Table 2. Decision Algorithm to Answer the Question: Is this a Clinical Trial with Drugs?17

Translation of the table included in Chapter 5 of Volume 10 of EUDRALEX entitled “Questions and Answers” of April 2006. Available at URL: http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/homev10.htm The following algorithm and its clarifying notes help answer this question. Start in COLUMN A and follow the instructions. Please read the clarifying notes in the following sheet.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| A | B | C | D | E |
| Clinical Trial With Drugs | Observational Study |
| Is it a drug? | Is it not a drug? | What effect do we wish to achieve with the drug? | Why are these effects sought? |  |
| If the answer to all questions in column A is **NO** then the study performed is not a clinical trial with drugs.If the answer to any of the following questions is **YES** then we must continue to column B.**A.1** Is it a substance **(2)** or combination of substances that is presented as having properties for treating or preventing diseases in humans?**A.2** Does the substance act as a drug? e.g., can it be administered to humans to restore, correct or modify physiological functions by means of a pharmaceutical, immunological or metabolic action or to perform a medical diagnosis or to be administered for some other medical purpose?**A.3** Is it an active ingredient in a pharmaceutical form? | If the answer to the question in column B is **YES** then the study is not a clinical trial with drugs.If the answer to this question is **NO**, we must continue to column C.**B.1** Are any of the following substances to be administered alone?• Completehuman blood **(3)**• Human blood cells• Human plasma• Tissue or cells, except for somatic cell therapy drugs **(4)**• A food product **(5)** (including dietary supplements) that are not presented as a medication• A cosmetic product **(6)**• A medical product. | If the answer to all questions in column C is **NO** then the study is not a clinical trial within the scope of Directive 2001/20/CE (RD 223/2004).If the answer to any of the following questions is **YES** then we must continue to column D.**C.1** To discover or verify/compare its clinical effect?**C.1** To discover or verify/compare its pharmacological effect, e.g., pharmacodynamics?**C.3** To identify or verify/compare its adverse reactions?**C.4** To study or verify/compare its absorption, distribution, metabolism or excretion? | If the answer to all of the questions in column D is **NO** then the study is not a clinical trial within the scope of Directive 2001/20/CE (RD 223/2004). If the answer to any of the following questions is **YES** then we must continue to column E.**D.1** To determine or verify/compare the efficacy (7) of the drug?**D.2** To determine or verify/compare the safety of the drug? | If the answer to all of the following questions is **YES** then the study is observational, which is outside the scope of Directive 2001/20/CE (RD223/2004).If the answers to the questions in columns A, B, C and D lead us to column E and the answer to any of the following questions is **NO** then the study is a clinical trial within the scope of Directive 2001/20/CE (RD223/2004).**E.1** Does this study refer to one or more drugs marketed in Spain?**E.2** Are the drugs prescribed in accordance with the authorized conditions of use (datasheet)?**E.3** Is the assignment of patients to a specific therapeutic strategy determined by standard clinical practice and not determined beforehand by a clinical trial protocol? (8)**E.4** Is the decision to prescribe a specific drug clearly disassociated from the decision to include the patient in the study?**E.5** Are the applied diagnostic and follow-up procedures those of standard medical practice?**E.6** Are epidemiological methods used in the analysis of data derived from the study? |

(1) Definition of drug as listed in Article 8a of Law 29/2006 of 26 July on Guarantees and Rational Use of the Medicines and Healthcare Products.

(2) Substance refers to all material, regardless of human, animal, plant or chemical origin that can be administered to humans.

(3) This does not include derivatives of complete human blood, human blood cells and human plasma in which manufacturing processes are involved.

(4) Somatic cell therapy drug (definition listed in Article 47.2 of Law on Guarantees and Rational Use of the Medicines and Healthcare Products): The use in humans of live somatic cells (autologous, which are derived from the patients themselves; allogeneic, which are derived from other humans; or xenogeneic, which are derived from animals) whose biological characteristics have been substantially altered as the result of their manipulation to obtain a therapeutic, diagnostic or preventive effect by metabolic, pharmacological or immunological means. This manipulation includes the expansion or activation of autologous cell populations “ex vivo”, such as adoptive immunotherapy, and the use of allogeneic and xenogeneic cells associated with healthcare products used “in vivo” or “ex vivo”, such as microcapsules, matrices and intrinsic cell scaffolds, biodegradable or nonbiodegradable.

(5) Food is considered any ingested product that is not a drug. A food should not be classified as a drug unless it contains one or more ingredients considered a drug and that are indicated with a medical purpose.

(6) Article 8n of the Law on Guarantees and Rational Use of the Medicines and Healthcare Products defines cosmetics as all substances or preparations for application to various surfaces of the human body (epidermis, hair and capillary system, nails, lips and external genitals), teeth or oral mucosa, with the exclusive or main objective of cleaning them, perfuming them, protecting them, modifying their appearance, keeping them in good condition and/or correcting body odors.

(7) The concept of efficacy, derived from the pharmaceutical legislation of the European Union, consists of the scientific demonstration that a drug is capable of diagnosing, preventing or treating diseases.

(8) The randomization of patients to a predetermined treatment group in a clinical trial protocol should not be considered standard clinical practice.