EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Meeting Report - Multi-stakeholder Workshop on ICH E6(R3) - Public Consultation – Day 1

13 July 2023, 13:30-18:10 CEST – Virtual meeting

Co-Chairs: Marita Kailajärvi (FIMEA) & Peter Twomey (EMA)

1. Welcome and Setting the scene

Welcome

Marita Kailajärvi (FIMEA), Peter Twomey (EMA) and Emer Cooke (EMA) welcomed participants and panellists. Emer Cooke also gave introductory remarks outlining the importance of the ICH E6 guideline and its revision.

Outline of the Day & Objectives

Peter Twomey and Kim Pietsch (DE-PEI/EMA) provided technical considerations and the outline of the Day 1 agenda.

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2. Background to Renovation of GCP & Road to ICH E6(R3)

Introduction

Momir Radulovic (JAZMP) introduced the topic of the first session as well as the speakers.

2.1 Perspective on the GCP renovation work in ICH

Lenita Lindström (EC) outlined the background for the ICH harmonisation project, its governance, products and guidelines. She then presented an overview of the ICH harmonisation activities, the reflection paper on GCP renovation and E6(R3), the stepwise approach to the guideline revision development and its structure.

2.2 The Road to ICH E6(R3) Public Consultation

Peter Twomey acknowledged the contribution of the previous Regulatory Chair, Spiros Vamvakas (EMA), and presented the current status of the ICH E6(R3) Principles, Annex 1 and Annex 2. The process for submitting comments in the public consultation was also described. It was highlighted that a high volume of comments is expected, and therefore that the categorisation of comments would be helpful for the expert group to focus the review on the main issues for stakeholders.

2.3 What is new? – An overview of ICH E6(R3)

M. Khair ElZarrad (US FDA) highlighted the importance of the clinical trial requirements harmonisation across regions, then detailed the background for the revisions and presented the high-level changes related to the structure and content. It was confirmed that work on Annex 2, which will cover amongst others decentralised elements, pragmatic elements and real-world data sources, is ongoing. The additional efforts from the global community that will be needed since guidelines alone will not be enough in addressing all scenarios and evolving innovations were also outlined.

2.4 Question & Answer Session

Lenita Lindström, Peter Twomey, M. Khair ElZarrad and Kim Pietsch addressed questions from stakeholders.

- Training: ICH has engaged training associates that will help in developing the training material. It is planned for the training to be in-depth, with concrete scenarios. A European supplementary training may be developed under the umbrella of ACT EU. If particular areas are of interest for training, stakeholders are invited to specify them when submitting their comments.
- Submission of comments: Stakeholders are strongly encouraged to submit comments as an organisation where applicable, but comments can also be submitted individually. All comments will be taken into account, however, a trend of similar (major) comments would lead to a greater likelihood of modifying the guideline accordingly. Consultation dates for stakeholder within the EU are from 26 May to 26 September 2023 and mailed to iche6_r3@ema.europa.eu using the following form.

Wrap-up

Momir Radulovic wrapped up the session and thanked the panellists and participants for their contributions.

3. Principles of ICH E6(R3) & Annex 1

Introduction

Marita Kailajärvi introduced the topic of the second session as well as the speakers.

2.1 The Principles of ICH E6(R3)

Susanne Nørskov (EFPIA) and Lisbeth Bregnhøj (DKMA) who are both representing the EC in the EWG provided a detailed overview of the 11 principles in the ICH E6(R3) revision, with a reference to the previous ICH E6(R2) principles where applicable.

2.2 Annex 1

Gabriele Schwarz (DE-BfArM), Rebecca Stanbrook (EFPIA) and Lisbeth Bregnhøj then provided an overview of the Annex I (including the new data governance section), glossary and appendices, focusing on the main considerations and changes. It was highlighted that the appendices bring no new requirements, as requirements are covered in the principles and Annex 1.

Wrap-up

Marita Kailajärvi wrapped up the session and thanked the panellists and participants for their contributions.

4. Panel Discussion, Q&A on Principles & Annex 1

Introduction

Spiros Vamvakas (EMA) introduced the panel discussion and panellists.

1. Panel Discussion: Exploring stakeholder's perspectives

Each panellist - Pirkko Lepola (Enpr-EMA – paediatric research network representative), Piotr Szymański (ESC – healthcare providers representative), Gunilla Andrew-Nielsen (MPA – CTCG representative), Rob Camp (EUPATI Spain – patient's representative), Herman Goossens (Universiteit van Antwerpen – academia representative, excused, statement presented by Spiros Vamvakas) and Fergus Sweeney (Good Clinical Practice Expert) - provided a statement outlining their perspectives on the guideline.

These statements and the key points they made are provided in the presentations with this report.

2. Panel facilitated Q&A Session – Principles & Annex 1

Rebecca Stanbrook and Gabriele Schwarz joined the previous panellists in the Q&A session.

Questions collected from participants were then discussed and gave rise to the following points:

- Remote consenting: Rob Camp indicated that there is no one-size-fits-all approach as some patients are happy to go to the hospital often for comfort and support, while others prefer staying at home as much as possible; and there is no clear distinction between older and younger patients, as long as all the necessary information is available and clear. Pirkko Lepola outlined the importance of the adequacy of the technology used, as well as the confirmation of understanding. Re-consenting when reaching the age of adulthood and summary of the results were also briefly touched upon.
- Education of patients on GCP: Rob Camp confirmed that involving patients in the revision and implementation of the guideline would be appreciated. Gabriele Schwarz noted that the inclusion of patient perspective in the development was included as a dedicated sub-section in ICH E8 and therefore these considerations were not repeated in ICH E6(R3). Pirkko Lepola recommended the inclusion of a cross-reference to ICH E8 in the ICH E6(R3) document.
- Lay summary of results: Rebecca Stanbrook confirmed that the intent of the new language in the guideline is to encourage sponsors provide summaries of the results in understandable language to the participants should the participant request their results.
- Education of investigator personnel on GCP: Piotr Szymański stated that a risk-based approach should be used and that appropriate measures should be undertaken to reduce opportunities for over-interpretation. Fergus Sweeney confirmed that the change in mindset should encompass all stakeholders; kick-off meetings could be used to train site personnel. It was also outlined that a good protocol is essential. In the longer term, teaching in medical school, updates to the curriculum of medical professionals and publications in scientific journals could be other training opportunities. In all cases, it was agreed that training would need to be concise due to the limited time that the personnel have. Gunilla Andrew-Nielsen then discussed the stakeholders' view of burden coming from complying with GCP. It was emphasised that in general ICH E8 and E6 should be read together by researchers, E8 first, and that those groups publishing E6 in booklet form should consider including ICH E8(R1) as the first half of such booklets.
- Investigator sites and trial participant's homes: Gabriele Schwarz clarified that the definition of an investigator site in the context of a decentralised trial is being discussed (during the drafting of annex 2). If significant parts of the trial are conducted at a trial participant's home, then the supervision of these activities at the trial participant's home remains under the responsibility of the investigator and the participants' home falls within in the definition of investigator site.
- Service provider: Rebecca Stanbrook clarified that this term is meant as an extension of the sponsor when the service provider is contracted by the sponsor, and as an extension of the investigator when the service provider is contracted by the investigator. Gabriele Schwarz added that it also depends on the related task, as service providers may be contracted by a sponsor to undertake investigator's tasks, with due regard to EMA GCP Q&A No. B.11.
- ICH E6(R3) approach: Piotr Szymański confirmed that publishing first principles then Annex 1 was the appropriate road to take and emphasized that Annex-1 should be a supporting document to the Principles and that Good Clinical Practice should be understood as approaches that satisfy the principles. Rebecca Stanbrook added that the training material should provide operational advice.

Peter Twomey then wrapped up the discussion, highlighting the importance of the patient's perspective which is at the core of this regulatory work. Rebecca Stanbrook highlighted the importance of thoughtful design to clinical trials, including ensuring appropriateness of endpoints, proportionate approaches and collecting input from participants and healthcare professionals. Rob Camp added that training would also be necessary on the patient's side to make sure they are able to contribute to review of the necessary documents. It was noted that additional questions were received on data governance and computer systems, which will be passed on to the Rapporteurs for the break-out sessions of Day 2. Peter Twomey then thanked all the panellists.

5. Presentation on Annex 2 & Q&A

Peter Twomey introduced Andrew Thomson (EMA) who then presented on the Annex 2 which is currently being developed, highlighting some of the issues discussed so far. It was noted that every region is engaged and that it will be important to keep the focus of the Annex to the challenges at hand.

Fergus Sweeney noted that trials with decentralised trials can already be run, using the principles and Annex 1, and that Annex 2 would provide some additional help when published. Gunilla Andrew-Nielsen referred to the corresponding recommendation paper, and added that from an assessor's perspective, proper arguments will need to be presented in the application to use decentralised elements.

Pirkko Lepola highlighted additional challenges for paediatric trials that will also need to be taken into consideration for decentralised clinical trials, particularly regarding data collection.

6. Closing Remarks

Marita Kailajärvi then closed the Day with the following remarks:

- The revision does not change the fundamental principles of ICH E6.
- In terms of main changes, the guidance now embraces quality by design, risk-based approach and proportionality, and aims to retain its relevance in the event of evolving technologies and specific situations such as emergency clinical trials.
- Thoughtfulness, thinking and flexibility were key words used during the day and should be considered during the entire lifecycle of the trial.
- A brief introduction to Annex 2 was presented.

Participants were reminded to submit their comments via the official channel (for EU: iche6_r3@ema.europa.eu by 26 September 2023 using this form with the appropriate categorisation of comments).

Finally, all participants were thanked for their attendance, and the registered participants were invited to attend the break-out sessions on Day 2.