EUROPEAN COMMISSION
DIRECTORATE- GENERAL FOR HEALTH AND FOOD SAFETY

Health systems and products
Medicinal products – quality, safety and innovation

Brussels, SANTE B4/LA

MEETING OF THE CLINICAL TRIAL EXPERTS GROUP

Webex meeting

06 July 2022

MINUTES

(from 09.00 till 13.00)

1. Welcome and introductions

The Commission opened the meeting of the Clinical Trial Expert Group (CTEG) by welcoming the participants.

The CTEG is the Commission's informal forum to discuss regulatory issues on clinical trials in the EU with both representatives of the National Competent Authorities and the Ethics Committees.

The Commission informed the Group that the minutes of the previous CTEG meeting were disseminated for adoption via written procedure and then made available on the Commission's webpage of the 'Register of Commission Expert Groups and Other Similar Entities' dedicated to CTEG.

The Commission outlined the objectives of the meeting:

i. to discuss some topics covered in the Questions & Answers document;

ii. to discuss a few templates to be used by sponsors when submitting their clinical trial applications; and

iii. to share information on other items.

2. Adoption of the draft agenda

When reviewing and adopting the agenda, none of the attendees indicated any conflict of interest.

Two items have been proposed for A.O.B., namely (i) the interplay between the Clinical Trials Regulation (EU) 536/2014 (CTR) and Regulation (EU) 2017/745 or /746 on (In vitro) medical devices and (ii) labelling language.

3. Updates on Q&A

a. Patient facing documents

The Commission explained that in the past weeks the Group has worked on a few topics covered in the Q&A in order to better clarify some sentences but also to add new elements, such as a chapter on patient facing documents.

Indeed, as a follow up action stemming from the previous CTEG meeting that took place on 16 March, the Commission and some members of the Group worked on a text related to patient facing documents and CTEG members were invited to contact the national contact points for internal alignment where needed.

b. Transition trials

In the past weeks, the Commission consulted both CTAG and CTEG on the approach for transition trials. Divergent feedback and perspectives on the Q&A chapter related to transition trials were received. At the CTEG meeting, the Commission underlined the main principles of the transitions trials which are as follows:

i. The validity of previous assessments and decisions under the CTD needs to be respected (no re-assessment of the documentation and information that was part of the Clinical Trial Directive (CTD) submissions);

ii. A minimum application with harmonised (or consolidated in case of the protocol) documentation is to be submitted in the transition application;

iii. The sponsor is expected to complement the missing documentation in line with the CTR requirements at the time of the first substantial modification – addition of Member States Concerned only possible after the transition when the full CTR documentation is available;

iv. Voluntary submission of other annex I documents is recommended at the time of submission of the initial transition application.

It is sponsor's responsibility to bring the transition trial in line with the rules of the CTR, including for emergency trials, possibly contacting the national contact point where needed.

The Commission will revise the specific transition trials Q&A by balancing the input received and will publish the revised version on Eudralex volume 10 upon adoption by CTAG via written procedure.

c. Labelling of the investigational medicinal products (IMP)

Ahead of the meeting, the CTEG representative of IE proposed to update the Q&A document, in particular to the wording relating to labelling of the investigational medicinal products (IMP) under 2.6 Question.

The text, that was circulated via email, received positive reactions from some CTEG members.

The Commission will therefore revise the text and update the Q&A n. 2.6 accordingly in the next iteration upon CTAG adoption.

d. Reference to clinical trials authorised under the CTD

Sponsors have been asking whether the "Table 1: Content of the simplified IMPD" illustrated in annex II of the CTR, which contains a table with the possibility to refer to other trials, could also make reference to trials authorised under the CTD.

The CTEG considered it would be unfeasible to refer to documentation submitted under the CTD. As the text is within the CTR, the references to other clinical trials is within the same system and makes reference to documentation available in CTIS. The Commission concluded by saying that it will bring this topic to the attention of CTAG together with the other Q&As.

4. Templates

Over time, the Commission uploaded various templates on Eudralex volume 10 that can be used by sponsors to submit the information required in the CTR (under part II).

The first template discussed is a new template for the statement related to the proof that data will be processed in compliance with union law on data protection.

a. Statement GDPR compliance

NL presented the proposed template for the statement related to the proof that data will be processed in compliance with union law on data protection.

The objective of the new template is to harmonise as much as possible the statement across the EU with regards to the GDPR compliance to be submitted in part I. This form does not require signature, unless explicitly required by national legislation, as it is implied with the submission via CTIS.

National authorities will be able to continue to require to fill in national forms for GDPR as part of part II application.

b. Updates Part II templates

The CTR does not require signing individual documents in the clinical trial application, but the inclusion of "signature" somewhat implies the need for signature. Hence, the request for signature has been removed from the following documents available on EudraLex volume 10 and which are part of part II of the clinical trial application:

- Declaration of Interest
- Investigator Curriculum Vitae
- Site Suitability

In addition, a footnote has been added to flag that a request for signature could be subject to national legislation. The same approach has been applied for the statement on GDPR compliance.

With regards to signatures, the Commission will include a footnote to clarify that documents should be signed in the sponsor or investigators file as appropriate.

c. Update Qualified Person (QP) template

The Commission revised the Qualified Person (QP) declaration form to make it in line with the requirements of the CTR. The revised document continues to require the signature as requested by the CTR. The Commission received a few proposals to improve the template; it will implement them and upload on Eudralex volume 10 the up-to-date document upon CTAG adoption.

5. Interpretation of Article 61 § 5

NL presented the challenges with the interpretation of Article 61 paragraph 5 of the CTR. The specific aspect that raises some questions is around the interpretation of the wording "intended to be used exclusively".

NL pointed out that if the wording means that the investigational medicinal products are exclusively to be *administered* to the trial participant at the same location as were the re-labelling/re-packaging or magistral officinal formula took place, only a very small number of clinical trials will benefit from this exception.

The Commission explained that the purpose of the Article 61.5 is to limit the cross-border movement of magistral and officinal products since the production and the delivery of these products are not harmonised across the Union, whilst allowing their use in clinical trials (not for administration in hospital) which was not foreseen in the CTD.

There was a general consensus with having a flexible approach with the interpretation because an oral /topic preparation may be taken by non-hospitalized patients participating in the clinical trials. The Commission will ask for advice to the legal service.

6. DCT project work

The progress on the decentralised clinical trials project, its governance, the challenges and solutions, were presented.

The objective is to have a paper that outlines similarities and divergences across the member states and find a harmonised way to conduct decentralised clinical trials.

After a consultation process, a first draft of the proposed text report will be shared in September 2022 and the intention is to publish the report of the similarities and differences across the Union at the end of 2022.

7. Updates on the Delegated Regulation on labelling requirements for unauthorised investigational and unauthorised auxiliary medicinal products for human use

The Commission provided an overview of the steps that have been taken with regards to the Delegated Regulation on labelling requirements for unauthorised investigational and unauthorised auxiliary medicinal products for human use.
The proposed text and its annex have been subject to public consultation for feedback on the 'Have your say' webpage for a period of 4 weeks that ended on 29 June at midnight.

The Commission will analyse the responses received and describe how these will be treated in the explanatory memorandum of the delegated act.

The Commission will send the text to CTAG for information. *[Post meeting note: the Delegated Regulation amending Regulation (EU) No 536/2014 as regards "Unauthorised investigational and auxiliary medicinal products - labelling requirements" has been adopted by the Commission on 6 September 2022.]*

After that, the Commission adopts the act and sends it to the Council and the EP for scrutiny. The Council and the European Parliament cannot make comments, only they can accept or reject.

8. ICH-GCP guideline updates

The EMA shared some updates related to the revision of the ICH-GCP guideline. It was mentioned that Spiros Vamvaka is the new Head of Scientific Advice after the departure of Fergus Sweeney from the EMA due to retirement.

The EMA presented the steps that will ultimately lead to a complete revision and re-organisation of the ICH E6(R2) Guideline for interventional clinical trials. Annex I will reflect the content of E6(R2) with updates where needed. Annex II will include guidelines on the design of pragmatic clinical trials, decentralized clinical trials and trials that incorporate real world data sources (e.g., electronic health records, hospital discharge summaries, claims data, patient/disease registries). ICH E6 should be read in conjunction with other ICH guidelines relevant to the design and conduct of clinical trials.

The draft principles were published in April 2021 and will be open for consultation in November/December 2022 together with Annex I. The stakeholder engagement is a key aspect of this revision, involving also patients and healthcare professionals.

Some CTEG members will be involved in the consultation process and the Commission will inform the entire Group of the developments in due course.

It is critical that the ICH documents do not contradict the CTR also with relation with ICH rules.

9. Call for speaker for a workshop on Digital health Technology 8th and 9th November

The CTCG Vice-Chair and observer of the CTEG informed the group of a workshop taking place on 8 and 9 November 2022 on digital health technology. This topic nicely fits into the broader framework of the EU activities related to boosting clinical trials in the EU. The CTEG observer invited attendees to put themselves forward before the end of July to speak at the event and bring the regulatory perspective to the workshop.

10. AOB and next steps

It was asked to discuss the interplay between CTR (EU) 536/2014 regulation and Regulation (EU) 2017/745 or /746 on (In vitro) medical devices also based on the recently published Q&A guidance document (https://ec.europa.eu/health/document/download/59abcc81-fd32-4546-a340-24c8fad4e2ac_en?filename=mdcg_2022-10_en.pdf).

It was highlighted that one single protocol should be submitted, but it requires two combined trials and notifications for each of the aspects included in the protocol. The formulation of the primary objective is the main driver of the final decision on how to handle the clinical trial.

The Commission will liaise with the DG SANTE Unit dedicated to medical devices to align on the topic and avoid confusion, incoherence, and duplication.

The second and the last AOB item was about the Annex II of the Q&A version 6.1 on 'Language requirements for part I document'. One of the column reports the requested language for labelling, including in some cases a footnote that in certain countries exceptions are allowed when the IMP is being administered by physician/authorised health care professional. Nevertheless, there is the need to harmonise this because the information is not available for all Member States.

The Commission will revise the Q&A on the 'Language requirements for part I document', including a footnote that in certain countries exceptions are allowed when the IMP is being administered by physician/authorised health care professional.

In terms of next steps, the draft minutes of the CTEG meeting will be adopted after CTEG's review and feedback via written procedure.

The Commission will share the Q&A texts and the up-to-date templates with the CTAG for written adoption and update the Q&A on Eudralex volume 10 accordingly. *[Post meeting note: the adoption of the revised Q&A and templates by CTAG via written procedure closed on 26 August].*

The next CTEG meeting is planned for 08 November 2022 and it will be virtual.