



EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Health systems, medical products and innovation
Medicinal products: quality, safety and innovation

Brussels,

MINUTES OF THE MEETING OF THE EXPERT GROUP ON CLINICAL TRIALS (FINAL)

26 JANUARY 2017

1. WELCOME AND OPENING

The Chair welcomed the participants and asked the new members of the group to introduce themselves. The Chair, welcoming new participants, invited members of the group to revise the members list in order to update it.

2. ADOPTION OF THE AGENDA

The Agenda was adopted without amendments.

3. ADOPTION OF THE MINUTES OF THE MEETING HELD ON 30 JUNE 2016

EMA requested an amendment to the minutes in order to clarify the EMA contribution to the discussion on the transitory period. COM informed that revised minutes will be shared with the group.

4. UPDATE BY EMA ON THE DEVELOPMENT OF THE EU CT PORTAL AND DATABASE

The EMA representative gave a presentation on the progress of the development of the EU CT portal and database informing on the project timelines, the milestones achieved and the ideas to mitigate the risks of the delay. The presentation covered also the details of user management system and roles matrix.

The presentation was followed by questions of the group regarding the assignment of tasks and the simultaneous work on the document by more than one user. The experts asked about the procedures of nomination of the Member State administrator. EMA clarified the high level administrators (Member States super users) will be nominated outside the Portal.

COM informed that on the 14th February a workshop on the implementation of the clinical trials regulation will be held in London, organised by the Coordination Group with the collaboration of EMA.

5. DRAFT TEXT OF THE REVISED Q&A DOCUMENT ON THE CT REGULATION

5.1. The Question and Answer document: General question on GLP and specific question on GLP for ATMPs

COM reminded the discussions of the June meeting on the text of the question on GLPs for ATMPs as well as the general GLP question, intended to be integrated to the Question and Answer document on the Clinical Trials Regulation.

Following the feedback received and further discussion with the group, COM amended the text of the Q&A on the GLP for ATMPs by removing the examples of the situations where the sponsor does not need to provide confirmation on compliance of the study with GLP or equivalent standards, leaving the assessment for the NCAs.

The group agreed to amended text.

COM concluded that text as agreed by the Expert Group will be sent to its members and to DG GROW contact point.

6. DISCUSSION ON THE PRINCIPLES FOR THE TRANSITORY PERIOD.

COM gave a presentation basing on the outcomes of the discussion on the principles for transitory period, discussed at the June meeting. COM raised specific questions in the light of the feedback received from the stakeholders. COM invited the group to provide their input.

As regards the first question, concerning whether the requirement to transition a trial should apply to a trials where the last visit of the last patient took already place, the group supported flexible approach.

As regards the documents required for transitioning a trial authorized under the Directive 2001/20/EC, the group agreed that the requirements should be limited to documents that already exist and have been approved. The group considered that the documents with the old EudraCT number should be acceptable for that purpose. EMA added that the EudraCT number could be used to link the trial to the one authorized under the Directive. As regards Part II the group suggested that a flexible solution should be proposed and, in any case, a sponsor should not be requested to produce new documents for that purpose. COM stated that the sponsors need a detailed guideline what exactly should be uploaded in the Portal if the responsibility for assessing the compliance of a trial with the Regulation is primarily on them. It is to be expected that they will not take risk of relying on authorization under the Directive if the requirement as regards the documents expected to be uploaded will not be clear. EMA stressed the importance of identifying a list of those documents so that the system can support the functionality. The members of the group were requested to provide the feedback on the list of documents required for transitioning trials by the 27 of February 2017.

EMA clarified that the specific functionality for switching from the EurdaCT to the new regulation will be available not earlier than one year after the Regulation becomes applicable.

COM invited the group to discuss the transitioning of multinational trials. Initially, COM proposed that, in order to benefit from the rules for transitioning, all clinical trials should be treated as mono-national clinical trials unless a sponsor wishes to reapply for re-authorisation. This principle was criticized by EMA as well as by some stakeholders. COM proposed to create a group of volunteers to come up with a proposal for transitioning of multinational trials which will propose alternative solution.

On the margin of this discussion the ES representative group raised the question what would happen with the cluster trails, currently not covered by the Directive. COM stated that as from the entry into application of the Regulation on clinical trials all clinical trials should comply with the requirements of the new Regulation

7. OUTCOME OF THE PUBLIC CONSULTATION ON THE AD HOC GROUP RECOMMENDATIONS

7.1. Risk proportionate approach in clinical trials

The DE representative informed on behalf of the responsible task group on the state of play of the revision of the draft *Recommendation on the risk proportionate approaches in clinical trials*. The revision of the recommendation was triggered by the comments received in the public consultation.

COM informed that the intention is to finalize the revision and present the guideline for expert group approval at the April meeting. The text will be distributed to the participants before that meeting.

7.2. Lay person summary

The UK representative on behalf of the task group responsible for developing the *Recommendation on lay person summary* presented the revised version of the recommendation. The modifications proposed in the recommendation on Layperson's summary aimed at further improving the readability of the summaries (e.g. the recommendation proposed simplified subtitles for the summaries).

The document was adopted by the group.

7.3. Ethical considerations in pediatric CT

The NL representative, on behalf of the task group in the lead for the revision of the *Recommendation on the ethical consideration in pediatric clinical trials* in order to adapt it to revised legal framework of the Clinical Trials Regulation, informed the expert group about the state of play. It was highlighted that there was important number of comments on this document. In the light of the comments received in the consultation it was also agreed that the document should be redacted in order to be more user friendly.

COM informed that the intention is to finalize the revision and present the recommendation for expert group approval at the April meeting. The text will be distributed to the participants before that meeting.

7.4. IMP and AxMP

The DE representative gave a presentation on the progress of the revision of the comments received in the public consultation on the *Recommendation on Auxiliary Medicinal Products* (former *Guideline on investigational medicinal products and non-investigational medicinal products*).

COM informed that the intention is to finalize the revision and present the guideline for expert group approval for the April meeting. The text will be distributed to the participants before that meeting.

8. REVISION OF THE GCP PROCEDURAL GUIDELINES

EMA gave an overview of guidance documents finalized and under revision.

COM recalled that the revised guidelines were circulated to the group before the meeting and that the feedback should be sent to EMA by 9 February. At this opportunity COM informed the Group that the Commission Implementing Regulation on GCP inspection procedures will be sent in the coming days for vote to the Standing Committee on human medicinal products in a written procedure. The Committee members will have 21 days to express their position.

9. DOCUMENTS REQUIRED IN APPLICATION DOSSIER PART II

COM informed the group that would like to launch the exchanges on the requirements as regards application dossier for Part II. COM explained that COM representatives were approached by stakeholders expressing concerns that Member States may diverge as regards types, as well as level of detail, of documents required. These concerns were expressed in particular as regards a statement on the suitability of the sites, a description of financial arrangements, and a proof that personal data will be processed in accordance with the data protection legislation. The group welcomed the initiative. The NL representative informed that similar discussion was initiated in the context of Member State task group working on the template for the assessment report as regards the Part II. COM informed that will liaise with the chair of that group. Independently on that COM asked MS to provide feedback what types of documents Member States will require in Application Dossier Part II.

10. AOB

10.1. MS readiness for the entry into force of the CT Regulation

The DE representative, in her capacity of the vice-chair of CTFG, gave a presentation on this issue, relying on the information provided to CTFG by the participating Member States. The presentation focused on different aspects of the Member States preparedness. As it was stressed in the presentation, not all Member States inform on the state of play of their preparation.

COM stressed that the preparation for application of the new Regulation presents several challenges. In this context it is of importance to share the best practices between MS. For that reason, COM offered the forum of the Expert Group for discussing some of the aspects of

Member State preparedness. COM announced that will send the list of topic to be possibly discussed on the forum of the Expert Group.

10.2. General Data Protection Regulation implementation by MS of the clauses allowing them to impose additional conditions for processing health related data.

COM informed that the implementation of the GDPR is now being discussed at national level. In this context COM stressed that it is important that the national competent authorities in the field of health research are informed how the flexibility clause allowing Member States to impose the additional conditions on the processing of health related data in the GDPR (Article 9(4) of the GDPR) is being implemented at national level.

COM clarified that the discussions on the impact of the new General Data Protection Regulation (GDPR) on Clinical Trials Regulation will be continued with the expert group.

10.3 Interplay between Pharma and GMO legislation

COM informed about the Workshop organized by COM on the 9 February, involving different authorities to discuss GMO and pharmaceutical legislation. One of the issues identified for the discussion was how to articulate the requirements stemming from the GMO legislation (GMO authorization) with the new Clinical Trials Regulation. In case an investigational medicinal product contains a GMO, a sponsor needs to ask for the GMO authorization independently on the necessity to ask for the clinical trials authorization. The differences in the Member States requirements, procedures and timelines for authorizations of GMO may impede the sponsor from taking full advantage from the quick and streamlined procedures for clinical trials authorization in the new Clinical Trial Regulation. The workshop offers possibility to discuss with both, national competent authority responsible for clinical trials authorisation, as well as with GMO authorities, possible best practices. COM will come back to the group on that issue.

10.4 Reminder to inform COM on fees

COM reminded MS to give a feedback on the national requirements as regards the fees.

10.5 Long term safety follow-up of patients

COM gave a presentation about the long term safety follow-up of patients, which is of particular relevance for the clinical trials on the advanced therapy medicinal products. COM raised an issue that the requirement of long term follow up is treated differently in the Member States and was seeking the group feedback what should be legal framework for those situations.

The AT, IT, DE, IE, ES and UK representatives agreed that the differences in understanding in the Member States are an issue and that a common approach should be found at the European level. The issue should be covered by the Q&A document.

EMA pointed out the registries that are considered in the legislation and GVP module 8 as non-interventional CT. COM explained there is no consensus about how to classify the registries, because in some MS they are considered as low interventional clinical trials.

COM highlighted the importance of patient's follow-up after the treatment. However, COM considered that the very long term follow up cannot be considered as a part of a clinical trial, since the formal end of a trial triggers certain obligations under the Regulation (e.g. submission of results). It does not seem justified to delay those actions in case the trial is considered as on-going only for the reason of long term safety follow up. COM indicated that this issue should be kept in mind by assessors when assessing the clinical trial application dossier.

COM concluded that a questionnaire will be sent to the NCA's legal services.

10.6. Questions raised by MS

The IE representative raised 2 questions regarding the joint assessment under the Clinical Trials Regulation.

1. What are the options for an appeal in case the reporting MS gives a negative opinion in the conclusions on the Part I assessment, to which Member State concerned cannot object (no opt-out option). COM committed to come back to this issue on the meeting of April.

2. What should be the timing for the notification of an opt out from conclusion of reporting Member State of the joint assessment of the Part I, in case of the applications on a basis of Article 11 of Clinical Trial Regulation (assessment limited to Part I)? According to Regulation the sponsor is notified on the outcome of the joint assessment once the Reporting Member State issues it. In case Member State concerned opts out, he will be informed at the moment of the decision on this opt out. It implies, in case of the applications was submitted on a basis of Article 11, he may not know before submitting Part II for assessment that MS considers opt out. COM confirmed the letter of the Regulation but at the same time recalled the conclusions of the discussions on that issue in November 2015, that informing a sponsor that a member state concerned consider an opt-out at the moment of notification is advisable as a good administrative practice.

The LV representative raised the question of interpretation of Article 9 as regards the independence of the Ethic Committee of the CT site. COM recalled that it will depend on the national legislation to clarify this concept, and that globally recognized standards (such as ICH) may be helpful to clarify this.

The Chair closing the meeting congratulated the Expert Group for an adoption of the *Recommendations of the expert group on summaries of clinical trial results for lay persons* and summarized the follow up actions for the Expert Group and the Commission.

COUNTRY	ORGANISATION
AT	AGES - Austrian Medicines & Medical Devices Agency
BE	Ethics Committee of the Hospital Erasme - ULB
BE	Federal agency for medicines and health products
BG	Ethics Committee for Multicentre Trials – Bulgaria
BG	Bulgarian Drug Agency
CZ	State Institute for Drug Control
DE	IBE - Ludwig Maxmilians University - Association of Research Ethics Committees
DE	BFARM
DK	The Danish Ministry of Health
DK	Danish Health and Medicines Authority
EE	State Agency of Medicines
EL	National Organisation of Medicines
ES	RESEARCH Institute of Universitary Hospital "12 de Octubre"
ES	AEMPS
	EMA
FI	Finnish Medicines Agency Fimea
FI	National Committee on Medicinal Research Ethics
HU	National Institute of Pharmacy and Nutrition
IE	Department of Health Ethics Committee
IE	Health Products Regulatory Authority
IT	Agenzia Italiana del Farmaco (AIFA)
LV	CLINICAL RESEARCH ETHICS COMMITTEE at PAULS STRADINS CLINICAL UNIVERSITY HOSPITAL DEVELOPMENT SOCIETY
LV	State Agency of Medicines of Latvia
NL	Central Committee on Research Involving Human Subjects (CCMO)
NL	Health Care Inspectorate
NO	Norwegian Medicines Agency
PL	Main Pharmaceutical Inspectorate
PL	Office for Registration of Medicinal Products, Medical Devices and Biocidal Products
PL	Ministry of Health
PT	National Ethics Committee for Clinical Research - CEIC
SK	Ministry of Health of the Slovak Republic
SI	JAZMP
UK	Medicines and Healthcare products Regulatory Agency
UK	Health Research Authority
EMA	