Harmonised approach to **E**arly **F**easibility **S**tudies for Medical Devices in the **E**uropean **U**nion **(HEU-EFS)**

WP4 Development and Validation of a Standard EFS CIP Template

DELIVERABLE 4.1 (3/3)

CIP Checklist for a Clinical Investigation Plan for EFS clinical investigations involving Medical Devices

Co-funded by the European Union

Disclaimer:

The Harmonised approach to Early Feasibility Studies for Medical Devices in the European Union (HEU-EFS) project is funded by the European Union, the private members, and those contributing partners of the IHI JU. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the aforementioned parties. Neither of the parties can be held responsible for them.

Project Acronym	HEU-EFS
Project Title	Harmonised approach to Early Feasibility Studies for Medical Devices in the European Union
Project Coordinator	Giuditta Callea giuditta.callea@unibocconi.it
Grant Agreement Number	101112185
Project Duration	October 2023 – September 2027 (48 months)
Deliverable Number	4.1
Work Package	4
Task	4.2
Lead Beneficiary	Meditrial, Abbott
Status	Completed
Dissemination Level	Public
Type	R – Document, report
Due Date of Deliverable	30 September 2025
Actual Submission Date	17 October 2025
Author(s) & Organization(s)	Dr Monica Tocchi, Donatella Mariani, Vivienne Kayser-Soltys, Silvia Ruggieri, Davide Decandia, Paola Antonini, Eleonora Russo, (Meditrial); Alessandra Denaro, Karine Miquel, Karolien Timmermans, Katie Ludwig, Keshav Kohli, Jeff Sturm (Abbott), Giuditta Callea, Francesca Pissarello (Bocconi University), Alexandra Herborg Cornelius Poulsson, Marit Erna Austeng (Norwegian Institute of Public Health (NIPH), Nicolas Martelli, Armelle Arnoux, Ornella Tangila Kayembe (APHP Paris), Adrian Valledor, Daniel Beltran Argudo, Laura Sampietro (FCRB & HCB), CIMT, Yasemin Zeisl, European Patient Forum (EPF), Marta Bragagnolo Global Heart Hub (GHH), Newronika, Jessie Catarina Verwaard, Kostine Lyubava, (Edwards), Manon Gielkens, Alicia Panadero, Sebastiaan de Jongh (Medtronic), Marlen Peseke (UMR) Gabriella Di Santo, Antonio Balsamo (AGENAS), Carmen Furno, Benedetta Brancadoro, Arianna Salvatori (GEMELLI), Tom Melvin, Majella Geraghty (TCD), Yasemin Zeisl, Claudia Louati (EPF), Cinzia Santin (Gore), Marta Kestan (JNJ), Sebastian Kuhn, Marlen Peseke, Ilja Michaelis (UMR)

Reviewer(s) & Organization(s)	Majella Geraghty (TCD); Marta Kerstan (JNJ)
Contact	Giuditta Callea giuditta.callea@unibocconi.it

File History

Version	Date	Status	Author	Review
1.0	10-12-2024	V1.0	Monica Tocchi, Meditrial	Giuditta Callea (UB)
2.0	03-13-2025	V2.0	Monica Tocchi, Meditrial	Nicolas Martelli, Armelle Arnoux, Ornella Tangila Kayembe (APHP), Alexandra Poulsson, Marit Erna Austeng (NIPH)
3.0	06-12-2025	V3.0	Monica Tocchi, Meditrial	Tom Melvin (TCD), Alexandra Poulsson, Marit Erna Austeng (NIPH)
3.1	22-07-2025	V3.1	Monica Tocchi, Meditrial	Nicolas Martelli, Ornella Tangila Kayembe (APHP), Marta Bragagnolo (GHH), Marlen Peseke (UMR) Alexandra Poulsson, Marit Erna Austeng (NIPH), Gabriella Di Santo (AGENAS), Antonio Balsamo (AGENAS)
3.2	31-07-2025	V3.2	Monica Tocchi, Meditrial	Carmen Furno, Benedetta Brancadoro and Arianna Salvatori (GEMELLI), Laura Sampietro-Colom (HCB), Adrián Valledor (FCRB), Yasemin Zeisl (EPF), Lyubava Kostine (Edwards), Jessie Verwaard (Edwards) Majella Geraghty (TCD), Cinzia Santin (Gore), Marta Kestan (JNJ), Sebastian Kuhn, Marlen Peseke, Ilja Michaelis (UMR), Sebastiaan de Jongh (Medtronic), Claudia Louati (EPF)
4.0	30-09-2025	V3.3	Monica Tocchi, Meditrial	Giuditta Callea (UB), Francesca Pissarello (UB), Helen Banks (UB), Federico Facciolo (UB)

Table of Contents

Table of Contents **5**

1 CIP EFS Checklist **6**

1 CIP EFS Checklist

CIP EFS Name: **CIP EFS Version:**

All questions must be answered. If the information required will be provided with a separate cover, this shall be specified in the comments. The user can still use "Yes" to report compliance in these cases. If there are no comments, this shall be specified in the comments (e.g. N/A or no comments).

	CIP Plan Requirements	Y/N	Comments
	Front page: including title, type of investigation (EFS), Registration number, CIP identifier, Principal Investigator, Sponsor, Legal Representative if applicable, CRO if applicable, Medical Device, CIP version and date – confidentiality statement		
	Protocol Change History		
	Signature Page(s): To be completed with name and title of the person(s) authorised to sign the CIP and the CIP amendment(s): Sponsor, medical expert, Principal Investigator responsible for conducting the investigation Add more lines, functions and pages as needed. If the Sponsor and PI are the same person, replace both lines with Sponsor-Investigator.		
	Signature of Principal Investigator at the local investigational site. In multicentre investigations, this page must be individually signed by all participating Local Principal Investigators.		
	Table of Contents		
	Index of Tables		
	Index of Figures		
	Abbreviations		

	CIP Plan Requirements	Y/N	Comments
1	Investigation Administrative Structure a. Sponsor, Sponsor-Investigator (complete contact details of the Sponsor (name and address), role in the investigation, role in the investigation design, collection, management, analysis, and interpretation of data, writing of the report) b. Principal Investigator(s) (If available, provide information on the PI at each investigational site, the coordinating investigator for the investigation, the address details for each investigational site and the emergency contact details for the PI at each site) - If you refer to another document, this document should be annexed to the CIP c. Core Laboratory (if applicable) - name of the core laboratory that is involved in the investigation (may be referred to different document, e.g., agreement between Sponsor and core Laboratory). d. Monitoring Institution - name of the institution, place and country that monitors the investigation, if other than the Sponsor (may be referred to different document, e.g., agreement between Sponsor and the Monitoring Institution). e. Data Safety Monitoring Board - composition of data safety monitoring board (DSMB); summary of its role and reporting structure; statement of whether it is independent from the Sponsor and competing interests; and reference to where further details about its charter can be found, if not in the CIP. Alternatively, provide an explanation of why a DSMB is not needed. f. Clinical Events Committee (CEC) – role of the CEC; how it works (i.e. adjudication of events, criteria and methodologies); reference to CEC charter g. Any other relevant Committee, Person, Organisation, Institution - If applicable e.g., coordination, data management, Patient organization, etc . Alternatively, write “not applicable”. h. Funding - Provide brief statement of sources and types of financia support for the investigation. If applicable, reference to other places or contracts/documents where this information is captured. Provide brief statement of any other type of support received to conduct the investigation (MD, comparator, investigation material, software’s, …). If applicable, reference to other places or contracts/documents where this information is captured.		

	CIP Plan Requirements	Y/N	Comments
2	Synopsis: including Title, Short Title, Investigation ID, CIP version and date, Sponsor/Sponsor-Investigator name and address, Registration number, Name of the Medical Device, Unique Device Identification if applicable, Name of the manufacturer, Stage of Development, Intended Use, Clinical Need, Study Design, Study Objective, Primary Endpoints, Secondary Endpoints, Subject Population, Number of subjects with rationale, Site Selection (number and location of study centers), Study Timelines (FPI, expected enrolment completion, LPO, total duration of study, planned study end, regulatory submission), Inclusion/exclusion criteria, Screening and Enrolment, Intervention, Control Intervention (if applicable), Additional Assessments, Follow-up Schedule, Risk Mitigations and Risk Benefit Considerations, Compliance Statement, Study Governance (committees/safety boards), Core Labs (Echo, CT,…), Sponsor Contact, CRO Contact (if applicable), Investigator(s) (names and full contact details), DSMB/CEC/other relevant Committees - Study Workflow - graphic flowchart or table detailing the clinical investigation design and stages - Schedule of Assessments - Insert a flow chart (graphic) or tabular listing of schedule of events and assessments and procedures of the specific investigation.		
3	Background - Background and Rationale for the Clinical Investigation		

	CIP Plan Requirements	Y/N	Comments
4	Investigational Device a. Identification and Description of the Investigational Medical Device – indicate: brand name(s), manufacturer(s), name or number of the model(s) / type(s), incl. software(s), materials, and accessories if any, whether CE marked, intended use, populations target, deviations from IFU; – indicate necessary training and experience required for the use of the MD – include risk management steps to minimize risks through design and manufacturing – reference to IB b. Device Changes during EFS Studies c. Types of Device Changes (modifications to the design, materials, manufacturing processes, labelling, intended use, or software) a. Regulatory Requirements for Device Changes (determination by manufacturers whether a device change is substantial or non-substantial) b. Documentation and Reporting of Device Changes (documentation and evaluation and risk assessment) c. Impact on Clinical Study (on study design, clinical endpoints, or patient population, including: Informed Consent, safety monitoring, Investigational Data Integrity) d. Timing and communication of Device Changes e. Storage of Biological Materials and Related Health Data		

	CIP Plan Requirements	Y/N	Comments
5	Justification for the design of the clinical investigation (shall be based on the conclusions of the evaluation; specific elements to consider: patient input into design, justification for dose or exposition regime (when applicable), rationale for study design, intervention model, duration, objectives, endpoints, interim analysis (when applicable), comparator (when applicable), start of study / end of study definition, access to study intervention after end of study) - Preclinical Evidence (Summarise, if applicable, the available non-clinical data (published or available unpublished data) that could have clinical relevance and justify its use in humans. There may be a reference to the IB, for more details about preclinical data, but still including a short summary) - Clinical Evidence to Date (There may be a reference to the IB for more details about preclinical data, but still including a short summary. This shall include an analysis of adverse device effects, benefits, and any history of modification or recall. If none is available, include a statement that there is no available clinical experience to date on the MD. Also include post-market experience if applicable)		
6	Benefits and Risks of the Investigational Device, Clinical Procedure, and Clinical Investigation - Expected Benefits - Anticipated Adverse Device Effects - Potential Risks of Study Participation (Describe the risks and inconveniences of participating in the study itself, e.g., procedure-related complications, required examinations or concomitant medications that are recommended for use with the device) - Minimization of Risks - Risk/Benefit Consideration (rationale)		

	CIP Plan Requirements	Y/N	Comments
7	Objectives and Hypotheses of the Clinical Investigation - Overall Objective (Provide a clear, simple statement describing the overall purpose(s) of the investigation, explaining why the investigation is performed) - Safety Objective - Device Functionality, Performance and Technical Success Objectives - Description of Study Design (purpose of the clinical investigation risks and anticipated adverse device effects) - Study Hypothesis (if applicable)		
8	Design of the Clinical Investigation a. General Clinical Investigation Design and Justification of Design b. Study Duration (Expected duration of subject participation and a description of the sequence and duration of all investigation periods, including follow-up, if any) c. Methods for Minimising Bias (if applicable) d. Clinical Investigation Outcomes a. Safety Outcomes b. Device Functionality and Performance Outcomes c. Other Outcomes (such as human factors and usability: observation on how clinicians interact with the device)		

	CIP Plan Requirements	Y/N	Comments
9	Study Population - Eligibility Criteria o Inclusion Criteria o Exclusion Criteria - Eligibility Assessment (qualified physician assessing each potential subject, taking final decision to include subject and documenting this decision) - Recruitment and Screening (Describe how, where and by whom subjects are recruited / preselected for the investigation) - Criteria for Withdrawal / Discontinuation of Subjects (Describe the criteria and procedures when and how subjects are withdrawn from the investigation and if and under which circumstances subjects will be replaced; describe reasons that would lead to investigation and/or intervention discontinuation) - Justification of the Choice of the Investigation Population		

10	Study Conduct - Procedures at Each Phase (including informed consent procedure and screening) - Split into Subtitles by Type of Visit (e.g. Screening visit, Day (e.g., -10 to 0): List all exams/tests and other actions to be performed) - Adverse Events - Device Deficiencies (Provide a clear definition of what constitutes a device deficiency within the context of this specific investigational device. Detail the procedures for their identification, assessment, and reporting during the clinical investigation) - Imaging and Core Laboratory Parameters - Vital Signs (if applicable) - Concomitant Interventions (Treatments) - Clearly state any specific or relevant concomitant care and interventions that are permitted (additional treatments) during the investigation including contraindications and interactions for the investigational device, comparators, and required treatments. Their use should be recorded in the CRF. Describe their potential impact on the objectives of the investigation. - Clinical Investigation Specific Preventive Measures (Describe any specific preventive measures, including rescue medication for the subjects or treatments that are prohibited (restrictions). Their use should be recorded in the CRF. Describe their potential impact on the objectives of the investigation) - Follow-up of the Subjects After the Regular Termination of the Clinical Investigation (Specify duration and method) - Assessments of Outcomes (If not already described under chapter 5: Describe for each endpoint (if applicable) what variables will be assessed/observed and how it will be done (e.g., questionnaires, laboratory tests), including any related processes to promote data quality (e.g., duplicate measurements, training of assessors; equipment to be used and arrangements for maintenance and calibration). Provide the rationale or justification to use certain methods and not others etc. Define the time windows allowed) - Assessments of Safety Outcomes - Assessments of Device Functionality and Performance Outcomes - Assessments of Other Outcomes of Interest - Site and Data Monitoring (reference to Monitoring Plan)		

	CIP Plan Requirements	Y/N	Comments
	- Protocol Deviations (write a statement that it is not allowed to deviate from the protocol; describe the procedure for recording, reporting and analysing CIP deviations, providing notification requirements and time frames; describe corrective and preventive actions and investigator disqualification criteria)		

	CIP Plan Requirements	Y/N	Comments
11	Statistical Design and Analysis This section describes the statistical plan for managing, analysing, and presenting data from this clinical study. In EFS studies, the statistical design is predominantly descriptive and exploratory, focusing on preliminary safety, initial performance, and feasibility. Demonstrations of statistical significance or formal hypothesis testing for the primary objectives are not envisaged, but rather the identification of trends and issues. - Statistical Design and Considerations - Planned Analysis o Datasets to be Analysed, Analysis Population o Primary Analysis o Secondary Analyses o Exploratory/Tertiary/Other Objectives o Safety Analysis o Other Analysis o Interim Analyses o Deviation(s) from the Original Statistical Plan - Data Management o Data Management System o Data Security, Access and Back-up - Analysis and Archiving - Data Handling and Record Keeping/Archiving o Handling of Missing Data and Drop-outs - Electronic and Central Data Validation - Case Report Forms o Specification of Source Data and Source Documents o Archiving of Essential Clinical Investigation Documents o Audits and Inspections o Confidentiality, Data Protection		

	CIP Plan Requirements	Y/N	Comments
12	Device Accountability (Provide plans of accurate and adequate records maintenance from shipment to the sites until return or disposal, including any comparator) - Return, Analysis or Destruction of the Medical Device - Labelling and Supply (Re-supply) - Storage Conditions		
13	Ethical and Regulatory Aspects - Ethical Conduct of the Investigation - Declaration of Interests - Insurance (Give proof of insurance cover or indemnification of subjects in case of injury) - Registration of the Investigation (The investigation must be registered in a registry listed in the WHO International Clinical Trials Registry Platform (ICTRP, http://www.who.int/ictrp/en/) - Competent Authorities (CA) and Ethics Committees (EC) o Reporting Duties to the Competent Authorities and Ethics Committees - Protocol Amendments (State who is allowed to amend the CIP or to provide suggestions for a CIP amendment; provide plans for communicating important CIP modifications) - Informed Consent Process - Subject Privacy and Confidentiality		

	CIP Plan Requirements	Y/N	Comments
14	Safety Reporting - Definition and Assessment of (Serious) Adverse Events, Device Deficiencies and Other Safety Related Events - Adverse Events Categorization o Foreseeable Adverse Events and Anticipated Adverse Device Effects o Reporting of (Serious) Adverse Events, Device Deficiencies, and Other Safety Related Events (to the sponsor, pregnancies if applicable, to the National CA and EC, Periodic Safety Reporting) o Follow-up of (Serious) Adverse Events o Documentation and Reporting		
15	Suspension/Premature Termination of the Clinical Investigation (Description of the "stopping rules"; statement that the Sponsor may terminate the investigation prematurely according to certain circumstances) - Discontinuation or Modifications of the Intervention (Description of criteria) - Compliance with Clinical Investigation Intervention		
16	Publication Policy (Describe plans to communicate the results of the investigation to the subjects, healthcare professionals, the public, and other relevant groups; Mention the protection of trade secrets, if applicable)		
17	Bibliography		

	CIP Plan Requirements	Y/N	Comments
18	Appendices (Documents that frequently change during the course of the investigation can be mentioned as 'documents provided separately' and listed here. Investigator's Brochure General Insurance Conditions, insurance certificate List of norms List of investigational sites / PIs (List of countries or centres where data will be collected) Specific protocols (e.g., MRI) Case Report Form (ISO14155 Annex C) Other material handed over to the patients Definitions Rates of foreseeable AE Labels ICF Monitoring Plan		

The Harmonised approach to Early Feasibility Studies for Medical Devices in the European Union (HEU-EFS) project is supported by the Innovative Health Initiative Joint Undertaking (JU) under grant agreement No 101112185. The JU receives support from the European Union's Horizon Europe research and innovation programme and life science industries represented by MedTech Europe, COCIR, EFPIA, Vaccines Europe and EuropaBio.