

Harmonised approach to **Early Feasibility Studies** for Medical Devices in the **European Union (HEU-EFS)**

WP2 Research and analysis on regulatory framework, and institutional and organizational characteristics of EU competent authorities

DELIVERABLE 2.3

Recommendations for HEU-EFS on the
current state of play of pre-market
programs and EFS, of regulatory
framework and institutional and
organizational characteristics of EU
competent authorities

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.

Project Acronym	HEU-EFS
Project Title	Harmonised approach to Early Feasibility Studies for Medical Devices in the European Union
Project Coordinator	Giuditta Callea
Grant Agreement Number	101112185
Project Duration	October 2023 – October 2027 (48 months)
Deliverable Number	D2.3 Recommendations for HEU-EFS on state of play of regulatory framework and institutional and organizational characteristics of EU competent authorities
Work Package	WP1, WP2
Task	Task 2.4 Development of recommendations
Lead Beneficiary	TCD, UB (Task 2.4)
Status	Final
Dissemination Level	PU
Type	R – Document, report
Due Date of Deliverable	31-03-2025
Actual Submission Date	31-03-2025
Author(s) & Organization(s)	Tom Melvin, Majella Geraghty, Ali McDonnell (TCD), Giuditta Callea, Rosanna Tarricone, Helen Banks, Maria Luisa Buzelli, Federico Facciolo, Carlo Federici, Francesco Malandrini, Franco Luigi Zurlo (UB), Marta Kerstan (JNJ), Nicolas Martelli, Ornella Tangila Kayembe, Tess Martin (APHP), Sebastian Kuhn, Ilja Michaelis, Marlen Peseke (UMR)
Reviewer(s) & Organization(s)	Rosanna Tarricone (UB), Rob Nelissen (EFORT) Claudia Louati, Yasemin Zeisl (EPF), Laura Sampietro-Colom (HCB), Adrian Valledor (FCRB), Marta Bragagnolo (GHH), Donal O'Connor (HPRA), Peter McCulloch (IDEAL), Carlo M. Petrini (ISS), Alexandra H.C. Poulsson, Marit Erna Austeng (NIPH).
Contact	MELVINTO@tcd.ie , giuditta.callea@unibocconi.it

File History				
Version	Date	Status	Author	Review
1.0	24-02-2025	V1.0	Giuditta Callea, Rosanna Tarricone, Helen Banks, Maria Luisa Buzelli, Federico Facciolo, Carlo Federici, Francesco Malandrini, Franco Luigi Zurlo (UB), Marta Kerstan (JNJ), Tom Melvin, Majella Geraghty, Ali McDonnell (TCD), Nicolas Martelli, Ornella Tangila Kayembe, Tess Martin (APHP), Sebastian Kuhn, Ilja Michaelis, Marlen Peseke (UMR)	
2.0	06-03-2025	V2.0	Maria Luisa Buzelli, Giuditta Callea, Francesco Malandrini, Niccolò Palminteri Matteucci (UB), Tom Melvin, Majella Geraghty, Ali McDonnell (TCD), Nicolas Martelli, Ornella Tangila Kayembe, Tess Martin (APHP), Sebastian Kuhn, Ilja Michaelis, Marlen Peseke (UMR).	
3.0	24-03-2025	V3.0	Maria Luisa Buzelli, Giuditta Callea, Francesco Malandrini (UB), Tom Melvin, Majella Geraghty, Ali McDonnell (TCD), Nicolas Martelli, Ornella Tangila Kayembe, Tess Martin (APHP), Sebastian Kuhn, Ilja Michaelis, Marlen Peseke (UMR).	

TABLE OF CONTENTS

ABBREVIATIONS	5
EXECUTIVE SUMMARY	7
1. Regulatory background	13
2. Methodology	13
3. Recommendations of WP1 and WP2 for HEU-EFS	15
3.1. Harmonisation of applications and assessments for EFS	15
3.2. Dialogue	17
3.3. Expertise and awareness	19
3.4. Transparency	21
3.5. Stakeholder involvement	23
3.6. Facilitators for R&D in the EU	25
3.7 Ensuring EFS program also reflects DHT-specific needs	26
Appendix 1	29

ABBREVIATIONS

AB	Advisory Board
AIeMDs	Artificial Intelligence-enabled Medical Devices
APHP	Assistance Publique Hôpitaux De Paris
CA	Consortium Agreement
CI	Clinical investigation
CIE	Clinical Investigation and Evaluation
CIP	Clinical Investigation Plan
CIRCABC	Communication and Information Resource Centre for Administrations, Businesses and Citizens
CRO	Contract Research Organisation
DHT	Digital health technology
EFS	Early Feasibility Study
EMA	European Medicines Agency
EU	European Union
FDA	Food and Drug Administration
GA	Grant Agreement
HEU-EFS	Harmonised Approach to Early Feasibility Studies for Medical Devices in the European Union
HTA	Health Technology Assessment
IB	Information Brochure
ICF	Informed Consent Form
ICTRP	International Clinical Trials Registry Platform
IHI	Innovative Health Initiative
J&J	Johnson & Johnson
MD	Medical device
MDCG	Medical Device Coordination Group
MDIC	Medical Device Innovation Consortium
MDR	Medical Device Regulation
MCTA	Master Clinical Trial Agreements
MS	Member state
NB	Notified body
NCA	National Competent Authority

PAG	Patient Advisory Group
PEA	Patient Engagement Ambassador
PREM	Patient Reported Experience Measure
PRO	Patient Reported Outcome
PROM	Patient Reported Outcome Measure
REC	Research Ethics Committee
SME	Small and Medium Enterprise
TCD	Trinity College Dublin
UB	Bocconi University
UMR	Philipps-Universität Marburg
WP	Work Package

EXECUTIVE SUMMARY

The Harmonised approach to Early Feasibility Studies (EFS) for Medical Devices in the European Union (HEU-EFS) project aims to streamline the regulatory processes for Early Feasibility Studies (EFS) of medical devices (MDs) and digital health technologies (DHTs) in the EU. Through extensive research and analysis conducted within Work Packages (WP) 1 *Research and analysis on state of play of pre-market programs and implementation barriers to EFS* and 2 *Research and analysis on regulatory framework, and institutional and organizational characteristics of EU competent authorities*, the project identified key challenges in the current regulatory landscape and proposes actionable recommendations to create a harmonised, efficient, predictable, and transparent regulatory environment for EFS in the EU, which will contribute to advancing medical technology innovation within the member states (MSs) while maintaining patient safety and ethical standards.

The recommendations are aimed to inform the activity of the WPs in charge of developing the HEU-EFS methodology, who will then provide final recommendations to external stakeholders, to be tested through pilot use-cases.

This report outlines seven main recommendations:

1. Harmonisation of applications and assessments for EFS. This recommendation focuses on the need for harmonising regulatory pathways and establishing clear, dedicated guidance for EFS under the Medical Device Regulation (MDR). This would help to lay the foundation for a standardised process that enhances efficiency and expedites approval timelines for EFS, particularly for innovative devices, thereby fostering innovation.

2. Dialogue. This recommendation further advocates for enhanced dialogue between sponsors and National Competent Authorities (NCAs) through the introduction of structured advisory processes that mirror successful models from other jurisdictions such as the Food and Drug Administration (FDA) Q-Submission program.

3. Awareness and expertise. This recommendation underscores the importance of increasing expertise and awareness among stakeholders, including regulatory bodies, clinical sites, sponsors including small and medium enterprises (SMEs), and patient groups. The introduction of training programs and the development of centralised repositories for EFS-related resources are proposed to bridge existing knowledge gaps and facilitate better preparation for early-stage clinical investigations.

4. Transparency. This recommendation stresses the necessity of transparency in EFS reporting and the establishment of publicly accessible databases and dashboards for clinical investigation (CI) data, ensuring that EFS outcomes are easier to track, assess, and utilise by all stakeholders.

5. Stakeholder involvement. This recommendation focuses on improving processes to involve key stakeholders, such as patient panels, specific clinical expert panels, regulators, and Health Technology Assessment (HTA) bodies, at early stages of device development to ensure that MDs and DHTs meet real-world needs and align with patient and payer expectations.

6. Support for R&D in the EU. This recommendation focuses on developing support measures, grounded on lessons learnt from other jurisdictions, for conducting R&D in the EU to support EFS and reduce financial burdens on manufacturers.

7. Ensuring that the EU EFS program also reflects DHT-specific needs. This recommendation addresses the unique challenges faced by DHTs and proposes tailored pathways for their EFS, ensuring that the specificities of software-driven technologies and Artificial Intelligence-enabled Medical Devices (AIeMDs) are appropriately addressed. Highlighting the areas of risk assessment that are problematic for DHTs, we must follow the harmonisation process of the interplay between the MDR and the EU AI Act, and ensuring that EFS templates and protocols can be used for innovative DHTs.

Summary of recommendations for WPs and tasks

The table below provides a consolidated summary of the recommendations influencing each WP and/or task.

Recipient	Area	Recommendation	Actionable steps
WP 3	Expertise and awareness	Establish targeted training programs.	Develop educational and informational materials (e.g., pre-recorded and live training sessions, briefing documents) to train organisations (i.e., health technology developers and SMEs, NCAs, trialists, clinical sites, CROs) participating in pilot use-cases.
	Harmonisation of applications and assessments for EFS	Enhance the efficiency and predictability of pre-market CIs.	Develop specific EFS guidance within the MDR framework.
T 3.1.6	Facilitators for R&D in the EU	Develop incentives for conducting R&D in the EU to support EFS and reduce financial burdens on manufacturers.	Conduct a review of various mechanisms for investigational device reimbursement and provide evidence-based recommendations.
			Clarify the type of coverage available (device costs and routine care costs).
T 3.2	Dialogue	Establish the foundation for a harmonised, standardised EU dialogue and collaborative engagement process.	Standardize regulatory dialogue types (i.e., outlining different types of regulatory interactions required before and during an EFS and developing a structured methodology to involve patients in early dialogue).

Recipient	Area	Recommendation	Actionable steps
	Stakeholder involvement	Ensure MDs and DHTs meet real-world needs through a structured approach to stakeholder engagement.	<p>Establish structured engagement pathways for patient panels, patient associations, Expert Panels, and HTA bodies.</p> <p>Propose methodologies and best practice guidelines for early patient involvement in CIs.</p> <p>Propose NCA participation in structured stakeholder engagement initiatives.</p> <p>Encourage the use of patient experience data to inform regulatory decisions.</p> <p>Facilitate knowledge sharing and capacity building among stakeholders (i.e., providing guidance and best practices, which can support sponsors and regulators for involving patients).</p>
T 3.3	Harmonisation of applications and assessments for EFS	Enhance the efficiency and predictability of pre-market CIs.	Develop and suggest a harmonised process for EFS assessments together with the NCAs (EFS-eligibility assessment criteria).
			Reduce regulatory assessment timelines (i.e., encouraging NCAs to harmonise assessment processes to avoid clock-stops).
			Identify device and protocol modifications, by defining the procedural steps to be undertaken by CI sponsors for iterations.
	Dialogue	Establish the foundation for a harmonised, standardised EU dialogue and collaborative engagement process.	Establish a possible process for seeking regulatory feedback and develop a map detailing regulatory interactions.
			Develop iterative feedback mechanisms and elaborate mechanisms to plan and manage device and protocol modifications and ensure transparent communication about iterative changes.
			Standardize regulatory dialogue types, outlining different types of regulatory interactions required before and during an EFS.
	Stakeholder involvement	Ensure MDs and DHTs meet real-world needs, a structured approach to stakeholder engagement should be implemented.	Establish structured engagement pathways for patient panels, patient associations, Expert Panels, and HTA bodies.
			Propose NCA participation in structured stakeholder engagement initiatives.
	Ensuring that the EU EFS program also reflects DHT-specific needs	Establish a structured EFS pathway for DHTs to reduce regulatory uncertainty, enhance industry participation, and accelerate safe adoption.	Describe the pathway for DHTs within the harmonized EU EFS programme (outlining the scope, eligibility criteria, and objectives of EFS for DHTs).

Recipient	Area	Recommendation	Actionable steps
WP 4	Expertise and awareness	Facilitate knowledge sharing among stakeholders and enhance the overall quality of EFS applications.	Develop educational and informational materials (i.e., pre-recorded and live training sessions, briefing documents) to train those organisations (i.e., health technology developers and SMEs, NCAs, trialists, clinical sites, CROs) taking part in the pilot use-cases.
	Stakeholder involvement	Ensure MDs and DHTs meet real-world needs, a structured approach to stakeholder engagement should be implemented.	Propose possible pathways for incorporating PROMs and PREMs data into EFS evaluations.
T 4.2	Harmonisation of applications and assessments for EFS	Enhance the efficiency and predictability of pre-market CIs.	Establish standardised templates for essential EFS documents.
	Dialogue	Establish the foundation for a harmonised, standardised EU dialogue and collaborative engagement process.	Standardize regulatory dialogue types (establish standardised templates to streamline interactions).
	Ensuring that the EU EFS program also reflects DHT-specific needs	Establish a structured EFS pathway for DHTs to reduce regulatory uncertainty, enhance industry participation, and accelerate safe adoption.	Ensure that templates and protocols also suit DHT specificities. Clarify the AI Act–MDR Interplay in EFS, providing guidance on how AI-related regulatory obligations apply in the context of EFS).
WP 5	Expertise and awareness	Facilitate knowledge sharing among stakeholders and enhance the overall quality of EFS applications.	Develop educational and informational materials (e.g., pre-recorded and live training sessions, briefing documents) to train those organisations (i.e., health technology developers and SMEs, NCAs, trialists, clinical sites, CROs) that will take part in the pilot use-cases.
T 5.2	Harmonisation of applications and assessments for EFS	Enhance the efficiency and predictability of pre-market CIs.	Monitor and evaluate the implementation of harmonised procedures by developing a framework and key performance metrics to track the adoption of EFS-specific processes and the level of harmonisation across jurisdictions.
	Dialogue	Establish the foundation for a harmonised, standardised EU dialogue and collaborative engagement process.	Define key performance indicators (KPIs) for the dialogue process and design metrics specifically aimed at measuring participation and outcomes of the EFS Dialogue & Collaborative Engagement Process.
	Transparency		Develop an online database which includes submitted and approved EFS.

Recipient	Area	Recommendation	Actionable steps
		Enhance transparency in EFS by ensuring adherence to FAIR principles.	<p>Improve the quality and availability of data on EFS by promoting more transparent and systematic collection of EFS data and integrate into the clinical development pathway.</p> <p>Implement reporting and evaluation systems for EFS (Create EU EFS Performance Dashboard).</p>
	Stakeholder involvement	Ensure MDs and DHTs meet real-world needs, a structured approach to stakeholder engagement should be implemented.	Encourage the use of patient experience data to inform regulatory decisions, including PROMs and PREMs data into Dashboard metrics to monitor EFS collecting them.
T 5.3	Transparency	Enhance transparency in EFS by ensuring adherence to FAIR principles.	Improve the quality and availability of data on EFS and incorporate information flows on EFS within the EU regulatory processes and data structures.
WP 6	Expertise and awareness	Facilitate knowledge sharing among stakeholders and enhance the overall quality of EFS applications.	Develop educational and informational materials (e.g., pre-recorded and live training sessions, briefing documents) to train those organisations (i.e., health technology developers and SMEs, NCAs, trialists, clinical sites, CROs) that will take part in the pilot use-cases.
	Stakeholder involvement	Ensure MDs and DHTs meet real-world needs, a structured approach to stakeholder engagement should be implemented.	Co-design the HEU-EFS ICF with patients and their associations and experts (e.g., members of ethics committees) to improve clarity, tone, and structure.
T 6.1	Harmonisation of applications and assessments for EFS	Enhance the efficiency and predictability of pre-market CIs.	Develop standardised templates for essential EFS documents and provide guidance for drafting Master Clinical Trial Agreements (MCTA) Informed Consent Form (ICF), for EFS and Insurance Agreement.
WP 7	Harmonisation of applications and assessments for EFS	Enhance the efficiency and predictability of pre-market CIs.	Test the proposed harmonised process for EFS assessments together with the NCAs process through pilot use-cases.
T 7.2	Transparency	Enhance transparency in EFS by ensuring adherence to FAIR principles.	<p>Fill in the online database with information from pilot use-cases.</p> <p>Test the functionality of the dashboard through the provision of information by the pilot use-cases.</p>

Recipient	Area	Recommendation	Actionable steps
	Ensuring that the EU EFS program also reflects DHT-specific needs	Establish a structured EFS pathway for DHTs to reduce regulatory uncertainty, enhance industry participation, and accelerate safe adoption.	Ensure that templates and protocols also suit DHT specificities.
T 7.3	Dialogue	Establish the foundation for a harmonised, standardised EU dialogue and collaborative engagement process.	Evaluate how the regulatory advice was provided during pilot use-cases and propose adjustments where necessary.
T 8.2	Expertise and awareness	Facilitate knowledge sharing among stakeholders and enhance the overall quality of EFS applications.	Develop an online portal that can serve as a central repository for EFS-related documents, guidance, template and best practices.

1. Regulatory background

Early Feasibility Studies (EFS) are defined by ISO 14155:2020 as limited clinical investigations of a device early in its development, typically before the device design is finalised. These studies are relevant for evaluating initial clinical safety and performance or effectiveness (if appropriate), particularly for innovative, technologies. EFS are proposed to streamline clinical evidence generation for medical devices (MDs), fostering innovation and a more structured approach to clinical evidence generation, while maintaining regulatory compliance, ethical standards and patient safety. The Medical Device Regulation (MDR) explicitly recognizes the role of CIs in device evaluation, with EFS aligning with the principles set forth in Article 62 *General requirements regarding clinical investigations conducted to demonstrate conformity of devices* and Annex XV *Clinical investigations*.

EFS can benefit from synergies with existing EU mechanisms such as MDR expert panels, CA early regulatory advice, HTAR, and coordinated assessment procedures. Article 78 of the MDR introduces the concept of coordinated CI assessments, allowing for a single review process across multiple European Union (EU) member states. In 2025, the Clinical Investigation and Evaluation (CIE) Working Group has launched a pilot program for Article 62 studies utilizing the CIRCABC (Communication and Information Resource Centre for Administrations, Businesses and Citizens) platform, common templates and national documentation.

By establishing an EFS regulatory framework, enhancing regulatory clarity, promoting early dialogue between sponsors of CIs and National Competent Authorities (NCAs), and leveraging coordinated assessment mechanisms, the HEU-EFS project aims to optimize the implementation of EFS in the EU. These efforts will strengthen clinical evidence generation processes, streamline regulatory pathways, and foster innovation in the EU MD sector.

2. Methodology

The development of the future EU EFS Program must be rooted in a deep understanding of the EU regulatory framework and international standards and a thorough comprehension of strengths, weaknesses, and opportunities of current pre-market clinical evidence generation in the EU. For this reason, the first phase of the HEU-EFS project was dedicated to an in-depth analysis of the current situation. Secondary research was conducted to gather existing data through scoping reviews of scientific and grey literature, analysis of relevant regulations in force in the EU and international standards, and data collection from public sources (e.g., EFS registered on public registries). Primary research was conducted after ethics approval to gather data and perceptions and discuss research findings with stakeholders (i.e., sponsors including small and medium enterprises – SMEs, NCAs,

Notified Bodies – NBs, Health Technology Assessment – HTA – bodies, members of professional and scientific clinical associations, contract research organisations – CROs, members of the Patient Advisory Group - PAG) through surveys, one-to-one structured/semi-structured/unstructured interviews, and semi-structured/ unstructured focus groups. The research methodologies used and the results of work in WP1 on *Research and analysis on state of play of pre-market programs and implementation barriers to EFS*, and in WP2 on *Research and analysis on regulatory framework, and institutional and organizational characteristics of EU competent authorities*, are described in detail in the following deliverables, some of them public: D1.1 *Characteristics, gaps, and best practices of premarket programs*, D1.2 *Pre-Market Program Database*, D1.3 *Characteristics and state of play of EFS*, D2.1 *EU regulatory framework and international standards*, D2.2 *Professional and organizational characteristics of competent authorities*, and D2.4 *Research report summarizing the current EU regulatory framework for clinical evidence generation for MDs and DHTs and relations with the future EU EFS Program*.

This document presents a set of recommendations informed by WP1 and WP2 research and analysis activities within the HEU-EFS project that serves as a foundation for the work of WP3 *Methodology development: rationale, processes and procedures*, WP4 *Methodology development: evidence requirements, data, and statistical tools*, WP5 *Methodology development: EU EFS Program monitoring system*, and WP6 *Methodology development: ethical and legal aspects*. For every recommendation provided, the WPs and tasks in charge of the implementation are specified. Information on the full name of WPs and tasks can be found in Appendix 1. The methodology of the HEU-EFS project, developed by WP3-6 based on the findings of WP1-2, will subsequently be tested and refined the pilot phase conducted under WP7 *Testing the methodology: pilot use-cases*. The recommendations focus specifically on pre-market CIs for MDs (e.g. first in human studies), including digital health technologies, with an emphasis on EFS. There are both synergies and distinctions with EFS for general MDs compared to DHTs, as both seek to demonstrate proof of concept in a clinical setting. For general MDs, this relates to clinical and technical proof of concept *in vivo*, whereas DHTs tend to explore proof of concept in clinical workflows.

The recommendations we proposed are compliant with the EU regulatory framework, identify opportunities for process optimization and improve stakeholder engagement. To ensure clarity and practical applicability, each recommendation follows a structured format:

- **Context:** description of the current situation and context.
- **Recommendations:** proposed recommendations based on identified challenges and opportunities.
- **Actionable steps:** concrete measures addressed to the HEU-EFS WPs to implement the recommendation. [OBJ]

3. Recommendations of WP1 and WP2 for HEU-EFS

3.1. Harmonisation of applications and assessments for EFS

Context

A key challenge in the EU is the lack of a harmonised, structured pathway for conducting EFS and harmonised evaluation criteria across NCAs. Currently, applications for EFS fall under Article 62 of the MDR. This article groups all pre-market CIs together without providing specific requirements tailored to different study types (e.g., first-in-human, EFS, pivotal studies). Within this regulatory environment, there may be room for improvement in defining clear and consistent rules and specific procedures to be followed for the submission, assessment, and conduct of EFS across EU Member States (MSs).¹

Specifically, there is no guidance describing key phases of EFS and how EFS should be distinguished from other types of early-phase CIs. Moreover, there is no dedicated guidance clarifying the eligibility criteria for patients for participating in EFS. In addition, the roles and responsibilities of the different stakeholders involved—sponsors, NCAs, research ethics committees (IEC), MDCG, and potentially external experts—are not clearly defined. The internal organisations of some of these actors is also problematic. For instance, the organisation of IECs hugely differs between different MSs, causing further uncertainties. This lack of clarity not only increases the administrative and regulatory burden for sponsors, especially for those conducting multi-centre or multi-national studies, but also limits the predictability and transparency of the authorisation process, ultimately discouraging the use of EFS as a valuable tool to generate early clinical evidence within the EU.

The lack of standardised templates for essential EFS documents, including EFS-specific Clinical Investigation Plan (CIP), Informed Consent Form (ICF), Investigator’s Brochure (IB) and Master Clinical Trial Agreements (MCTAs), further increases administrative burden, delaying approvals.²

In addition, while clinical trial insurance coverage is a mandatory component of the submission dossier as outlined in Annex XV (4.3) of the MDR, there is no common guidance or standardised approach across EU countries to assist sponsors in navigating insurance requirements specifically related to EFS. NCAs typically assess whether a valid policy is in place, with reasonable coverage for study-

¹ See D2.4 for further information.

² See D1.2 for further information.

related injuries and a duration that covers the entire study period. However, sponsors often face inconsistent expectations across jurisdictions, and certain policy provisions, such as restrictive reporting timelines, can create unforeseen challenges for study teams.

There is also significant variability in the time from initial application to authorization for innovative MDs reported by the NCAs, reflecting differences in the use of stop-clock mechanisms for additional test data, reliance on external expert consultations, and resource constraints affecting assessment efficiency.³

As a result, sponsors must navigate a fragmented system, where national processes vary significantly across jurisdictions. This can lead to confusion and inefficiencies in the development of regulatory, market access strategies and decision-making processes across the stakeholders involved.

Recommendations

To enhance the efficiency and predictability of pre-market CIs, particularly for EFS, reduce administrative burden, and minimise delays caused by procedural discrepancies, harmonisation of regulatory pathways across EU countries is essential. Establishing structured and dedicated guidance for EFS within the MDR framework would help address existing inconsistencies. This includes having EFS-specific guidelines and application templates to streamline the process.

Actionable steps

Based on the findings from WP1 and WP2, we have identified recommendations for the future WPs of the HEU-EFS project, with the aim to increase harmonisation in EFS:

- **Develop specific EFS guidance within the MDR framework.** Based on the findings identified in previous research, we recommend that WP3 draft guidance describing key phases, eligibility criteria, indicative timelines, roles and responsibilities of stakeholders, but also advice on how to handle iterative changes to the investigational device and protocol modifications, which are the most valuable aspect and one of the main characteristics of EFS studies (WP3). Such tailored guidance would help distinguish EFS from other types of CIs and ensure appropriate flexibility while maintaining patient safety and data integrity. While MDCG 2024-3 *Guidance on content of the Clinical Investigation Plan for clinical investigations of medical devices* provides general guidance on CIs, further EFS-specific guidance is needed to address the unique characteristics of these early-phase studies. As a recommendation aimed at external stakeholders, project partners could suggest to NCAs to put together some best practices to aid the development of innovative MDs.

³ See D2.2 for further information.

- **Establish standardised templates for essential EFS documents.** We suggest that WP4 and WP6 develop predefined templates for essential regulatory and ethics documents, including the CIP and ICF, and consider the information that patients should have access to about the study. When providing standardised templates, one option may be to lay out a list of minimum requirements which need to be set out and explained in these documents, with the aim to ensure a degree of flexibility. In addition, WP6 colleagues are also recommended to provide guidance for drafting MCTAs, to promote consistency in defining roles, responsibilities, and financial arrangements between sponsors and sites, reducing the risk of conflicts and delays in study initiation, and develop clear guidance on insurance coverage requirements, to ensure that policies provide reasonable and adequate protection for participants, covering the entire duration of the study (WP4 Task 4.2, WP6 Task 6.1).
- **Develop and suggest a harmonised process for EFS assessments together with the NCAs.** We recommend that WP3 develop EFS-eligibility assessment criteria to be tested in the HEU-EFS pilot use-cases (WP7) and further refined in collaboration with the NCAs (WP3 Task 3.3). Those items not tested in the pilots may be assessed together with stakeholders and NCAs after the pilots are conducted.
- **Define the procedural steps for device and protocol modifications.** We recommend that WP3 Task 3.3 identify the acceptable device and protocol iterations for MDs undergoing EFS, along with the necessary process guidelines for CI sponsors to follow when implementing these iterations. The pilot use-cases in WP7 will then provide a practical validation of these steps, assessing their applicability in real-world scenarios and identifying any necessary refinements.
- **Reduce regulatory assessment timelines** for both initial assessments and modifications to the device. Although not solely responsible for delays, this may be done by encouraging NCAs to harmonise assessment processes, and hence timelines for EFS applications evaluation, and support sponsors with their CI applications aligned with the EU-EFS framework to avoid clock-stops and support complete and comprehensive applications (WP3 Task 3.3).
- **Monitor and evaluate the implementation of harmonised procedures.** We recommend that WP5 Task 5.2 develops a framework and key performance metrics to track the adoption of EFS-specific processes and the level of harmonisation across jurisdictions. We also recommend the establishment of a dedicated dashboard, that one day can be merged into a European platform such as EUDAMED, to analyse regulatory performance data, such as common non-conformities, and key procedural bottlenecks reported by sponsors and NCAs, to identify areas for improvement.

3.2. Dialogue

Context

Regulatory advice helps both sponsors and regulators by ensuring clinical evidence generation strategies meet expectations and facilitating discussions on potential challenges.⁴ In the EU, systematic regulatory advice design is partially available via different processes.⁵ The EU has some national advice structures through NCAs, and MDR Expert Panels provide advice for high-risk devices (Article 61(2)). There is currently no advice structure to help sponsors to understand whether an EFS is needed similar to the FDA's Q-Submission program, that offers a structured Pre-Submission (Pre-Sub) pathway, providing a model for early dialogue, allowing sponsors to seek feedback on development plans and key topics such as biocompatibility, bench testing, and cybersecurity before conducting EFS.³⁻⁶ The EU does not have a centralised advisory system to provide guidance at key stages of the CI process;⁴ however, for high-risk devices there is the aforementioned path covering MDR Expert Panels Scientific Advice, and from 2025, Joint Scientific Consultations under HTAR can also be performed in parallel with the Expert Panels, where the relevant Notified Body is invited as an observer. Some NCAs offer pre-submission or innovation meetings, but these interactions vary in consistency.³ Some are informal and *ad hoc*, occurring via email or teleconference, while larger NCAs offer a formal, paid 'scientific advice' process that requires an application.³ Nevertheless, these interactions are not always part of a structured framework.³

A structured dialogue between sponsors and NCAs is crucial both prior to and during EFS. It has the potential to enhance study design, improve clinical evidence quality, prevent clock stops due to lack of needed evidence, shorten time to market, and reduce unnecessary testing costs.³ Furthermore, it fosters trust, transparency, and greater alignment between sponsors and regulatory bodies ultimately accelerating EFS timelines, and enhancing the quality of data generated.

Recommendations

Establish the foundation for a harmonised, standardised EU Dialogue and Collaborative Engagement Process to facilitate structured interactions between sponsors and NCAs and enable early and continuous communication throughout the EFS lifecycle, enhancing regulatory clarity and efficiency.

Actionable steps

With the aim to develop a standardised EU-wide EFS regulatory advice structure and increase interactions among stakeholders involved in EFS, the following actions are suggested:

⁴ See D1.1 for further information.

⁵ See D2.1 for further information.

⁶ FDA. Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program Guidance for Industry and Food and Drug Administration Staff, 2023. Available at: <https://www.fda.gov/media/114034/download>

- **Standardize regulatory dialogue types.** We propose that WP3 Task 3.3 outline the various regulatory interactions necessary prior to and throughout an EFS. This should encompass preliminary guidance on regulatory pathways and processes, protocol design advice, pre-submission consultations once a protocol is prepared, and continuous dialogue during the EFS for discussing potential modifications. We recommend our colleagues in WP3 Task 3.2 provide resources and examples of methodology to involve patients in early dialogue to support sponsors in developing appropriate risk profiles and risk benefit analyses. Finally, standardised templates being developed in WP4 Task 4.2 should be assessed for consistency with the processes for dialogue mentioned above (WP4 Task 4.2).
- **Establish a possible process for seeking regulatory feedback.** Towards this aim, we recommend that WP3 Task 3.3 develop a map detailing the regulatory interactions.
- **Develop iterative feedback mechanisms.** We recommend that our colleagues in WP3 Task 3.3, possibly involving external stakeholders such as NCAs, elaborate mechanisms to plan and manage device and protocol modifications and ensure transparent communication about iterative changes. Such mechanisms may be tested and refined through pilot case studies in WP7, or assessed together with stakeholders and NCAs after the pilots are conducted.
- **Assess and refine the advisory process.** We recommend that WP7 Task 7.3 evaluate how the regulatory advice was provided during pilot use-cases and propose adjustments to either the process or the standardised templates if deemed necessary, engaging with NCAs and the CIE Working Group to present the refined template for potential incorporation into MDCG guidance.
- **Define key performance indicators (KPIs) for the dialogue process.** We recommend that WP5 Task 5.2 develop metrics specifically aimed to measure participation and outcomes of the EFS Dialogue & Collaborative Engagement Process and assess the impact of regulatory advice.

3.3. Expertise and awareness

Context

The level of expertise among stakeholders involved in EFS preparation, approval, and conduct varies considerably, affecting the efficiency and quality of CIs. For instance, NCA assessors exhibit significant diversity in professional training and areas of expertise when assessing EFS applications.⁷ Some NCA assessors have no, or limited experience of assessing early-stage CIs. This can lead to

⁷ See D2.2 (section 3.2.1) for further information.

inconsistent decision-making across different jurisdictions. Additionally, the absence of a structured competency framework for NCA assessors results in gaps in assessment quality.

Beyond NCAs, other key stakeholders also experience challenges related to expertise and awareness, including clinical trialists, clinical sites, NBs, HTDs, especially SMEs, CROs, and patient representatives supporting sponsors in study development. SMEs, particularly those operating in countries with fewer regulatory resources, often struggle to navigate the fragmented EU regulatory landscape due to limited access to expert networks and focused regulatory guidance. Lack of awareness also affects patient engagement, with many patients unaware of opportunities to participate in the CI design process or lacking the necessary training to contribute effectively.

Contributing to the lack of clarity is the absence of a centralised repository containing guidance documents, templates, and best practices for EFS applications, as CIs fall within the national legislative remit. Unlike the US, where the Food and Drug Administration (FDA) and the Medical Device Innovation Consortium (MDIC) provide structured guidance, templates, and resources through dedicated online platforms, the EU lacks a comprehensive and easily accessible source of information for stakeholders involved in early-stage CIs. This gap results in inefficiencies, as sponsors and regulatory bodies must independently navigate a complex and fragmented regulatory landscape.

Recommendations

Adopt a multifaceted approach, including targeted training programs and the establishment of a structured and accessible repository containing all relevant EFS-related documents, including final HEU-EFS guidance, standardised templates, and regulatory insights, to facilitate knowledge sharing among stakeholders and enhance the overall quality of EFS applications. These actions would enhance clarity and foster the establishment of a more informed and capable ecosystem for EFS.

Actionable steps

To increase expertise among stakeholders involved in EFS, the following actions are recommended:

- **Develop training materials.** We suggest that WPs 3-6 in charge of developing the HEU-EFS methodology develop educational and informational materials (e.g., pre-recorded and live training sessions, briefing documents) to train those organisations (i.e., HTDs and SMEs, NCAs, trialists, clinical sites, CROs) that will take part in the pilot use-cases to improve expertise in applying for, assessing and conducting EFS. At a later stage, once the final guidance on the EU-EFS Program is released, we recommend preparing additional educational contents and interactive online tools (e.g., a navigator) to create awareness regarding the EU EFS Program among all the interested stakeholders, including patients, and support sponsors, especially SMEs and university spin-offs, wishing to undertake an EFS in the EU.

To improve clarity and comprehensiveness the following actions could be implemented:

- **Develop an online portal that can serve as a central repository for EFS-related documents, guidance, templates and best practices.** We advise colleagues working on Tasks 8.2 of WP8 to make sure that the dedicated HEU-EFS web portal includes final WP reports and scientific publications, final EU EFS Guidance, and standardised templates and forms (e.g., for CIP, regulatory submissions, ICF, MCTA, case studies). This platform should also serve as a knowledge hub featuring questions, webinars, and regulatory updates. A medium-term sustainability plan for the online portal should be carefully designed to ensure that it remains viable while awaiting the approval of the future EF EFS Program by the European Commission. For instance, in the transitional period, while waiting for the contents to be hosted on a European repository (e.g., Communication and Information Resource Centre for Administrations, Businesses and Citizens - CIRCABC), the portal could also help for sharing assessments conducted by NCAs to improve knowledge sharing between NCAs.

3.4. Transparency

Context

EFS have been proposed as means to streamline and enhance the generation of clinical evidence for MDs, aiming to foster innovation in medical technology and anticipate the 'business case,' while upholding ethical standards and acceptable levels of patient risk. While conducting an EFS may add time upfront, the insights gained can help streamline later stages and accelerate development. Without EFS, many products may face prolonged delays or fail to reach the market at all, making it essential to consider not just time, but also the risk of attrition. In some cases, the adoption of EFS could also avoid waste of resources, failed pivotal studies and patient exposure to unnecessary risks, and the production of useless technologies, generating real value for society.

Despite their suggested role, little is known and there is a lack of routine monitoring about the extent to which EFS are currently conducted, where and how they fit into manufacturers' overall evidence generation plans (i.e., whether EFS represent the first step in the lifecycle of the clinical evidence generation process), whether they indeed enhance evidence quality or accelerate the time to market for novel technologies, and their overall performance. Experience gained so far through other initiatives, e.g., IDEAL Collaboration, suggests that well-designed EFS are currently rare, largely due to a lack of knowledge among innovators and insufficient guidance and advice from NCAs and NBs.

Currently, access to information on EFS remains limited. No public databases or repositories currently classify studies as EFS, either in the US or globally. Even well-established international clinical trials databases, such as ClinicalTrials.gov or the International Clinical Trials Registry Platform (ICTRP), do not require studies to indicate their classification as EFS, not even as an optional field. The clinical module of EUDAMED will contain CI and EFS results in the future. In the interim, a temporary

to locate, access, integrate, and reuse for various purposes, including research and innovation, while ensuring intellectual property rights are not compromised. Further research within HEU-EFS will generate recommendations on how to best incorporate information flows on EFS within the EU regulatory processes and data structures (WP5 Task 5.3).

- **Implement reporting and evaluation systems for EFS.** An EU EFS Performance Dashboard aimed at ensuring transparent, reliable, and continuous monitoring and evaluation of the EU EFS Program should be established to determine whether EFS can effectively enhance the quality of evidence and ultimately improve patient outcomes (WP5 Task 5.2). The functionality of the Dashboard must be tested through the provision of information by the pilot use-cases (WP7 Task 7.2). Such data and evidence would provide essential tools to monitor EFS as a critical component of evidence generation for MD.

3.5. Stakeholder involvement

Context

The involvement of patient panels, patient associations, Expert Panels, and HTA bodies in the development of MDs, including DHTs, is currently limited. When device design is still evolving, engaging these stakeholders could provide valuable insights to improve usability, accessibility, and alignment with patient needs as well as societal and payer expectations.

Despite the recognized benefits, as highlighted in D1.3 and D2.2, most NCAs and sponsors have yet to meaningfully integrate these stakeholders into pre-market CI pathways for MDs. The lack of structured involvement results in missed opportunities to refine study designs, enhance clinical relevance, and address potential barriers to product uptake and reimbursement.

Integrating the patient's perspective early into MD and DHT development is often limited, leading to potential misalignments with real-world needs and patient expectations. This gap can hinder product acceptance while delaying market entry. A structured approach to patient involvement in both product development and EFS planning is crucial to improving usability, accessibility, and measurement of patient-relevant outcomes.

In addition, patients face significant barriers to accessing and participating in pre-market CIs, including fragmented awareness of trials, complex informed consent processes, logistical challenges, and limited transparency. The absence of clear, accessible, and easy-to-read information for patients on trial procedures, risks, and benefits further limits engagement. Additionally, limited coordination and awareness of patient involvement opportunities, coupled with perceived expertise barriers, prevent patients from actively contributing to the design and execution of pre-market CIs.

Despite the benefits of patient involvement early in MD and DHT development, its implementation is often inconsistent, which results in missed opportunities to refine study design and enhance the

relevance of CIs. This inconsistency arises from a lack of methodological guidance and unclear mechanisms of integration in the early stages of development in Europe. This lack of structure not only limits the potential benefits of patient contributions but also hinders sponsors from effectively engaging patients in a way that enhances study quality, helps align study design with patient priorities, enhances clinical trial relevance, and improves overall product acceptance and informs HTA processes.

Recommendations

To ensure that MDs and DHTs meet real-world needs, a structured approach to stakeholder engagement should be implemented from the early stages of development, particularly during EFS. Involving patients and their associations, Expert Panels, and representatives of HTA bodies in a systematic way would help align study design with patient priorities, enhance clinical trial relevance, and improve overall product acceptance.

In addition, mechanisms should be introduced to involve HTA bodies in the planning and review process of EFS, either through early dialogue opportunities or by consulting HTA representatives during the assessment process. This would help align early evidence generation with the long-term data needs of HTA bodies, ensuring that the evidence collected during EFS is more relevant for future value assessments and ultimately improving the efficiency of the evidence generation process across the lifecycle of the device.

Actionable steps

To favour more patient-centred early CIs, reduce inefficiencies, and enhance the overall impact of medical device innovations, these strategies are recommended:

- **Establish structured engagement pathways for patient panels, patient associations, Expert Panels, and HTA bodies.** We recommend that WP3 Tasks 3.2 and 3.3 suggest procedures for involving these stakeholders in EFS planning and study design and encourage NCAs to integrate formal advisory mechanisms and ensure systematic engagement in pre-market CIs.
- **Propose methodologies and best practice guidelines for early patient involvement in CIs.** We recommend that WP3 Task 3.2, in collaboration with the Patient Engagement Ambassadors (PEAs) of each WP, develop a roadmap which identifies the most important development activities that would benefit from incorporating patient perspectives into EFS study design.
- **Propose NCA participation in structured stakeholder engagement initiatives.** Colleagues from Tasks 3.2 and 3.3 of WP3 are recommended to involve external

stakeholders, including NCAs, and encourage them to adopt formalised approaches for engaging patient representatives and promote the integration of structured patient involvement requirements into national regulatory frameworks to ensure a harmonised approach.

- **Develop patient-friendly ICFs for EFS.** We recommend WP6 suggests an ICF draft template and recommendations to improve clarity, readability, and transparency for patients, facilitating their clear understanding of trial procedures, potential risks, and expected benefits. Enhancing the quality and accessibility of trial information, among other actions, would contribute to more informed decision-making and better patient engagement throughout the EFS.
- **Encourage the use of patient experience data to inform regulatory decisions.** We recommend that WP3 Task 3.2 and WP4 propose possible pathways for incorporating patient-reported outcomes measures (PROMs) and patient-reported experience measures (PREMs) data into EFS evaluations, ensuring that patient insights contribute to decision-making, and that WP5 Task 5.2 include such measures in Dashboard metrics to monitor the number/share of EFS collecting PROMs and PREMs.
- **Support knowledge sharing on patient engagement.** As part of developing a roadmap for patient engagement, we recommend WP3 Task 3.2 to provide guidance and best practices, if available, which can support sponsors and regulators involving patients. Where feasible, Task 3.2 will review materials and plans for activities for training and capacity building.

3.6. Facilitators for R&D in the EU

Context

High financial regulatory costs and the expenses associated with generating clinical evidence in the EU have been identified as significant barriers to MD innovation.¹¹ This is why it has become a priority to understand the root causes of these high costs. As the costs associated with CIs may outweigh the potential return on investment, manufacturers may discontinue certain devices or delay their market entry. Stricter technical and administrative requirements, combined with lack of clarity on regulators' and notified bodies' expectations, have further contributed to extended timelines and increased financial burdens, prompting companies to reconsider their regulatory strategies in the region.¹¹ In addition, significant financial and administrative burdens disproportionately impact SMEs, causing some to delay, avoid, or abandon EFS. The absence of targeted funding or support measures further make it harder for smaller organisations to generate robust early clinical evidence.

¹¹ See D1.1 (section 4.8) for further information.

Under the U.S. Medicare program, investigational devices in Category A (Experimental) and Category B (Nonexperimental/investigational) Investigational Device Exemption IDE studies may receive reimbursement for certain costs. For Category A IDE, while Medicare does not cover the device itself, it may reimburse routine care costs. For Category B IDE, since similar devices may already have FDA premarket approval (PMA) or clearance (510(k)) for similar devices, Medicare covers both the device and routine care costs.^{11,12}

The FDA and CMS coverage mechanisms for investigational device studies may offer a model the EU could evaluate to lower financial barriers for MD innovation, although substantial differences between the EU and US healthcare systems limit the transferability of this model. Furthermore, EU healthcare systems differ in their organization, levels of coverage, and support for the development of innovative health technologies, which would have to be studied and taken into account to determine how and where the future EU EFS Program might help manage early-stage costs, boost clinical research participation, and accelerate access to new technologies.

Recommendations

Explore regulatory and financial support measures for conducting R&D in the EU to support EFS and reduce financial burdens on manufacturers.

Actionable steps

To review various mechanisms for R&D support measures and clarify coverage and responsibilities across stakeholders:

- **Conduct a review of various mechanisms for investigational device reimbursement** (e.g., DiGA) and provide evidence-based recommendations, considering options such as reimbursing the device/study, helping cover study design, ethics submissions, or data management, or providing innovation support funds or tax relief for companies, including SMEs (WP3 Task 3.1.6).
- **Clarify the type of coverage available**, distinguishing between device costs and routine care costs, and outlining conditions under which each may be reimbursed (WP3 Task 3.1.6)

3.7 Ensuring EFS program also reflects DHT-specific needs

Context

¹² Medicare Coverage of Items and Services in Category A and B Investigational Device Exemption (IDE) Studies. Available at <https://www.cms.gov/medicare/coverage/investigational-device-exemption-ide-studies>

Despite its critical role in early-stage device assessment, EFS remains underutilised in DHTs, with a primary focus on high-risk MDs. Many sponsors do not consider EFS, opting instead for simulation studies, *in silico* trials, or pilot studies that do not meet EFS criteria. This avoidance is primarily due to regulatory uncertainties, a lack of pre-market DHT-specific guidance, and fragmented approval processes across EU Member States. As a result, DHT companies miss valuable opportunities to refine prototype design, validate the ‘proof of concept’ of the digital-human interaction in clinical settings, and identify unforeseen safety issues in real-world clinical environments before finalizing product design.

In the context of Artificial intelligence-enabled medical devices (AIeMDs), most qualify as both MDs of various risk classes under MDR and “high-risk AI systems” under the EU AI Act, creating potential duplications in risk management, clinical evidence needs, and post-market obligations. Without integrated guidance, DHT companies face confusion over meeting parallel requirements, resulting in either redundant efforts or non-compliance risks.

Recommendations

By ensuring that the future EU EFS program also reflects DHT-specificities, the EU can reduce regulatory uncertainty, encourage greater industry participation, and accelerate the safe and effective introduction of innovative DHTs and AIeMDs into clinical practice. Moreover, ensuring clearer coordination between the AI Act and MDR will help prevent regulatory bottlenecks, reduce the burden on manufacturers, and maintain robust safeguards, thus allowing AI-driven DHTs to reach clinical settings efficiently and responsibly. Towards this aim, it will be important to create synergies with existing projects in other ongoing EU-funded initiatives throughout the HEU-EFS timeframe.

Actionable steps

- **Describe the pathway for DHTs within the harmonized EU EFS program** that outlines the scope, eligibility criteria, and objectives of EFS for DHTs. The alignment with the iterative nature of software-driven technologies and AI-enabled MDs will be analysed by the HEU-EFS taskforce on DHTs (WP2 Task 2.2).
- **Ensure that templates and protocols also suit DHT specificities** to facilitate smoother regulatory submissions and ensure consistency across Member States (WP2 (ongoing), WP4 Tasks 4.2, WP7 Task 7.2).
- **Clarify the AI Act–MDR interplay in EFS** by providing specific guidance on how AI-related regulatory obligations apply in the context of EFS, detailing expectations for risk assessment, pre-EFS algorithm validation, and CIP. This should include concrete examples to help sponsors align early-stage compliance efforts with both regulatory frameworks. (WP2 (ongoing), WP4 Task 4.2).

Appendix 1

Table 1 Full names of work-packages and tasks mentioned in the document

Work packages	Tasks
WP1: Research and analysis on state of play of pre-market programs and implementation barriers to EFS	
WP2: Research and analysis on regulatory framework, and institutional and organizational characteristics of EU competent authorities	
WP3: Methodology development: rationale, processes, and procedure	<p>T3.1: Identification of eligibility criteria for the EU EFS Program (T 3.1.6 conditions for reimbursing investigational devices).</p> <p>T3.2: Identification of patient contribution to EFS</p> <p>T3.3: Development of processes, procedures, actors, and timelines.</p>
WP4: Methodology development: evidence requirements, data, and statistical tools	<p>T4.1: Evaluation of state of play of regulation and international standards to inform CIP development.</p> <p>T4.2: Development and validation of a standard EFS CIP Template.</p>
WP5: Methodology development: EU EFS program monitoring system	<p>T5.1: Research on the EU EFS Performance Dashboard compliance with EU data Regulations, links with the European Database of Medical Devices (EUDAMED) and level of confidentiality.</p> <p>T5.2: Design and implementation of the EU EFS Performance Dashboard.</p> <p>T5.3: Formulation of recommendations for the European Commission regarding performance monitoring of the future EU EFS Program.</p>
WP6: Methodology development: ethical and legal aspects	T6.1: Development of standard templates for the EU EFS Program.

Work packages	Tasks
<p>WP7: Testing the methodology: pilot use-cases</p>	<p>T7.1: Undertaking of preliminary activities in preparation for pilot use-cases.</p> <p>T7.2: Undertaking of EFS use-cases to test the methodology.</p> <p>T7.3: Evaluation and assessment.</p>
<p>WP8: Web portal, dissemination, exploitation, and communication</p>	<p>T8.1: Development of the Dissemination, Exploitation and Communication (DEC) Plan.</p> <p>T8.2: Implementation of Dissemination, Exploitation and Communication (DEC) Plan.</p> <p>T8.3: Design and provision of educational activities to stakeholders involved in the HEU-EFS project.</p>



Co-funded by
the European Union

The Harmonised approach to Early Feasibility Studies for Medical Devices in the European Union (HEU-EFS) project is supported by the Innovative Health Initiative Joint Undertaking (JU) under grant agreement No 101112185. The JU receives support from the European Union's Horizon Europe research and innovation programme and life science industries represented by MedTech Europe, COCIR, EFPIA, Vaccines Europe and EuropaBio.