"Please do take into account that this is a translation of the original French version validated in the Quality Management System (QMS) of Cliniques universitaires Saint-Luc through the SharePoint PaCo GED. Therefore in case of doubt, differences, inconsistency or discrepancy in this English version, the French version shall prevail"

By default, any clinical study project is covered by the following regulations:

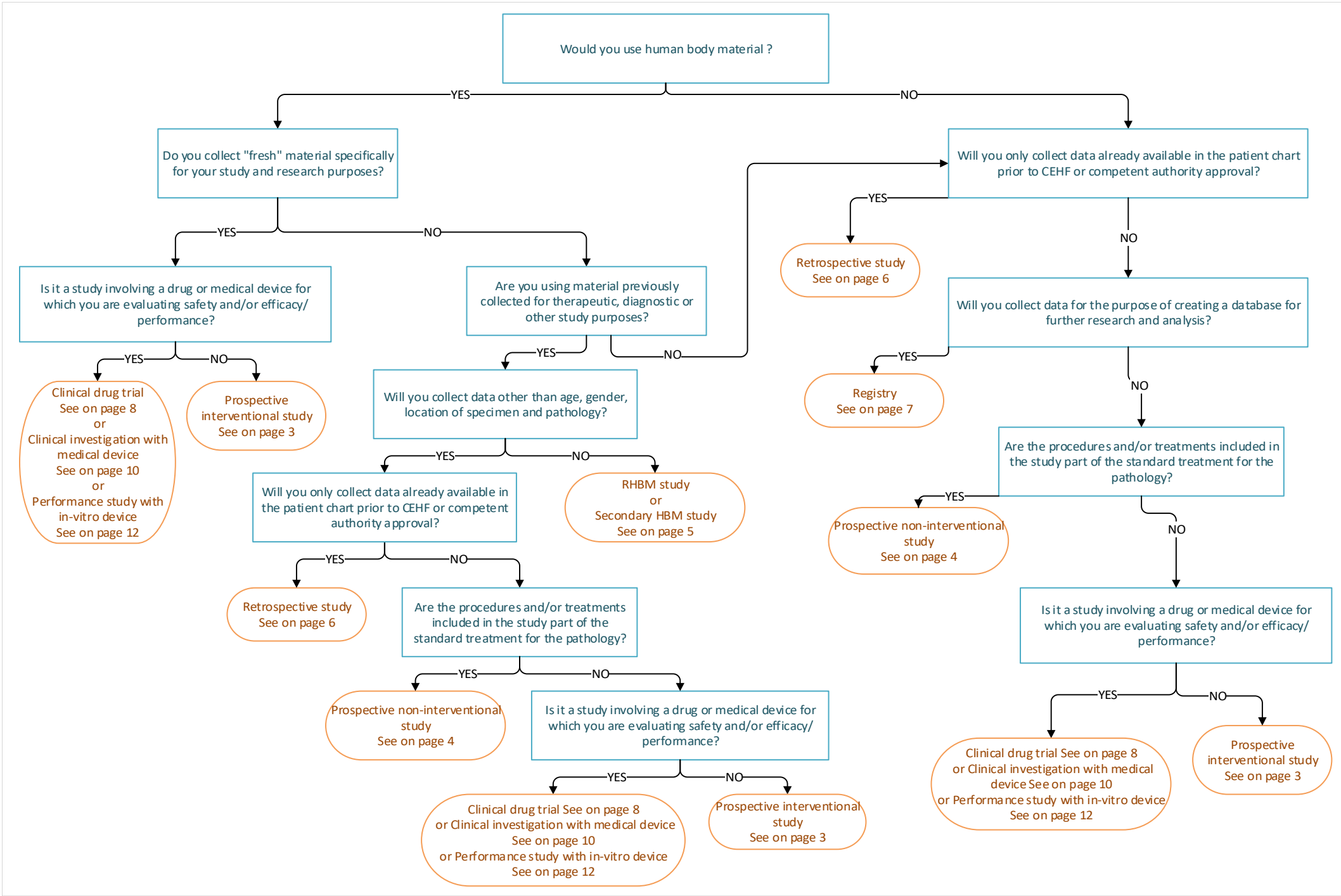
- European Regulation 2016/679 of 27 April 2016 on the protection of individuals with regard to the processing of personal data and on the free movement of such data
- Belgian Law of July 30, 2018 on the protection of individuals with regard to the processing of personal data
- Belgian law of 22 August 2002 on the rights of the patient
- Declaration of Helsinki
- ICH Guidelines for Good Clinical Practice E6(R2)

The regulatory assessment flowchart on page 2 allows you to identify specifically for your research project

- the corresponding type of study
- the applicable regulation
- the submission procedure to follow
- the reference document(s) of the AAHRPP quality system

Follow the flowchart according to the characteristics of your project and refer to the page indicated to consult the various useful information.

The referenced documents are accessible via the Paco - Clinical Research or the research pages of CuSL web site https://www.saintluc.be/en/commercial-studies or https://www.saintluc.be/en/recherche-clinique-etudes-academiques


Would you use human body material ?
YES
NO
Do you collect "fresh" material specifically for your study and research purposes?
YES
NO
Is it a study involving a drug or medical device for which you are evaluating safety and/or efficacy/ performance?
YES
NO
Clinical drug trial
See on page 8
or
Clinical investigation with medical device
See on page 10
or
Performance study with in-vitro device
See on page 12
Prospective interventional study
See on page 3
Are you using material previously collected for therapeutic, diagnostic or other study purposes?
YES
NO
Will you collect data other than age, gender, location of specimen and pathology?
YES
NO
RHBM study
or
Secondary HBM study
See on page 5
Will you only collect data already available in the patient chart prior to CEHF or competent authority approval?
YES
NO
Retrospective study
See on page 6
Are the procedures and/or treatments included in the study part of the standard treatment for the pathology?
YES
NO
Prospective non-interventional study
See on page 4
Is it a study involving a drug or medical device for which you are evaluating safety and/or efficacy/ performance?
YES
NO
Clinical drug trial See on page 8
or Clinical investigation with medical device
See on page 10
or Performance study with in-vitro device
See on page 12
Prospective interventional study
See on page 3
Will you only collect data already available in the patient chart prior to CEHF or competent authority approval?
YES
NO
Retrospective study
See on page 6
Will you collect data for the purpose of creating a database for further research and analysis?
YES
NO
Registry
See on page 7
Are the procedures and/or treatments included in the study part of the standard treatment for the pathology?
YES
NO
Prospective non-interventional study
See on page 4
Is it a study involving a drug or medical device for which you are evaluating safety and/or efficacy/ performance?
YES
NO
Clinical drug trial See on page 8
or Clinical investigation with medical device See on page 10
or Performance study with in-vitro device
See on page 12
Prospective interventional study
See on page 3

PROSPECTIVE INTERVENTIONAL STUDY

❖ Definition

Any study in which the risk to the participant is greater than the minimal risk due to routine treatment (known as "standard of care" or "SOC").

A study is interventional if :

- Intentional contact with the patient takes place as part of organized research, even if the data collected are only processed/used in a subsequent study and/or publication (e.g. a questionnaire to be completed at home, telephone follow-up).
- The patient is asked to make an additional effort (e.g. additional diagnostic or monitoring procedure, additional blood test or additional blood tube taken during a routine analysis).

❖ Applicable regulations

Belgian law of May 7, 2004 on human experimentation

Belgian law of December 19, 2008 on the collection and use of human body material intended for human medical applications or for scientific research purposes

❖ Submission procedure

Submission to the ethics committee(s) of the site(s) involved in the study

For Saint-Luc / UCLouvain : CEHF - Document 1

❖ Useful documents

213 - AAHRPP-SOP-066 Commercial Central Desk - Initial Submission (Procedure)

053 - AAHRPP-DSQ-102 Commercial study – Submission documents (Checklist)

211 - AAHRPP-SOP-064 Academic Central Desk - Initial Submission (Procedure)

058 - AAHRPP-DSQ-111 Academic study – Submission documents (Checklist)

112 - BIOBANQUE-SOP-016 Use of human body material (Procedure)

PROSPECTIVE NON-INTERVENTIONAL STUDY (OBSERVATIONAL)

❖ **Definition**

Any study that does not require any additional act beyond routine treatment or follow-up procedures, in this case observing one or more interventions or responses to standard treatments.

Studies involving only questionnaires for study participants, completed during a consultation or routine follow-up, are considered non-interventional studies.

❖ **Applicable regulations**

Belgian law of May 7, 2004 on human experimentation

Belgian law of December 19, 2008 on the collection and use of human body material intended for human medical applications or for scientific research purposes

❖ **Submission procedure**

Submission to the ethics committee(s) of the site(s) involved in the study

For Saint-Luc / UCLouvain : CEHF - Document 1

❖ **Useful documents**

213 - AAHRPP-SOP-066 Commercial Central Desk - Initial Submission (Procedure)

053 - AAHRPP-DSQ-102 Commercial study – Submission documents (Checklist)

211 - AAHRPP-SOP-064 Academic Central Desk - Initial Submission (Procedure)

058 - AAHRPP-DSQ-111 Academic study – Submission documents (Checklist)

112 - BIOBANQUE-SOP-016 Use of human body material (Procedure)

RESIDUAL HUMAN BODY MATERIAL STUDY (RHBM)

OR

SECONDARY HUMAN BODY MATERIAL (HBM)

❖ **Definition**

Any study involving the analysis of human body material (blood, organs, tissues, cells, sweat, tears, etc.). Human body material can either be collected specifically for research purposes, or surplus material collected for diagnostic purposes is analyzed as part of the study. The latter is referred to as residual human body material.

Residual human body material intended for research purposes is registered in the CUSL biobank. Any transfer of this material to an external entity requires the establishment of a Material Transfer Agreement.

❖ **Applicable regulations**

Belgian law of December 19, 2008 on the collection and use of human body material intended for human medical applications or for scientific research purposes

❖ **Submission procedure**

Submission to the ethics committee(s) of the site(s) involved in the study

For Saint-Luc / UCLouvain : CEHF - Simplified submission form

❖ **Useful documents**

213 - AAHRPP-SOP-066 Commercial Central Desk - Initial Submission (Procedure)

053 - AAHRPP-DSQ-102 Commercial study – Submission documents (Checklist)

211 - AAHRPP-SOP-064 Academic Central Desk - Initial Submission (Procedure)

058 - AAHRPP-DSQ-111 Academic study – Submission documents (Checklist)

112 - BIOBANQUE-SOP-016 Use of human body material (Procedure)

RETROSPECTIVE STUDY

❖ **Definition**

Any study for which the data analyzed are already available at the time of approval by the ethics committee. These are mainly analyses of patient medical records. In this case, no other data are acquired prospectively. This type of study does not require consent (the "opting-out" principle). The patient must be informed of the use of his or her medical data in a retrospective study, and the absence of a refusal in the medical file must be verified before any data is used.

❖ **Applicable regulations**

Retrospective studies are excluded from the Belgian law of 07 May 2004.

European Regulation 2016/679 of 27 April 2016 on the protection of individuals with regard to the processing of personal data and on the free movement of such data

Belgian Law of July 30, 2018 on the protection of individuals with regard to the processing of personal data

Belgian law of 19 December 2008 on the collection and use of human body material intended for human medical applications or for scientific research purposes

❖ **Submission procedure**

Submission to the ethics committee(s) of the site(s) involved in the study

For Saint-Luc / UCLouvain : CEHF - Simplified submission form

❖ **Useful documents**

213 - AAHRPP-SOP-066 Commercial Central Desk - Initial Submission (Procedure)

053 - AAHRPP-DSQ-102 Commercial study – Submission documents (Checklist)

211 - AAHRPP-SOP-064 Academic Central Desk - Initial Submission (Procedure)

058 - AAHRPP-DSQ-111 Academic study – Submission documents (Checklist)

112 - BIOBANQUE-SOP-016 Use of human body material (Procedure)

REGISTRY

❖ **Definition**

A systematic collection of [health] data of an epidemiological and/or scientific nature, in the form of an organized system of data collected on the basis of defined criteria, relating to the field concerned, allowing a population of persons to be characterized in a longitudinal perspective.

The purpose of the registry is preparatory processing for subsequent research and analysis in the epidemiological and/or scientific field. Data from the registry may be used by duly authorized persons to facilitate recruitment for studies or to carry out retrospective studies with the following objectives: to understand or better treat the disease, to participate in the evolution of the quality of care, treatments, the cost of care for the disease, etc... These studies must be submitted to the Ethics Committee

The creation of registers is in line with the healthdata approach advocated by the European Union, which aims to optimize the use of health data for the benefit of patients, notably by :

- providing a better understanding of diseases (mapping the mechanisms that lead to illness)
- enabling the evaluation of disease prevention and screening tools,
- optimizing and accelerating diagnosis (detecting early signs of health problems, comparing approaches, issuing guidelines),
- by enabling treatments to be evaluated (comparing the efficacy of therapies, particularly drug therapies)
- ensuring greater safety for patients (identification and monitoring of adverse effects of drugs, vaccines or medical interventions).

❖ **Applicable regulations**

Registries are excluded from the Belgian law of 07 May 2004.

European Regulation 2016/679 of 27 April 2016 on the protection of individuals with regard to the processing of personal data and on the free movement of such data

Belgian Law of July 30, 2018 on the protection of individuals with regard to the processing of personal data

❖ **Submission procedure**

Submission to the ethics committee(s) of the site(s) involved in the study

For Saint-Luc / UCLouvain : CEHF - Simplified submission form

❖ **Useful documents**

211 - AAHRPP-SOP-064 Academic Central Desk - Initial Submission (Procedure)

058 - AAHRPP-DSQ-111 Academic study – Submission documents (Checklist)

CLINICAL DRUG TRIAL

❖ **Determine that it is a clinical trial :** The table below will help you identify if your project is a clinical trial.

A	B	C	D	E
Is a medicinal product being investigated ?	**What effects of the medicinal product are you looking for?**	**Why are you looking for those effects?**	**How are you looking for those effects?**	**Is your clinical trial a low-intervention clinical trial?**
If you answer NO to the question in column A below, the investigation does not fall within the scope of Regulation EU No 536/2014. If you answer YES to the question below go to column B	If you answer NO to all the questions in column B below, the investigation does not fall within the scope of Regulation EU No 536/2014. If you answer YES to any of the questions below go to column C.	If you answer NO to all the questions in column C below, the investigation does not fall within the scope of Regulation EU No 536/2014. If you answer YES to any of the questions below go to column D - the investigation is a clinical study as described in article 2(2)(1) of Regulation EU No 536/2014.	If you answer NO to all the questions in column D below, the clinical study is a non-interventional study that does not fall within the scope of Regulation EU No 536/2014. If you answer YES to any of the questions below go to column E – the study is a clinical trial according to Regulation EU No 536/2014.	If your answer NO to any of the questions below in column E, the trial is a clinical trial within the scope of Regulation EU No 536/2014 but is NOT a low-intervention clinical trial as defined in Regulation EU No 536/2014. If you answer YES to ALL of the questions below, the trial is a low intervention clinical trial. A specific set of risk adaptations can be applied.
A. Is the investigated substance or product either presented as a medicinal product or does it function as such, in accordance with point 2 of article 1 of Directive 2001/83/EC ? The following substances are not considered to be medicines : - Human whole blood, blood cells, or plasma (this does not include derivatives of human whole blood, human blood cells and human plasma that involve a manufacturing process) - Food products, including dietary supplements - Cosmetic products - Medical device	B. Is the aim of the investigation on the medicinal product : B.1. To discover or verify/compare its clinical effects? B.2. To discover or verify/compare its pharmacological effects, e.g. pharmacodynamics? B.3. To identify or verify/compare its adverse reactions? B.4. To study or verify/compare its pharmacokinetics, e.g., absorption, distribution, metabolism or excretion?	C. Is the objective of the investigation on a medicinal product : C.1. To ascertain or verify/compare the efficacy of the medicine? C.2. To ascertain or verify/compare the safety of the medicine?	D.1. Is the assignment of any patient involved in the study to a particular therapeutic strategy decided in advance by a clinical trial protocol, and does the assignment not fall within normal clinical practice in the Member State(s) Concerned ? D.2. Is the decision to prescribe a particular medicinal product clearly taken together with the decision to include the patient in the study? D.3. Are diagnostic or monitoring procedures applied to the patients included in the study, other than those which are applied in normal clinical practice in any of the Member State(s) concerned?	E.1. Is this a study of one or more medicinal products, which all have a marketing authorization in the Member State(s) concerned? E.2. Does the protocol of the clinical trial specify that (i) the investigational medicinal products are used in accordance with the terms of the marketing authorization; or (ii) the use of the investigational medicinal products is evidence-based and supported by published scientific evidence on the safety and efficacy of those investigational medicinal products in any of the Member States concerned; E.3.Do the additional diagnostic or monitoring procedures not pose more than minimal additional risk or burden to the safety of the subjects compared to normal clinical practice in any Member State concerned? (“Yes” to this answer means that the additional procedures do not pose more than minimal risk or burden; “No” means that the additional procedures do pose more than minimal risk or burden)

❖ **Definition**

Any prospective study designed:

a) demonstrate or verify the clinical, pharmacological or other pharmacodynamic effects of one or more drugs;
b) identify any adverse effects of one or more drugs; or
c) to study the absorption, distribution, metabolism and excretion of one or more drugs;

with the aim of ascertaining the safety and/or efficacy of these medicinal products;

And meeting one of the following conditions:

a) the participant's assignment to a particular therapeutic strategy is predetermined and not part of standard clinical practice;
b) the decision to prescribe investigational medicinal products is taken at the same time as the decision to enrol the participant in the clinical trial; or
c) in addition to standard clinical practice, diagnostic or monitoring procedures are applied to participants.

❖ **Applicable regulations**

European Regulation 536/2014 of 16 April 2014 on clinical trials on medicinal products for human use, also known as CTR for Clinical Trial Regulation

Belgian Law of 07 May 2017 on clinical trials on medicinal products for human use.

Belgian law of 19 December 2008 on the collection and use of human body material intended for human medical applications or for scientific research purposes

❖ **Submission procedure**

Submission to the FAMHP and the competent authorities of the other participating countries via the CTIS portal. No joint submission to the ethics committee(s) of the centers involved in the trial.

❖ **Useful documents**

112 - BIOBANQUE-SOP-016 Use of human body material (Procedure)

External sponsor

213 - AAHRPP-SOP-066 Commercial Central Desk - Initial Submission (Procedure)

053 - AAHRPP-DSQ-102 Commercial study – Submission documents (Checklist)

211 - AAHRPP-SOP-064 Academic Central Desk - Initial Submission (Procedure)

058 - AAHRPP-DSQ-111 Academic study – Submission documents (Checklist)

CuSL Sponsor

038 - AAHRPP-SOP-007 Clinical drug Trial - Initial Submission CTR (Procedure)

243 - AAHRPP-DSQ-009 Clinical drug trial – Submission documents for CuSL sponsor (Checklist)

CLINICAL INVESTIGATION WITH A MEDICAL DEVICE

❖ **Definition**

Any prospective study designed to evaluate the safety or performance of a medical device.

❖ **Determine if the study is a clinical investigation with a medical device**

The table below will help you identify if your project is a clinical investigation.

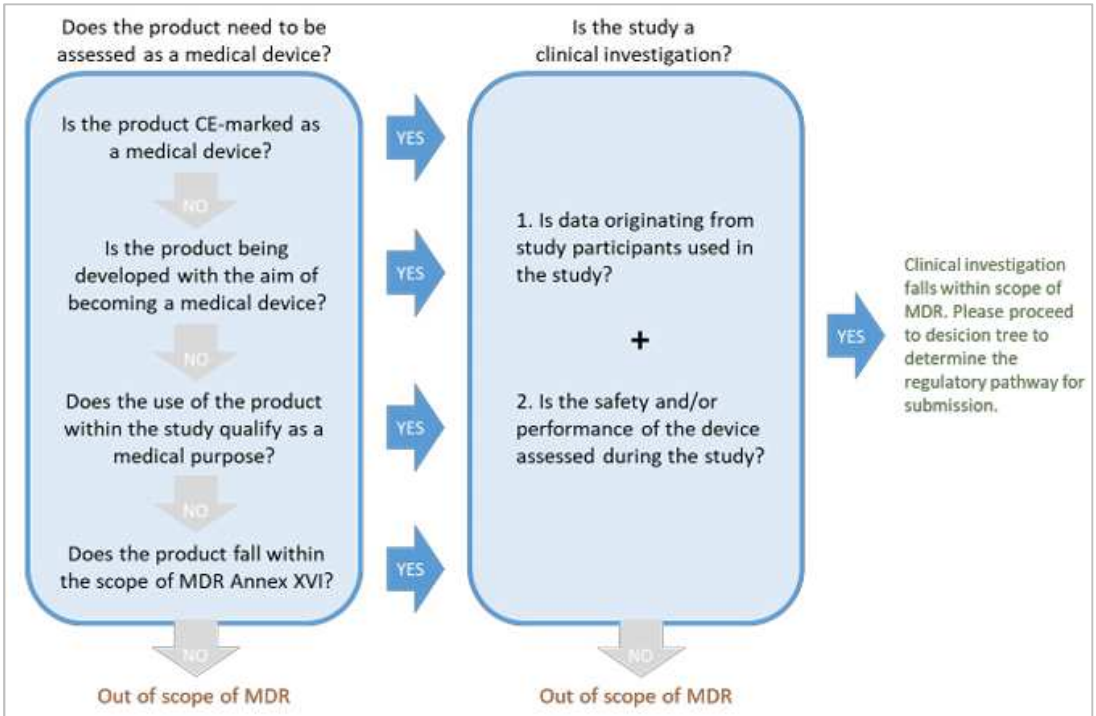


Figure 1. Does the study fall within scope of MDR?

❖ **Applicable regulations**

European Regulation 2017/745 of 5 April 2017 on medical devices, also known as MDR for Medical Device Regulation

Belgian law of 22 December 2020 on medical devices

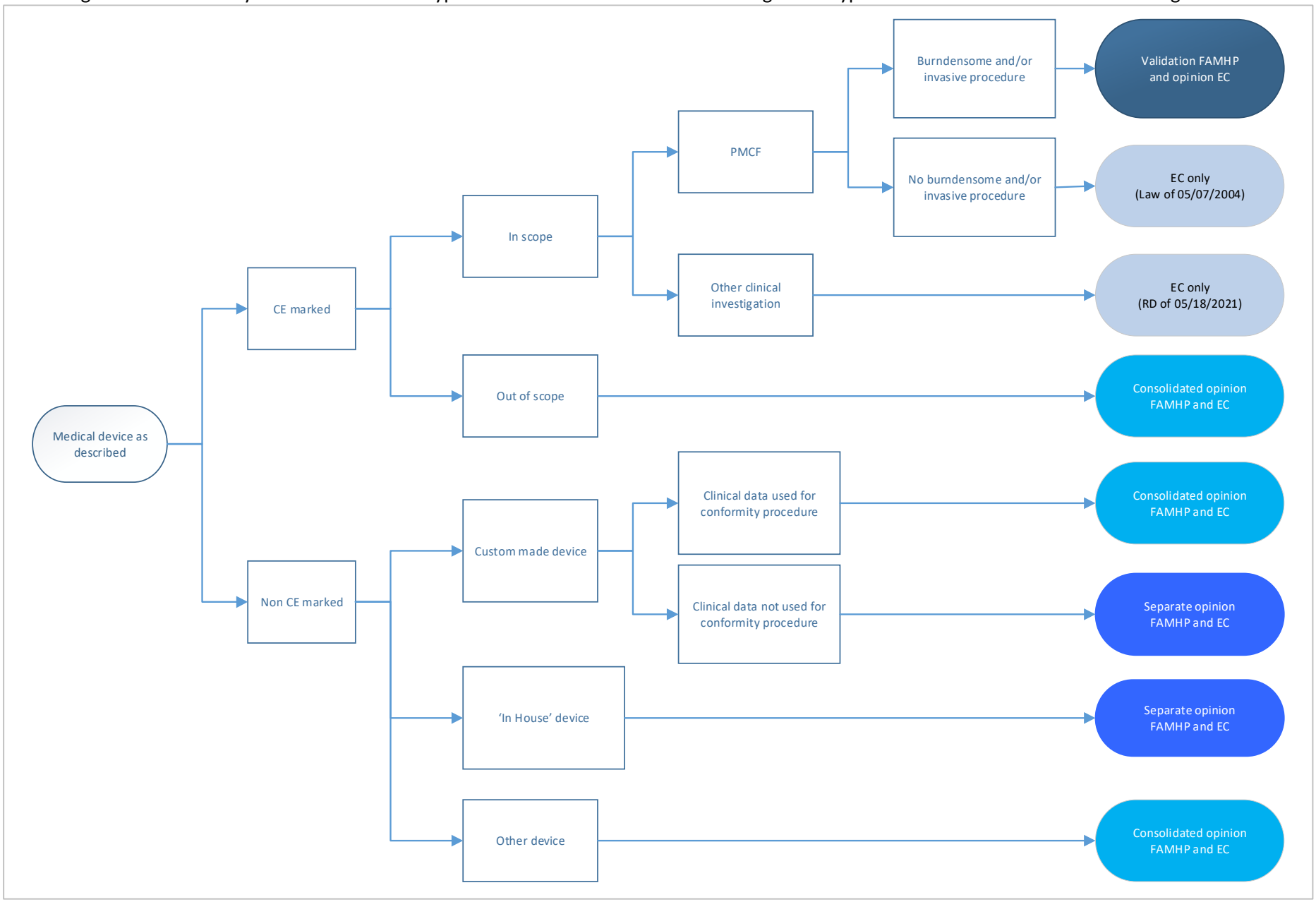
Royal Decree of 18 May 2021 on clinical investigations of medical devices

The good clinical practices of the international standard ISO 14155:2020 (07-2020)

Belgian law of 19 December 2008 on the collection and use of human body material intended for human medical applications or for scientific research purposes

❖ **Submission procedure**

The diagram below allows you to determine the type of submission to be made according to the type of device used in the clinical investigation



❖ **Useful documents**

112 - BIOBANQUE-SOP-016 Use of human body material (Procedure)

External sponsor

213 - AAHRPP-SOP-066 Commercial Central Desk - Initial Submission (Procedure)

053 - AAHRPP-DSQ-102 Commercial study – Submission documents (Checklist)

211 - AAHRPP-SOP-064 Academic Central Desk - Initial Submission (Procedure)

058 - AAHRPP-DSQ-111 Academic study – Submission documents (Checklist)

CuSL Sponsor

039 - AAHRPP-SOP-008 Medical Device - Initial Submission MDR (Procedure)

217 - AAHRPP-DSQ-008 Medical device – Submission documents for CuSL sponsor (Checklist)

PERFORMANCE STUDY WITH AN IN VITRO DIAGNOSTIC DEVICE

❖ **Definition**

Any prospective study designed to establish or confirm the analytical (ability to correctly detect or measure a given analyte) or clinical (ability to produce results correlated with a given clinical condition or physiological or pathological process or state, depending on the target population and intended user of the device) performance of a device.

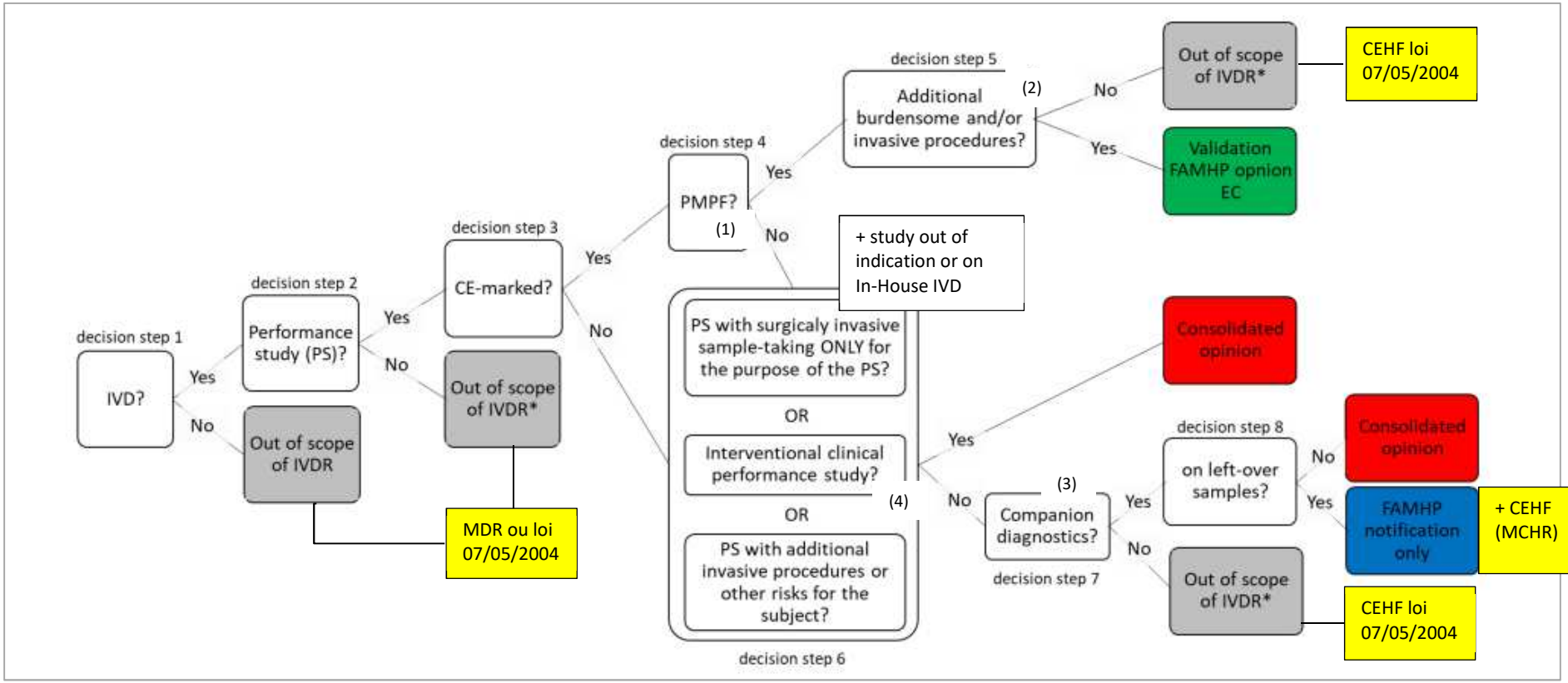
❖ **Applicable legislation**

European Regulation (EU) 2017/746 of April 5, 2017 on in vitro diagnostic medical devices, also known as IVDR for In-Vitro Device Regulation

Belgian law of June 15, 2022 on in vitro diagnostic medical devices

Belgian law of December 19, 2008 on the procurement and use of human body material intended for human medical applications or scientific research purposes

❖ **<u>Submission procedure</u>:** The diagram below shows the type of submission to be carried out, depending on the type of device used in the performance study.



Source : Guideline on the Submission Processes for Performance Studies according to the IVDR in Belgium – version 4.0, 30/03/2023

(1) PMPF: Post-marked performance follow-up: a post-marketing performance study conducted to further evaluate a CE-marked IVD in the context of its intended purpose, in order to proactively collect clinical data that could confirm safety and/or performance.

(2) Compulsory and/or invasive procedure: a procedure which is not foreseen by the manufacturer in the instructions for use of the diagnostic device, or which is not foreseen in standard clinical practice. See non-exhaustive list in Appendix 1 at the end of this document.

(3) Companion diagnostic: any device essential for the safe and effective use of a given drug, designed to:

- identify, before and/or during treatment, patients most likely to benefit from the drug in question; or
- identify, before and/or during treatment, patients likely to present an increased risk of serious adverse reactions in response to treatment with the drug in question.

(4) An interventional clinical performance study is a clinical performance study whose results may influence patient management decisions and/or may be used to guide treatment.

❖ **Useful documents**

112 - BIOBANQUE-SOP-016 Use of human body material (Procedure)

External sponsor

213 - AAHRPP-SOP-066 Commercial Central Desk - Initial Submission (Procedure)

053 - AAHRPP-DSQ-102 Commercial study – Submission documents (Checklist)

211 - AAHRPP-SOP-064 Academic Central Desk - Initial Submission (Procedure)

058 - AAHRPP-DSQ-111 Academic study – Submission documents (Checklist)

CuSL Sponsor

088 - AAHRPP-SOP-003 In vitro diagnostic Device – Initial Submission IVDR (Procedure)

229 - AAHRPP-DSQ-072 In vitro diagnostic Device – Submission documents for CuSL sponsor (Checklist)