From where we start: The current state of play of EFS in Europe

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EFS characteristics

Key elements for an EU EFS program

Early and continuous dialogue between sponsors and regulators

Processes for **iterative changes** for both **device design or study design** during EFS

Limited **number of patients** (staged enrolment), adequately **informed and engaged** in the research

Experienced clinical sites (patient populations, ethical and legal issues, contracting)

Potential **benefits outweigh risks**

Source: HEU-EFS Scoping literature review (LINK)

EFS are feasible in the EU

EFS in the EU: feasible but not yet facilitated

MDR and International Standards mainly focus on general clinical investigations (CIs)

MDGC guidance theoretically allows similar flexibility to the US EFS program

Existing templates and standards for general CIs only partly applicable to EFS and rarely address EFS-specific needs

Limited detail and lack of EFS provisions make applications difficult

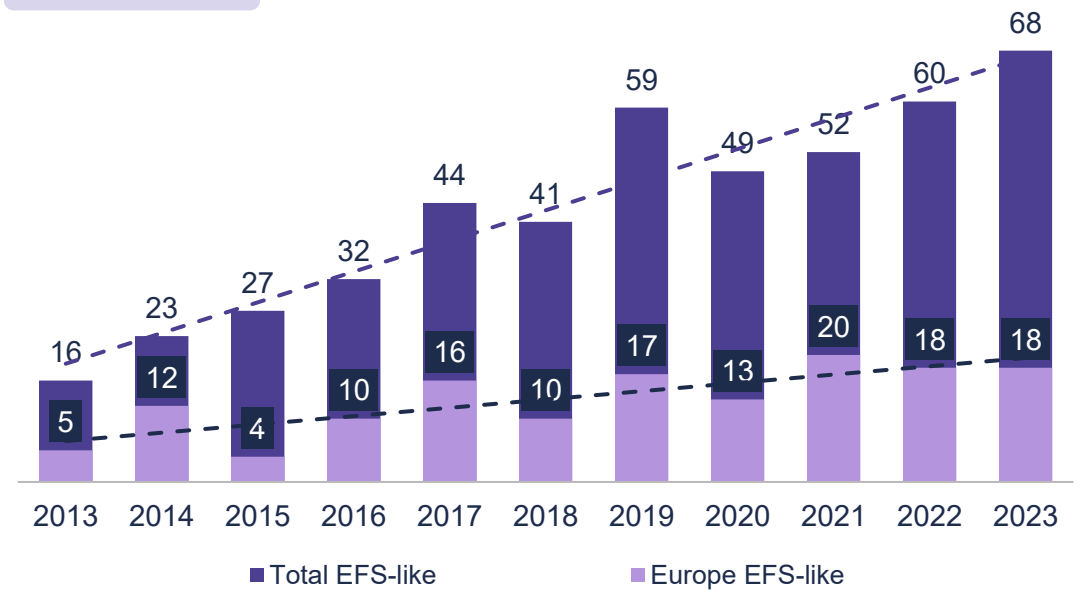
Urgent need for EFS-tailored EU guidance and templates

During interviews, NCAs reported a lack of formal EFS definition and homogeneous assessments across Member States

Source: HEU-EFS Scoping literature review (LINK) and NCA Interviews (n=8, 2025) (LINK)

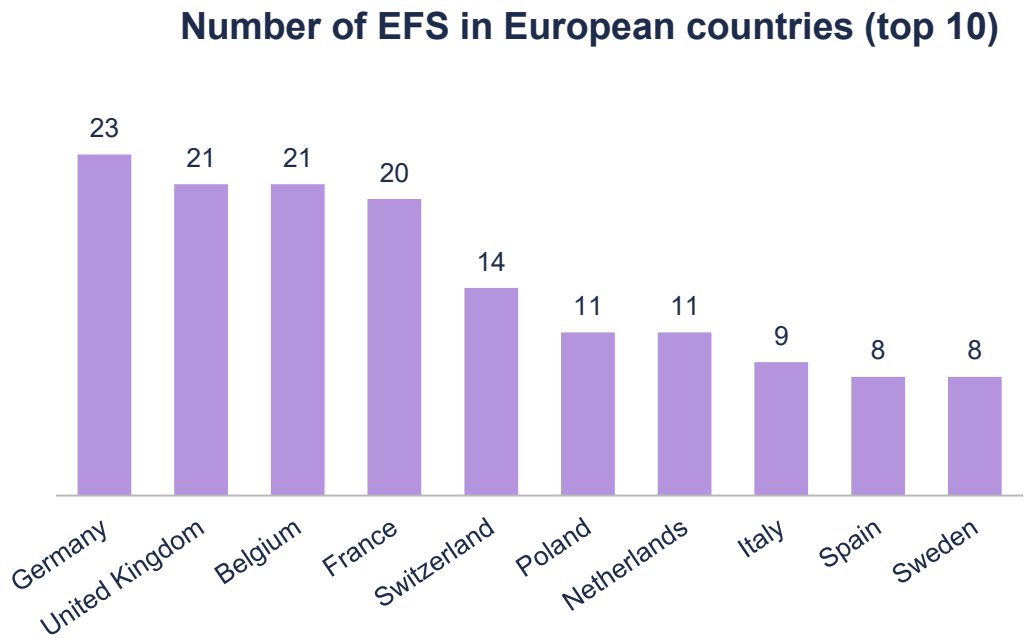
EFS are implemented in the EU

559 studies



In 2013-2024:

- **24%** of EFS conducted in **Europe only**
- **4%** of EFS conducted in **Europe and other jurisdictions**



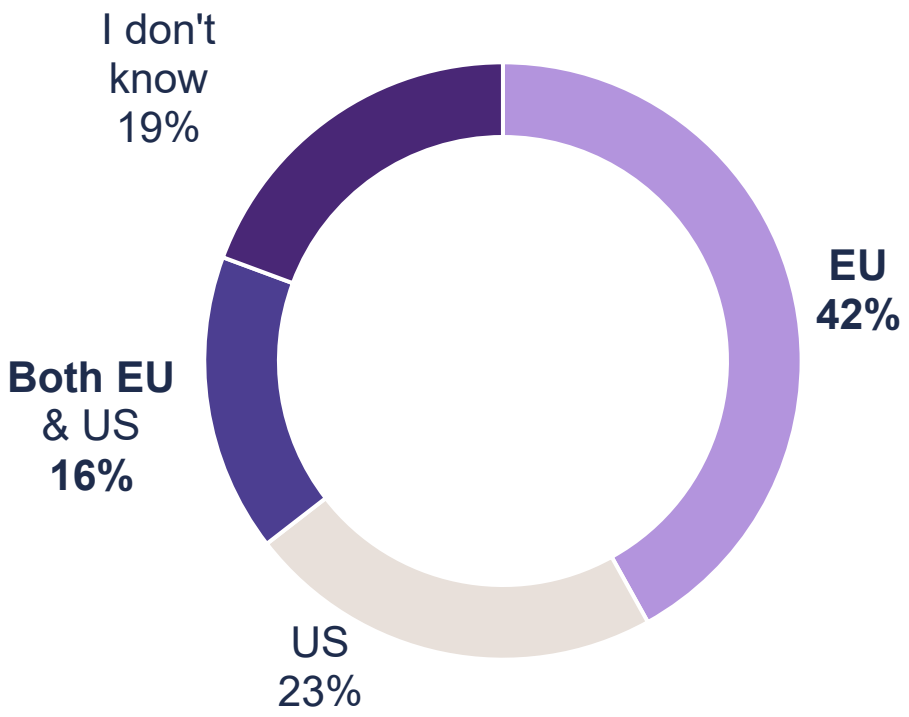
EFS address different patient conditions:

- 46% Diseases of circulatory system
- 15% Endocrine, nutrition and metabolic diseases
- 11% Diseases of the nervous system

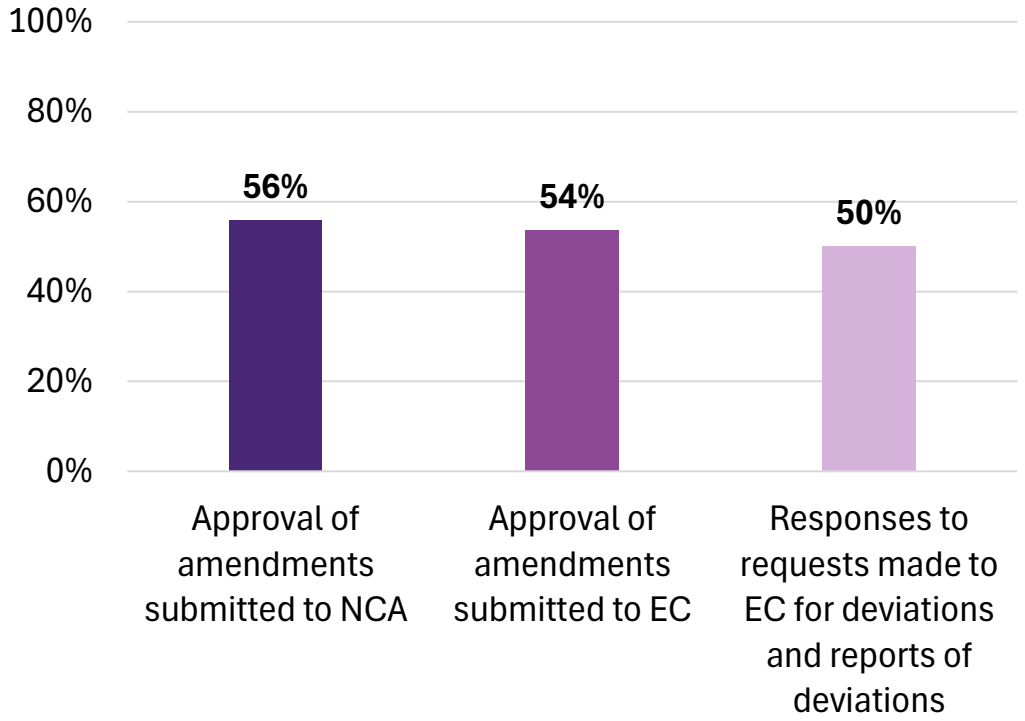
Source Analyses based on HEU-EFS EFS-DB (Dec 2024) (LINK)

Is the EU attractive for clinical investigations?

Sponsors' favourite location for conducting pilot clinical investigations?



Sponsors' level of satisfaction with EU NCA and EC response times during the conduct of the study

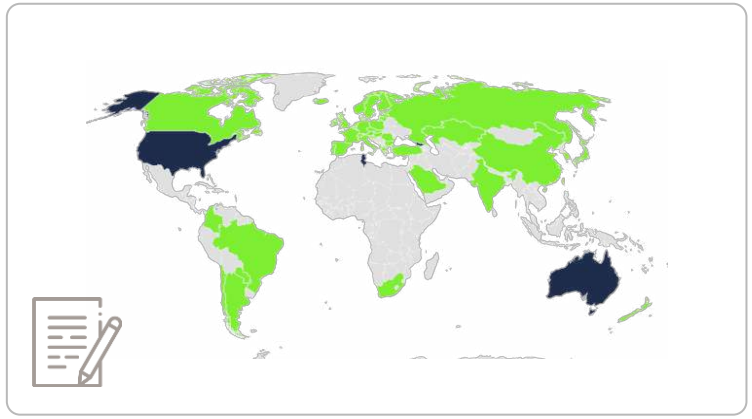


Source: HEU-EFS Sponsors Survey (n=83, 2024) (LINK)

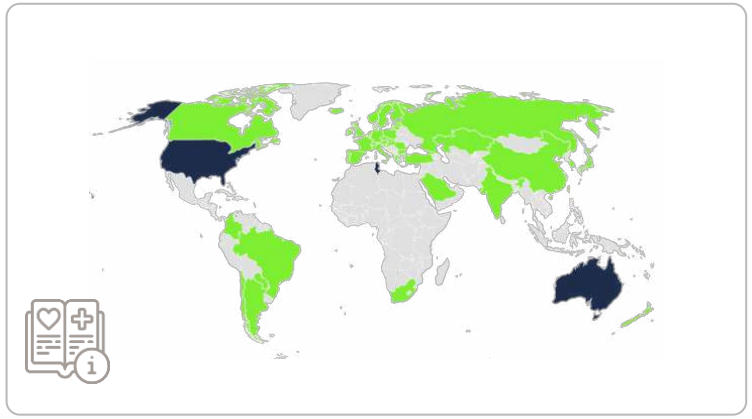
NCA: National Competent Authority
EC: Ethics Committee

Attractive, but more documents required

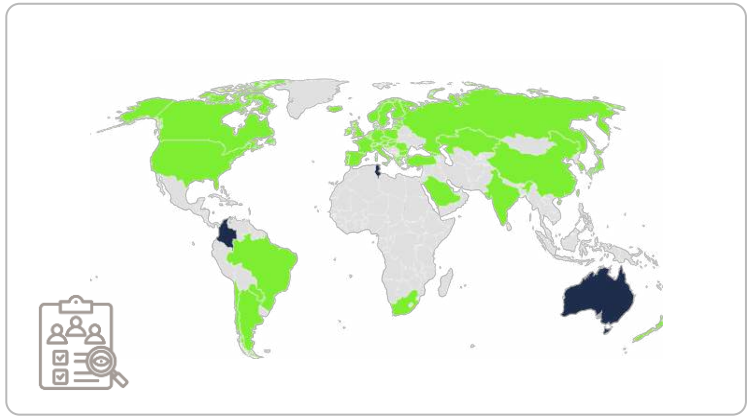
Application Form



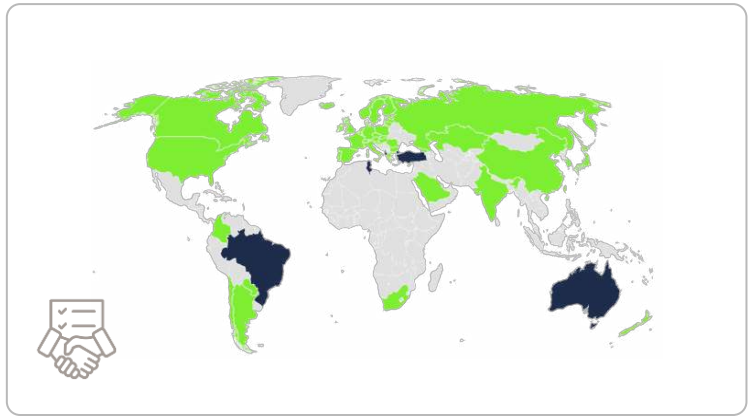
Investigator's Brochure



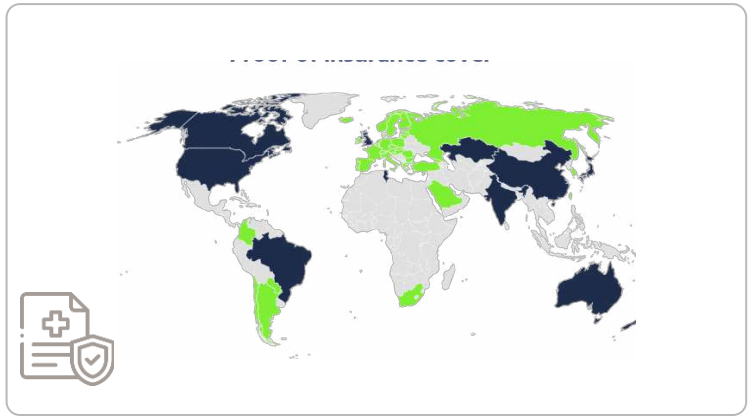
Clinical Investigation Plan



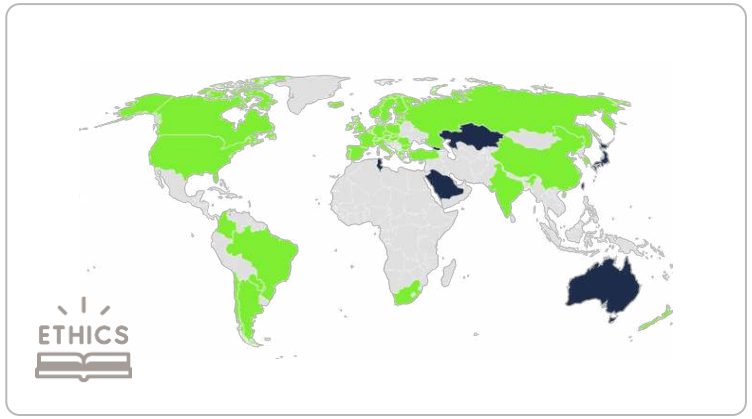
Informed Consent Form



Proof of Insurance Coverage



Copy of Ethics Committee Opinion



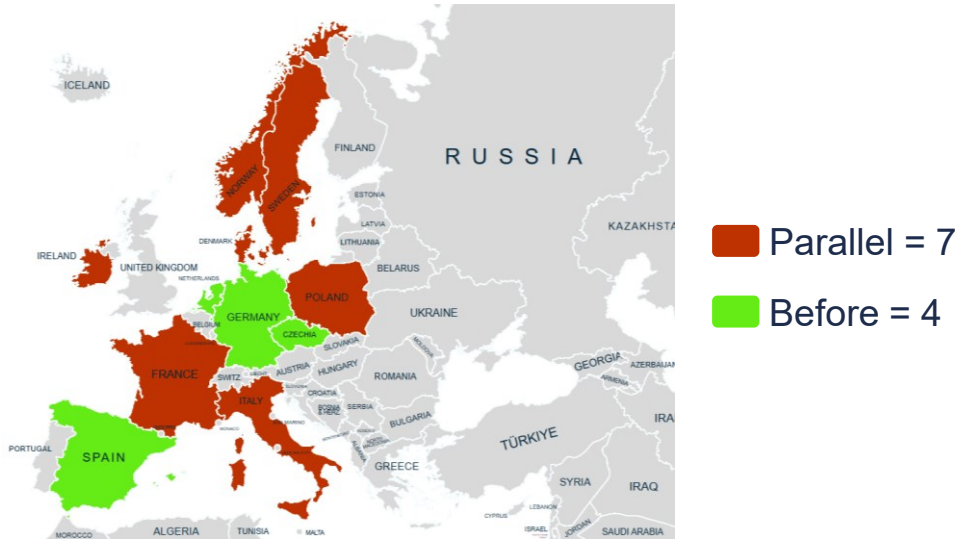
Yes, mandatory

Yes, optional, No, or n/a

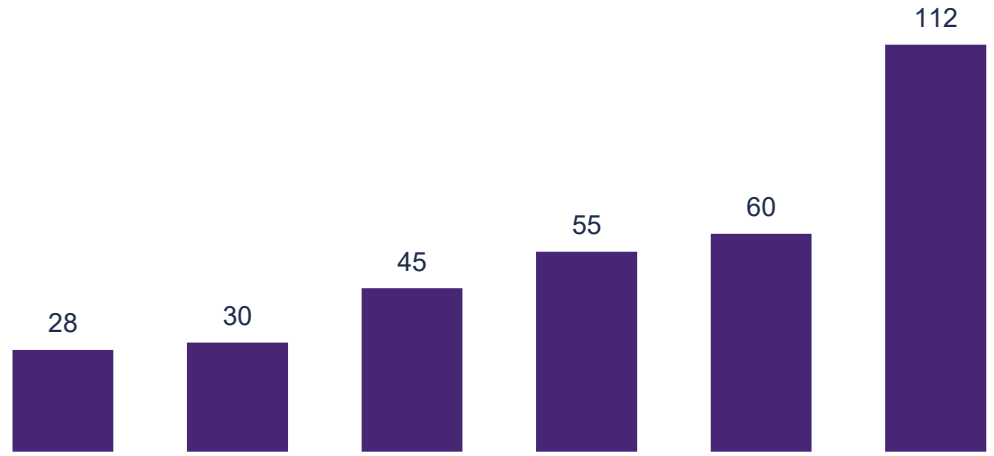
Source: HEU-EFS PMAP database (2024)

Fragmented ethics approval

Timing of ethics approval process with respect to NCA



Maximum ethics approval duration (calendar days)



During interviews, NCAs reported that the diverse ethics approval models across EU generate struggles and underscore need for harmonized model

"There are different approaches to ethics [approvals], and *that is a problem."*

"A more *harmonised approach* to ethics [approval] *would be very helpful."*

Source: HEU-EFS analysis of ethics review of a sample of countries (2025); NCA Interviews (n=8, 2025); (Deliverable D3.2 under evaluation by IHI)

Lack of standardised dialogue

NCAs report:

- **63%** offer the possibility of **dialogue** through ‘pre-submission’ or ‘innovation’ meetings or scientific advice, **32%** do not.
  - Dialogue may occur either **before** submission, **during** assessment or **after** assessment has been completed.
- Dialogue relates to **administrative aspects** of submissions (all NCAs), the extent of **pre-clinical testing** or advice on **study design** (33% each).

82% of NCA believe **dialogue improves quality** of clinical investigation application.

NCA interviews revealed that dialogue improves assessment efficiency and speed through NCA adaptability and sponsor cooperation

“when there was a scientific advice, the solution and *the assessment [was] quicker [and] easier for both sides.”* “If [sponsors] are cooperative, they basically speed up our evaluation.”

Source: HEU-EFS NCA Survey (n=19, 2024) (LINK) and HEU-EFS NCA Interviews (n=8, 2025); (Deliverable D3.2 under evaluation by IHI)

What challenges should be addressed to develop an EU EFS Program?

Lack of Regulatory Harmonization

Fragmented approval systems

Inconsistent interpretation of MDR

Capacity & Expertise Gaps

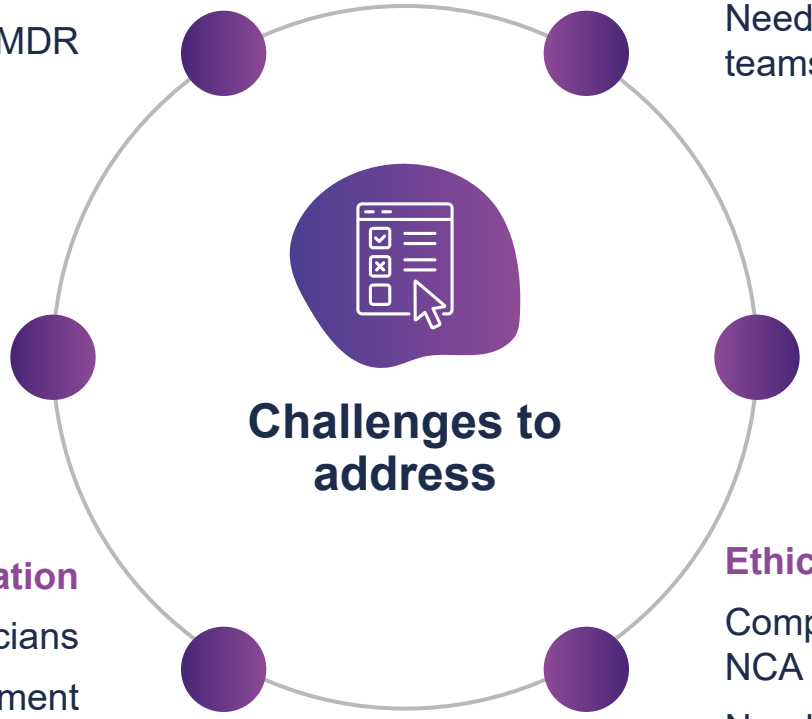
Shortage of trained investigators & infrastructure

Need for structured training for ethics & research teams

Evidence & Evaluation Quality

Lack of evidence & poor documentation

Missing data & non-standard templates



Financial & Structural Limitations

High costs for SMEs, no proportional fee scaling

Limited funding for early-phase studies

Limited Stakeholders' Coordination

Weak dialogue among regulators & clinicians

Need for early alignment

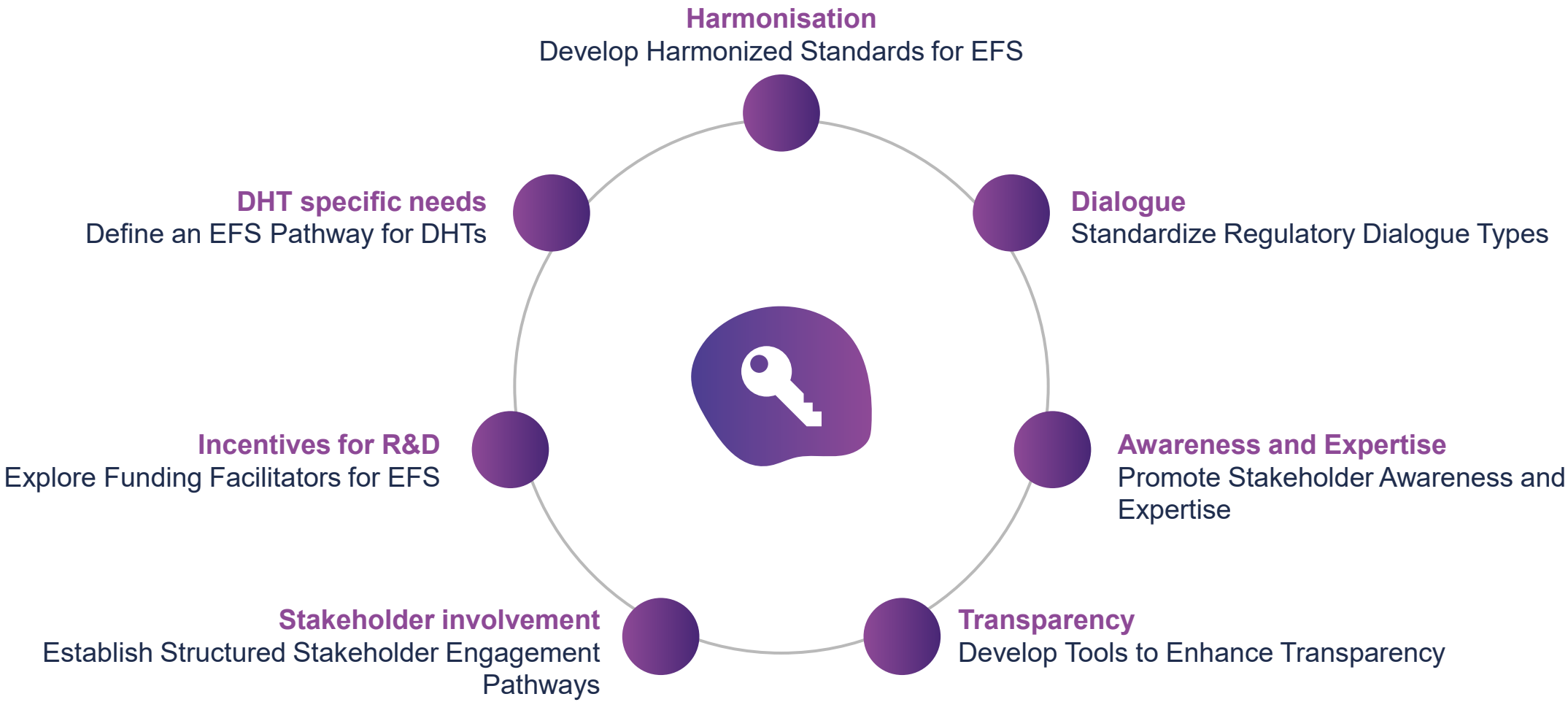
Lack of structured consultation

Ethics Approval Process Issues

Complex frameworks across ethics approval and NCA assessments causing delays

Need for clear ethical guidance & reviewer training

7 Key Recommendations



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