Harmonised approach to **E**arly **F**easibility **S**tudies for Medical Devices in the **E**uropean **U**nion **(HEU-EFS)**

Executive summary

Co-funded by the European Union

Disclaimer:

The Harmonised approach to Early Feasibility Studies for Medical Devices in the European Union (HEU-EFS) project is funded by the European Union, the private members, and those contributing partners of the IHI JU. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the aforementioned parties. Neither of the parties can be held responsible for them.

Background and rationale

European Union (EU) regulations mandate a lifecycle approach to generate clinical evidence for health technologies. Technological innovations must demonstrate to be worth spending, which means that an added value compared to the standard of care must be measured and demonstrated at the time of market authorization. Anyhow, the developmental process is long and costly, and needs to be carefully planned from the beginning to minimize late-stage pipeline failures, which very often depend on a lack of correct understanding of the market needs (Campbell et al, 2018;[1] Tarricone et al, 2020[2]). Manufacturers should develop an evidence-generation plan from the earliest stages of product development, involving all stakeholders, particularly regulators, to ensure that the product actually meets their expectations in terms of safety and efficacy. By building a robust business case from the earliest pre-market stages, developers can maximize the chances to invest time and money in generating evidence that really responds to the regulators and payers' needs. This approach to product development is essential to allow patients timely access to innovative medical technologies that actually protect and improve their health.

Early Feasibility Studies (EFS) are pre-market clinical studies formally recognized by the International Standard ISO 14155 *Clinical investigation of medical devices for human subjects – Good clinical practice* and can play a critical role in achieving these objectives.

Definition of EFS by ISO 14155

> 'A limited clinical investigation of a device early in development, typically before the device design has been finalized, for a specific indication (e.g. innovative device for a new or established intended use, marketed device for a novel clinical application). It can be used to evaluate the device design concept with respect to initial clinical safety and device clinical performance or effectiveness (if appropriate) as per intended use in a small number of subjects when this information cannot practically be provided through additional nonclinical assessments or appropriate nonclinical tests are unavailable. Information obtained from an early feasibility clinical investigation can guide device modifications. An early feasibility clinical investigation does not necessarily involve the first clinical use of a device.'

[1] Campbell B, Campbell M, Dobson L, et al. Assessing the value of innovative medical devices and diagnostics: the importance of clear and relevant claims of benefit. Int J Technol Assess Health Care. 2018;34(1): 419–424. doi: 10.1017/S0266462318000466.

[2] Tarricone R, Ciani O, Torbica A, et al. Lifecycle evidence requirements for high-risk implantable medical devices: a European perspective. Expert Rev Med Devices. 2020 Oct;17(10):993-1006. doi: 10.1080/17434440.2020.1825074.

EFS can contribute to increasing the efficiency and the effectiveness of the whole evidence generation process for MDs market access, providing a unique opportunity to collect relevant data at an early stage, inform the business case, and maximize the chances to develop innovative, cost-effective, safe MDs in the interest of patients, end-users, payers, and policymakers. EFS can be particularly impactful when applied to innovative, high-risk technologies, with lifesaving potential for patients with no alternative treatment options.

The US has been the first jurisdiction to recognize the potential impact of EFS on innovation in the MedTech sector. In 2013, the Food and Drug Administration (FDA) published a guidance on Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies,[3] as part of a broad review process aimed at contrasting the decline in clinical investigations on MDs conducted in the US, attract R&D investments, and facilitate early access for US patients to innovative technologies. Preliminary evidence on the FDA EFS program is based on data collected on a voluntary basis from study sponsors by the Medical Device Innovation Consortium (MDIC) and shows that the program has been successful in boosting the undertaking of EFS: since its implementation, there has been an increase in the number of EFS submitted in the US and an improvement in the efficiency of the approval process.

The need for an EU EFS program

Callea and colleagues (2022) showed that over 80% of EFS are conducted in the US and only 10.7% in the EU.[4] This is explained by the fact that, even if it is legally possible to undertake EFS in the EU, at present, there is neither a standardized procedural framework nor guidelines or common reference standards for this type of study in the EU.

An EU EFS program would be strategic to attract clinical research and investments in innovation development and strengthen the EU competitiveness and attractiveness versus other jurisdictions, one of the key goals of the EU4HEALTH Program 2021-2027. Moreover, it would play a pivotal role to ensure that public money is spent only on innovations that bring added value to society.

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[3] US Food and Drug Administration, Investigational device exemptions (IDEs) for early feasibility medical device clinical studies, including certain first-in-human (FIH) studies: guidance for industry and food and drug administration staff. 2013.

[4] Callea G, Federici C, Freddi R, Tarricone R. Recommendations for the Design and Implementation of an Early Feasibility Studies Program for Medical Devices in the European Union. Expert Rev Med Devices. 2022;19(4):315-325. doi: 10.1080/17434440.2022.2075729.

The need to develop a common, harmonized EU EFS program was recently recognized as a strategic priority by the European Commission and included in a call for proposals issued by the Innovative Health Initiative (IHI),[5] a public-private partnership between the European Commission and major industry associations in the life science sector.

The HEU-EFS Project

At the end of a two-stage competitive selection process, IHI awarded the 4-year project called Harmonised Approach to Early Feasibility Studies for Medical Devices in the European Union (HEU-EFS), which started in October 2023. The project is co-funded by IHI and 6 industry partners for a total budget of €19 million.

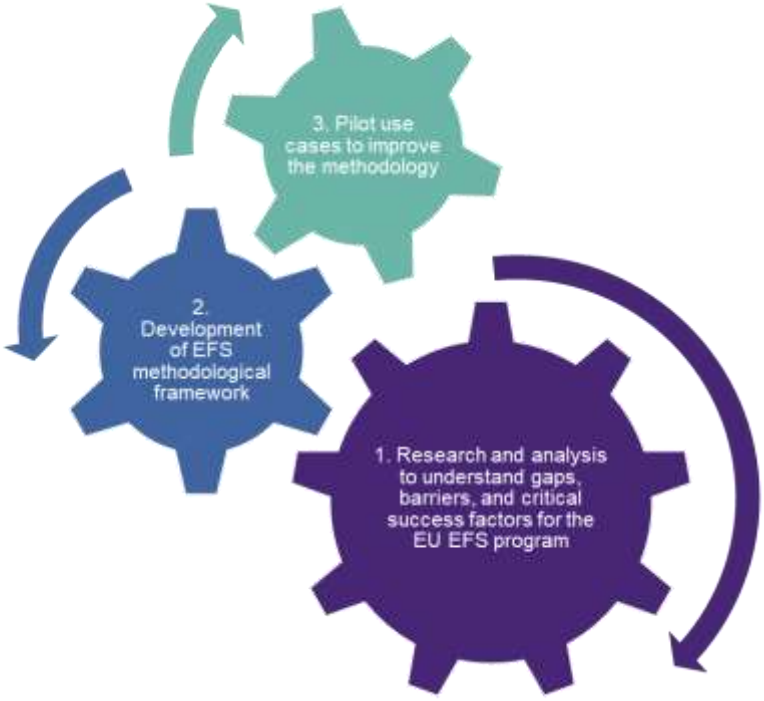
Aims, objectives and phases of the project

The overall goal of the initiative is to develop a harmonised methodology and enhance the uptake of EFS in the EU. This will be achieved through the pursuit of six specific project objectives:

1. Conduct research and analysis on state of play of regulatory framework and characteristics and impacts of pre-market programs.
2. Build a sustainable network of stakeholders to promote the implementation of EFS in the EU.
3. Develop a sound, widely applicable and harmonised EU methodology and recommendations to uptake EFS.
4. Undertake pilot use cases to test the proposed methodological framework.
5. Develop instruments to monitor the performance of the EU EFS program.
6. Implement a dedicated, sustainable, open access informative online portal dedicated to EFS and disseminate the project results and recommendations.

[5] https://www.ihi.europa.eu/apply-funding/ihi-call-2

The project will progress through three main phases:



The HEU-EFS Consortium

To achieve these objectives, the project will leverage on the expertise of 22 public and private partners and 16 affiliated entities, from 12 countries worldwide: Belgium, Denmark, France, Germany, Ireland, Italy, Spain, the Netherlands, Norway, Switzerland, the United Kingdom, and the United States. The consortium includes representatives of a wide range of relevant stakeholders:

Academia	Health care provider	HTA body	Patient organization	SME	Industry partner
• Bocconi University (coordinator) • Trinity College Dublin • University of Marburg	• Fundació Clínic per a la Recerca Biomèdica & Hospital Clínic de Barcelona • Assistance Publique Hôpitaux de Paris • Odense University Hospital • Fondazione Policlinico Agostino Gemelli	• Norwegian Institute of Public Health • Italian National Agency for Regional Healthcare Services	• European Patients' Forum • Global Heart Hub	• Carmat • Newronika • IdrisOncology BV • Qurasoft • Meditrial	• Edwards Lifesciences • Medtronic • Abbott • J&J • Philips Medical • WL Gore

The external Advisory Board

To ensure a comprehensive engagement of relevant stakeholders, the HEU-EFS project has appointed an external Advisory Board with representatives from EU competent authorities, notified bodies, clinical and biomedical engineering professional associations, members of national ethics committees, the European Trade Association for Medical Devices, and independent experts.

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