Topic 2: Setting a harmonised methodology to promote uptake of Early Feasibility Studies for clinical and innovation excellence in the European Union

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.

Expected impacts to be achieved by this topic

By setting a harmonised methodology to promote the uptake of Early Feasibility Studies (EFS)[1], this topic will improve patients' access to health technologies including digital technologies and support technological innovation, as well as contribute to a smoother development process of these health technologies. As such it will contribute to the following IHI JU 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 early feasibility study (EFS).
- Facilitate uptake of early feasibility studies in health technologies development, including 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 for patients, especially in medical conditions that have limited or no alternative therapeutic options, with streamlined access to treatment in the EU.
- Better refined patient populations and strengthened understanding of diseases management and treatment options.

Expected outcomes

The project 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 that are directed, tailored and contributing to all of the expected outcomes:

- Patients are engaged and contribute from the start of the development process of innovative health technologies.

INDICATIVE TEXT

[1] 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

- EU-wide and national regulators, and health technologies assessment (HTA) bodies, 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 the understanding of diseases management and treatment options that could inform future medical guideline development,

    - provide input on innovation development, and

    - 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:

    - controlled opportunity to assess their technologies as well as 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.

    - 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 set 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 such 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 allow for optimising design and gaining necessary information before running a large clinical investigation.

INDICATIVE TEXT

Even if it is legally possible to undertake EFS in the EU such studies are not yet widely taken up in the EU. Indeed, most EFS are run today outside of the EU, and primarily in the United States.[2]

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

This topic seeks to develop and validate a methodology for EFS 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 the framework and inform any adjustments to be made to the methodology.

The project would entail the following:

- **Research & Analysis,** including review of existing guidelines, experiences, a survey on potential current barriers and challenges to undertake EFS in the EU**,** taking into account the interplay between the different relevant current and future EU regulations.

- Development of methodology for EFS

    - The methodological framework would include: i) definition and scope, including legal considerations, ii) 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) methods and tools, including statistical tools adapted to the analysis of EFS results and tailored to the needs of different health technologies, v) contribution of EFS to making more patient-centered devices, vi) contribution of EFS to the development of training plans for health care professionals that would in turn improve the use of devices.

    - Recommendations for best practices, addressing also ethical aspects and contractual elements.

    - Development of a permanent online portal, hosted and maintained by the consortium acting as a repository for the methodological framework and the best practices, and which will 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, healthcare professionals, research institutions and hospitals, health technology developers, including SMEs, regulators, and HTA bodies.

INDICATIVE TEXT

[2] US National Library of Medicine, ClinicalTrials.gov. Out of the 300 EFS referenced, only 8 are conducted in Europe as per September 2020.

- **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 on 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, consortium will define specific criteria and process to determine which use-cases can be selected.

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

Experience from other regions outside the EU has shown[3] 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.[4]

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

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

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

Pre-identified industry consortium

In the spirit of partnership, and to reflect how IHI JU 2-stage call topics are built upon identified scientific priorities agreed together with a number of proposing industrial beneficiaries, it is envisaged that IHI JU 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.

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[3] 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

[4] 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)

Indicative budget

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 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 delivery of impacts in terms of clinical development excellence and attractiveness of EU for innovation.

Contribution of the pre-identified industry consortium

The industry consortium expects to contribute to the IHI JU 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 survey to stakeholders already engaged in EFS, with potential interviews.
    - Contribution to the development of methodology, including best practices
    - Assessment of regulatory and ethical provisions to 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 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, health care professionals, patients, 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 to ensure a wide applicability of the methodology and valorise innovations of SMEs for the citizen’s benefit. Moreover, SMEs notably with expertise in

INDICATIVE TEXT

legal, regulatory and ethical matters are encouraged joining the consortium to support setting relevant criteria for the methodology.

The composition of the consortium should also ensure a broad geographical representation of European countries. Sex and gender aspects 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

To be determined

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