

# D1.2 Report from EAB

WP1. Project coordination



Funded by  
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### Document History

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V0.1	12 Aug 2024	Draft
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## Abstract

Initially, this deliverable D1.2 should have provided with the feedback from the Ethics Advisory Board regarding the project framework in terms of patient rights, data privacy, study risk/benefits aspects. However, the EORTC realized that the project (a clinical trial) is already fully reviewed for ethics and legal aspects by ethics committees from all participating countries as requested by the Clinical trial Regulation. Therefore, there is no justification to repeat such review by a panel of experts organised by EORTC. This document aims to explain how the review is defined under the Clinical Trials Regulation.



## Deliverable

### Introduction

This document aims to explain how the project (a clinical trial) was fully reviewed by official ethics committees according to the Clinical Trial Regulation<sup>1</sup> (CTR). Clinical trial approval under the CTR is mandatory for starting the clinical trial in any member state. Therefore, the EORTC believes that the project was already fully reviewed for ethics aspects in all involved member states and this ethics review should not be duplicated.

### Why additional ethics review is not needed?

The project will investigate health intervention, collect clinical data and make direct use of these clinical data in specified analyses. All project research activities (including health economics) are detailed in the clinical trial protocol and assessed by regulators and ethics committees from all member states involved in the clinical trial according to the CTR.

The application for clinical trial approval under the CTR is structured in two parts: part I (scientific aspects and information about the investigational medicinal product, etc.) and part II (patient consent, GDPR aspects, proof on insurance, credentials of investigators, various compliance aspects, etc.).

According to the CTR:

- The clinical trial protocol (part I and part II) was reviewed and approved by all the involved countries (CTR art. 4, 7 and 8).
- The assessment was made by national regulatory bodies but also by ethics committees. National ethics committees are composed by independent experts including lay people according to applicable laws and standards (CTR art. 9).
- We will need to request a new approval under the CTR, should we change anything to the protocol after its initial approval (CTR art. 14, 15, 18). Every involved member state will review the modifications on part I and/or part II and inform the trial sponsor about its decision (CTR art. 19, 22, 23).

Therefore, it will make no sense to convey ethic experts in an advisory board and to ask them to duplicate what official ethics committees already did under the CTR.

### What about evidence and documentation?

The officially approved clinical trials including the list of involved member states are publicly available from the EU Clinical Trials Register website [Search for clinical trials - EMA \(euclinicaltrials.eu\)](https://www.eudra.org/eudra/doing/researchers/search-for-clinical-trials-ema).

The formal approval documents (incl. ethics review) for the first approved country were already provided in deliverable D2.1 Study initiation package.

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<sup>1</sup> REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL OF 16 APRIL 2014 ON CLINICAL TRIALS ON MEDICINAL PRODUCTS FOR HUMAN USE, AND REPEALING DIRECTIVE 2001/20/EC

## Specific information about the CTR

Information about the CTR extracted from the EMA dedicated website [Clinical Trials Regulation | European Medicines Agency \(EMA\) \(europa.eu\)](https://clinicaltrialsregulation.europa.eu/)

- European Union (EU) pharmaceutical legislation known as the Clinical Trials Regulation (CTR) entered into application on 31 January 2022.
- The main characteristics of the new Regulation are:
  - A streamlined application procedure via a single entry point - an EU portal and database, for all clinical trials conducted in EEA. Registration via the portal will be a prerequisite for the assessment of any application;
  - A single set of documents to be prepared and submitted for the application defined in Annex I of the Regulation;
  - A single authorisation procedure for all clinical trials, allowing a faster and thorough assessment of an application by all Member States concerned, and ensuring one single assessment outcome and authorisation per Member State;
  - A harmonised procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is jointly assessed by all Member States concerned. Part II is assessed by each Member State concerned separately;
  - The involvement of the ethics committees in the assessment procedure in accordance with the national law of the Member state concerned but within the overall timelines defined by the Regulation;
  - Union controls in Member states and third countries to ensure that clinical trials rules are being properly supervised and enforced.
- Extracts from the CTR <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R0536>

## CHAPTER II

### AUTHORISATION PROCEDURE FOR A CLINICAL TRIAL

#### Article 4. Prior authorisation

A clinical trial shall be subject to scientific and ethical review and shall be authorised in accordance with this Regulation. The ethical review shall be performed by an ethics committee in accordance with the law of the Member State concerned.

The review by the ethics committee may encompass aspects addressed in Part I of the assessment report for the authorisation of a clinical trial as referred to in Article 6 and in Part II of that assessment report as referred to in Article 7 as appropriate for each Member State concerned.

Member States shall ensure that the timelines and procedures for the review by the ethics committees are compatible with the timelines and procedures set out in this Regulation for the assessment of the application for authorisation of a clinical trial.

## **Article 7 Assessment report — Aspects covered by Part II**

1. Each Member State concerned shall assess, for its own territory, the application with respect to the following aspects: (a) compliance with the requirements for informed consent as set out in Chapter V; (b) compliance of the arrangements for rewarding or compensating subjects with the requirements set out in Chapter V and investigators; (c) compliance of the arrangements for recruitment of subjects with the requirements set out in Chapter V; (d) compliance with Directive 95/46/EC; (e) compliance with Article 49; (f) compliance with Article 50; (g) compliance with Article 76; (h) compliance with the applicable rules for the collection, storage and future use of biological samples of the subject.

The assessment of the aspects referred to in the first subparagraph shall constitute Part II of the assessment report.

2. Each Member State concerned shall complete its assessment within 45 days from the validation date and submit, through the EU portal, Part II of the assessment report, including its conclusion, to the sponsor.

## **Article 8 Decision on the clinical trial**

1. Each Member State concerned shall notify the sponsor through the EU portal as to whether the clinical trial is authorised, whether it is authorised subject to conditions, or whether authorisation is refused.

## **Article 9 Persons assessing the application**

1. Member States shall ensure that the persons validating and assessing the application do not have conflicts of interest, are independent of the sponsor, of the clinical trial site and the investigators involved and of persons financing the clinical trial, as well as free of any other undue influence.

In order to guarantee independence and transparency, the Member States shall ensure that persons admitting and assessing the application as regards the aspects addressed in Parts I and II of the assessment report have no financial or personal interests which could affect their impartiality. These persons shall make an annual declaration of their financial interests.

2. Member States shall ensure that the assessment is done jointly by a reasonable number of persons who collectively have the necessary qualifications and experience.

3. At least one layperson shall participate in the assessment.

## **Article 14 Subsequent addition of a Member State concerned**

1. Where the sponsor wishes to extend an authorised clinical trial to another Member State ('additional Member State concerned'), the

sponsor shall submit an application dossier to that Member State through the EU portal.

The application dossier may be submitted only after the notification date of the initial authorisation decision....

7. The additional Member State concerned shall assess, for its territory, the aspects addressed in Part II of the assessment report within the period referred to in paragraph 3 and submit, through the EU portal, Part II of the assessment report, including its conclusion, to the sponsor....

10. The additional Member State concerned shall refuse to authorise the clinical trial if it disagrees with the conclusion of the reporting Member State as regards Part I of the assessment report on any of the grounds referred to in second subparagraph of paragraph 4, or if it finds, on duly justified grounds, that the aspects addressed in Part II of the assessment report are not complied with, or where an ethics committee has issued a negative opinion which, in accordance with the law of the additional Member State concerned, is valid for that entire additional Member State. That additional Member State concerned shall provide for an appeal procedure in respect of such refusal.

### **CHAPTER III**

## **AUTHORISATION PROCEDURE FOR A SUBSTANTIAL MODIFICATION OF A CLINICAL TRIAL**

### **Article 15 General principles**

A substantial modification, including the addition of a clinical trial site or the change of a principal investigator in the clinical trial site, may only be implemented if it has been approved in accordance with the procedure set out in this Chapter.

### **Article 18 Assessment of a substantial modification of an aspect covered by Part I of the assessment report**

1. The reporting Member State shall assess the application with regard to an aspect covered by Part I of the assessment report, including whether the clinical trial will remain a low-intervention clinical trial after its substantial modification, and draw up an assessment report.

### **Article 19 Decision on the substantial modification of an aspect covered by Part I of the assessment report**

1. Each Member State concerned shall notify the sponsor through the EU portal as to whether the substantial modification is authorised, whether it is authorised subject to conditions, or whether authorisation is refused.

5. The Member State concerned shall assess the application and shall submit to the sponsor, through the EU portal, Part II of the assessment report, including its conclusion, and the decision as to whether the substantial modification is authorised, whether it is authorised subject to conditions, or whether authorisation is refused.

**Article 22 Assessment of a substantial modification of aspects covered by Parts I and II of the assessment report — Assessment of the aspects covered by Part II of the assessment report**

1. Each Member State concerned shall assess, for its own territory, the aspects of the substantial modification which are covered by Part II of the assessment report and submit, through the EU portal, that report, including its conclusion, to the sponsor within 38 days from the validation date.

**Article 23 Decision on the substantial modification of aspects covered by Parts I and II of the assessment report**

1. Each Member State concerned shall notify the sponsor through the EU portal as to whether the substantial modification is authorised, whether it is authorised subject to conditions, or whether authorisation is refused