II

(Information)

INFORMATION FROM EUROPEAN UNION INSTITUTIONS AND BODIES

COMMISSION

Communication from the Commission — Guidance on the information concerning paediatric clinical trials to be entered into the EU Database on Clinical Trials (EudraCT) and on the information to be made public by the European Medicines Agency (EMEA), in accordance with Article 41 of Regulation (EC) No 1901/2006

(2009/C 28/01)

1. INTRODUCTION AND SCOPE

Regulation (EC) No 1901/2006 on medicinal products for paediatric use ([1]) (hereafter the 'Paediatric' Regulation) entered into force on 26 January 2007. Article 41(3) of the Regulation requires the Commission to draw up guidance on the nature of the information on paediatric clinical trials to be entered into the database of clinical trials (EudraCT ([2])), on which information shall be made available to the public, on how clinical trials results shall be submitted and be made public and on the European Medicines Agency (EMEA)'s responsibilities and tasks in this regard.

This obligation aims to increase the availability of information on the use of medicinal products in the paediatric population and to avoid unnecessary repetition of studies. The information is aimed at the public which includes lay persons, patients and families, health professionals, researchers and academics as well as industry and regulators.

This guidance sets out the nature of the information to be entered into EudraCT, the information to be made accessible to the public, the paediatric clinical trial results to be submitted and made public and on the responsibilities of the EMEA and related tasks in this context.

The information referred to in this guidance comprises paediatric clinical trial protocol-related information and paediatric trial results. Such information is to be entered into EudraCT in cases where the respective paediatric trial has at least one investigator site in the European Economic Area (EEA), and/or is part of an agreed Paediatric Investigation Plan (PIP ([3])). It concerns paediatric trials planned, ongoing or completed in the EEA and those that are planned, ongoing or completed in any other country ('third countries') provided these latter trials are included in a PIP. The status of each paediatric trial will be identified (e.g. under assessment, authorised or refused, ongoing, prematurely ended or completed). This status will be listed for each Member State.

The EudraCT data fields are for the most part consistent with international initiatives relating to clinical trial registries, e.g. WHO International Clinical Trials Registry Platform (ICTRP) and the International Committee of Medical Journal Editors (ICMJE). Although EudraCT may have additional fields, the convergence of the information to be made public with the WHO ICTRP facilitates the work of sponsors and researchers submitting information to different registries for different purposes, and facilitates access to this information.

The Commission's Directorate-General for Enterprise and Industry (DG ENTR) ([4]) will make available the list of the specific data fields to be included in EudraCT, and those to be made public.

([1]) OJ L 378, 27.12.2006, p. 1.
([2]) http://eudract.emea.europa.eu/
([3]) See point 2, Article 2 of the Paediatric Regulation.
([4]) http://ec.europa.eu/enterprise/pharmaceuticals/index_en.htm

2. NATURE OF THE INFORMATION TO BE ENTERED INTO EUDRACT AND TIMING

2.1. Nature of the information

The nature of the required information to be entered into EudraCT is based on its importance to clinical trials contained in an agreed PIP. Two sets of information are required:

— paediatric trial protocol related information — supplied prior to the start of the trial and updated if needed during the trial describing the trial protocol, investigational medicinal products (IMPs), therapeutic indication, trial population, the trial authorisation and the current status of the trial,

— paediatric trial results related information — supplied after the completion of the trial and containing a summary of the results and conclusions.

2.2. Timing of entering of the information into EudraCT

2.2.1. *Protocol related information*

All interventional paediatric clinical trials with at least one site in the EEA are required to be entered into EudraCT no later than at the time of the valid application for authorisation of a clinical trial to the National Competent Authorities (NCA).

All clinical trials that are included in an agreed PIP should also be included, whether the trials are planned, ongoing, or completed.

In particular, all paediatric trials conducted with at least one site in a third country and included in an agreed PIP, should be entered into EudraCT no later than one month after, either, the EMEA decision agreeing a PIP, or, the first approval/positive opinion of the trial by a third country competent authority and/or third country ethics committee, whichever is the latest.

2.2.2. *Result related information*

Result-related information for paediatric trials should be submitted to the EMEA, for entry into EudraCT, no more than six months after the trial has ended, whether the trial has been completed or prematurely terminated, whichever occurs first.

However, notwithstanding the above, if

— the clinical trial does not fall within the scope of Article 46(1) of the Paediatric Regulation, and

— it is for objective scientific reasons not possible to submit the result-related information within six months, which has been demonstrated by the submitting party,

result-related information for paediatric trials may be submitted to the EMEA, for entry into EudraCT, at the latest within twelve months after the trial has ended, whether the trial has been completed or prematurely terminated, whichever occurs first.

For the purpose of submitting result-related information, a trial is considered completed when the last visit of the last patient has occurred, as foreseen in the latest version of the protocol. This means that, for the purpose of submitting result-related information for inclusion into EudraCT, open trial extensions, e.g. for maintenance treatment, are not considered as part of the trial.

2.2.3. *Submission of the information into EudraCT*

The sponsor, PIP holder or Marketing Authorisation Holder (MAH) submits the information electronically to the EudraCT staging area, once such a staging area is operational.

In the interim, the information is submitted in electronic format.

3. INFORMATION TO BE MADE AVAILABLE TO THE PUBLIC

3.1. Protocol related information

The information to be included in EudraCT and to be made public will include details of the following elements:

— identification of the clinical trial and its protocol,

— sponsor,

— source of funding,

— contact point for public use,

— identification and description of the treatment arms of the study (IMPs) to be used,

— therapeutic objective of the trial (disease under investigation),

— major objectives and endpoints,

— trial design including the countries in which it is to be conducted,

— trial population,

— inclusion/exclusion criteria,

— trial status (per country or region as applicable), and if refused for ethical reasons the reasons for refusal.

3.2. **Results related information**

The information to be included in EudraCT and to be made public should take into account the format for summary of results set out in the ICE E3 guideline ([1]). It will cover the following elements:

— administrative information and trial identification,

— trial design,

— scientific background and explanation of rationale for the trial,

— participants in the trial — information on the subject population including inclusion exclusion criteria and demographic information,

— interventions — the treatments used,

— objective(s) of the trial,

— outcome measures,

— randomisation implementation,

— blinding,

— statistical methods,

— patient disposition,

— protocol deviations,

— recruitment,

— baseline data,

— trial interruption,

— outcomes and estimation,

— ancillary analysis,

— adverse events,

— trial termination,

— discussion and interpretation of study results (interpretation of trial results by sponsor, if available and by competent authority, if available),

— a declaration of the submitting party on liability for the accuracy of the submitted information.

([1]) http://www.ich.org/

3.3. **Timing of making information accessible to the public**

Protocol-related information will be made public automatically, once the data has been entered into EudraCT and the trial bas been approved by the NCA concerned. Where a negative opinion bas been issued by an Ethics Committee, the information on the trial will still be published, together with a field indicating the reason for the negative opinion.

Public release of result-related information takes places automatically once this information has been included by the EMEA in the EudraCT database.

3.4. **How information is made public**

The information will be made available through a dedicated public website containing a subset of information regularly updated from EudraCT. Appropriate disclaimers will be included to reflect the stage of regulatory evaluation of the trial.

Studies not registered in EudraCT and for which protocol-related information is not available, e.g. because the conduct of the studies predated requirements for inclusion in EudraCT, should be specifically identified.

Result-related information is not validated prior to its inclusion into EudraCT. Responsibility for the result-related information lies with the sponsor, PIP holder or MAH submitting the results.

EudraCT will contain a disclaimer to this effect.

If and when the results are submitted for assessment (e.g. in a marketing authorisation application), a link to the public assessment report will be made.

4. **RESPONSIBILITIES OF THE EMEA AND TASKS IN THIS REGARD**

4.1. **The EMEA's responsibilities**

The EMEA should:

— make public the protocol-related information on paediatric clinical trials in accordance with this guideline and the lists of data fields made public by DG ENTR,

— make public the result-related information on trials included in EudraCT and on any paediatric studies submitted according to Article 45 and 46 of the Paediatric Regulation,

— coordinate the exchange of information,

— manage the EudraCT database.

4.2. **The related tasks**

The responsibility for the initiation of the process, electronic submission of protocol and result related data, and maintenance of data lies with:

— the MAH, in the case of provision of the results of an authorised medicinal product in accordance with the obligations in Articles 45 and 46 of the Paediatric Regulation,

— the sponsor of trials referred to by Article 41, whether or not it is the MAH,

— the PIP addressee.

The EMEA should:

— enter into EudraCT the protocol information received electronically for third-country trials including their authorisation status and information regarding the end of trial status,

— enter the result information received electronically into EudraCT,

— make public data from the protocol-related and result-related information in accordance with Section 3.4.

The NCAs should:

— enter the protocol information received electronically into EudraCT,

— enter information concerning the review and oversight of the paediatric trial,

— exchange information with the EMEA on the studies submitted,

— enter additional data relating to the review and authorisation, amendment and end of the trial, to be recorded directly into EudraCT by the NCAs or by transmission of the information from national clinical trial databases.

5. **IMPLEMENTATION**

The guidance set out in this Communication applies:

— as regards the protocol-related information, as soon as the programming of EudraCT has been finalised,

— as regards the result-related information, once the detailed guidelines for the reporting format have been published and the related programming has been finalised.

Finalisation of the programming will be publicly announced.