innovative health initiative

HEU EFS

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

US vs. EU: 10 Years of Experience with EFS vs. a Program Starting to Emerge in Europe

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Privileged Talk | Milan, 18 March 2025

Acknowledgement

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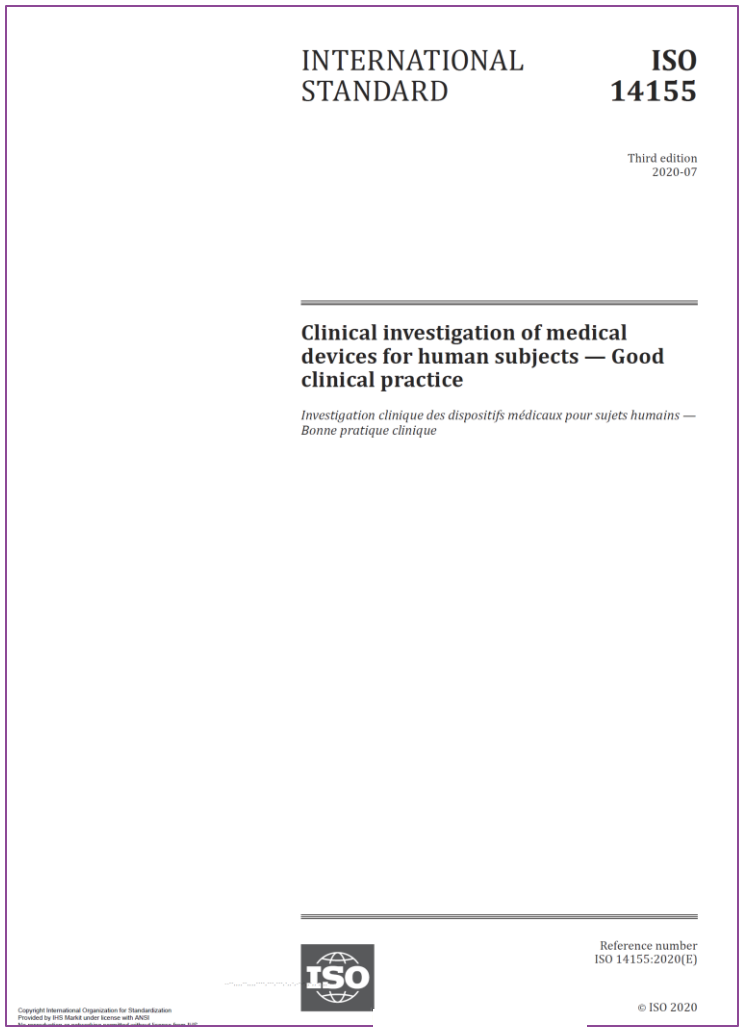
Early Feasibility Studies (EFS)



INTERNATIONAL STANDARD **ISO 14155**

Third edition
2020-07

Clinical investigation of medical devices for human subjects — Good clinical practice

Investigation clinique des dispositifs médicaux pour sujets humains — Bonne pratique clinique

Reference number
ISO 14155:2020(E)

WHAT?

A **limited clinical investigation** of a device **early in development.**

WHEN?

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).

WHY?

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.

The broad review of pre-market device programs in the US

% MDs clinical studies in US

87% → 45%

2004 — 2009

02/2011

Innovation Pathway

- Aim: improve pre-market review.
- Focus: revolutionary technology with important public health implications that would challenge CDRH's current approach.

10/2011

Network of Experts Program

- Aim: overcome the internal lack of experience and expertise needed to review emerging, innovative medical technologies.

11/2011

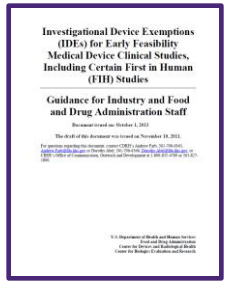
Pilot program for EFS investigational device exemption (IDE)

- Aim: recoup the US leading role in pre-market research for MDs and accelerate access to medical technologies.

04/2012

Innovation Pathway 2.0

- Aim: offer new and modified tools and methods to deepen collaboration between the FDA and innovators early in the process, prior to pre-market submission, with the goal to shorten the overall time and cost it takes for the development, assessment and review of MDs.


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

10/2013

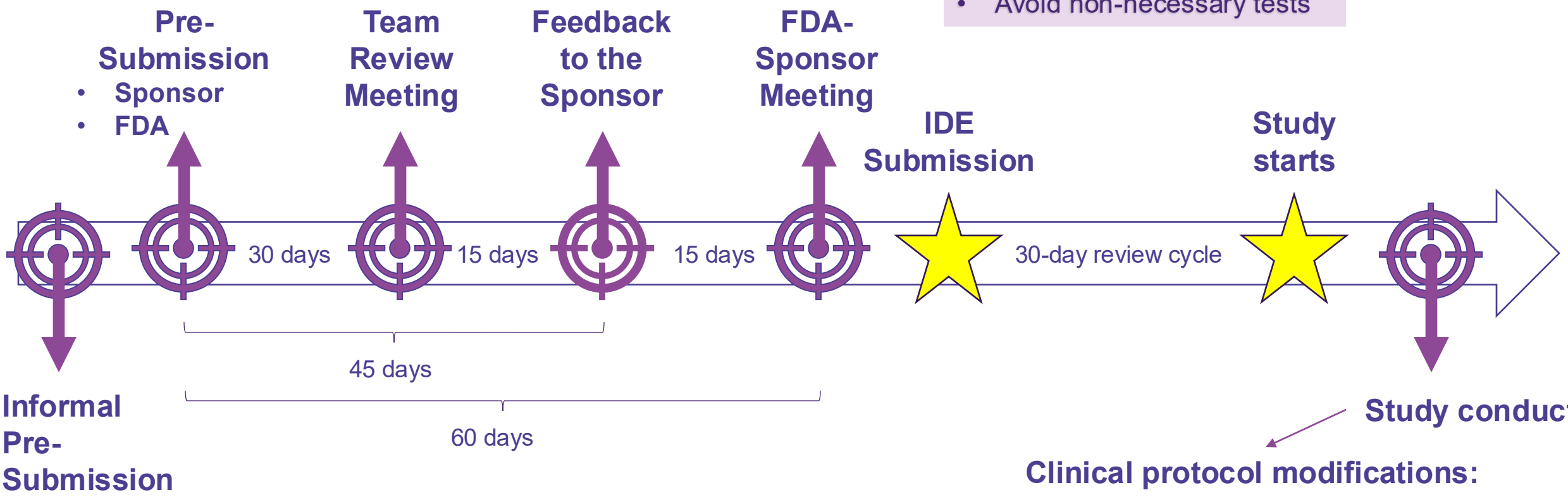
Guidance on Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies

Source Holmes et al, 2016

The FDA EFS process

Strengths

- Dialogue
- Flexibility
- Predictability
- Iterations
- Modification(s)
- Safety
- Avoid non-necessary tests



Clinical protocol modifications:

- 5-day notification changes.
- Changes that require FDA approval:
  - Contingent approval.
  - Interactive approval: 30-day review cycle.

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

Goal

Formulate recommendations for the establishment of an EFS Program within the EU, with a focus on ensuring patient safety and enhancing the EU single market competitiveness and attractiveness for R&D funds.

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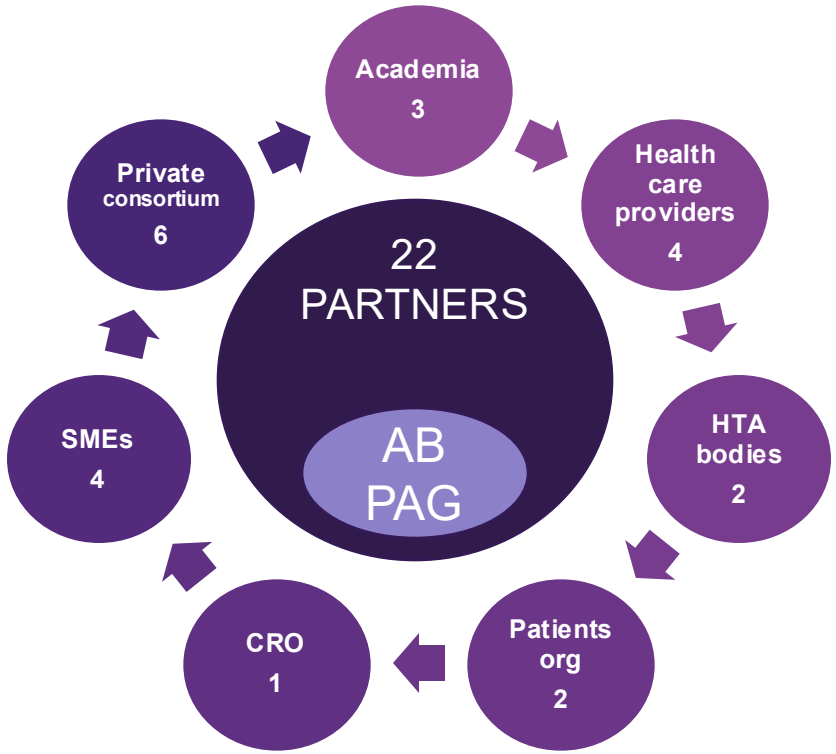
Consortium



WP 9 Scientific supervision and project management

Research and analysis

- WP 1 State of play of pre-market clinical evidence generation programs and implementation barriers to EFS
- WP 2 Regulatory framework and organization of clinical evidence generation programs in the EU

Methodology development

- WP 3 Rationale, processes, and procedure
- WP 4 Evidence requirements, data, and statistical tools
- WP 5 Program monitoring system
- WP 6 Ethical and legal aspects

Methodology test

- WP 7 Pilot use cases

WP 8 Web portal, dissemination, exploitation, and communication

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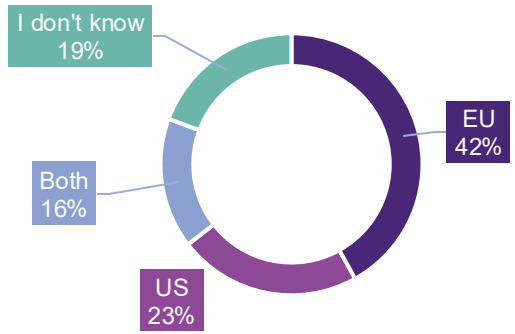
Co-funded by the European Union

Research and analysis

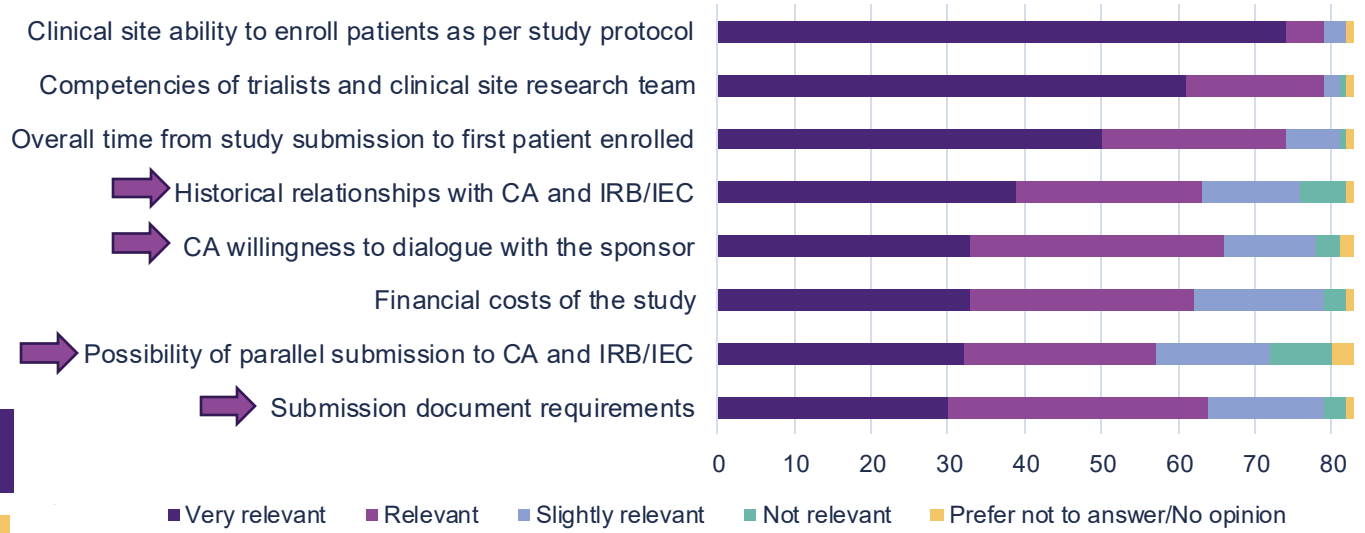
- Analysis of EU and US regulatory frameworks and international standards.
- Deep dive into FDA EFS program.
- Analysis of the approval pathways for pre-market clinical investigations in 56 EU, EEA, non-EU countries.
- Collection of quantitative data and analysis of the characteristics of EFS.
- Analysis of NCAs institutional and organisational characteristics.
- Surveys with clinical investigation sponsors.
- Discussion of challenges of pre-market clinical research in Europe with NCAs, NBs, HTA bodies, ethical committees, hospitals, professional associations, patients, CRO, technology developers, including SMEs.

Pre-market clinical investigations for MDs in the EU

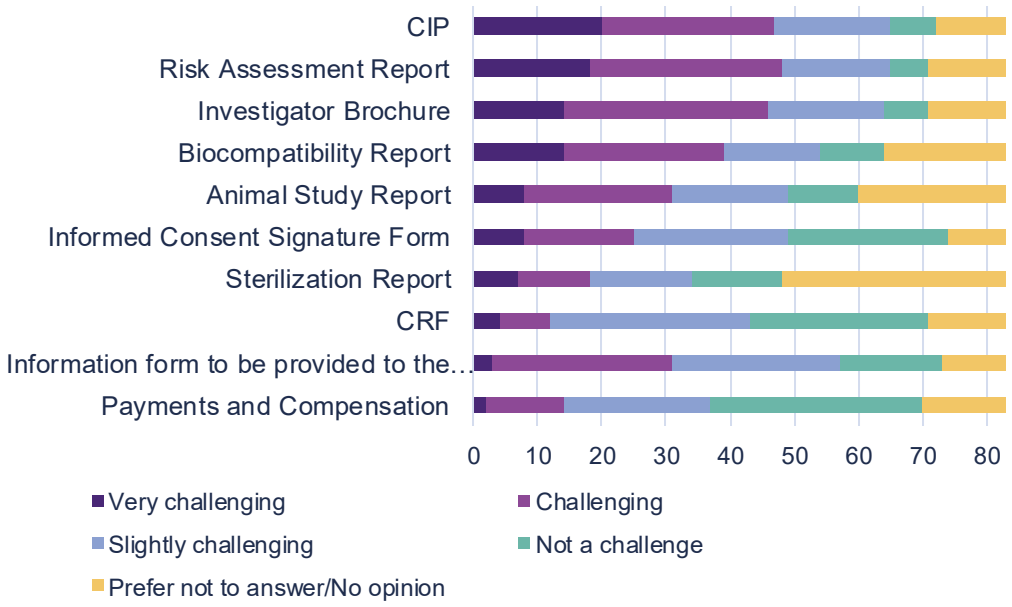
Favourite location for conducting pilot CIs (n=83)



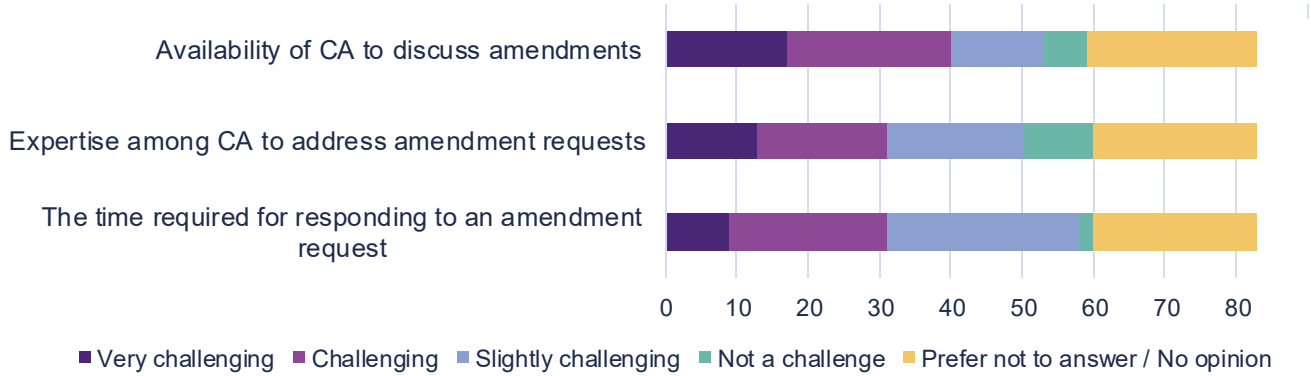
Key criteria influencing the selection of the country



Most challenging documents to get approved by NCAs



Challenges of the dialogue with NCAs when managing amendments to the CI

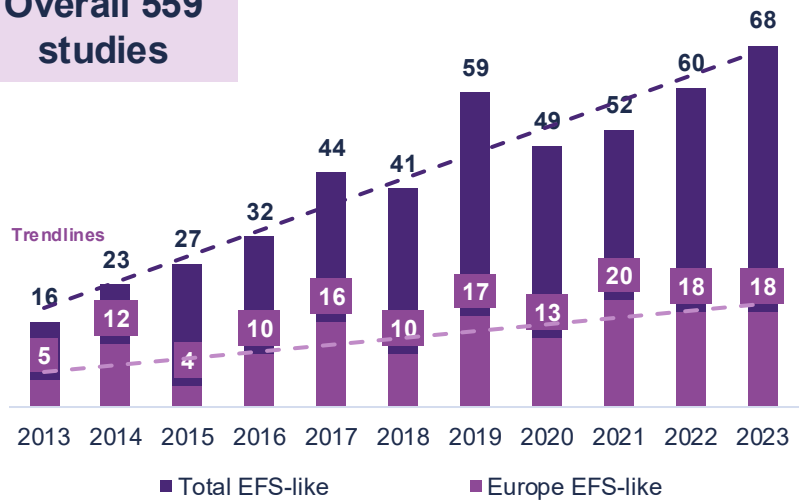


Source HEU-EFS Survey for CI sponsors (Oct-Nov 2024), n=83

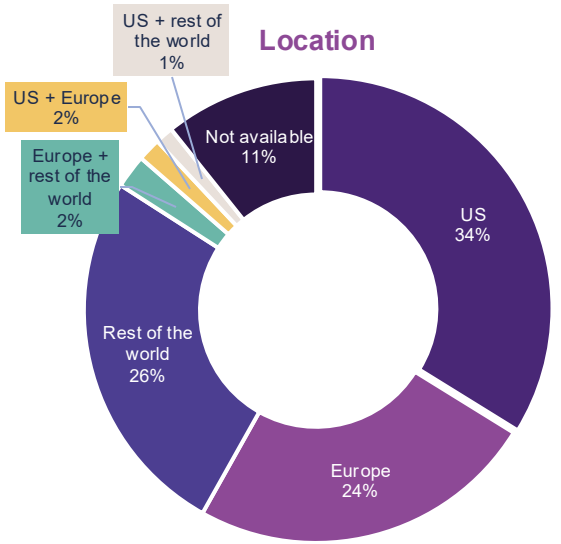
Characteristics of EFS

Overall 559 studies

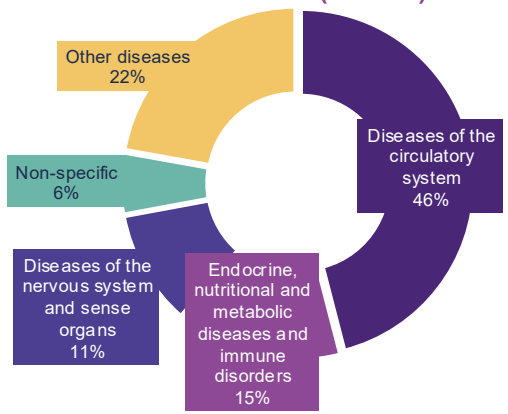
Global trend



Location

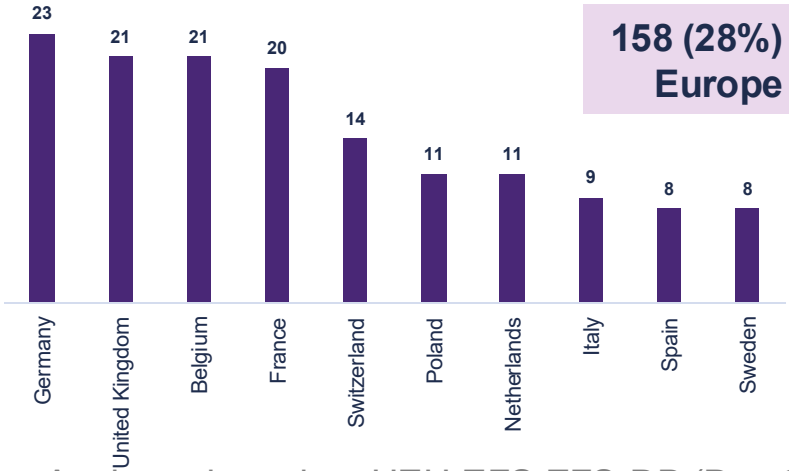


Patient conditions (ICD-10)



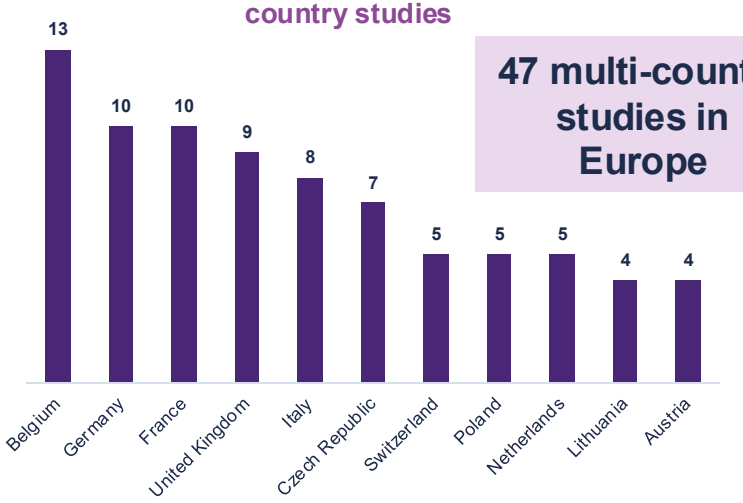
Country location - Europe

158 (28%) in Europe

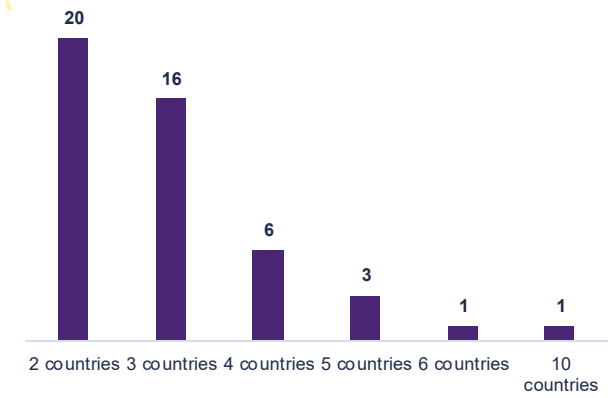


European countries involved in multi-country studies

47 multi-country studies in Europe



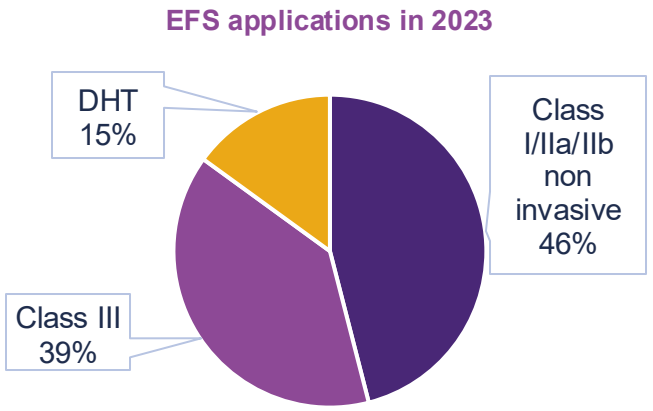
Number of collaborating countries in EFS-like studies (Europe only)



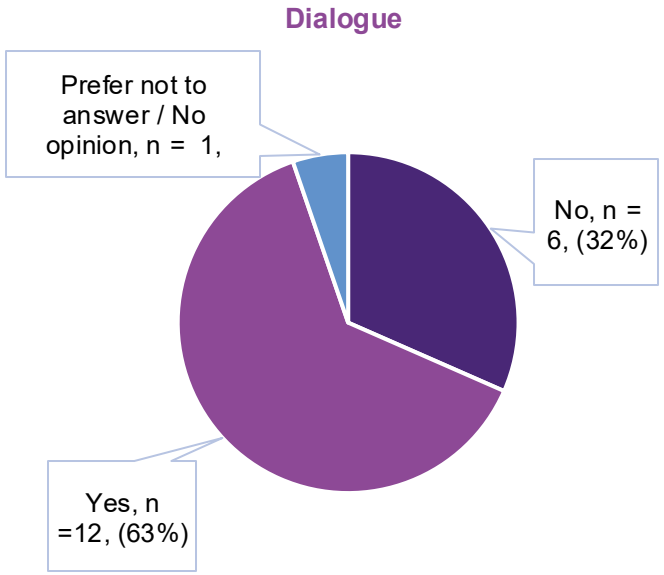
Source Analyses based on HEU-EFS EFS-DB (Dec 2024)

Institutional and organizational characteristics of NCAs

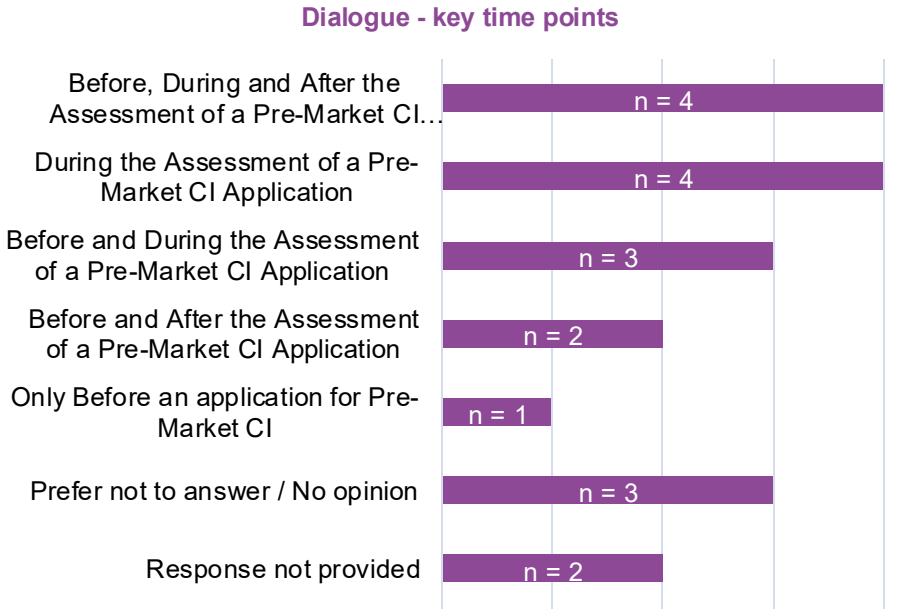
- 11 NCAs (58%) record the clinical development stage.
  - 6 NCAs record EFS.
- 46 EFS in 2023 reported by 4 NCAs.

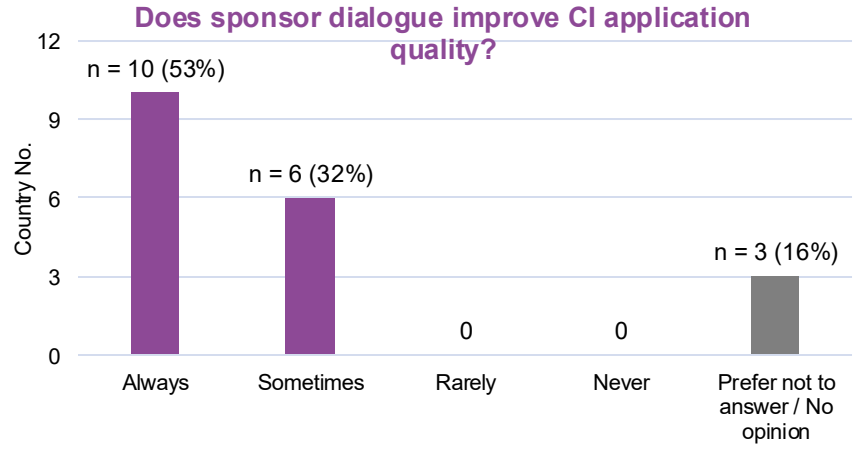


Source HEU-EFS Survey for NCAs (Dec 2024 - Jan 2025), n=19/30 (61%)

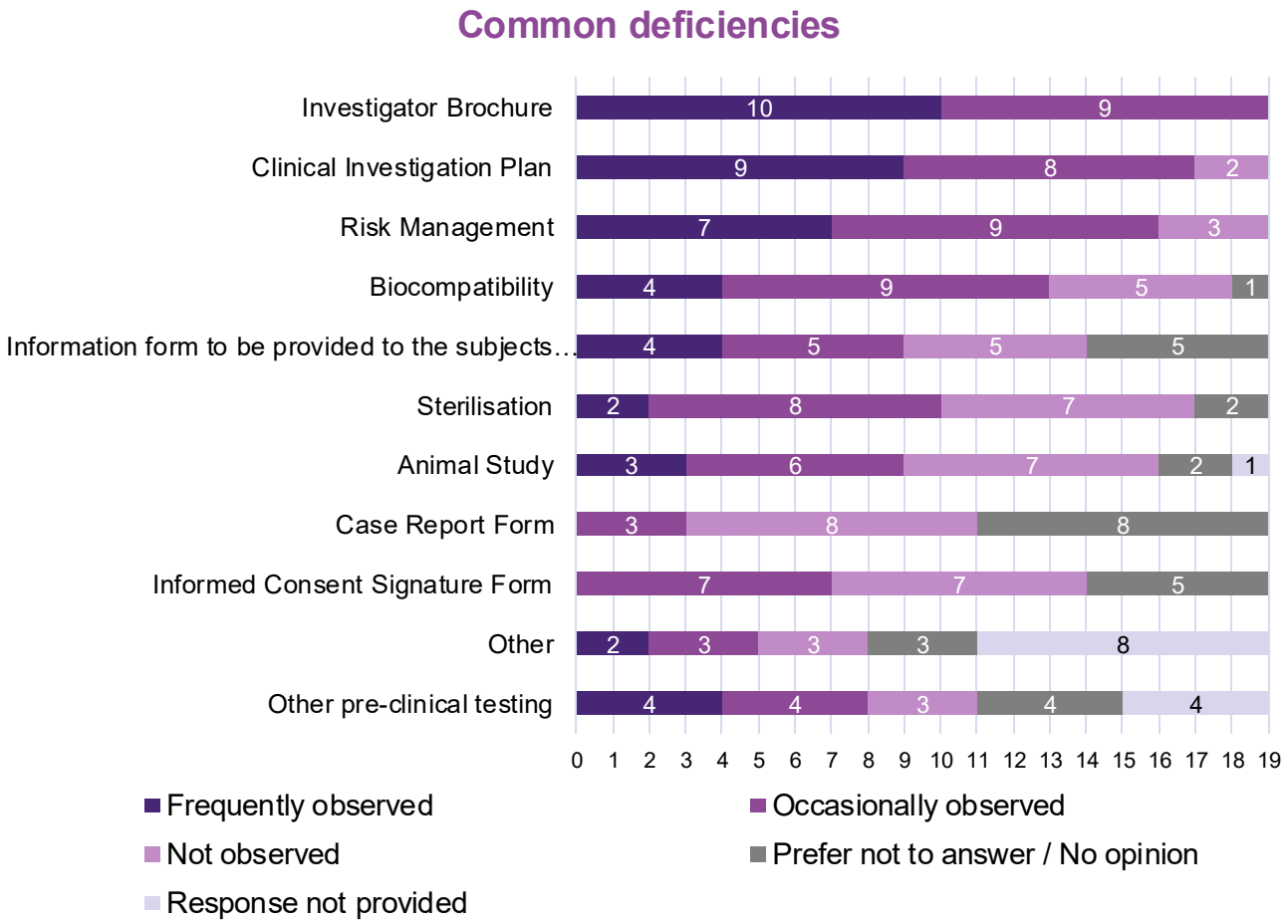


- 'Pre-submission' or 'innovation' meetings.
- Scientific advice is possible in some NCAs, in some cases associated with a fee.
- Sometimes the process is official, and in some cases, it is ad hoc or sporadic.





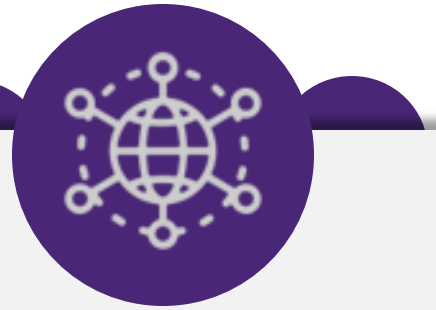
Institutional and organizational characteristics of NCAs



Most likely causes:

- Poor understanding of the content of standards.
- Inadequate documentation demonstrating compliance to standards.
- Price of standards.
- Lack of understanding of the CI process and applicable MDCG guidance documents.

Recommendations from extensive research and analysis



- Develop specific **EFS guidance** within the MDR framework.
- Establish **standardised templates** for essential EFS documents.
- Develop a **harmonised process** for EFS assessments together with the NCAs.
- Identify **device and protocol modifications**.
- Reduce regulatory **assessment timelines**.
- Monitor and evaluate the implementation of **harmonised procedures**.

HARMONISATION

- Standardize **regulatory dialogue types.**
- Establish a possible process for seeking **regulatory feedback**.
- Develop **iterative feedback mechanisms**.
- Assess and refine the **advisory process**.
- Define **key performance indicators** (KPIs) **for** the **dialogue process**.

DIALOGUE

Recommendations from extensive research and analysis

- Identify **types of expertise** needed by stakeholders involved.
- Deliver **training program**.
- Develop an online **repository for EFS-related documents**, guidance, template and best practices.

EXPERTISE & AWARENESS

- Develop an **online database** with granular information regarding submitted and approved EFS.
- Improve **quality and availability of data on EFS.**
- Implement **monitoring and evaluation systems** for EFS.

TRANSPARENCY

- Establish **structured engagement pathways** for patient panels, patient associations, expert panels and HTA bodies.
- Propose **methodologies and best practice guidelines** for early patient involvement in CIs.
- Increase **NCA participation** in structured stakeholder engagement initiatives.
- Develop **patient-friendly ICF** for EFS.
- Encourage the use of **patient experience data** to inform regulatory decisions.
- Facilitate **knowledge sharing** and capacity building among stakeholders.

STAKEHOLDER INVOLVEMENT

Recommendations from extensive research and analysis

- Conduct a comprehensive review of various **economic and fiscal mechanisms** to foster R&D.
- Propose **types of coverage** available, the **responsible authority** for verifying coverage eligibility and providing coverage.
- Develop a **structured coverage application** process for sponsors.

INCENTIVES FOR R&D IN THE EU

- Develop an inclusive **EFS pathway, tailored to** the specificities of **DHTs.**
- Develop **DHT-specific templates and protocols.**
- Clarify the **AI Act–MDR Interplay in EFS.**

REFLECT DHT-SPECIFIC NEEDS

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Thank you!

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