innovative health initiative

HEU EFS
HARMONISED APPROACH TO EARLY FEASIBILITY STUDIES FOR MEDICAL DEVICES IN THE EUROPEAN UNION

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

WP6 - Methodology development: ethical and legal aspects

DELIVERABLE 6.2

Set of templates for the EU EFS Programs

- Master Clinical Trial Agreement Checklist

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Master Clinical Trial Agreement Checklist

This guideline-checklist is intended to assist the parties in drafting the Master Clinical Trial Agreement (MCTA) for an Early Feasibility Study (EFS).

While recognising the autonomy of the parties in drafting agreements, including those of an economic nature, these guidelines are intended to provide the contracting parties with specific information on the clauses that must be included in the contract in order to comply with the obligations laid down by regulations and good practice for EFS in particular.

The parties must comply with all rules laid down by sector regulations relating to the conduct of clinical investigations (CI), even if they are not expressly contained in the contract and its annexes.

The contract sections to which the parties must pay particular attention, bearing in mind the specific nature of CIs for EFS, are indicated below:

i) Detailed description of the CI for EFS and detailed description of the roles and obligations of both parties.

ii) Detailed indication of the system for protecting subjects recruited for the CI.

iii) Detailed indication of the authorisations to proceed with the clinical investigation CI and of the devices involved, with particular regard to the traceability system and the obligations of each of the parties.

iv) Detailed indication of the monitoring system and the adverse event reporting system.

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*Please return the completed form to*_____[Entity/Office or Name and Surname and his/her qualify] *by e-mail* [*insert e-mail address or other like address, register electronic mail, website upload etc.*]

Relevant regulatory references

a) Required per Regulation (EU) 2017/745 on medical device

b) Required per International Organization for Standardization (ISO) 14155

c) International Conference on Harmonisation's international guideline for Good Clinical Practice (ICH-GCP) guidance E6(R3)

d) Helsinki declaration

***Note: Some elements do not have a specific origin and therefore will not have a footnote but are suggested by legal staff**

Part 1: Contract details

Instructions: *Complete blank sections of Part 1 of this checklist. If any of the sections cannot be completed, please specify the reason.*

Study Title:	Indication of the CI to be conducted and the name of the medical device (in the contract header)
Study Code:	
Union-wide unique single identification number [Art. 70 MDR]:	
Study approval date:	
Authority that authorised the study [ART. 71 MDR Authority of the Member State where the study is conducted, regardless of whether the study is conducted in several States]:	
Sponsor:	Any individual, company, institution or organisation which takes responsibility for the initiation, for the management and setting up of the financing of the CI [a) art. 2 n. 49; b) par. 3.49]. Where the sponsor of a CI is not established in the Union, that sponsor shall ensure that a natural or legal person is established in the Union as its legal representative. Such legal representative shall be responsible for ensuring compliance with the sponsor's obligations pursuant to this Regulation and shall be the addressee for all communications with the sponsor provided for in this Regulation. Any communication with that legal representative shall be deemed to be a communication with the sponsor. Member States may choose not to apply the first subparagraph to CIs to be conducted solely on their territory, or on their territory and the territory of a third country, provided that they ensure that the sponsor establishes at least a contact person on their territory in respect of that CI who shall be the addressee for all communications with the sponsor provided for in this Regulation [a) art. 62 par. 2; b) Annex A.1.3; c) Chapter III, Annex 1, par. 3].

Principal Investigator(s)	An individual responsible for the conduct of a CI at a CI site [a) art. 2 n. 54; b) par. 3.39, Annex A.1.4; c) Chapter III, Annex 1, par. 2.1.1, 2.1.2]. The investigator shall be a person exercising a profession which is recognised in the Member State concerned as qualifying for the role of investigator on account of having the necessary scientific knowledge and experience in patient care. Other personnel involved in conducting a CI shall be suitably qualified, by education, training or experience in the relevant medical field and in clinical research methodology, to perform their tasks [a) art. 62 par. 6; b) par. 6.1].
Site: **[Name of the Health Care Facility, registered office, VAT number, Legal Representative and his or her position]:**	The facilities where the CI is to be conducted shall be suitable for the CI and shall be similar to the facilities where the device is intended to be used [a) art. 62 par. 7; b) par. 6.8; c) Chapter III, Annex 1, par. 2.1.2].

Part 2: Premises

Instructions: *Check the appropriate box for each element within the MCTA. For any "No" or "NA" answers, please type a comment into the statement box as to the reason it is not included (i.e., does not apply to type of study or site declines to include).*

2.1. Preliminary premises			
Y	**N**	**NA**	
□	□	□	Declaration of interest by the Sponsor to conduct the trial for EFS on the medical device indicated, subject of the CI (identified by Union-wide unique single identification number [Art. 70 MDR]) at the investigator's site, under the responsibility of the physician appointed as scientific director of the CI
□	□	□	Description of what this EFS entails
□	□	□	Indication of the purpose of the CI. Indicate that the device is currently being tested and has not yet been placed on the market [a) art. 62 par. 1].
□	□	□	Declaration that the facilities where the CI is to be conducted shall be suitable for the CI and shall be similar to the facilities where the device is intended to be used [a) art. 62 par. 7, b) par. 6.8].

□	□	□	Declaration that each phase of the CI will be conducted in accordance with recognised ethical principles [a) Annex XV, Chapter I, par. 1; b) par. 4, 5.1, Annex A.12; c) Chapter II, par. 1; d) art. 10].
□	□	□	Declaration that a brief description of the CI funding arrangements and a brief description of the agreement between the sponsor and the site were attached to the CI application [a) Annex XV, Chapter II, par. 3.1.4; b) par. 5.6.2; c) Chapter III, Annex 1, par. 3.5; d) art. 22].
□	□	□	Declaration that the investigator possesses the technical and scientific expertise required for the CI and that the facility is suitable for conducting the CI in compliance with current regulations. [b) par 6.1].
□	□	□	Statement that the CI has been designed to cause as little pain, discomfort, burden, fear and other foreseeable risks to the subject as possible, and that both the risk threshold and the degree of discomfort are expressly defined in the CI plan and are subject to continuous review; [a) art. 62, par. 4 (i); b) par 4, 7.1; c) Chapter II, par. 1.1, 1.3; d) art. 17]..
□	□	□	The Sponsor submitted an application to the National Competent Authority (NCA) for a CI of the device without the CE mark on [specify date], and on [specify date] the authority validated the application [a) art. 70; c) Chapter III, Annex 1, par. 3.8.1].

Part 3: Specific Section

Instructions: *Check the appropriate box for each element within the MCTA. For any "No" or "NA" answers, please type a comment into the statement box as to the reason it is not included (i.e., does not apply to type of study or site declines to include).*

3.1. Documents annexed the contract			
Y	**N**	**NA**	
□	□	□	Clinical investigation plan (CIP) [a) Annex XV par. 2.4 ; b) par. 6, 6.4, Annex A ; c) Appendix B].
□	□	□	Investigator's brochure (IB) [a) Annex XV Chapter II, par. 2 ; b) par. 6.5, Annex B ; c) Appendix A].
□	□	□	Monitoring plan [a) Annex XV Chapter II, par. 3.6.6 ; b) par. 6.7, Annex A.6.5 ; c) Chapter III, Annex 1, par. 3.11.4.3].
□	□	□	Annex relating to personal data protection [a) art. 62, par. 4; b) 7.7, 7.8; c) Chapter II, art. 1.6 – Chapter III, Annex 1 par. 3.16].
□	□	□	Case report forms (CRFs) [b) Annex C].
□	□	□	Ethics Committee (EC) responsibilities [b) Annex G].
□	□	□	Budget plan [c) Chapter III, Annex 1 par. 3.5].
□	□	□	Other documents.

3.2. Object of the contract **In any case, the contract must specifically mention the obligations of the Parties that guarantee the rules of clinical conduct** [a) Art. 72].			
Y	**N**	**NA**	
□	□	□	The NCA and EC have authorised the clinical use of this device in an EFS for a specific medical indication.
□	□	□	Declaration that all conditions for conducting the CI have been met [a) art. 62; b) par. 7.1].
□	□	□	Indication of how the CI will be conducted, specifying the respective duties and obligations of the parties [b) par. 7].
			Given the specific nature of the CI as an EFS, the parties undertake to provide the following essential records […] "*Many records are generated before and during the conduct of a clinical trial. The nature and extent of those records generated and maintained are dependent on the trial design, its conduct, application of risk proportionate approaches and the importance and relevance of that record to the trial*" [b) 7.1, 9.2; c) Appendix C, par. C.1.1.].
□	□	□	Description of device characteristics, function, mode of operation, innovative features and how it is different from currently available therapy [a) art. 62; b) par. 6.10, Annex A.2].
□	□	□	Statement that the parties undertake to conduct CI in such a way that the rights, safety, dignity and well-being of the subjects participating in a CI are protected and take precedence over any other interest [a) art. 62; b) par. 4, 5.5; c) Chapter III, Annex 1, par. 3.10; d) art. 9, 10].
□	□	□	The parties undertake to obtain scientifically valid, reliable and robust clinical data [a) art. 62; b) par. 4 (e); c) Chapter II, par. 4, 9].
□	□	□	Indication by the sponsor of its scientific representative (the sponsor may change the scientific representative for the part under its responsibility by giving written notification to the trial center)
□	□	□	Declaration of the site where the CI will be conducted that it possesses all the resources necessary to conduct the study [b) par. 6.8; c) Chapter III, Annex 1, par. 3.11.4.5.2].
□	□	□	Declaration that the investigator will undertake directly to the Sponsor to conduct the CI in accordance with the terms and conditions set out in the contract [b) par. 10; c) Chapter III, Annex 1, par. 3.6.3].
□	□	□	The sponsor and the investigator shall ensure that the CI is conducted in accordance with the approved CIP [a) art. 72 par. 1; c) Chapter III, Annex 1, par. 2.5.2; d) art. 22].

□	□	□	In order to verify that the rights, safety and well-being of subjects are protected, that the reported data are reliable and robust, and that the conduct of the CI follows the requirements of this Regulation, the sponsor shall ensure adequate monitoring of the conduct of a CI. The extent and nature of the monitoring shall be determined by the sponsor on the basis of an assessment that takes into consideration all characteristics of the CI including the following: (a) the objective and methodology of the CI; and (b) the degree of deviation of the intervention from normal clinical practice [a) art. 72 par. 2; b) 6.7, 9.2.4; c) Chapter III, Annex 1, par. 3.11.4].
□	□	□	The parties shall facilitate any inspection of the CI site(s) requested by the NCAs in order to verify that the CIs are being conducted in accordance with the requirements of the Regulation and the approved trial plan [a) art. 72 par. 5; b) par. 7.7, 9.2.4.5; c) Chapter III, Annex 1, par. 2.3.5].
□	□	□	The investigator must record and immediately notify the sponsor the following: (a) any adverse event of a type identified in the CIP as being critical to the evaluation of the results of that CI; (b) any serious adverse event; (c) any device deficiency that might have led to a serious adverse event if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate; (d) any new findings in relation to any event referred to in points (a) to (c) [a) art. 80; b) par. 7.4.2, 9.2.5, 10.8; c) Chapter III, Annex 1, par. 2.7.2].
□	□	□	Device traceability requirements [a) art. 25]. The sponsor shall establish a procedure for emergency situations which enables immediate identification and, where necessary, an immediate recall of the devices used in the investigation [a) art. 72 par. 6; b) par. 7.8.1, 9.2.4.5 (n); c) Chapter III, Annex 1, par. 2.12.10 (d)].
□	□	□	Obligations of the parties in the event of accidents or adverse events [b) par. 9.2.5; c) Chapter III, Annex 1, par. 2.7.2 (b), 3.13.2 (b), 10.8].
□	□	□	Declaration that all parties involved in the conduct of the clinical study share the responsibility for its ethical conduct in accordance with their respective roles in the clinical study [b) par. 5.5, 7.9, 9, 10, ; c) Chapter II, par. 10.2].
3.3. Investigator (assumed by the institution in the agreement if the investigator is not a contracting party)			
Y	**N**	**NA**	
□	□	□	Indication of the principal investigator, and their respective obligations [b) par. 10].

□	□	□	The principal investigator must ensure that all subjects, including any co-investigators who will perform any part of the CI under the supervision of the principal investigator, are eligible to conduct the CI in accordance with applicable regulations, are familiar with the protocol and good clinical practice standards, and meet the necessary regulatory and legal requirements, including those concerning compliance with current regulations on conflicts of interest [b) per 10.1; c) Chapter III, Annex 1, par. 2.3.2].
□	□	□	Investigators shall have access given by the sponsor to technical and clinical data regarding the device. Personnel involved in the conduct of a CI shall be adequately trained by the sponsor in the proper use of the investigational device, and as regards the CIP and good clinical practice. This training shall be verified and arranged where necessary by the sponsor and documented appropriately [a) Annex XV Chapter I, art. 2.7; b) par. 9.2.1; c) Chapter III, Annex 1, par. 2.3.2].
□	□	□	Investigators and co-investigators undertake not to make any changes to the CIP [a) Annex XV Chapter II, art. 3.10; b) par. 10.6].
□	□	□	Declaration that there are no conflicts of interest and obligation to notify the sponsor of any change that could give rise to a conflict of interest [b) par. 10.2].
3.4 Subject and recruitment method			
Y	**N**	**NA**	
□	□	□	Subjects involved in the investigation and recruitment methods [b) par. 5.6.2 (d), 7.5.2, 7.7, 7.10, Annex A 6.3, c) Chapter III, Annex 1, 2.2.1].
□	□	□	Declaration on compliance with informed consent policies, including based on the category of subject involved, and on privacy [a) art. 63, 64, 65,66; b) par. 5.7, 5.8; c) Chapter II, par. 1.2.7, 2; Chapter III, Annex 1, par. 2.8; d) 24-28].
3.5 Medical devices			
Y	**N**	**NA**	
□	□	□	Indication of medical devices necessary for conducting the CI [a) Annex XV, Chapter II, par. 1.9].
□	□	□	Indication of the type of device, with particular reference to the lack of CE marking, as this is an EFS [b) Annex A, A.2; c) Chapter III, Annex 1, par. 3.15].
□	□	□	Accessory materials provided by the sponsor or investigator, if any.
□	□	□	A list of the technical and functional features of the device and the related expected clinical outcomes shall be provided [a) Annex XV Chapter I, art. 2.5].
3.6. Loan for use			

Y	N	NA	
□	□	□	Indication of equipment provided to the investigator on loan for use and conditions of the loan [b) par. 7.9; c) Chapter II, par. 11].
□	□	□	Equipment disposal methods [c) Chapter II, par. 11.6, Chapter III, Annex 1, art. 3.11.4.5.3].
3.7. Financial agreements			
Y	**N**	**NA**	
□	□	□	Indication of the total budget, the detailed budget for all activities, and the payment method, in accordance with national law. [b) 9.2.2 (f); c) Chapter III, Annex 1, par. 3.2, 3.5].
□	□	□	Provision of payment arrangements in the event of discontinuation of the CI, including, where appropriate, by differentiating the reasons for discontinuation [b) 9.2.2 (f); c) Chapter III, Annex 1, par. 3.2, 3.5].
3.8. Fees/Reimbursements for Participating subjects			
Y	**N**	**NA**	
□	□	□	Indication of the fee/refund for participants and payment methods, also in accordance with national law [b) par. 5.3, 5.6.2 (g); c) Chapter III, Annex 1, par. 3.14].
□	□	□	Obligation of the parties not to subject the participants to any financial conditioning [a) art. 63; b) Annex G G.2.; c) Chapter II, par. 1.2.8].
3.9. Duration, withdrawal and termination			
Y	**N**	**NA**	
□	□	□	Contract duration and rules governing possible unforeseen circumstances affecting the duration of the investigation, the need for withdrawal, suspension, discontinuation and termination for justified reasons [b) par. 8; c) Chapter III, Annex 1, par. 2.2.2, 2.6., 3.17.1].
□	□	□	If the sponsor intends to make changes to a CI that are likely to affect the safety, health or rights of the subjects participating in the investigation or the robustness or reliability of the clinical data generated by the investigation, it shall proceed in accordance with Article 75 of the MDR and notify the investigator [a) art. 75; b) par. 6.5, Annex D., D.6.1.; c) Chapter III, Annex 1, par. 3.6.2].
□	□	□	The end of a CI shall be deemed to coincide with the last visit of the last subject unless another point in time for such end is set out in the CIP [a) art. 77; b) par. 8.1; c) Chapter III, Annex 1, par. 2.9].
3.10. Insurance coverage and assistance to the subject			
Y	**N**	**NA**	

□	□	□	Detailed indication of the type of insurance coverage for the subjects involved, including the policy and the insurance company [a) art. 69; b) par. 5.6.2. (j), 9.2.2 (e); c) Chapter III, Annex 1, par. 3.14].
□	□	□	Detailed indication of the type of medical assistance to be provided to the subject involved and indication of the party responsible for providing it [a) Annex XV, Chapter II, par. 3.16; b) 10.7; c) Chapter I, par. 1.5, Chapter III, Annex 1, par. 2.7.
□	□	□	Guarantees included in the follow-up [a) Annex XV, Chapter II, art. 3.16; b) par. 10.7; c) Chapter III, Annex 1, par. 2.8.10].

Part 4: Results of the Clinical Investigation

Instructions: *Check the appropriate box for each element within the MCTA only for the specific frail participant. For any "No" or "NA" answers, please type a comment into the statement box as to the reason it is not included (i.e., does not apply to type of study or site declines to include).*

4.1. Confidentiality and dissemination of results – Data protection			
Y	**N**	**NA**	
			All parties involved shall respect the confidentiality of information and data obtained in carrying out their tasks. This obligation applies, in particular, to: i) personal data of study subjects, investigators and site staff, which shall be processed in accordance with Regulation (EU) 2016/679 (General Data Protection Regulation, GDPR) and applicable data protection requirements; ii) commercially confidential information and trade secrets of any natural or legal
□	□	□	Indication of how information obtained as a result of the CI will be managed and how the data will be used **[b) par. 7.8, c) Chapter III, Annex 1, par. 3.16, 4].**
□	□	□	Ownership and dissemination of data obtained as a result of the CI, including for the scientific dissemination of results **[b) par. 7.8; Annex A. A.17; c) Chapter III, Annex 1, par. 2.8.10 (p, v), Appendix B, B.16; d) art. 36].**
□	□	□	Regulations on the protection of personal data relating to CIs **[b) par. 7.8; c) Chapter II, par. 1.6; par. 3.16.1].**
□	□	□	Regulations on the protection of personal data concerning the Parties to the contract and all parties involved in the trial other than the subjects **[b) par. 5.8.4 (e.5, I.2), 5.8.5 (f). 6.7 (j); c) Chapter III, Annex 1, par. 2.12.7, par. 3.16.1 (t); d) 24].**
□	□	□	All CI information shall be recorded, processed, handled, and stored by the sponsor or investigator, as applicable, in such a way that it can be accurately reported, interpreted and verified while the confidentiality of records and the personal data of the subjects remain protected in accordance with the applicable law on personal data protection **and data retention policies [a) art. 72 par. 3; b) par. 7.8.2, 7.8.3; c) Chapter II, par. 9.4, 9.5; d) art. 35].**
□	□	□	Appropriate technical and organisational measures shall be implemented to protect information and personal data processed against unauthorised or unlawful access, disclosure, dissemination, alteration, or destruction or accidental loss, in particular where the processing involves transmission over a network **[a) art. 72 par. 4; b) par. 7.8.2, 7.8.3; c) Chapter III, Annex 1, par. 2.12;].**

Part 5: Other Clauses of the Contract

Instructions: *Check the appropriate box for each element within the MCTA only for the specific frail participant. For any "No" or "NA" answers, please type a comment into the statement box as to the reason it is not included (i.e., does not apply to type of study or site declines to include).*

5.1. Intellectual and industrial property			
Y	**N**	**NA**	
□	□	□	Rules governing intellectual and industrial property rights relating to scientific discoveries and merchandising rights.
5.2. Modifications			
Y	**N**	**NA**	
□	□	□	Rules governing amendments to the contract and annexes, requirement that all amendments be made in writing.
□	□	□	Modifications relating to the CI and the manner in which it is conducted must be authorized [b) par. 7.5.1, 10.6 (e); c) Chapter II, par. 4.3].
5.3. Anti-corruption policy			
Y	**N**	**NA**	
□	□	□	Anti-corruption statements (according to national law).
5.4. Transfer of rights, assignment of contract			
Y	**N**	**NA**	
□	□	□	Rules governing the transfer of rights or assignment of the contract (according to national law).
5.5. Tax Charges			
Y	**N**	**NA**	
□	□	□	If required by national legislation.
5.6. Applicable law and jurisdiction			
Y	**N**	**NA**	
□	□	□	Indication of the applicable law, especially when the contract is signed in different countries by the same sponsor, and indication of the place of jurisdiction.
5.7. Language			
Y	**N**	**NA**	
□	□	□	Indication of the language of the contract, but above all, if it is drawn up in two languages, indication – in the event of discrepancies between the versions – of which language will prevail.

Form completed by	
Professional qualification	
Optional comments	
Editing date	
Signature	

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