innovative health initiative

HEU EFS

HARMONISED APPROACH TO EARLY FEASIBILITY STUDIES FOR MEDICAL DEVICES IN THE EUROPEAN UNION

Harmonised approach to EFS in the EU

Meeting with DGSANTE

July 3rd, 2025

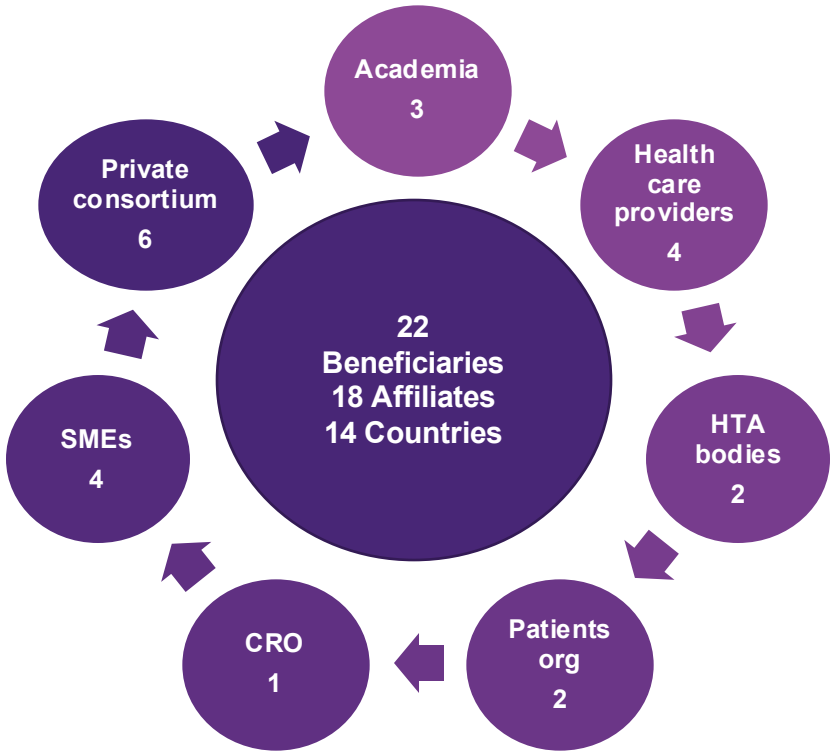
Harmonized Approach to Early Feasibility Studies for Medical Devices in the European Union (HEU-EFS)

Project information

Start date: 1 October 2023
End date: 30 September 2027

DOI: 10.3030/101112185
Total cost: € 19 008 438,75

Consortium



Advisory Board

- Competent Authorities
- Notified Bodies
- National Ethics Committees
- Medical societies
- Networks
- Independent Experts
- Trade Association

Patient Advisory Group

- 11 members

Goal

Formulate recommendations for the establishment of an Early Feasibility Studies Program within the European Union, with a focus on ensuring **patient safety** and enhancing the EU single market **competitiveness**.

Objectives

1. Conduct **research and analysis** on 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 **harmonised EU methodology** and recommendations using the **legal pathways available** to tailor the process for EFS.
4. Undertake **pilot use cases** to test the proposed methodology.
5. Develop **performance measurement instruments** for the EU EFS Program
6. Implement an open access **online portal** dedicated to EFS and **disseminate** results and recommendations.

Filling the gap

- **Feasible** in the EU:
  - **ISO 14155:2020** Clinical investigation of medical devices for human subjects — good clinical practice.
  - **MDR 2017/745** and **HTAR 2021/2282** early dialogue and life cycle approach for clinical evidence generation.
  - **MDCG 2021-6** – Rev 1. December 2023 Q&A regarding clinical investigation.
- **Beneficial** to patients, clinical sites & trialists, technological innovation developers, regulators.
- But **no standardized procedural framework**, guidelines or common reference standards to conduct EFS in the EU.
  - **No operational definition.**
  - We proposed a novel definition of **EFS-like.**
- The EU is at **risk of losing competitiveness and attractiveness** for innovation and investments.

EFS

- **limited** clinical investigation of a device **early in development**
- typically **before the device design** has been finalized, for a specific indication
- to evaluate the device design concept with respect to **initial clinical safety** and device **clinical performance** […] as per intended use in a **small number of subjects**
- Information obtained from an EFS can **guide device modifications**.

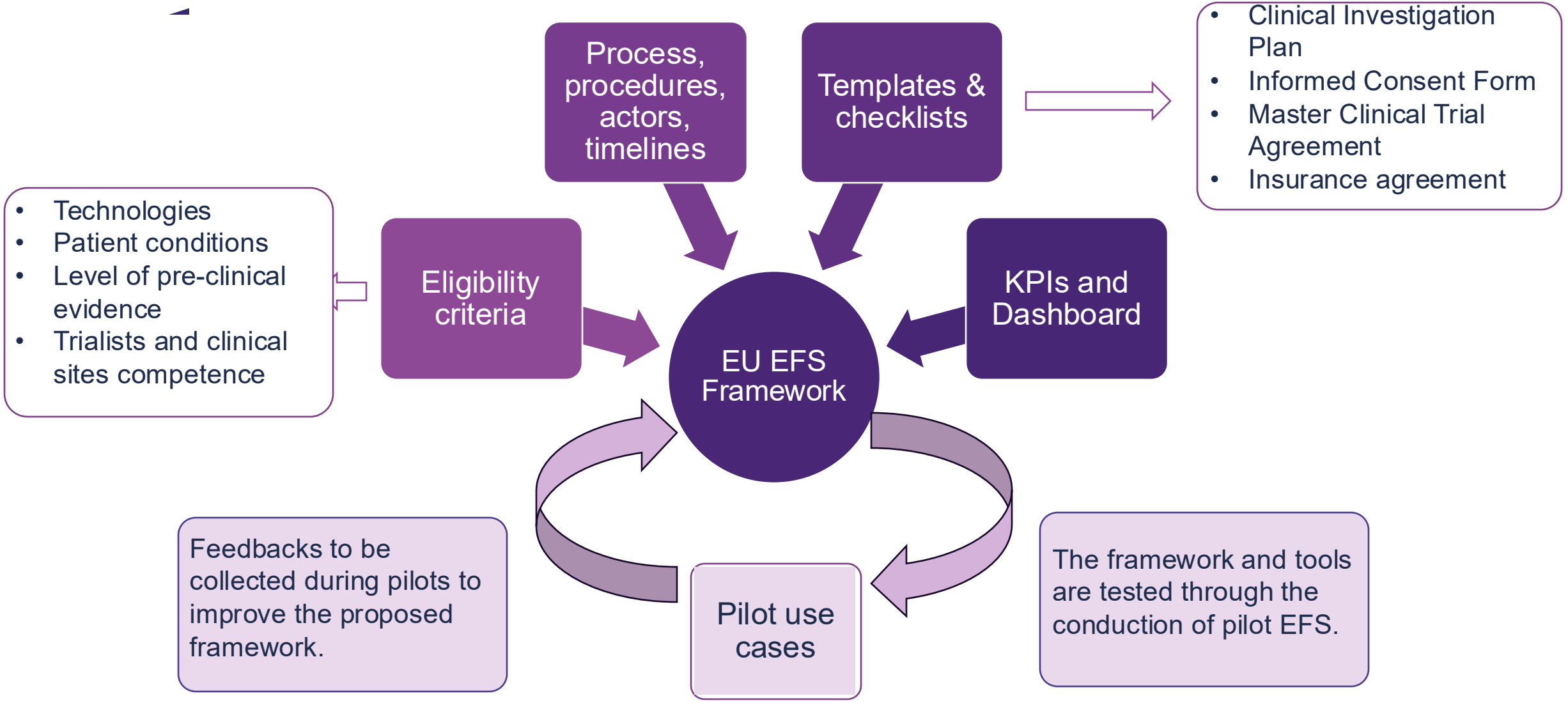
Regulatory status	Pre-market		Post-market	
Clinical development stage	Pilot stage (I.3.2)	Pivotal stage (I.3.3)	Post-market stage (I.3.4)	
Type of design	Exploratory or confirmatory (I.4.2)	Confirmatory (I.4.3)		Observational (I.4.4)
Descriptors of clinical investigations	First in human clinical investigation (I.5.2) Early feasibility clinical investigation (I.5.3) Traditional feasibility clinical investigation (I.5.4)	Pivotal clinical investigation (I.5.5)	Post-market clinical investigation (I.2.3)	Registry[a] (I.5.6) Post-market clinical investigation[a] (I.2.3)
Burden to subject	Interventional (I.6.2)			Non-interventional (I.6.3)

HEU-EFS Progress (update M21)

Completed	Completed	Ongoing – Deliverables due September 2025	Ongoing - pilots begin January 2026
Research & analysis	Recommenda-tions	Framework development	Framework test
• Pre-market CI approval pathways • Barriers & challenges of pre-market CI • Characteristics of EFS • EU regulatory framework and international standards • Organisational characteristics of NCA • Mapping ethics approval	• Harmonisation • Dialogue • Expertise and awareness • Transparency • Stakeholder involvement • Incentives for R&D • Reflect DHT-specific needs	• Eligibility criteria • Process, procedures, actors, timelines • Templates & checklists • KPIs and Dashboard	• Preparation for pilot use cases • Definition of selection criteria for technologies

HEU-EFS approved deliverables can be downloaded from https://cordis.europa.eu/project/id/101112185/results

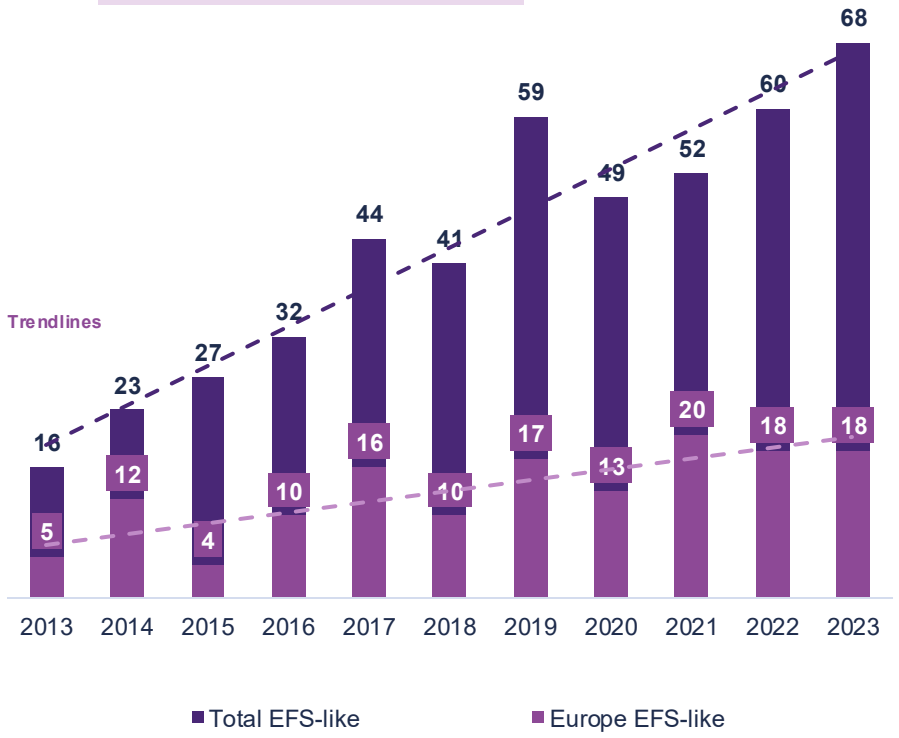
EU EFS Framework

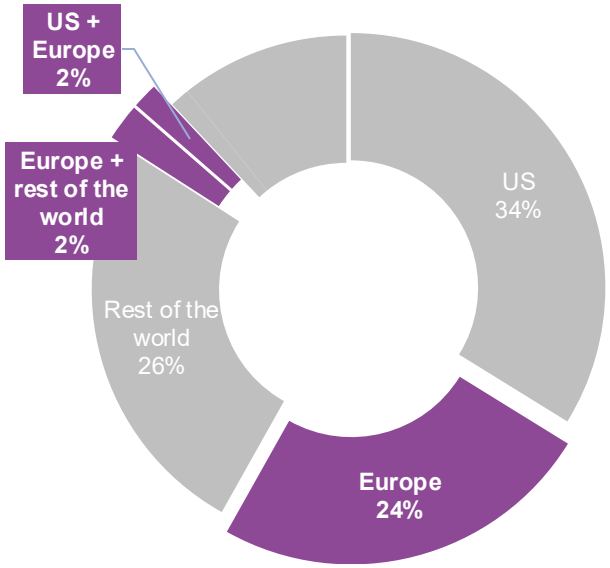


Synergies with breakthrough guidance, coordinated assessment, and other EU pathways (e.g., HTAR JSC, Expert Panel Scientific Advice).

EU NCAs have EFS expertise

A global, increasing trend





Overall 559 studies in the EFS-DB, of which **28% in European countries**

21 EU countries + Norway conducted **124 EFS-like studies, 1300 CI Applications in 2023**

Source: analyses on HEU-EFS Early Feasibility Studies Database (see deliverable D1.3)

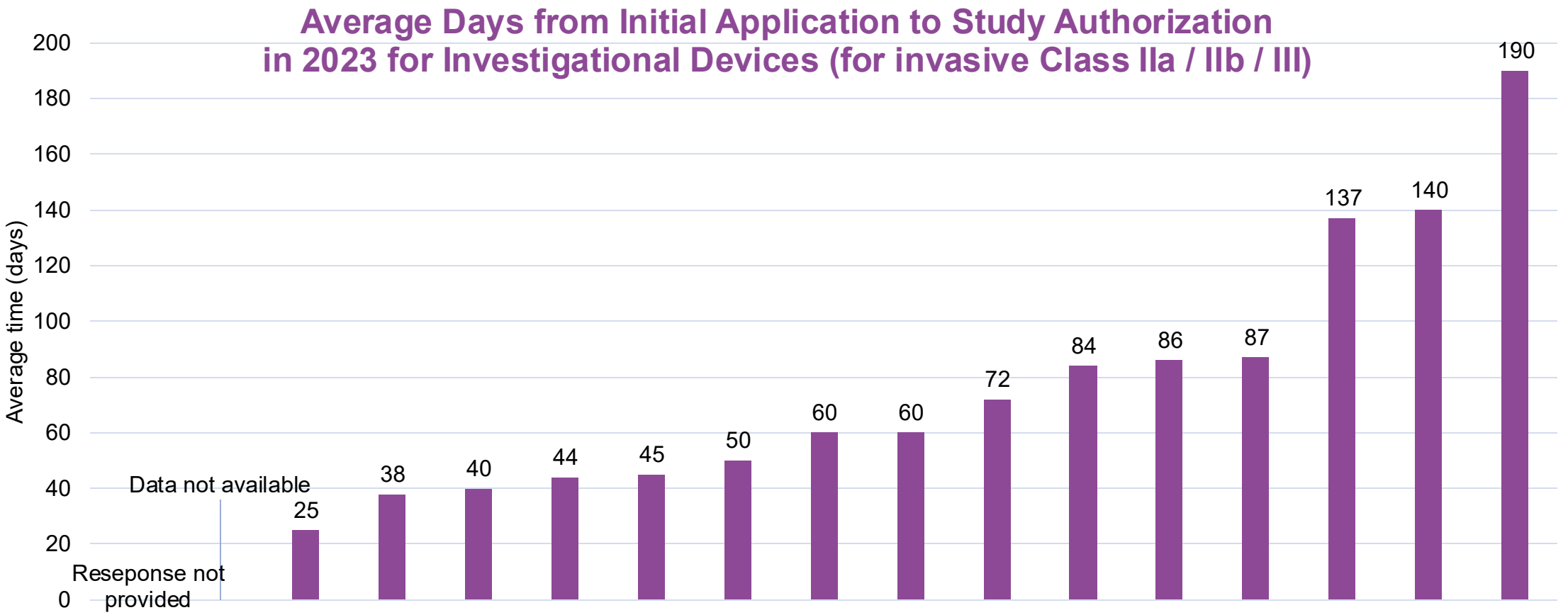
EFS are regarded as standard pre-market CIs

- Accompanying documentation (Annex XV)*
  - Application form
  - IB
  - CIP
  - Other information (e.g., proof of insurance cover, ICF)
- MS notifies sponsor about scope and completeness of application
- Sponsor comments or completes the application
- MS notifies sponsor about scope and completeness of application
- For any device other than Class I or non-invasive Class IIa and IIb (Art. 70(b))

For Class I or non-invasive Class IIa and IIb, the CI may start, unless otherwise stated in national law, provided that a negative opinion has not been issued by an ethics committee (art. 70(7a)).

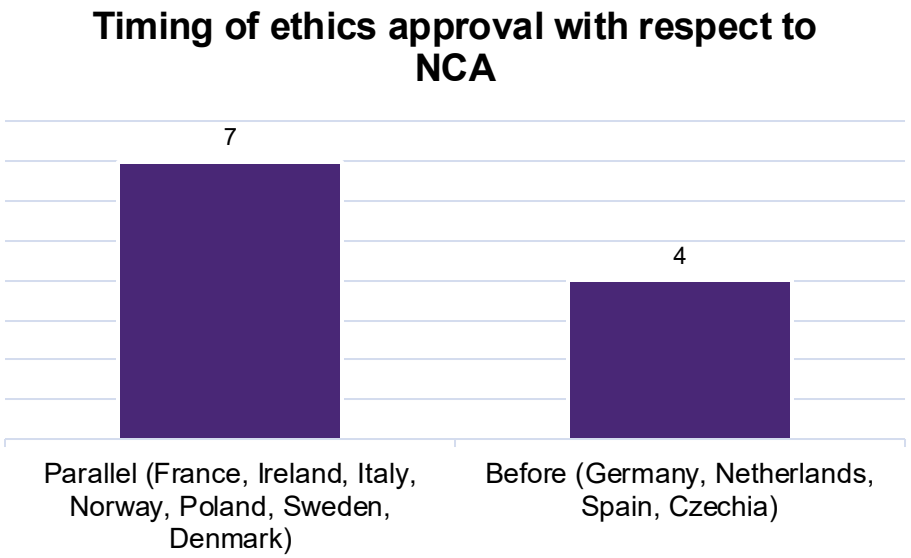
*For devices covered by Art. 62.
Abbreviations Art. = article of the MDR, d=days, CIP =Clinical Investigation Plan, IB = Investigator's Brochure, ICF = informed consent form),

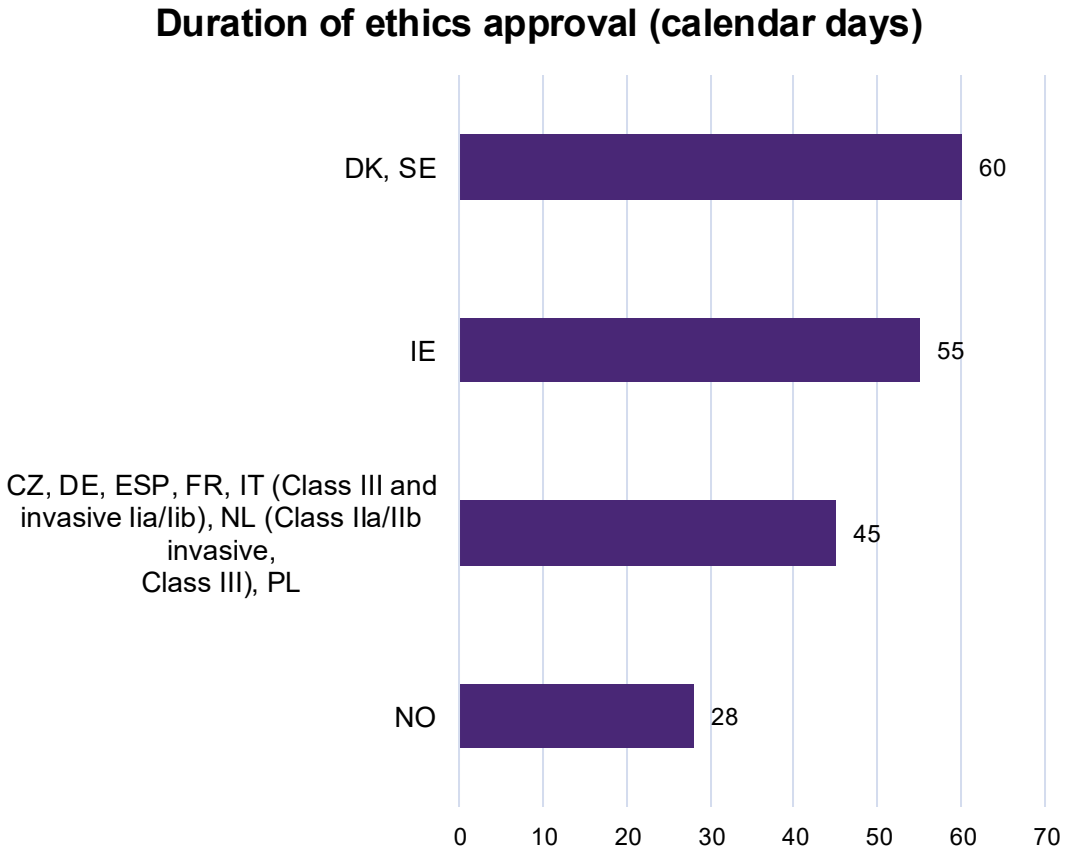
Current timelines



Source HEU-EFS Survey for NCAs (Dec 2024 - Jan 2025), n=19/30 (61%)

Preliminary mapping of ethics approval



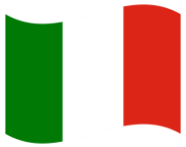


Preliminary mapping of ethics approval

	Czechia	Ireland	Norway	Netherlands	Denmark	France	Germany	Italy	Spain	Poland
Application form / Letter of Intents	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)
Cover letter	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	No	Yes (mandatory)	NA (not avaliable)	Yes (mandatory)	Yes (mandatory)
Investigator's brochure (IB)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)
Synopsis	Yes (mandatory)	NA (not avaliable)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (optional)	Yes (mandatory)
Clinical trial protocol / Clinical investigation plan (CIP)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)
Clinical evaluation plan (CEP)	No	NA (not avaliable)	NA (not avaliable)	Yes (mandatory)	No	Yes (mandatory)	Yes (mandatory)	Yes (optional)	Yes (optional)	Yes (mandatory)
Pre-clinical data (if not present in the protocol)	Yes (mandatory)	NA (not avaliable)	No	Yes (mandatory)	No	Yes (mandatory)	NA (not avaliable	NA (not avaliable)	Yes (mandatory)	Yes (optional)
Clinical data (if not present in the protocol)	Yes (mandatory)	Yes (mandatory)	Yes (optional)	Yes (mandatory)	No	Yes (mandatory)	NA (not avaliable	NA (not avaliable)	Yes (mandatory)	Yes (optional)
List of documents sent for scrutiny	Yes (mandatory)	Yes (mandatory)	Yes (optional)	Yes (mandatory)	No	No	NA (not avaliable	Yes (optional)	NA (not avaliable)	Yes (optional)
Case report form (CRF)	Yes (mandatory)	Yes (mandatory)	NA (not avaliable)	No	No	No	NA (not avaliable	Yes (mandatory)	Yes (mandatory)	Yes (optional)
Letter of delegation	No	Yes (mandatory)	NA (not avaliable)	NA (not avaliable)	No	NA (not avaliable)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (optional)
Safety requirements	Yes (mandatory)	NA (not avaliable)	Yes (mandatory)	NA (not avaliable)	Yes (mandatory)	NA (not avaliable)	Yes (mandatory)	Yes (mandatory)	No	Yes (optional)
Letter to general practitioner (PLS)	No	Yes (mandatory)	NA (not avaliable)	No	No	Yes (mandatory)	NA (not avaliable	Yes (optional)	No	Yes (optional)
Risk management documentation	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	No	No	Yes (mandatory)	Yes (mandatory)	NA (not avaliable)	No	Yes (mandatory)
Instructions for use of the MD	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	No	Yes (optional)	Yes (mandatory)	NA (not avaliable)	Yes (mandatory)	Yes (mandatory)
Dossier on the active substance, if the MD incorporates a medicina	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	No	No	Yes (mandatory)	Yes (mandatory)	NA (not avaliable)	Yes (mandatory)	Yes (optional)
Signed statement that the sponsor is aware that the competent aut	No	NA (not avaliable)	Yes (mandatory)	NA (not avaliable)	No	Yes (mandatory)	NA (not avaliable	NA (not avaliable)	No	Yes (optional)
Subject related										
Informed consent form (ICF)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)
Consent form for processing of personal data	Yes (optional)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)
Documents to be delievered to patients (e.g. Diaries, Questionnaire	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (optional)	Yes (optional)	Yes (mandatory)	Yes (optional)
Subject information leaflet	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (optional)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)
Arrangements for recruitment of subjects	Yes (optional)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	NA (not avaliable	NA (not avaliable)	Yes (optional)	Yes (mandatory)
Facilities & staff related										
CV of each investigator responsible for the conduct of the trial in a s	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)
Conflict of interest declaration for each investigator	No	Yes (mandatory)	Yes (optional)	No	No	NA (not avaliable)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)
Center eligibility	No	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	No	Yes (optional)	Yes (mandatory)	Yes (mandatory)	Yes (optional)	Yes (optional)
Financial and Insurance Information										
Insurance certificate	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)
Contract between sponsor-financing entity	Yes (mandatory)	NA (not avaliable)	Yes (mandatory)	No	No	NA (not avaliable)	Yes (mandatory)	Yes (mandatory)	No	Yes (optional)
Master clinical trial agreement	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)	No	NA (not avaliable)	Yes (mandatory)	Yes (mandatory)	No	Yes (optional)
EC fees payment receipt	No	Yes (mandatory)	No	No	No	NA (not avaliable)	NA (not avaliable	Yes (mandatory)	Yes (mandatory)	Yes (mandatory)
For non-profit investigations, fee exemption letter	NA (not avaliable	NA (not avaliable)	NA (not avaliable)	NA (not avaliable)	No	NA (not avaliable)	NA (not avaliable	Yes (mandatory)	Yes (mandatory)	Yes (optional)
Compensation for trial participants	NA (not avaliable	NA (not avaliable)	NA (not avaliable)	Yes (mandatory)	No	Yes (mandatory)	Yes (mandatory)	NA (not avaliable)	Yes (mandatory)	Yes (mandatory)

Deep dive into NCA experience with EFS

Seven 1-to-1 interviews conducted with EEA NCA from April-June 2025


ITALY§


NORWAY


IRELAND §,*


PORTUGAL§


CZECH REPUBLIC


BELGIUM*


FRANCE*

- Questions approved by Bocconi University Research Ethics Committee.
- Facilitated by CIE WG and European Commission.

§ Member of HEU-EFS Advisory Board
* Coordinating Member States for pilot coordinated assessments

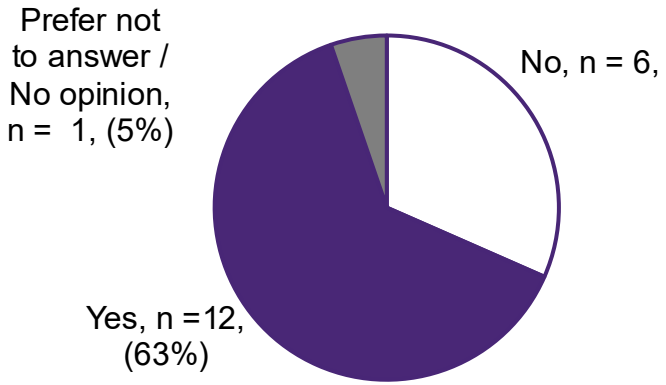
Insights from NCA interviews

- **Lack of formal EFS definition** results in disparate EFS assessment practices across NCAs and heterogeneous thresholds for risk evaluation and preclinical evidence requirements - highlighting a fragmented regulatory environment where they struggle.
- **Poor submission documentation quality** challenge NCAs' validation and evaluation of EFS.
- **Harmonised templates and checklists** developed by HEU-EFS project may improve the quality of applications.
- **Coordinated assessment pilot** are regarded as a critical opportunity for learning from each other, ensuring a unified EFS assessment approach in the EU, paving the way for a MDCG-endorsed guidance.

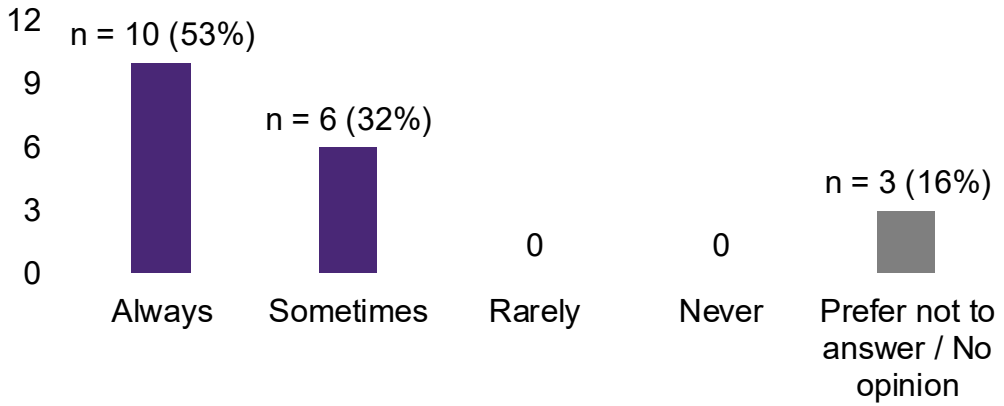
Insights from NCA interviews

- **Dialogue** - regardless of whether dialogue is formal or informal - improves efficiency and speed of EFS assessment through NCA adaptability and sponsor cooperation.

Dialogue between NCA and sponsors for pre-market CIs



Does dialogue improve CI application quality?



But some NCA consider dialogue illegal

Source HEU-EFS Survey for NCAs (Dec 2024 - Jan 2025), n=19/30 (61%)

What a future EFS process could look like: initial concept

- Ensure readiness and efficiency for key actors, both on the side of authorities as well as EFS initiator.
- Improve resource and timing planning, clarify EFS objectives and needs, and identify key potential challenges early on.
- Enhance opportunity to conduct EFS in more than 1 Member State

1

CONTACT POINT AND EARLY DIALOGUE

Opportunity to engage more early on, and build trust

2

VALIDATION PROCESS

A structured and timed validation process for all involved stakeholders

3

EFS REVIEW

Predictable, timed documentation review for eligible technologies with opportunity for acceleration

ELIGIBITY CRITERIA

Structured approach to ensure only fit-for-purpose technologies undergoing new EFS process

EU EFS Proposals overview

Pre-submission

Submission & Review

Presubmission phase

- Contact point early on in the process to allow for planification and resource allocation
- Multistakeholder early dialogue for sponsor, NCA, and where appropriate and relevant Ethics Committee, experts of the NCA, principal investigator of clinical site. Option to invite other Member States if EFS is conducted in multiple countries.

National Competent Authority (NCA) Timeline (30% reduction)

Initial "Validation" Phase → completeness of submission file

- *NCA assessment time*
- *Proceed to Review Phase or Additional Information Request (AIR)*
- *AIR Cycle time for sponsor and NCA*

Review Phase → Scientific Review of submission file

- *NCA review time, including utilizing a "stop-clock" approach, and encouraging "rolling review process" to facilitate timely review*
- *Approval or Additional Information Request (AIR)*
- *AIR Cycle time for sponsor and NCA*

In case of more than 1 NCA: Coordination Process to follow Coordinated Assessment

Measuring EFS performance

KPIs

- # of EFS submitted
  - total, per country, per year
- # of EFS submitted by SMEs
  - total, per country, per year
- # of NCA involved in EFS assessment
- List of NCA involved in EFS assessment
- # of EFS involving patient / patient assoc in study design

- # of clinical sites involved in EFS
  - total, per country, per year (EU only)
- # of single-centre, multi-centre, multi-country EFS
- # of EFS per device risk class
- # of EFS per health condition
- # of EFS assessing PROMs
- # of EFS assessing PREMs
- Dialogue
  - Participation, modality, topics, helpfulness

- # of EFS approved
  - total, per country, per year
- # of EFS approved by SMEs
  - total, per country, per year
- EFS approval rate (%)
- Avg time for EFS approval
- # of EFS applications rejected
- # of NCAs requests for comments
- # of ethics committee involved in EFS assessment
- List of ethics committee involved in EFS assessment
- Avg time from ethics committee submission to approval

- Avg time from signature w clinical site to 1st patient enrolled
- Avg # of patients enrolled in EFS
- Avg time from EFS approval to signature w clinical site
- % of EFS transitioning to pivotal
- # of EFS with patient withdrawal
- # of EFS terminated, withdrawn, or suspended
  - with explanations
- Additional pre-market CIs after EFS termination, withdrawn, or suspension
  - Number, list

Modality of data collection to calculate KPIs

Data required to calculate KPIs will be collected using four online forms completed by sponsors of EFS pilots

KPIs

- # of EFS submitted
  - total, per country, per year
- # of EFS submitted by SMEs
  - total, per country, per year
- # of NCA involved in EFS assessment
- assoc in study design

Online Form #1
"Self Evaluation Checklist"

- # of clinical sites involved in EFS
  - total, per country, per year (EU only)
- # of single-centre, multi-centre, multi-country EFS
- # of EFS per device risk class
- # of EFS per health condition
- # of EFS assessing PROMs
- # of EFS assessing PREMs

Online Form #2
"Application to NCA(s)"

- # of EFS approved
  - total, per country, per year
- # of EFS approved by SMEs
  - total, per country, per year
- EFS approval rate (%)
- Avg time for EFS approval
- # of EFS applications rejected
- # of NCAs requests for comments
- Avg time from ethics committee submission to approval

Online Form #3
"Validation by NCA(s)"

- Avg time from signature w clinical site to 1st patient enrolled
- Avg # of patients enrolled in EFS
- Avg time from EFS approval to signature w clinical site
- % of EFS transitioning to pivotal
- # of EFS with patient withdrawal
- # of EFS terminated, withdrawn, or su
  - with
- suspension
  - Number, list

Online Form #4
"EFS Pilot"

Key Discussion Points

- Early dialogue in the context of targeted evaluation – open discussion.
- Synergies with breakthrough guidance, coordinated assessment, and other EU pathways (e.g., HTAR JSC, Expert Panel Scientific Advice).
- Engagement with CIE WG.
    - Online workshop end of August – beginning of September.
    - NCA feedback regarding process, templates, checklists (in preparation of pilots).
    - Slot at CIE meeting n November.
- EU CIRCABC system for pilots?
- DGSANTE invited to join HEU-EFS yearly consortium meeting in Barcelona (15-16 September).

innovative health initiative

COCIR

efpia

EuropaBio

MedTech Europe
from diagnosis to cure

Vaccines Europe

Co-funded by
the European Union