

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

WP7 Testing the methodology: pilot use-cases

DELIVERABLE 7.2

Recommendations for the
selection of pilot use cases

Disclaimer:

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ABBREVIATIONS

CIP	Clinical Investigation Plan
D	Deliverable
EDWARDS	Edwards Lifesciences
EFS	Early Feasibility Studies
EU	European Union
GEMELLI	Fondazione Policlinico Universitario Agostino Gemelli
GSPR	General Safety and Performance Requirements
HEU-EFS	Harmonized Approach to Early Feasibility Studies for Medical Devices in the European Union
ICH-GCP	International Council for Harmonisation Good Clinical Practice
ISO	International Organization for Standardization
MS	Milestone
NCAs	National Competent Authorities
NIPH	Norwegian Institute of Public Health
PAG	Patient Advisory Group
T	Task
UB	Bocconi University
WP	Work Package

EXECUTIVE SUMMARY

The Harmonised approach to Early Feasibility Studies for Medical Devices in the European Union (HEU-EFS) project aims to develop a sound, widely applicable, and harmonised framework for EFS implementation at the EU level. Within the scope of the HEU-EFS project, this methodological framework is tested through pilot use-cases to validate the processes, procedures, actors involved, timelines of the phases, templates, performance monitoring defined in WP3, WP4, WP5 and WP6. The pilot use cases also aim to provide feedback and recommend any necessary adjustments needed to improve the methodology.

The pilots are key step to gain real-life experience of a new EU EFS pathway to help inform, refine and validate the framework. They leverage the results of the developed HEU-EFS eligibility criteria and methodological framework (WP3), template for clinical investigational plan (CIP) for EFS and CIP EFS checklist (WP4), metrics for performance monitoring of the EFS project (WP5), and a set of standard templates for the EU EFS Program, including Informed Consent Form, Master Clinical Trial Agreement, and Insurance Agreement (WP6), and take into considerations the recommendations from WP1 and WP2.

1. Introduction

Deliverable 7.2 *Recommendations for the selection of pilot use cases* is a part of Task T7.1 *Undertaking of preliminary activities in preparation for pilot use-cases*, the aim of which is to prepare for the submission of pilot use cases and enable a smooth and timely execution of the pilots. As such, the deliverable summarizes key elements and strategies that guided development of a system for selection of use cases, including:

- Summary of processes, templates and checklist defined in WP3 *Methodology development: rationale, processes, and procedure*, 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* reflected in the self-evaluation checklist and guidelines.
- Self-evaluation checklist which was developed as a tool to ensure alignment of proposed pilots with HEU-EFS methodologies and templates.
- Submission procedure.

In the next step and within the scope of Task 7.2 *Undertaking of EFS use-cases to test the methodology*, the pilots will test the:

- Process defined in Task 3.3 *Development of processes, procedures, actors, and timelines*.
- Templates and checklists defined in WP4 *Methodology development: evidence requirements, data, and statistical tools*, and WP6 *Methodology development: ethical and legal aspects*.
- Key performance metrics and dashboard defined in WP5 *Methodology development: EU EFS program monitoring system*.

2. Methods

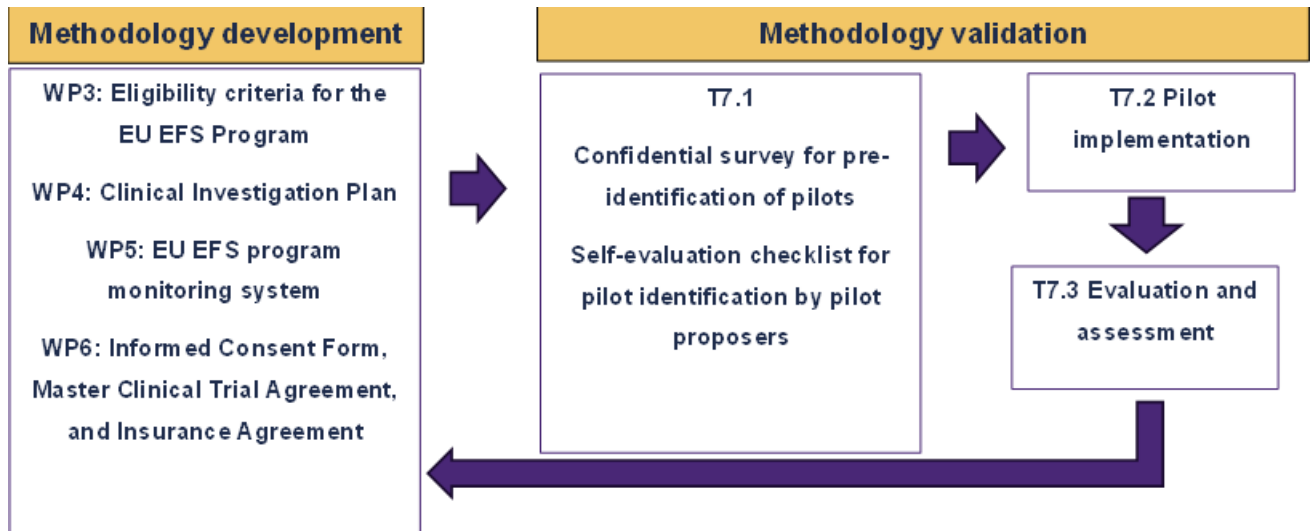
To launch the validation of the HEU-EFS eligibility criteria, methodological framework, process, and templates, within the Task T7.1, a two-fold approach was undertaken:

1. Development of a confidential survey for pilot use-case submitters to pre-identify types of technologies, medical conditions (based on deliverable D3.1 *Eligibility criteria and patient contribution to EFS*) and prioritised member states where the future EFS may be undertaken. This survey was developed by WP7 leaders (EDWARDS, ABBOTT, MEDTRONIC, and GEMELLI) in close alignment with WP3 leaders (NIPH and UB). The aim of the survey was to enable other WPs - particularly WP3 - to consider those results in further WP development and during the interview process with NCA.
2. Development of a self-evaluation checklist together with a process for its submission by the pilot proposers. The purpose of the self-evaluation checklist was to provide pilot proposers with a tool to self-assess consistency of the pilots with eligibility criteria defined in Task 3.1 Identification of eligibility criteria for the EU EFS Program as a gateway to qualify pilots for the validation process. Pilot submissions are based on self-evaluation rather than consortium assessment to ensure complete confidentiality. The checklist was co-developed by WP7 leaders (EDWARDS, ABBOTT, MEDTRONIC, and GEMELLI), with continuous input by the leaders of WP3 (NIPH and UB) and of WP5 and 6 (UB). Further information about the self-evaluation checklist methodology is provided below in chapters 2.1. *Self-evaluation checklist inputs*; 2.2. *Self-evaluation checklist* and 2.3. *Submission process*.

Development of the survey for pilot use-case submitters, the self-evaluation checklist and the checklist submission process were a key step to transition from the methodology development to validation by pilot use-cases (Figure 1).

All documents were developed and discussed through regular working meetings (average every two-week meetings). The process for development of both the survey and the self-evaluation checklist was presented to the Steering Committee of the HEU-EFS consortium, as well as to the private consortium so as to ensure alignment. A separate meeting with patient organisations was held to ensure planning of engagement with the Patient Advisory Group (PAG) and to ensure that patient feedback is sought at the right points of the validation process. A plan was made to seek PAG feedback to patient specific documents and comments to be prepared as a part of Task 7.2, which will implement the pilots.

Figure 1: Self-evaluation checklist and pilot submission process as a step to transition from methodology development to validation by pilot use-cases.



2.1. Self-evaluation checklist inputs

The self-evaluation checklist was developed based on inputs from WP3 – 6 and the confidential survey for pilot use-case submitters which pre-identified possible pilots and key stakeholders and supported activities of other WPs by providing key pilot insights. Moreover, with the checklist submission, was a step for proceeding with pilot preparation during absence of inputs from other WPs and the pilot proposers tested the online Qualtrics submission format.

The baseline for the development of the self-evaluation checklist (T7.1) were eligibility criteria defined in Deliverable D3.1. The D3.1 eligibility criteria informed the structure and content of the checklist. Specifically, the self-evaluation checklist adopted the key characteristics of technologies proposed to undergo an EFS, patient engagement and population to be recruited for EFS, requirements and types of tests to be conducted prior to initiating an EFS, and requirements that should be met by clinical sites selected for EFS. Any adaptations or feedback given on D3.1 have continuously been captured to ensure a continuous feedback mechanism in view of developing final recommendations towards the methodology.

Further to D3.1, the following documents have informed the design of the pilot self-evaluation process:

- D3.2 *HEU-EFS methodological framework* which defines the regulatory pathway to be tested in the pilots (T7.2).
- D4.2 *Template for a Clinical Investigation Plan for EFS clinical investigations involving Medical Devices*, which defines the clinical information to be included in the document (T7.2).
- WP4 *CIP EFS Checklist* to be tested during implementation of the pilots (T7.2).

- D5.1 *Measuring the EU EFS Performance*, which defines the metrics to monitor EFS performance as a part of T7.2.
- D6.2 *Set of templates for the EU EFS Programs - methodological document*, which defines the templates – Informed Consent Form, Master Clinical Trial Agreement, Insurance Agreement – to be tested during implementation of the pilots (T7.2).

2.2. Self-evaluation checklist

To assess consistency of the proposed pilots with eligibility criteria for EFS defined in D3.1, a self-assessment by the pilot proposers was chosen as a preferred pilot selection methodology over evaluation conducted by the consortium in order to ensure confidentiality of the proposed pilots.

The checklist was developed as an online document placed on the HEU-EFS Share Point. Comments and feedback were gathered directly *via* the online document and during regular WP7 leader calls, to which WP3 leaders were consistently invited. All comments and suggestions have been addressed and iteratively implemented. Draft of the checklist was also presented to the Steering Committee as well as during plenary meeting of the consortium.

For the self-evaluation checklist submission, there was no prescriptive list of disease areas provided. The consortium aims to reach a minimum of 3 pilot use cases to test the methodology.

The following topics have defined the structure of the self-assessment checklist:

1. Pilot overview information
2. Technology characteristics
3. Patient engagement
4. Level of pre-clinical evidence
5. Clinical expertise and clinical sites

The description of the checklist content is provided in Chapter 3 *Results*.

2.3. Submission process

Phasing the pilot launch

The submission process was launched in June 2025 with release of the self-evaluation checklist. With that, Milestone MS5 *Launch of submission of technologies for use cases* has been achieved. The submission process has been phased as follows:

1. Phase 1: submission open for private partners who articulated their intention to propose pilots in the project preparation phase was launched in June 2025.
2. Phase 2: all members of the consortium are invited to propose pilots by submitting completed self-evaluation checklists. This phase was launched in July 2025.
3. Phase 3: opening the pilots to the public has been identified as a potential risk mitigation measure of Risk number 10 *Limited number of technology proposed to run pilot*. The consortium will discuss whether this mitigation measure needs to be implemented or not. Decision on the launch of this phase will be made by the consortium upon alignment with the Innovative Health Initiative (IHI). If implemented, active outreach will be planned for the project network, including participants in the Survey for health technology developers implemented in WP1 *Research and analysis on state of play of pre-market programs and implementation barriers to EFS*.

Submission format

The final self-evaluation checklist was implemented *via* an online format using the Qualtrics survey form developed by UB. This format allows full confidentiality and is also harmonised with other forms developed in WP5. Deliverable D5.1 *Measuring the EU EFS Performance* defined a uniform method for data collection, both for the checklists and for the information required to calculate the Key Performance Indicators (KPIs). This will allow for consistency and confidentiality in gathering feedback throughout the submission process.

The online form was designed to collect preliminary data from sponsors participating in the EFS pilot. For the submission, the pilot proposers are asked to provide only such information that is available or can be shared. Once submitted, the pilot proposers obtain a summary of provided responses downloadable in PDF form. Further details can be added by pilot proposers at later stages whenever they become available. The responses provided *via* submitted self-evaluation checklist remain confidential, and no individual sponsors or medical device technologies can be identified. UB is the only recipient of the submitted information, and the information is not shared with the other consortium members. For each submitted checklist, the pilot proposers generate a self-selected, 8-digit code that serves as unique identifier for the EFS pilot. The code may include letters, numbers, and special characters.

Submission timelines

The pilot submission process is expected to be implemented in two cut-offs:

- Cut-off 1 was launched in June 2025 with release of the self-evaluation checklist. The first cut-off period is expected to end by 30 September 2025. Pilot proposers have been invited to

regularly inform UB of their intended timing to submit pilots so as to ensure planning for the overall consortium deliverables.

- Cut-off 2 will be launched in October 2025 and is expected to end at the latest by 31 March 2026.

Cut-off 2 was added as a deviation from the original plan. Firstly, because pilot proposers were in need of a more solid understanding of the processes, templates and checklists developed in other Work Packages. In addition, the timelines could maximise appropriate identification of pilots by pilot submitters in accordance to their internal R&D pipelines. Finally, the additional cut-off (2) also would facilitate interest from other partners of the consortium and the wider public to submit pilots. This was therefore to mitigate Risk number 10 *Limited number of technology proposed to run pilot*.

3. Results

The self-evaluation checklist is the primary outcome of the earlier activities and contains these sections and details:

Pilot overview information

In this section, the pilot proposers are asked to provide sponsor profile and contact information as well as an overview of the pilot including the estimated submission timeline, pilot characteristics, target national competent authorities (NCAs), ethics committees, clinical sites, possible synergies with coordinated assessment (Figure 2).

Technology characteristics

In this section, the pilot proposers are asked to provide information on the device therapeutic area, device risk classification and its breakthrough character (as specified in Deliverable D3.1), technology specific purposes of the EFS pilot study, a description of why the study is considered EFS, expected number of subjects to be enrolled within EU, characteristics of the target patient population, and confirmation that the study includes phased or iterative enrolment (Figure 3).

Patient engagement

This section focuses on confirming whether patients / patient representatives have been consulted during the study design and justifying the inclusion, where applicable, of any vulnerable patient groups relevant to the health condition (Figure 4).

Level of pre-clinical evidence

In this section, pilot proposers are asked to complete information on pre-clinical evidence including confirmation of compliance to GSPR, with relevant ISO/ASTM (or other) standards, confirmation of prior generation of pre-clinical evidence and possibility to consult/leverage data from similar devices and previous versions (Figure 5). The pilot proposers have an option to add references to the Clinical Investigational Plan (CIP) or indicate if the data is not available or if the pilot proposers are not ready to disclose them.

Clinical expertise and clinical sites

In this section, pilot proposers are asked to provide information confirming that the clinical sites ensure compliance with ICH-GCP and ISO 14155 standard, whether the personnel to be involved in EFS have an extensive understanding of reporting of serious adverse events, whether the clinical sites have the capacity and equipment to offer adequate emergency care and support during and after

EFS, whether the clinical site staff have the needed experience and access to the patient population, confirm that there is a developed EFS technology-specific training program for the involved clinical personnel and whether proctors and clinical specialists are involved in the clinical staff training activities, and whether the sponsor will make staff available to support clinical staff during the procedures (Figure 6). As above, the pilot proposers have an option to add reference to the Clinical Investigational Plan or indicate if the data is not available or if the pilot proposers are not ready to disclose them.

Figure 2: Self-evaluation checklist - pilot overview information

Pilot overview information

Q1. Does the sponsor of the EFS identify itself as a SME?

Note: The European Commission defines Small and medium-sized enterprises (SMEs) as enterprises with fewer than 250 employees and either an annual turnover below €50 million or a balance sheet total under €43 million.

- Yes
- No

Q2. Company name (optional)

Q3. Representative name (optional)

Q4. Representative contacts (optional)

Q5. When are you planning to submit the EFS application?

Q6. Please select the option that describes the pilot EFS based on the number of countries and clinical sites involved:

- Single-country, single-centre
- Single-country, multi-centre
- Multiple-country, multi-centre

Recommendations for the selection of pilot use cases

Q7. Which of the following EU/EEA NCAs do you plan to submit the EFS application to? Please check all that apply.

- Austria (Austrian Agency for Health and Food Safety (AGES))
- Czech Republic (State Institute for Drug Control)
- Denmark (Danish Health and Medicines Authority)
- France (Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM))
- Germany (Federal Institute for Drugs and Medical Devices (BfArM))
- Ireland (Health Products Regulatory Authority)
- Italy (Ministero della Salute)
- Netherlands (Health and Youth Care Inspectorate)
- Poland (Office for Registration of Medicinal Products, Medical Devices and Biocidal Products)
- Spain (Spanish Agency for Medicines and Medical Devices)

Q8. If there were a coordinated assessment option under the EFS pilot, which NCA would you prioritize as the lead NCA?

Q9. Please list the ethics committees (EC) to be involved in the EFS pilot if known.

Q10. Please list the clinical sites to be involved in the EFS pilot if known.

Q11. Which of the following non-EU/EEA NCAs have you, or plan to, submit the EFS application to? Please check all that apply. If none, please select "None of the above."

- United States (FDA)
- UK (MHRA)
- Switzerland (Swissmedic)
- New Zealand (MedSafe)
- Georgia (RAMA)
- Other
- None of the above

Figure 3: Self-evaluation checklist - technology characteristics

Technology characteristics

Q12. What is the therapeutic area of the device?

- Circulatory system (cardiovascular / lymphatic)
- Endocrinology and diabetes
- Gastroenterology and hepatology
- General and plastic surgery, dentistry
- Nephrology and urology
- Neurology
- Obstetrics and gynecology (including reproductive health)
- Ophthalmology
- Orthopedics, traumatology, rehabilitation
- Respiratory, anesthesiology, intensive care
- Other

Q13. What is the highest risk classification of the device?

- Class I
- Class II A
- Class II B
- Class III

Q14. In case the technology is not Class III or Class IIb device (including DHTs) as per eligibility criteria (see deliverable D3.1), please provide a justification.

Q15. Is the technology a breakthrough device and/or addressing an unmet need (i.e. no equivalent device exists)?

- Yes
- No

Recommendations for the selection of pilot use cases

Q16. Is the technology already CE Marked or previously approved for clinical investigations such that the EFS pilot will be an expansion of the existing intended use in new patient population or application?

Yes

No

Q17. Is the purpose of the EFS pilot study to better understand the device interaction between the technology and physiology/ anatomy during development?

Yes

No

Q18. Is the purpose of the EFS Pilot study to evaluate a technology enhancement made to an existing design?

Yes

No

Q19. Please describe why you consider this study as an EFS.

Q20. Enter the number of subjects to be enrolled within EU.

Q21. In case the estimated enrolment exceeds 15 patients as per eligibility criteria (see deliverable D3.1), please justify.

Q22. What are the characteristics of the target patient population?

Male/Female	<input type="text"/>
Age range	<input type="text"/>
Other	<input type="text"/>

Q23. Does the study include phased or iterative enrolment?

Yes, please describe

No

Figure 4: Self-evaluation checklist - patient engagement

Patient engagement

Q24. Have patients / patient representatives been consulted during the study design?

Yes, please describe

No, please describe

Q25. In line with section 3 of Annex XV of MDR have the vulnerable patient groups relevant to the health condition been identified, specifically subjects such as children, pregnant women, immuno-compromised or, elderly subjects, if they are included, please justify.

Figure 5: Self-evaluation checklist - level of pre-clinical evidence

Level of pre-clinical evidence

Q26. Is the EFS planned to be conducted in accordance with ISO 14155:2020?

Yes

No

Q27. Is the technology developed utilizing the principles of ISO 14971?

Yes

No

Q28. Is the technology under investigation compliant to GSPR for pre-clinical testing (unless duly justified)?

Yes

As far as possible

No

No, the relevant data is planned to be collected during the EFS.

Q29. Was generation of pre-clinical evidence possible?

Yes

No

Q31. If available, has data from similar devices or previous versions been consulted/leveraged?

Yes

No

Figure 6: Self-evaluation checklist - clinical expertise and clinical sites

Clinical expertise and clinical sites

Q32. Are the clinical sites expected to comply with ICH-GCP standards?

Yes

No

Q33. Are the clinical sites expected to comply with ISO 14155:2020?

Yes

No

Q34. Does the personnel to be involved in EFS have an extensive understanding on how to report serious adverse events in line with requirements of the MDR and national law?

Yes

No, please describe which personnel

Q35. Does the clinical site have the capacity and equipment to offer adequate emergency care and support systems during and, where needed, after the EFS?

Yes

No

Q36. Does the clinical site staff have experience in the therapeutic field of the investigational devices?

Yes

No



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