# HEU-EFS Methodological Framework

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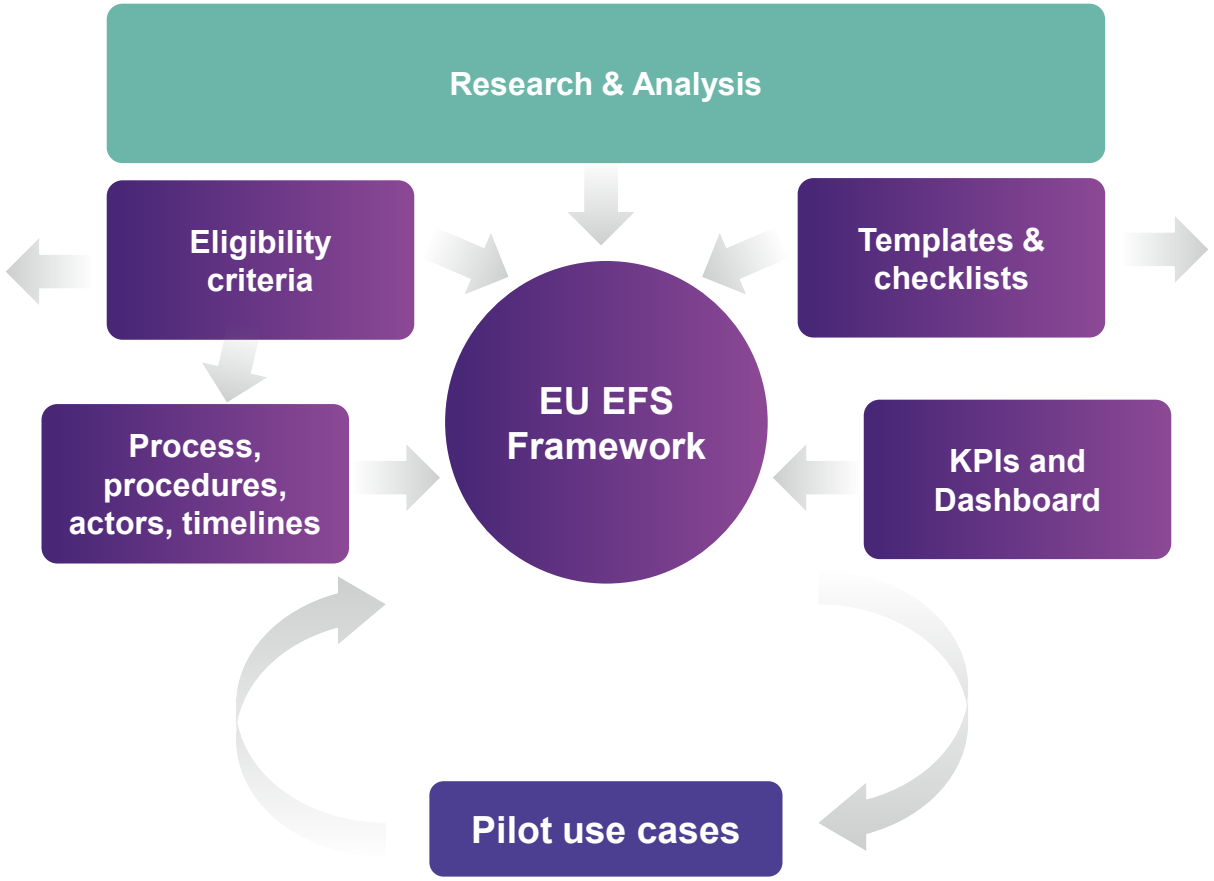
# EU EFS Framework

- Technologies
- Patient conditions
- Level of pre-clinical evidence
- Trialists and clinical sites competence




- Clinical Investigation Plan
- Informed Consent Form
- Master Clinical Trial Agreement
- Insurance agreement

*Taking into account synergies with Expert Panel Scientific Advice, HTAR JSC, Coordinated Assessment, draft MDCG Breakthrough Guidance, and other EU pathways.*

# Eligibility Criteria for the Pilots Technology

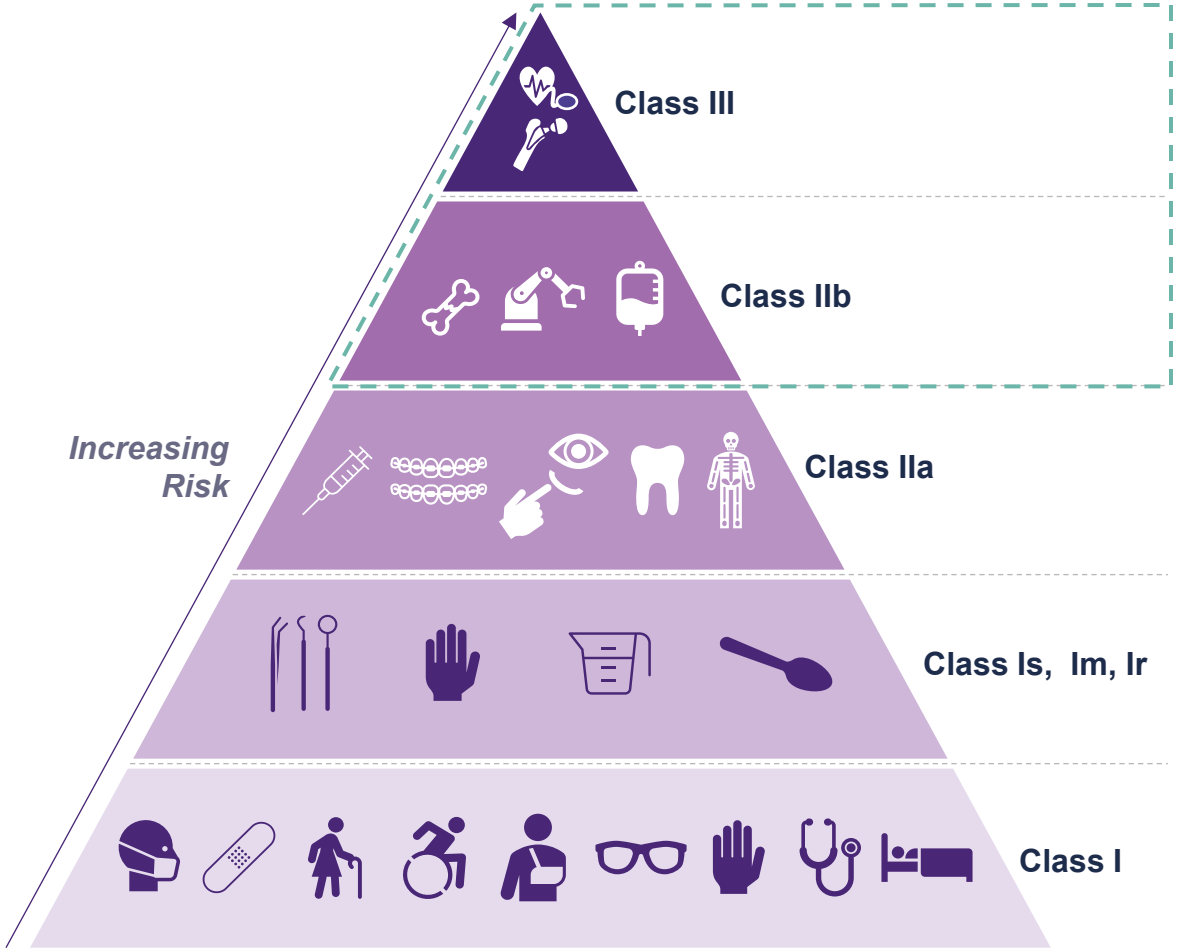
## General criteria:

**High-risk devices (Class III and Class IIb)**, where a clinical investigation will be required as part of the conformity assessment.

**Breakthrough Device / Unmet Patients Needs**

**Anatomical Understanding**

**New / Expanded Intended Uses or Indications for Use for Patients**



# Level of Pre-clinical Evidence for EFS Pilots

**GSPR*** must be the **foundation for pre-clinical testing** performed for an EFS. **Pre-clinical testing will not be finalised** as the design may remain in **a continuous iterative phase**

**Preclinical testing** shall be **performed as far as possible** unless;

The **goal of the EFS** may be to answer specific GSPRs which cannot be answered through preclinical testing

A **justification provided for limitations**, such as – further testing is not possible through preclinical testing due to e.g. anatomy or physiology

**Concurrent testing is planned to be performed** without causing greater risk to the patients enrolled in the EFS.

Allow for **leveraging data from similar (own) devices for some tests**

*GSPR - General Safety and Performance Requirements of the MDR

# Clinical Sites and Clinical Expertise for EFS Pilots

**The requirements defined by the MDR for sponsors, sites and investigators must be followed , in addition we identified**

Increase in **regulatory competence** on EFS is **beneficial for all parties;** need for **early dialogue between NCA and sponsors, and e.g. EC, PI**

**Personnel conducting EFS should be qualified under ICH-GCP*** and meet additional qualifications required at national level.

Ensure that the clinical site has the **capacity and equipment to offer adequate emergency care and support systems** during and also after the EFS.

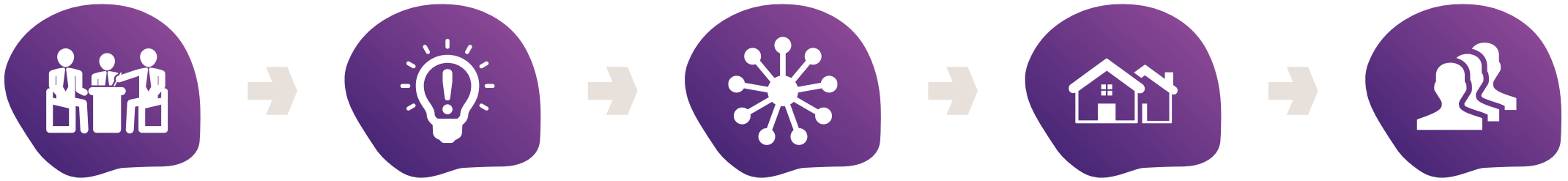
**Clinical staff** should have **experience in the therapeutic field**

Ensure **independence and transparency of clinical staff**

May have **dedicated units or personnel** specifically tasked with **coordinating regulatory submissions and contracts.**

*ICH-GCP – International Council for Hamonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use – Good Clinical Practice
PI – Principle Investigator

# Process Goals and Considerations



Enhance Early Dialogue Options

Accelerated EFS Process (~30% reduction in review times)

Streamlined Templates / Checklists and Performance Metrics

Parallel NCA & EC Review where Possible

- ✓ Timely
- ✓ Efficient
- ✓ Collaborative

# EFS Process Overview

**Pre-Submission** | **Submission & Review**

**Contact Point** → **Early Dialogue** → **Submission** → **Validation** → **Review**

### Pre-submission Phase

- Contact point early in the process to allow for planning and resource allocation
- Multi stakeholder early dialogue for sponsor, NCA and where appropriate and relevant Ethics Committee, NCA experts, Principal investigator of clinical site.

### National Competent Authority (NCA)

**Initial "Validation" Phase → Completeness of Submission File**

- NCA Assessment time
- Proceed to Review Phase or Request for Information (RFI)
- RFI 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 request for Information (RFI)
- RFI Cycle time for sponsor and NCA

**Target 30% Reduction in Overall Process Timelines Compared to Current MDR**

# Pre-Submission in Detail

Contact Point → Early Dialogue

## Contact Point

- Alerts NCA (and other recipients) to incoming application for an EFS
- Identifies key principles of Device Technology
- Outlines qualifications for Accelerated review
- Cycle timing: 1-2 weeks

## Early Dialogue (optional)

- Opportunity to have targeted discussions related to the device, Patient population, etc.
- Pre-submission to include appropriate background information
- Cycle timing: 30-60 days

# Submission: Validation and Review in Detail

Submission → Validation → Review

## Validation

### Validation under MDR (Article 70) Timing (10 - 55 days)

- NCA Assessment: 10 – **15** days
- Sponsor response to identified gaps: 10 – **30** days
- Final NCA Validation: 5 – **10** days

### Proposed Accelerated (HEU-EFS) Timing (7 - 39 days)

- NCA Assessment: 7 – **12** days
- Sponsor response to identified gaps: 7 – **17** days
- Final NCA Validation: 5 – **10** days

## Review

### Review under MDR (45 - 65 days)

- NCA Assessment: 45 – **65** days
- Sponsor response to identified gaps: Timing not specified
- Final NCA decision: Utilisation of remaining clock

### Proposed Accelerated NCA Assessment (30 - 45 days)

- Deficiency Communication:
  - Rolling Review/Interactive Questions approach
  - "Stop Clock" approach
  - "Approval with Conditions" approach
- Sponsor response to identified gaps: rapidly, be prepared
- Final NCA decision: Utilisation of remaining clock

# Proposed EFS Process vs MDR Art. 70

## CI for Implantable IIa, IIb and all Class III Devices

**Proposed HEU-EFS Process**

**Deficiency Communication:**
If the Sponsor is unable to respond within the set time of the accelerated process it will revert to normal Art. 70 process

### Pre-Submission

Contact Point → Early Dialogue

### Submission & Review

Submission → Validation → Review → Authorisation

**MDR Art. 70 Process**

Application for CI (MDR Art. 70) → NCA Notification (MDR Art. 70.1) 10d (+5d) → Sponsor Dossier Revision (MDR Art. 70.3) 10d (+20d) → NCA Validation (MDR Art. 70.3) 5d (+5d) → NCA Evaluation (MDR Art. 71) 45d (+20d) → NCA Notify of Authorisation

### Undefined Pre-Submission Process

### Submission & Review

*Abbreviations Art. = article of the MDR, d=days

# HEU-EFS Specific Checklists & Templates

**Self-Evaluation Checklist**

- **The checklist** aids sponsors to verify **internally** that **they are ready to start an EFS**

**Clinical Investigation Plan**

- **The template** based heavily on MDCG 2024-3 but tailored to EFS
- **The checklist** aids sponsors to verify **internally** that **CIP is completed appropriately** specifically for EFS

**Informed Consent Form**

- **The template based on MDR** provides a standardised format for sponsors — particularly SMEs — that may lack internal documentation resources.
- **The checklist** aids sponsors to verify **internally** that patient requirements are met, for the application to both NCA and Ethics Committee

**Master Clinical Trial Agreement**

- **The checklist** ensures all relevant and EFS-specific contractual elements are included

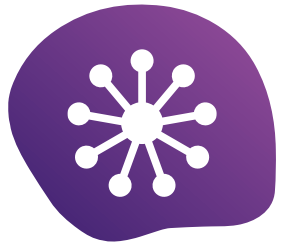
**Insurance Agreement**

- **The guidance** is a practical solution given that the insurance agreement is typically non-negotiable
- It serves as a reference document to ensure inclusion of the **minimum essential required elements**

# Collection of Data during the Pilots from Sponsors of the EFS Pilots and NCAs

**About the Pre-submission Process**

**After EFS Application has been Submitted to NCA**



**After Authorisation of the EFS Pilot by the NCA**

**After Completion of the EFS Pilot**

**Collect at Four Key Points along the Pilot Journey**

# Questions & Answers

1. Raise your Hand
2. Wait for the Moderator to Invite you to Speak
3. Unmute your Mic & ask your Question
4. Mute your Mic

# Thank you !

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