



EUROPEAN COMMISSION
DIRECTORATE- GENERAL FOR HEALTH AND FOOD SAFETY

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

Brussels, SANTE

Brussels, September 22, 2020

Minutes of the Meeting of the Expert Group on Clinical Trials

25 June 2020, webinar call

- 1. Welcome**
- 2. Adoption of the draft agenda**
- 3. Introductions of new CTEG members**
- 4. Member State preparedness (tour de table)**

The Clinical Trials Regulation (EU 536/2014) is foreseen to be applicable by end of 2021. It is essential that MS are ready by this date. CTEG/SANTE started monitoring MS readiness in collaboration with CTFG (Heads of Medicines' Clinical Trials Coordination and Facilitation Group) with the CTEG/SANTE focus being on national legislation to allow implementation and the preparedness of Ethics Committees. A traffic light table with directed questions regarding national/international pilots, reorganisation of ethics committees, training and resources has been created for regular updates. Based on feedback from 19 MS on 25 June, preparedness is variable, especially with regards to the organisation and preparedness of ethics committees. Some Member States will have to adopt national laws to be operational at the end of 2021.

5. Feedback from the working groups:

- Working group for harmonised part II documents

A draft template to collect information on financial transactions and compensation provided for participation in the trial, including to persons supporting a subject to participate has been presented to the expert group. The received comments were related to the scope of the document (e.g. to clarify that it is to collect information on payments as well as on compensation). The draft will be updated accordingly for submission at the next CTEG meeting.

In addition, a general guidance for part II documents was also prepared. This document provides additional clarifications in relation to a set of harmonised documents, which have been endorsed by the EU Clinical Trial Expert Group. It was not presented for

endorsement since the last template on financial compensation could not be finalised and thus endorsed.

- Subgroup for the classification of changes as SMs or non-SMs

A subgroup was created to add further clarifications to the definition of “substantial” and to identify data and documents where more specific guidance on what change could be potentially regarded as substantial modifications or non-substantial changes. The subgroup agreed to propose to CTEG to use the following main principles for the classification of changes in clinical trials:

- Three main categories of changes: substantial modifications, non-substantial changes which are relevant for the supervision of a clinical (Art 81.9) and non-substantial, not relevant changes;
- Changes to the same document can be substantial or non-substantial depending on their potential impact on subjects safety and rights or data reliability and robustness (eg. annual RSI update Q&A 7.15);
- Sponsor’s responsibility to decide if a change is substantial or not;
- MSs can impose corrective measures in case of disagreement (art 77) and penalties (art 94.2);
- Annex II provides examples (based on CT-1), but further guidance in the form of concrete examples per document type will be developed. This work will be carried out together with CTFG, EMA and select European organisations.

CTEG agreed with proposed approach.

6. Q&A document: discussion of new and updated Q&A’s

Q&A on the language requirements: Article 26 of the CTR asks the Member States to consider using a commonly understood language in the medical field for documentation that does not go to the subject. For sponsors, this is important information, as missing translations might impact the validation of their Clinical Trial Application. In March, SANTE has circulated a survey, inquiring on the language requirements from documents that constitute part I Member States have indicated in annex II which documents from the part I (i.e. CTR annex I, sections B to J). Input to this survey will be used to develop an overview on the language requirements to be included into COM Q&A document as an annex in the form of a table.

Q&A on the submission of SMs: CTEG endorsed this Q&A for publication on EudraLex-10. The Q&A was based on the position endorsed by CTEG in March 2020 and stakeholders’ feedback. The Q&A explains the rules to submit the first as well as consecutive SM following an initial application under Art 5 or 11. As a post-meeting note, this Q&A (3.4) is now available on EudraLex-10.

Art 11 and 14 applications:

Additional Q&A's (2.10, 2.11, 2.12, 2.13) were endorsed. SANTE explained that these Q&A clarify the mechanics of Article 11 / 14 applications, as there is the legal basis is different compared to the procedures foreseen for initial applications. Q&A 2.12 recommends sponsors not to perform additional article 14 procedures when an article 14 procedure is ongoing – it was explained that there is no legal basis to block parallel article 14 submissions.

Changes to the safety chapter of the Q&A

Several Q&As (7.9, 7.11, 7.15, 7.19, 7.28) with additional clarifications regarding safety reporting/assessment have been endorsed by CTEG, They are now published on EudraLex-10. Members of the group point out the importance of guaranteeing access to EudraVigilance for ethics committees in those countries where they have a mandate in line with Article 44(3) of the CTR.

Draft questionnaire on resources needs for safety assessment

Harmonised safety assessment will become a new requirement in the EU under CTR. DG SANTE understood from MS that preparation with its implementation is lagging behind and this is mostly because of insufficient national resources. Successful implementation of this requirement is high priority.

DG SANTE applied for a joint action, if accepted, the money can be used to support MS. In support of this application and to understand better expected workload, a questionnaire was drafted with questions to MS and EMA. The specific aim of the questionnaire is to collect information on the current/expected workload, national processes and positions regarding the assessment and about best ways to spend monetary support from the joint action. CTEG endorsed the questionnaire and it was circulated with MS for completion.

7. COVID-19 platform trials (14:00-14:45, RTD) for information

As RTD explained, the first ERAvsCorona Action Plan, supported by the EU National Ministers responsible for research and innovation, identifies 10 short-term priority actions one of them aiming at “extending and supporting large EU-wide clinical trials for clinical management of Coronavirus patients”. It is in this context that an ad hoc “Clinical Trials Sub-Group (CTSG)” was created with the overall purpose to support the implementation of large-scale, multi-centric clinical trials across Europe, in order to obtain robust results that can benefit patients and the healthcare systems in a timely manner.

8. ICH GCP renovation process and Reflection paper for patient focused drug development– update

ICH E8 has been rewritten and is being finalised following public consultation. It is foreseen to have a final text to be shared with CTEG by end of summer. In addition, CTEG members were asked to send comments to the ICH M11 protocol template.

9. CTIS update and collaboration between CTIS-EG and CTEG

EMA gave feedback on the current development status of the EU CT Portal and Database.

The recent discussion at the level of the EMA Management Board were presented. It was explained that the go-live date, set as a working assumption to December 2021 is mainly driven by the need to implement the CTR as soon as possible. A prioritisation exercise will take place to define which functionalities will be implemented for go-live and after go-live. Next to that, the current results from the development of CTIS were presented.

DG SANTE gave a short update on the implementation of the change on SM that was discussed during the March meeting. Due to the high impact of this change, it was not possible to cover it in the releases for the audit. It will be developed as part of the first release developed for the go-live package.

10. Union controls

The Commission will conduct union controls to MSs (in order to verify compliance with CTR provisions) and to 3rd countries (to verify equivalence with CTR provisions for patient safety and data robustness). DG SANTE gave an update on the progress with preparing for this new responsibility.

11. Lay summary guidance

The Commission was approached by EFGCP/EFPIA roadmap initiative drafting a detailed guidance to sponsors for the successful implementation of the new requirement for the preparation and publication of lay summaries. The guidance builds on the existing one including additional details on the preparation and dissemination. It was agreed that CTEG, CTFG and EMA will participate in the review of the document. In case the content is acceptable we aim for a joint endorsement and publication with CTFG and EMA. A small review group will be set up as a next step with a target date to complete the review in early September.

12. Post-trial treatment access for trial subjects subgroup

The subgroup will prepare a first draft of considerations as a basis for a guidance (and Q&A) to sponsors addressing specific concerns and about what information should be submitted with the application on this aspect (including trials for serious or life-threatening medical conditions with no available alternative treatments).