

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

WP5 Program monitoring system

DELIVERABLE 5.1

Assessing the Performance of Early Feasibility Studies in the EU

Disclaimer:

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ABBREVIATIONS

AB	Advisory Board
AleMDs	Artificial Intelligence–Enabled Medical Devices
CE	Conformité Européenne
CRO	Contract Research Organization
D	Deliverable
DHTs	Digital Health Technologies
EFS	Early Feasibility Study
EU	European Union
EUDAMED	European Database for Medical Devices
FDA	Food and Drug Administration
FSN	Field Safety Notice
HTA	Health Technology Assessment
HEU-EFS	Harmonized Approach to Early Feasibility Studies for Medical Devices in the European Union
IDE	Investigational Device Exemption
IRB	Institutional Review Board
KPI	Key Performance Indicator
MDCG	Medical Device Coordination Group
MDIC	Medical Device Innovation Consortium
NCA	National Competent Authority
PAG	Patient Advisory Group
PREMs	Patient Reported Experience Measures
PROMs	Patient Reported Outcome Measures
SME	Small and Medium-Sized Enterprise
UB	Bocconi University
USA	United States of America
WP	Work Package

EXECUTIVE SUMMARY

The Harmonized Approach to Early Feasibility Studies for Medical Devices in the European Union (HEU-EFS) Work Package (WP) 5 focuses on proposing a performance monitoring system of Early Feasibility Studies (EFS) in the European Union. Within this context, WP5 aims to deliver three main outputs: an approach to calculate performance metrics for EFS pilots, a performance dashboard displaying metrics related to EFS pilots, and a set of recommendations to integrate additional performance metrics into EUDAMED's Clinical Investigation and Performance Studies (CI/PS).

First, WP5 seeks to address the lack of knowledge about EFS overall performance and the current absence of EUDAMED functionality by proposing a temporary alternative approach for monitoring EFS performance that will be implemented through EFS pilots. This approach was developed by designing specific metrics to monitor EFS performance, identifying the necessary data for their calculation, and developing online forms to collect this information in the absence of EUDAMED [1]. Sponsors of EFS pilots – which will start in January 2026 – will be required to complete the online forms at key stages of the EFS pilot process: before the start of the EFS pilot, after submission of the application to the National Competent Authority (NCA), after validation of the application, and after the EFS pilot has been completed. The collected data will enable the calculation of Key Performance Indicators (KPIs), providing a basis for evaluating the performance and efficiency of the EFS process and support continuous, incremental improvements and long-term sustainability. Second, WP5 will deliver a performance dashboard as visual platform to display the KPIs related to EFS pilots. Third, upon completion of the EFS pilots, WP5 will make formal recommendations to integrate these metrics into the future Clinical Investigation and Performance Studies (CI/PS) module of EUDAMED.

To achieve the goals of delivering the three outputs, WP5 has followed four methodological steps: (1) development of a preliminary list of KPIs based on literature review and expert discussions; (2) a survey phase, which included a survey of the Patient Advisory Group (PAG), followed up by a consortium-wide survey, where KPIs were rated on their level of importance and additional indicators were suggested; (3) development of four online forms to be completed by sponsors of the EFS pilots at key stages of the EFS pilot process. These forms are designed to gather information on the EFS pilots and to collect data required to calculate performance metrics to monitor the performance of the EFS pilots; and (4) development of recommendations to modify the application form outlined in the MDCG 2021-08 guidance on *Clinical investigation application/notification documents* to adapt the form to meet the needs of EFS [2,3].

Background

A key limitation of EFS is the lack of knowledge about their performance due to the absence of systematic data collection for all submitted studies. In the USA, the only jurisdiction with an established EFS Program, the data is collected voluntarily by the Medical Device Innovation Consortium (MDIC) from selected study sites (Callea et al., 2022). The program evaluates performance based on approval rates and relevant timelines, such as Food and Drug Administration Investigational Device Exemption (IDE) approval, Institutional Review Board (IRB) approval, contract signing, and first patient enrolment [4].

The European regulatory framework for medical devices adopts a life-cycle approach, requiring data collection across all stages of device development and use. To support this, the European Commission has designated EUDAMED as the system for storing and managing such data. However, EUDAMED is not currently functional, and its official launch date has yet to be determined. One of the tools that EUDAMED will use to collect and store data is the application form outlined in the MDCG 2021-08 guidance on *Clinical investigation application/notification documents* [2,3], which sponsors will complete to provide general information on clinical investigations and medical device features. Despite the proposed use of this application form to collect data, further research and analysis conducted within Work Package 5 (WP5) revealed that EUDAMED's structure remains largely undefined, and several critical modules - especially those related to clinical performance and early feasibility studies - have not yet been developed.

To address the lack of systematic data collection and the current absence of EUDAMED functionality, the HEU-EFS project, through its WP5, proposes a temporary alternative approach for monitoring EFS performance. This approach will be implemented through EFS pilots and will enable the calculation of Key Performance Indicators (KPIs) to evaluate the performance and efficiency of the EFS process. WP5 developed this approach by designing specific metrics to monitor EFS performance, identifying the data required for their calculation, and developing online forms to collect this data in the absence of EUDAMED. WP5 proposes that the online forms will be completed by sponsors of EFS pilots. EFS pilots will be conducted within Work Package 7 (WP7), which aims to test the HEU-EFS methodological framework through several pilot use-cases. Within the work of WP5, sponsors of EFS pilots will be required to complete the online forms at key stages of the EFS pilot process: before the start of the EFS pilot, after submission of the application to the National Competent Authority (NCA), after validation of the application, and after the EFS pilot has been completed.

The aim of this work is to propose a process for measuring EFS performance metrics to monitor the HEU-EFS program. Upon completion of the EFS pilots, WP5 will make formal recommendations to the European Commission regarding the integration of these metrics into the future Clinical Investigation and Performance Studies (CI/PS) module of EUDAMED. These recommendations for the European Commission will enable systematic data collection for each EFS in the EU and to support continuous and incremental improvements.

Methods and steps

To support performance monitoring of EFS in the EU, leaders of WP5 followed a four-step methodological approach:

- 1. Development of a preliminary list of KPIs.** This process was conducted in two steps:
 - First, relevant indicators were retrieved from 1) the HEU-EFS First and Second Stage proposals submitted by the consortium to the European Commission as part of the grant application, and 2) NCA practices reported in the results of WP1 *Research and analysis on the state of play of pre-market programs and implementation barriers to EFS*, specifically, Deliverable D1.1 *Characteristics, gaps, and best practices of premarket programs* ([LINK](#)), completed in December 2024.
 - Second, internal discussions with consortium partners were conducted to review and refine the relevant indicators extracted from the first step and ensure their relevance and applicability for monitoring the HEU-EFS program. A preliminary list of 26 KPIs was generated.
- 2. Survey-based assessment of the relevance of KPIs involving the Patient Advisory Group (PAG) and the consortium.** The first survey consisted of an online survey targeting members of the Patient Advisory Group (PAG) that was developed using Qualtrics and distributed via email by the patients' associations in the consortium to all eleven members (March 2025). PAG members were included as participants to align with the patient engagement plan's intention to incorporate patient perspectives into the development of the overall EFS framework. The second survey consisted of an Excel form that was distributed via email in April 2025 to all consortium partners. Both surveys included an introduction describing the objectives, a demographics section, and a KPI relevance section consisting of one matrix question and one open-ended question. The matrix question asked respondents to rate the importance of 26 KPIs, grouped into six areas (Assessment and approval, Timing, Study characteristics, Patient involvement, Innovation and impact, Awareness) using five answer options (Not Important, Somewhat Important, Important, Very Important, Prefer Not to Answer / I Don't Know). Definitions of each KPI were provided to both groups in an attached document to support interpretation. The open-ended question invited respondents to suggest additional measurable KPIs. Responses were analysed using descriptive statistics to identify high-importance KPIs, defined as those rated "Important" or "Very Important" by at least 75% of respondents in both groups. Following the surveys, three plenary meetings were conducted

with WP5 partners in April, May, and July 2025 to refine the preliminary list of 26 KPIs based on the survey results, integrate selected KPIs suggested through the open-ended responses, and support the development of the final KPI list. Between May and July, WP5 partners also reviewed a preliminary version of this deliverable (V1.0) and provided additional comments to further refine and finalize the KPI list.

3. **Development of four online forms to be completed by sponsors of the EFS pilots at key stages of the EFS pilot process.** WP5 has developed four online forms that will be completed by sponsors of EFS pilots at key stages of the EFS pilots - before the start of the EFS pilot, after submission of the application to the NCA, after validation of the application, and after the EFS pilot has been completed - and that will collect data required to calculate performance metrics of the EFS pilots. Sponsors will be identified from the results of Work Package 7 (WP7), which describes the selection of pilot use cases (see Deliverable *D7.2 Recommendations for the selection of pilot use cases* for more details). This proposed process will collect information in the absence of EUDAMED. Bocconi University (UB) researchers will download the online form responses and conduct descriptive statistics analyses to calculate performance metrics. Data resulting from these analyses will be visually displayed into a performance dashboard.
4. **Development of recommendations to modify the application form outlined in the MDCG 2021-08 guidance on Clinical investigation application/notification documents.** To better understand the structure and content of the application forms currently in use in EU Member States, WP5 conducted a comparative analysis of nine countries (Italy, Netherlands, France, Ireland, Czech Republic, Denmark, Poland, Spain, Germany) and proposed recommendations to modify the current version of the application form outlined in the MDCG 2021-08 guidance on *Clinical investigation application/notification documents*, which is expected to serve as the basis for the future EUDAMED application form.

Results

Step 1 - Identification of a preliminary list of KPIs

Table 1 presents the outcome of this process: a preliminary list of 26 KPIs retrieved from the retrieved from 1) the HEU-EFS First and Second Stage proposals submitted by the consortium to the European Commission as part of the grant application, and 2) WP1 results (see Deliverable *D1.1 Characteristics, gaps, and best practices of premarket programs* ([LINK](#)) for more details), and further refined through internal discussions with consortium partners.

Table 1 Preliminary list of 26 KPIs

KPI
Assessment and approval
Number of EFS submitted (total, per country, per year)
Number of EFS submitted by SMEs (total, per country, per year)
Number of EFS approved (total, per country, per year)
Number of approved EFS submitted by SMEs (total, per country, per year)
Number of NCAs involved in EFS assessment
List of NCAs involved in EFS assessment
Percentage of EFS approved out of those submitted (approval rate)
Timing
Average time from EFS submission to approval
Average time from EFS approval to contractual signature with clinical site
Average time from contractual signature with clinical site to first patient enrolled
Study characteristics
Number of clinical sites involved in EFS in the EU (total, per country, per year)
Number of single-centre EFS
Number of multi-centre EFS
Number of multi-country EFS
Number of EFS per device risk class
Number of EFS per health condition
Average number of patients enrolled in EFS
Patient involvement
Number of EFS involving patients or patient associations in the study design
Number of EFS assessing health-related quality of life (e.g., PROMs)
Number of EFS assessing patients' clinical experiences (e.g., PREMs)
Innovation and impact

KPI
Average time from EFS approval to CE mark
Percentage of EFS transitioning to pivotal studies
Number of FSN issued
Number of recalls from the market
Awareness
Number of accesses to the HEU-EFS website
Number of downloads from the HEU-EFS website

Note. SMEs: Small and Medium-Sized Enterprises; PROMs: Patient-Reported Outcome Measures; PREMs: Patient-Reported Experience Measures; FSN: Field Safety Notice.

Step 2 - Survey-based assessment of the relevance of KPIs involving the PAG and the consortium

Table 2 reports the list of 26 KPIs ranked by perceived importance as evaluated by the PAG and consortium members via dedicated surveys. In the table, the KPIs highlighted in green are those perceived as 'very important' or 'important' by at least 75% of respondents in both groups.

Table 2 Percentage of PAG members and HEU-EFS consortium partners who rated KPIs as “Important” or “Very Important”

KPI	PAG survey %	Consortium survey %
	n=8	n=17
Assessment and approval		
Number of EFS submitted (total, per country, per year)	75	88
Number of EFS submitted by SMEs (total, per country, per year)	63	65
Number of EFS approved (total, per country, per year)	88	94
Number of approved EFS submitted by SMEs (total, per country, per year)	63	35
Number of NCAs involved in EFS assessment	75	76
List of NCAs involved in EFS assessment	63	76
Percentage of EFS approved out of those submitted (approval rate)	75	82
Timing		
Average time from EFS submission to approval	63	88
Average time from EFS approval to contractual signature with clinical site	75	65
Average time from contractual signature with clinical site to first patient enrolled	63	41
Study characteristics		
Number of clinical sites involved in EFS in the EU (total, per country, per year)	75	82

KPI	PAG survey %	Consortium survey %
	n=8	n=17
Number of single-centre EFS	88	65
Number of multi-centre EFS	88	65
Number of multi-country EFS	88	76
Number of EFS per device risk class	88	82
Number of EFS per health condition	75	71
Average number of patients enrolled in EFS	88	59
Patient involvement		
Number of EFS involving patients or patient associations in the study design	100	59
Number of EFS assessing health-related quality of life (e.g., PROMs)	100	59
Number of EFS assessing patients' clinical experiences (e.g., PREMs)	100	65
Innovation and impact		
Average time from EFS approval to CE mark	88	65
Percentage of EFS transitioning to pivotal studies	75	82
Number of FSN issued	88	47
Number of recalls from the market	88	53
Awareness		
Number of accesses to the HEU-EFS website	50	47
Number of downloads from the HEU-EFS website	38	29

Note. SMEs: Small and Medium-Sized Enterprises; PROMs: Patient-Reported Outcome Measures; PREMs: Patient-Reported Experience Measures; FSN: Field Safety Notice.

Survey of the PAG

Survey response rate was 73% (8/11 patient PAG members) with 18 out of 26 KPIs identified as important or very important by PAG survey respondents. KPIs of high importance spanned all categories, with particular emphasis on Patient Involvement. All respondents indicated that every indicator in this category is important or very important.

Based on the comments provided by respondents in the open-ended question, several insights emerged regarding indicators in the context of EFS. Respondents underscored the importance of having an indicator on the diversity of patients enrolled in EFS (e.g., sex, ethnicity, etc.) as *“this can be later useful when the EFS transitions into a pivotal study or when verifying causes of recalls from the market.”* Respondents also described the value of monitoring the timing of patient withdrawal from the study, with one respondent proposing *“an indicator about the moment when patients decide to withdraw from a study”* and noting that *“the moment when patients decide to quit is important for the*

designers of the study and can help identify potential issues in the design.” In addition, respondents reported the importance of including KPIs that monitor the success of EFS in terms of transition to market, with one respondent suggesting that such an indicator demonstrates “*its compliance to patient health improvement research as designed.*”

Consortium-wide survey

Survey response rate was 77% (17/22 partners). Of the 17 responses received, two (12%) were from academia, four (24%) from hospitals, two (12%) from HTA bodies, five (29%) from industry, two (12%) from patient associations, and two (12%) from SMEs.

Out of the total 22 consortium partners, the response rates within each group were: two out of three (67%) for academia, four out of four (100%) for hospitals, two out of two (100%) for HTA bodies, five out of five (100%) for industry, two out of two (100%) for patient associations, two out of four (50%) for SMEs, and 0 out of one (0%) for CROs.

Table 3 presents the perceived importance of KPIs as reported by each stakeholder category within the consortium.

Table 3 Percentage of respondents who rated KPIs as “Important” or “Very Important”, by category

KPI	Academia %	HTA body %	Hospital %	Industry %	Patient association %	SME %	Average consortium %
	n=2	n=2	n=4	n=5	n=2	n=2	n=17
Assessment and approval							
Number of EFS submitted (total, per country, per year)	100	100	75	100	100	50	88
Number of EFS submitted by SMEs (total, per country, per year)	100	100	25	40	100	100	65
Number of EFS approved (total, per country, per year)	100	100	75	100	100	100	94
Number of approved EFS submitted by SMEs (total, per country, per year)	100	50	0	40	0	50	35
Number of NCAs involved in EFS assessment	100	50	75	60	100	100	76
List of NCAs involved in EFS assessment	100	100	50	60	100	100	76
Percentage of EFS approved out of those submitted (approval rate)	100	100	75	80	100	50	82
Timing							
Average time from EFS submission to approval	100	100	100	100	50	50	88
Average time from EFS approval to contractual signature with clinical site	100	50	50	80	50	50	65
Average time from contractual signature with clinical site to first patient enrolled	100	50	0	60	50	0	41
Study characteristics							
Number of clinical sites involved in EFS in the EU (total, per country, per year)	100	100	100	60	100	50	82
Number of single-centre EFS	100	100	50	40	100	50	65
Number of multi-centre EFS	100	100	50	40	100	50	65
Number of multi-country EFS	100	100	50	80	100	50	76
Number of EFS per device risk class	100	100	75	60	100	100	82
Number of EFS per health condition	100	50	75	40	100	100	71
Average number of patients enrolled in EFS	100	50	0	80	100	50	59
Patient involvement							

KPI	Academia %	HTA body %	Hospital %	Industry %	Patient association %	SME %	Average consortium %
	n=2	n=2	n=4	n=5	n=2	n=2	n=17
Number of EFS involving patients or patient associations in the study design	100	50	50	60	100	0	59
Number of EFS assessing health-related quality of life (e.g., PROMs)	100	50	75	20	100	50	59
Number of EFS assessing patients' clinical experiences (e.g., PREMs)	100	50	75	40	100	50	65
Innovation and impact							
Average time from EFS approval to CE mark	100	100	75	0	100	100	65
Percentage of EFS transitioning to pivotal studies	100	100	50	100	100	50	82
Number of FSN issued	100	50	25	20	100	50	47
Number of recalls from the market	100	50	25	40	100	50	53
Awareness							
Number of accesses to the HEU-EFS website	100	0	50	40	100	0	47
Number of downloads from the HEU-EFS website	100	0	50	20	0	0	29

Several key aspects emerged from respondents' comments on additional indicators for monitoring the EFS Program as "Very Important." Table 4 provides a summary of the performance indicators recommended by respondents. Patient involvement was an aspect that was reported in the respondents' comments. Rather than limiting engagement to early stages, one respondent emphasized that *"for meaningful patient engagement it is important that it happens throughout the entire lifecycle of a device."* Relatedly, others suggested capturing whether *"insights from patients and patient organisations were implemented,"* not just whether patients were involved.

Inclusivity and diversity were also frequently noted. Respondents proposed indicators such as the *"percentage of under-represented groups participating in EFS"* and the *"number of EFS including a previously excluded patient population."* These suggestions reflect an interest in ensuring equitable access to clinical research. Comments also highlighted the need to monitor training and capacity building, with respondents reporting the importance of *"number of training sessions or materials provided to SMEs and NCAs"* and tracking the number of *"clinicians trained in EFS."*

Respondents also suggested operational performance indicators, such as the *"rate of amendments or resubmissions,"* *"average time between request and dialogue with NCA,"* and *"retention and dropout rates."* Financial indicators were described as particularly relevant for SMEs, with one comment identifying the *"cost associated with EFS"* as *"especially relevant for SMEs and possible implications for grants or other funding opportunities."* Finally, respondents reported the value of tracking longer-term outcomes, such as the *"number of EFS prematurely discontinued,"* *"serious adverse events,"* and assessments of *"economic"* and *"organisational impact."* As one respondent noted, *"A clear indicator of a failure is the discontinuation of the EFS. Reasons for discontinuation should be monitored,"* suggesting that such data can provide critical insights for program improvement.

Summary of additional KPIs suggested by PAG and consortium members

Table 4 shows the list of additional KPIs proposed by the PAG and consortium members.

Table 4 List of additional KPI suggested by PAG and consortium members

KPI suggested
Diversity of patients enrolled in EFS (in terms of age, sex/gender, ethnicity, etc.)
Timing of patient withdrawal from the study
Success of EFS in terms of transition to market
Number of EFS approved per Ethics Committee
Patient engagement throughout the entire lifecycle of a device

KPI suggested
Implementation of insights from patients and patient organisations
Percentage of under-represented groups participating in EFS
Number of EFS including a previously excluded patient population
Number of training sessions or materials provided to SMEs and NCAs
Number of “clinicians trained” in EFS
Rate of amendments or resubmissions
Average time between request and dialogue with NCA
Retention and dropout rates
Cost associated with EFS

The finalized list of KPIs, developed through refinements made during the plenary meetings and feedback on the preliminary version of this deliverable, is presented in Table 5 (located later in the document for layout clarity).

Step 3 - Development of four online forms to be completed by sponsors of the EFS pilots at key stages of the EFS pilot process.

Discussions and meetings with the consortium revealed the importance of reducing the burden of work for NCAs and maintaining confidentiality of data from sponsors during the proposed HEU-EFS methodological framework (see Deliverable D3.2 HEU-EFS methodological framework for more details). Based on this feedback, WP5 proposed to develop and distribute four brief, consecutive online forms to sponsors participating in the EFS pilots to collect data required to calculate performance metrics. Sponsors will complete the forms at specific stages of the EFS pilot process, and data collected will support both WP7 and WP5 (Table 5).

Table 5 Overview of online forms names, specific stage when they will be completed, and WPs using the data

Form name	Stage to complete it	Purpose of data collected through online forms
Form #1 - Self-Evaluation Checklist	Before the start of EFS pilot	Select medical device technologies for the EFS pilots;* Collect data required to calculate KPIs
Form #2 - Application to the NCA(s)	After EFS application has been submitted	Collect data required to calculate KPIs
Form #3 - Validation by NCA(s)	After EFS application has been validated	Collect data required to calculate KPIs
Form #4 - EFS Pilot	After EFS pilot has been completed	Collect data required to calculate KPIs

Notes. * See deliverable D7.2 Recommendations for the selection of pilot use cases for more details.

A detailed list of KPIs and online form that will collect data required to calculate each KPI is reported in Table 6.

Table 6 KPIs grouped per timing when information is provided and online form # to collect data

HEU-EFS KPI	KPI Source
Before the start of EFS pilot	
Number of EFS submitted (total, per country, per year)	Form #1 – Self-Evaluation Checklist
Number of EFS submitted by SMEs (total, per country, per year)	
Number of NCAs involved in EFS assessment	
List of NCAs involved in EFS assessment	
Number of EFS involving patient or patient associations in the study design	
After EFS application has been submitted to NCA	
Number of clinical sites involved in EFS in the EU (total, per country, per year)	Form #2 - Application to NCA(s)
Number of single-centre EFS	
Number of multi-centre EFS	
Number of multi-country EFS	
Number of EFS per device risk class (Class I, IIA, IIB, III)	
Number of EFS per health condition	
Number of EFS assessing health-related quality of life (e.g., PROMs)	
Number of EFS assessing patients' clinical experiences (e.g., PREMs)	
Participation in dialogue with sponsors	
Modality of dialogue with sponsors	
Topics discussed during dialogue with sponsors	
Perceived helpfulness of dialogue with sponsors in streamlining EFS application	
After EFS application has been validated by NCA	
Number of EFS approved (total, per country, per year)	Form #3 - Validation by NCA(s)
Number of approved EFS submitted by SMEs (total, per country, per year)	
Percentage of EFS approved out of those submitted (approval rate)	
Average time from EFS submission to approval	
Request of comments by NCAs during application assessment (per EFS)	
Number of EFS application rejected	
Reasons for EFS application rejection	
Number of ethics committee involved in EFS assessment (total, per EFS)	
List of ethics committee involved in EFS assessment (total, per EFS)	
Average time from ethics committee submission to approval	
After EFS pilot has been completed	
Average number of patients enrolled in EFS	Form #4 - EFS pilot
Average time from EFS approval to contractual signature with clinical site	
Average time from contractual signature with clinical site to site initiation visit	
Average time from site initiation visit to first patient enrolled	
Percentage of EFS transitioning to subsequent pre-market clinical investigation (e.g., pivotal studies)	
Number of EFS that experienced patient withdrawal	
Number of EFS that were terminated, withdrawn, or suspended	

HEU-EFS KPI	KPI Source
Explanations describing why EFS was terminated, withdrawn, or suspended	
Number of additional pre-market clinical investigations after the EFS was terminated, withdrawn, or suspended	
List of additional pre-market clinical investigations after the EFS was terminated, withdrawn, or suspended	

Pilot use case online forms anonymity and confidentiality

Anonymity and confidentiality of online forms responses provided by the sponsors during the pilot phase will be maintained across all four forms. To ensure this, each sponsor will be asked to generate a self-selected, unique code identifier at the beginning of the process. The unique code identifier will be used consistently across all four online forms, allowing Bocconi University (UB) researchers to link responses over time while fully preserving respondent anonymity. The use of sponsor-generated codes will also ensure that UB will not have access to sponsor names or information about the specific medical device technologies involved.

All online form responses will remain confidential and will be reported only in aggregate form in the performance dashboard where performance metrics will be displayed. No individual sponsor or associated medical device technology will be identifiable in the analyses or in any resulting graphs, tables, or dashboard visualizations. KPIs and all reported results will be aggregated to remain confidential.

Pilot use case online forms content

All four online forms have been developed and will be administered using Qualtrics^{XM}. As reported in Deliverable 9.10 *Data Management Plan*, Qualtrics^{XM} was selected by the HEU-EFS consortium as the primary platform for conducting online forms since it ensures high standards of personal data protection and security as requested by Bocconi University Ethics Committee.

Each online form consists of three sections:

- (1) an introduction, describing the objectives of the online forms; it includes a short text-entry field where sponsors will enter their self-generated, unique code identifier that will enable anonymous tracking of responses across the four online forms while maintaining full confidentiality;
- (2) a KPI data collection section that contains a mix of dichotomous, multiple-choice, matrix, and open-ended (short text entry) questions designed to systematically collect data required for KPI calculation;

- (3) a summary of responses section that includes a downloadable record of responses provided by each sponsor. Sponsors will be encouraged and required to download a PDF summary of their responses at the end of each form using the “Download PDF” button. This record may be needed to complete subsequent online forms and for the sponsor’s own reference.

Each online form is estimated to take approximately five to ten minutes to complete.

A Microsoft Word printable version of each online form is available at the following annexes:

- Annex I - Form #1 Self-Evaluation Checklist
- Annex II - Form #2 Application to NCA(s)
- Annex III - Form #3 Validation by NCA(s)
- Annex IV - Form #4 EFS Pilot

Pilot use case online forms data analysis

Bocconi University (UB) researchers will download the online form responses from Qualtrics and will conduct descriptive statistics analyses to aggregate responses and calculate KPIs. Data resulting from these analyses will be visualized through graphs and tables for integration into the performance dashboard. Because responses are linked using sponsor-generated unique identifiers, all analyses will be fully anonymized and confidential. Bocconi University (UB) researchers will not have access to sponsor names or the identities of the medical device technologies under investigation. All reported data will be presented in aggregate form, and no sponsor or specific technology will be identifiable in any analytical outputs. KPIs calculated from Form #1 will be also elaborated and submitted as part of Deliverable D7.2.

Pilot use case online forms distribution

Each of the four online forms will be distributed to a designated sponsor representative from each company participating in the pilot tests. Distribution will occur via personalized online form invitation emails, followed by tailored reminder emails.

The invitation email will include:

- A brief description of the study;
- A link to the Qualtrics online form;
- Instructions for creating and entering the sponsor-generated unique code identifier and for downloading a summary of responses;
- Information on informed consent and confidentiality.

At the beginning of each online form, sponsors will be prompted to enter the unique code before proceeding to the online form questions. Reminder content and timing of distribution will be tailored for each sponsor to help improve response rates, in accordance with Dillman tailored design principles [5].

Performance dashboard

Performance metrics calculated from the online forms analyses will be displayed using graphs (e.g., pie charts, bar charts, histograms) and tables in a performance dashboard. The performance dashboard will be made available in a subsection of the HEU-EFS website (<https://heuefs.eu/>). The performance dashboard will include data from EFS pilots only, but will be identified as an option recommended to the European Commission to collect data required to calculate performance metrics of EFS in general as EUDAMED’s full implementation will likely happen after the end of the project. The performance dashboard will be made available upon completion of EFS pilots.

Additional KPIs to be collected later in the device’s lifecycle

WP5 also suggested additional KPIs to be collected later in the device’s lifecycle (Table 7). Although collecting the KPIs indicated in Table 7 goes beyond WP5’s current data collection timeline, these KPIs are essential for fully capturing the medical device’s lifecycle. They also can support effective management and monitoring, provide valuable insight into the impact of conducting EFS, and help assess the device’s overall performance. These forms will not be used in the EFS pilots and have been developed as an informative suggestion to inform future practices to capture additional KPIs that are important in the medical device’s lifecycle.

Table 7 Additional KPIs suggested to be collected later in the device’s lifecycle

HEU-EFS KPI	KPI Source
After subsequent pre-market study following the EFS pilot	
Average time from approval of subsequent pre-market clinical investigation to contractual signature with clinical site	Form #5
Average time from contractual signature with clinical site to site initiation visit	
Average time site initiation visit to first patient enrolled	
After CE marking	
Average time from EFS approval to CE mark	Form #6
Adoption rate	
Number of Health Technology Assessment reports	
HTA recommendations	
Number of economic evaluations	
Results of cost-effectiveness studies	
Activation of coverage with evidence development schemes	
Special funding mechanisms	
Number of FSN issued	

HEU-EFS KPI	KPI Source
Number of recalls from the market	

A Microsoft Word printable version of each online form is available at the following annexes:

- Annex V - Form #5 (informative suggestion only)
- Annex VI - Form #6 (informative suggestion only)

Step 4 - Development of recommendations to modify the application form outlined in the MDCG 2021-08 guidance on Clinical investigation application/notification documents.

Comparative analysis results

The results from the comparative analysis of nine countries show that Italy and the Netherlands use the MDCG 2021-08 form, while seven countries (France, Ireland, Czech Republic, Denmark, Poland, Spain, Germany) use their own national forms. Despite overall consistency, national forms often include additional sections, especially related to ethics (e.g., Ethics Committee details) and administrative requirements (e.g., fee payments, local documentation) (Table 8). Sections without differences between the MDCG and the national application forms are highlighted in green in the table.

Table 8 Comparison of MDCG 2021-08 fields with national Application Forms in seven selected EU Countries

MCDG 2021-08	France	Ireland	Czech Republic	Denmark	Poland	Spain	Germany
Section 1: Clinical investigation identification							
1.1 Sponsor identification	x	x	x	x	x	x	x
1.2 Legal representative identification	x	x	x	x	x	x	x
1.3 Clinical investigation type	x	x	x	x	x	x	x
1.4 Submission type	x	x	x	x	x	x	x
1.5 Participating countries within the EU/EEA/UK (Northern Ireland), Turkey and Switzerland	x	x	x	x	Not explicitly requested	x	x
1.6 Participating countries outside EU/EEA/UK	x	x	x	x	Not explicitly requested	x	x
1.7 Clinical investigation plan (CIP)	x	x	x	x	x	x	x
1.8 Clinical investigation title	x	x	x	x	x	x	x
Section 2: Clinical investigation description							
2.1 Scientific opinion	x	x	x	x	x	x	x
2.2 Design of the clinical investigation	x	x	x	x	x	x	x
2.3 Design methodology	x	Not explicitly requested	x	x	x	x	x
2.4 Development stage	x	x	x	x	x	x	x
2.5 Objectives and endpoints	x	x	x	x	x	x	x
2.6 Synopsis of the clinical investigation	x	x	x	x	x	x	x

MCDG 2021-08	France	Ireland	Czech Republic	Denmark	Poland	Spain	Germany
2.7 Planned number of subjects	x	x	x	x	x	x	x
2.8 Duration of clinical investigation	x	x	x	x	x	x	x
2.9 Population	x	Not explicitly requested (None of these are broken down as individual fields. Instead, a general summary of the clinical investigation is requested, where such info may be included)	x	x	Not explicitly requested (None of these are broken down as individual fields. Instead, a general summary of the clinical investigation is requested, where such info may be included)	x	x
2.9.1 Medical condition	x	Not explicitly requested	x	x	Not explicitly requested	x	x
2.9.2 Therapeutic area	x	Not explicitly requested	x	x	Not explicitly requested	x	x
2.9.3 Gender of subjects	x	Not explicitly requested	x	x	Not explicitly requested	x	x
2.9.4 Inclusion criteria	x	Not explicitly requested	x	x	Not explicitly requested	x	x
2.9.5 Exclusion criteria	x	Not explicitly requested	x	x	Not explicitly requested	x	x
2.9.6 Type of subjects that the clinical investigation plans to recruit	x	Not explicitly requested	x	x	Not explicitly requested	x	x
2.9.7 Age range of the participants that the clinical investigation plans to include	x	Not explicitly requested	x	x	Not explicitly requested	x	x
2.10 Scope of the investigational device	x	x	x	x	x	x	x
2.10.1 Combined investigation Medical Device/In Vitro Diagnostic?	x	Not mentioned (No field in the HPRA form asks if this is a combined device/IVD study under Art. 74 MDR).	x	x	x	x	x
2.10.2 Is the application submitted in parallel with an application	x	x	x	x	x	x	x

MCDG 2021-08	France	Ireland	Czech Republic	Denmark	Poland	Spain	Germany
for a clinical trial on medicinal products							
2.11 Coordinating investigator	x	x	x	x	x	x	x
Section 3: Investigational device(s)							
3.1 Investigational medical device	x	x	x	x	x	x	x
3.1.1 Device purposes	x	Not specified (The form requests a general device description).	x	x	x	x	x
3.1.2 Device type	x	Not listed as predefined options	x	x	x	x	x
3.1.3 Invasiveness	x	Not explicitly requested	x	x	x	x	x
3.1.4 Device Identifiers	Not explicitly requested	x	Not explicitly requested	x	x	x	x
3.2 Previous clinical investigation	x	x	x	x	x	x	x
3.3 Scientific opinion/view	x	x	x	x	x	x	x
3.4 Manufacturer of the investigational device	x	x	x	x	x	x	x
3.4.1 Manufacturer information	x	x	x	x	x	x	x
3.4.2 Authorised representative	x	x	x	x	x	x	x
Section 4: Comparator							
4.1 Applicability of section 4	x	x	x	x	x	x	x
4.2 Type of comparator	x	x	x	x	x	x	x
4.2.1 Medical device as comparator	x	Only basic comparator info is requested (The HPRA form asks if a comparator is used and for its classification, but not for regulatory status or procedural impact).	x	x	Not explicitly requested	x	x
Section 5: National information							
5.1 Study site information	x	x	x	x	x	x	x

MCDG 2021-08	France	Ireland	Czech Republic	Denmark	Poland	Spain	Germany
5.2 Ethics committee information	x	x	x	x	x	x	x
5.3 Status of the clinical investigation	x	x	x	x	x	x	x
5.4 Expected number of subjects recruited within the Member State	x	x	x	x	x	x	x
Additional fields	Research-only procedures (Samples, invasive exams, dose/exposure data) Ancillary/marketed products (Drugs, devices, cosmetics – status, off-label use, import certification) Technical platforms, Comparator manufacturer, Legal/admin compliance	Payment details (e.g., wire transfer, account) Mandatory email to notify of submission Specification required for submission via CESP Signature and multiple statements on processing of application Detailed and guided list of documents to attach (43 items)	Administrative requirement: prior registration of the sponsor in the system, provision of fiscal details (e.g. VAT ID), proof of payment of the administrative fee, a signed declaration from the authorised representative (for non-Czech sponsors), explicit consent to receive official communications via the portal, and uploading of supporting documents following specific file naming and formatting standards	Monitor & CRO, Insurance and Liability, Regulatory Compliance (ISO 14155, Helsinki, GSPR), Signature and Billing, Attachments for MREC, Synopsis in Danish, Device Tracking and Handling		Ethics Committee designation, EUDAMED or internal identifiers, document checklist, site-specific investigation status, sponsor's prior drug trial activity, commitment to AEMPS communication, language of patient materials	Investigator site qualification Ethics opinion upload

The comparative analysis identified **three main submission models** used across the countries reviewed:

- Italy, Ireland, Poland and Denmark require sponsors to complete a national or MDCG-based application form offline (PDF/Word) and submit it via email or certified email, along with all supporting documents.
- France, Czech Republic, Germany, Spain, and the Netherlands use dedicated national online portals that combine structured data entry with the upload of annexes such as the clinical investigation plan and investigator's brochure.
- Some systems, such as those in Germany or the Czech Republic, also enable workflow tracking and amendment submissions.

These variations reflect different levels of digitalization and alignment with MDR procedures across Europe.

Recommendations for modifications to the MDCG 2021-08 application form

WP5 proposed the following recommendations to modify the MDCG 2021-08 application form. WP5 proposed **four light integrations** to the MDCG 2021-08 application form adding key fields required for EFS-specific monitoring and other aspects, but maintaining the original format and logic of the model (see Annex VII for more details):

2. Section 1.1 – Sponsor Identification:

A flag has been added to indicate whether the sponsor is an SME (Small or Medium-sized Enterprise) [6].

3. Section 2.2 – Design of the Clinical Investigation:

The options Early Feasibility Study (EFS) and Traditional Feasibility Study have been added.

4. Section 2.5 – Objectives and Endpoints:

A new item has been included on the use of patient experience data, with possible options:

- Patient-Reported Outcome Measures (PROMs)
- Patient-Reported Experience Measures (PREMs)
- Other

5. New Section – Patient or Patient Association Involvement:

A new section has been added to assess patient involvement in the design of the clinical investigation:

- Were patients or patient associations involved in the design of the clinical investigation?
(Yes/No)

- If yes, please briefly describe their role.

Discussion and next steps

WP5 has proposed three main outputs: an approach to calculate performance metrics for EFS pilots, a performance dashboard displaying metrics related to EFS pilots, and a set of recommendations to integrate additional performance metrics into EUDAMED's CI/PS.

Approach to calculate performance metrics of EFS pilots

The development of the approach to calculate performance metrics for EFS pilots included designing specific metrics to monitor EFS performance, identifying the necessary data required for their calculation, and developing online forms to collect this data. Performance metrics were designed by reviewing grant application materials and WP1 results to extract a preliminary list of metrics, conducting surveys with PAG and consortium partners to gather feedback on the perceived importance of the preliminary metrics, and conducting plenary meetings to refine and finalize the KPI list.

The necessary data for metrics calculation were identified by developing a mix of dichotomous, multiple-choice, matrix, and open-ended questions, which are included in online forms to be completed by sponsors of EFS pilots. The online forms were developed in Qualtrics to ensure anonymity and confidentiality. Sponsors participating in EFS pilots will be required to complete the forms at key stages: before the start of the EFS pilot, after submission of the application to the National Competent Authority (NCA), after validation of the application, and after the EFS pilot has been completed. Bocconi University (UB) researchers will download the online form responses and conduct descriptive statistics analyses to calculate performance metrics. Data resulting from these analyses will be visually displayed into a performance dashboard.

Performance dashboard displaying metrics related to EFS pilots

The performance dashboard will be created based on the analyses of the online form data. It will display graphs and tables and will be made available on a subsection of the HEU-EFS website (<https://heuefs.eu/>) upon completion of the EFS pilots.

Recommendations to integrate additional performance metrics into EUDAMED's CI/PS

Following completion of the EFS pilots, WP5 will make formal recommendations to the European Commission regarding integration of additional KPIs into the future Clinical Investigation and Performance Studies (CI/PS) module of EUDAMED. Based on work conducted so far, WP5 proposes

preliminary recommendations, which are subject to change as pilots progress. These include four light modifications to the MDCG 2021-08 application form, including adding: an option to indicate whether a sponsor is an SME, an option to indicate whether a study is an Early Feasibility Study or Traditional Feasibility Study, an item on the use of patient experience data (PROMs, PREMs), and a section to describe the patient involvement in design of the clinical investigation. In addition to being involved in the design of the clinical investigation, we recommend that patients are also more actively involved in the development of PROMs to ensure their relevance and usability for both patients and researchers. To implement these recommendations, further research and work would be needed. Currently, the number of validated instruments for PROMs and patient-centric PROMs for medical device clinical investigations is limited, especially for EFS. To help address this gap, we recommend referring to Deliverable 1.5 *Recommendations on PROMs for conformity assessment and post-market surveillance* authored by the European Patients' Forum (EPF) together with the University of Gothenburg, and produced within the CORE-MD [7].

In addition, based on PAG and consortium survey results - where at least 75% of both groups rated certain KPIs as important or very important - WP5 envisions recommending additional performance metrics for future EFS. These may include capturing countries of submission and approval, lists of NCAs involved, approval rates, and the number of clinical sites involved. However, WP5 recognizes that these recommendations may evolve as data from EFS pilots becomes available, and final recommendations will only be made after pilot completion.

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