Medicines & Healthcare products Regulatory Agency

MHRA Consultation on the International Council for Harmonisation (ICH) E6(R3) Good Clinical Practice (GCP) Guideline

The International Council for Harmonisation (ICH) Expert Working Group for ICH E6(R3) (EWG) has been updating the ICH E6(R2) Good Clinical Practice (GCP) guideline. The UK Medicines and Healthcare products Regulatory Agency (MHRA) represents the Pharmaceutical Inspection Co-operation Scheme (PIC/s) in the EWG.

The update is to address the application of GCP to new trial designs, technological innovations and to strengthen a proportionate risk-based approach of its application for clinical trials of medicines to support regulatory and healthcare decision making.

This was set out in the ICH Reflection paper on Renovation of Good Clinical Practice and the ICH E6(R3) Concept Paper.

A Business Plan was developed.

ICH E6(R3) will be composed of overarching principles, Annexe 1 (interventional clinical trials), Annexe 2 (additional considerations for non-traditional interventional clinical trials), Glossary and three Appendices. The overarching principles, Annexe 1, Glossary and Appendices will replace the current E6(R2). The development of Annexe 2 will commence once the principles, Annexe 1, Glossary and the three Appendices complete ICH step 1.

The draft principles of GCP have been released for transparency and common understanding in April 2021 followed by a global web conference to present progress.

ICH E6(R3) GCP Principles, Annexe 1, Glossary and the three Appendices have now reached Step 2 and are available for public consultation. These are attached here together with other information provided by ICH about the changes.

• ICH E6 (R3) Good Clinical Practice (obtained from ICH website)

(Annexe 2 is now starting to be developed by an ICH EWG subgroup and a concept paper has been agreed by the ICH Management Committee.)

The UK Medicines for Human Use (Clinical Trials) Regulations 2004 (as amended) are being updated following United Kingdom's departure from the European Union (EU) and the changes to the legislation have recently been subject to public consultation.

The Government response to the consultation on legislative proposals for clinical trials confirms that the principles of GCP, as set out in ICH E6(R3) section II will replace the current GCP principles in the UK legislation that are based on outdated EU legislation. Therefore, as stated in the Government response section 3.7, compliance with the ICH E6(R3) GCP Principles and not the entirety of the guideline will become a legal requirement in the UK.

The response can be found here: Government response to consultation on legislative proposals for clinical trials - GOV.UK (www.gov.uk). This response also covers the proposal for a new notification scheme for low interventional clinical trials.

As the UK sovereign medicines regulator following the UK departure from the EU, the MHRA became a full member of ICH in May 2022. Whilst feedback on the ICH E6(R3) can be provided via the ICH website, MHRA wishes to consult directly with UK stakeholders to compile and co-ordinate their comments to the ICH E6(R3) EWG. The period of consultation will end on 31 August 2023.

Before beginning the survey, please download and complete the MHRA spreadsheet for comments. You can use this to leave specific line by line comments on the guideline document. **This is a required part of the survey.** The spreadsheet can also collect general comments by entering the line reference “0” as per the instructions in the spreadsheet if you have no specific comments to make on particular line numbers in the guideline document.

When completing the spreadsheet, we strongly encourage you to consider the following when drafting your comments:

- Prioritizing or highlighting key comments.
- Correlating your comment with the corresponding line number of the draft guideline to make it easier for us to identify relevant text.
- Providing justification and any relevant examples to support suggested changes.
- Consolidating comments from the same organisation, if appropriate.

We are requesting inputs across all topics addressed in this draft guideline, but please focus on key issues and consider providing insights on:

- Areas that may need additional clarity or language that may be susceptible to misunderstanding.
- Areas that may not accommodate technological innovations and design elements that are being explored to make clinical trials more efficient (we welcome examples to help inform us).
- Training components that should be included to make global GCP training useful as the EWG is planning to develop training materials for ICH E6(R3).

You will be asked to re-upload the spreadsheet at the end of the survey.

Make sure to add your respondent ID to the spreadsheet:

If you would like to leave this survey and return after adding comments to the spreadsheet please feel free to do so. You may wish to bookmark this page. To help with your preparations for this survey, you can find a list of questions covered in the survey here.

About you

1. Which best applies to you?

- ○ I am responding on behalf of an organisation
- ○ I am responding as an individual

About You

2. Do you live in the United Kingdom?

- ○ Yes
- ○ No

3. What is your previous experience(s) with Clinical Trials of medicines (tick all that apply)

- ○ Clinical trial participant/carer of clinical trial participant
- ○ Investigator
- ○ Researcher/health care professional involved in clinical trial conduct
- ○ Sponsor employee involved in clinical trial activities
- ○ Service provider employee involved in clinical trial activities
- ○ Employee of funder
- ○ Employee of governance bodies e.g. regulator, HRA, REC etc.
- ○ Consultant/freelance involved in clinical trial activities
- ○ No experience
- ○ Other

4. Is your organisation involved in trials conducted in the United Kingdom?

- ○ Yes
- ○ No

5. Name of organisation for which you are responding

6. Type of Organisation

- ○ Central NHS organisation
- ○ Charity/Society/Not for profit/Network including CT funding and sponsorship
- ○ Disease specific charity/Society/Not for profit/Network including CT funding and sponsorship
- ○ Contract Research Organisation (for clinical trial operations)
- ○ Site Management Organisation/Investigator Site Service Provider
- ○ Non-Commercial Clinical Trials Unit
- ○ Organisation involved in Governance/Research Ethics/Good Research/Promotion/Transparency etc. (e.g. HRA, REC etc.)

- ( ) NHS Trust (hosting clinical trial investigator sites or other clinical trial activities)
- ( ) NHS Trust (non-commercial Sponsor)
- ( ) Pharmaceutical/Biotechnology Company (commercial sponsor)
- ( ) Phase 1 Unit
- ( ) eSYSTEM Vendor/Service Provider
- ( ) IMP Manufacturer/Distributor
- ( ) Trade/Professional Association/Society for Organisational Membership
- ( ) Commercial Investigator Site Organisation (excluding Phase 1)
- ( ) Consultant/Freelancer for Clinical Trial Activities of sponsors
- ( ) Non-Commercial Clinical Research Facility
- ( ) Trade Union/Professional Association/Society for Individual Membership
- ( ) University (non-commercial sponsor)
- ( ) University (hosting clinical trial investigator sites or other clinical trial activities)
- ( ) Other

GCP guideline related questions

7. The E6(R3) Principles and Annexe 1 guideline further advance the concept of a proportionate, risk-based approach to the design and conduct of clinical trials. Do you agree or disagree?

- Agree
- Disagree
- Uncertain

Please add any comments you may have about this question in the spreadsheet as a general comment using line reference “0”

8. The E6(R3) Principles and Annexe 1 guideline encourage relevant parties to utilise a proportionate, risk-based approach and focus on the protection of clinical trial participants and the reliability of the trial results. Do you agree or disagree?

- Agree
- Disagree
- Uncertain

Please add any comments you may have about this question in the spreadsheet as a general comment using line reference “0”

9. The E6(R3) Principles and Annexe 1 guideline conveys that the implementation of GCP principles should be a thoughtful, deliberative, and risk-based process (as clinical trials can vary greatly and certain aspects of GCP may not be applicable to every trial). Do you agree or disagree?

- Agree
- Disagree
- Uncertain

Please add any comments you may have about this question in the spreadsheet as a general comment using line reference “0”

10. The E6(R3) Principles and Annexe 1 guideline highlights that achieving compliance with GCP principles can be accomplished using multiple tools and methods? Do you agree or disagree?

- Agree
- Disagree
- Uncertain

Please add any comments you may have about this question in the spreadsheet as a general comment using line reference “0”

GCP guideline related questions

11. The E6(R3) Principles and Annexe 1 guideline, in particular the inclusion of the new section on Data Governance, flexibly addresses the requirements of the increased use of technology in clinical trials, for example validity of electronic systems, data sources and data integrity. Do you agree or disagree?

- Agree
- Disagree
- Uncertain

Please add any comments you may have about this question in the spreadsheet as a general comment using line reference “0”

12. The E6(R3) Principles and Annexe 1 guideline, in particular Appendix C, concerning essential records, allows a more thoughtful, flexible and proportionate approach to the collection and retention of essential records. Do you agree or disagree?

- Agree
- Disagree
- Uncertain

Please add any comments you may have about this question in the spreadsheet as a general comment using line reference “0”

13. The E6(R3) Principles and Annexe 1 guideline flexibly addresses innovations and complexities in investigator sites, test facilities or service provider activities in trial designs. Do you agree or disagree?

- Agree
- Disagree
- Uncertain

Please add any comments you may have about this question in the spreadsheet as a general comment using line reference “0”

14. The E6(R3) Principles can be successfully and proportionately applied to all clinical trials of medicines that require a clinical trial authorisation (or notification of low interventional trials as per the consultation on legislative proposals for clinical trials) from the MHRA. Do you agree or disagree?

- Agree
- Disagree
- Uncertain

Please provide any further comments you may have on the previous question

Comments on the document

15. Please upload the excel spreadsheet with your or your organisations comments on the document. Please make sure your respondent ID has been inserted into the spreadsheet. As a reminder, your respondent ID is:

Upload a file

Choose File No file chosen

Satisfaction survey - give feedback on participating

16. It was easy to participate in this opportunity

- Strongly agree
- Agree
- Neither agree or disagree
- Disagree
- Strongly disagree

17. The supporting information was understandable

- Strongly agree
- Agree
- Neither agree or disagree
- Disagree
- Strongly disagree

18. What could we do better?

Thank you for your time in completing this consultation.

Complete this survey again