakeholders already engaged in EFS, with potential interviews;
  - contribution to the development of the methodology, including best practices;
  - assessment of regulatory and ethical provisions with which EFS should comply.
- Potentially breakthrough technologies across disease areas to test the EFS methodology and inform any further adaptations.
- Project management, dissemination and communication.

### 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.

Applicant consortia should bring together partners with relevant expertise such as regulators, healthcare professionals, patients and patient representatives, health technology developers, research organisations, academia, biostatisticians, legal experts, ethicists.

For the development of the methodology, input from other relevant stakeholders, in particular HTA bodies would be necessary.

Participation of SMEs is encouraged with the aim of ensuring a wide applicability of the methodology and valorising innovations of SMEs for the benefit of citizens. Moreover, SMEs, particularly those with expertise in legal, regulatory and ethical matters, are encouraged to join the consortium to support the development of relevant criteria for the methodology.

The composition of the consortium should also ensure a broad geographical representation of European countries. Diversity aspects, including sex and gender, should be considered in carrying out the relevant activities.

At stage 2, the consortium selected at stage 1 and the predefined industry consortium 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<sup>10</sup> under “Specific conditions on availability, accessibility and affordability” do not apply.

<sup>10</sup> See section 4.2.3.2 of this amended Work Programme