Decision tree to establish a whether a study is a regulated clinical trial

This algorithm and its endnotes[1] will help you answer the question on whether a given investigation on humans is a clinical trial governed by the Regulation EU No 536/2014. Please start in column A and follow the instructions. Additional information is provided in the endnotes of the table. If you have doubts about the answer to any of the questions contact the national contact point(s) of the Member State(s) Concerned.

A	B	C	D	E
Is a medicinal product being investigated? (1) If you answer NO to I 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.**	**What effects of the medicinal product are you looking for?** 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**	**Why are you looking for those effects?** 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.	**How are you looking for those effects?** 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	**Is your clinical trial a low-intervention clinical trial?** 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? (2)	**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?(3) (4) **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, (5) and does the assignment not fall within normal clinical practice in the Member State(s) Concerned? (6) **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? (6)	**E.1.** Is this a study of one or more medicinal products, which all have a marketing authorisation 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 authorisation; 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 (6) in Regulation (EU) No 536/2014 any Member State concerned? ("YES" to this answer means that the additional procedures do not pose more than minimal risk or burden;(7) "NO" means that the additional procedures do pose more than minimal risk or burden

[1] Regulation (EU) No 536/2014 Questions & Answers July 2024 Version 6.9 (Page 130)

Endnotes

(1) Please refer to The rules governing medicinal products in the European Union VOLUME 10 - Guidance documents applying to clinical trials CLINICAL TRIALS REGULATION (EU) NO 536/2014 Q&A "Is the definition of 'medicinal product' relevant for the scope of the Clinical Trials Regulation?" and Q&A "Can a study be considered as clinical trial within the scope of Regulation (EU) No 536/2014 if it starts after administration/exposure of the investigational medicinal product has finished?

(2) 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 (Regulation on cosmetic products EU no 1223/2009, article 2.1.a.)
- Medical device (Medical Device Regulation EU no 2017/745, article 1.2 and 2.1)

The qualification of borderline products is a national competence. When there is an uncertainty on the status of a given product, this needs to be clarified with the national competent authorities.

(3) Efficacy is the concept of demonstrating scientifically whether and to what extent a medicine is capable of diagnosing, preventing or treating a disease and derives from EU pharmaceutical legislation.

(4)) This includes studies on "drug utilisation" of medicinal products used in normal clinical practice and trials on "palatability" intended to assess the suitability of a formulation for a particular population.

(5) Assignment of patients to a treatment group by randomisation planned by a clinical trial protocol cannot be considered as current practice

(6) Please refer to 2017_04_25_risk_proportionate_approaches_in_ct_0.pdf (europa.eu) Q&A "What is not considered as "normal clinical practice?" and the guidance for Risk proportionate approaches in clinical trials:

(7) In case of doubt whether an intervention poses only minimal burden or risk to participants, please contact the concerned national competent authorities