ICH GUIDANCE FOR CLINICAL TRIALS

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Session 4: Practicalities on Innovative Clinical Trials

Cancer Drug Development Forum

Amsterdam

19 September 2023

- Views expressed are those of the speaker only. They are not intended to present the views of EMA or ICH or other parties with whom the speaker may have worked previously.
- Speaker has no conflict of interest and is retired.

The benefits of properly powered (large scale) RCTs

- Too many trials are small, underpowered and poorly designed.
- Fewer, well designed, properly powered trials, run multinationally would deliver better information for regulatory and healthcare decision making
- In rarer diseases, sites over multiple countries are often needed to enable sufficient participant numbers

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International coordination needed to encourage conduct of large, decision-relevant COVID-19 clinical trials

Share

Press release 15/05/2020

Regulators are highlighting the need for a comprehensive international coordination mechanism to allow the conduct of adequately powered, randomised controlled trials, which can generate sound evidence on the effects of therapeutics or vaccines against COVID-19. This follows a call made by EMA's Human Medicines Committee (CHMP) for the research community to pool resources into large, well-designed, multi-arm clinical trials to determine which investigational or repurposed medicines would be safe and effective for the treatment or prevention of COVID-19.

Although the scientific community has responded to the COVID-19 challenge in an unprecedented manner, there are concerns about the growing number of COVID-19 stand-alone clinical trials with a small number of participants and observational studies, which might not generate the data required for regulatory decision-making.

Too many CTs are mono-national or in few MS

Commercial sponsor: average 3.1 MS per trial
Non-commercial sponsor: Average 1.2 MS per trial

Clinical Pharmacology & Therapeutics

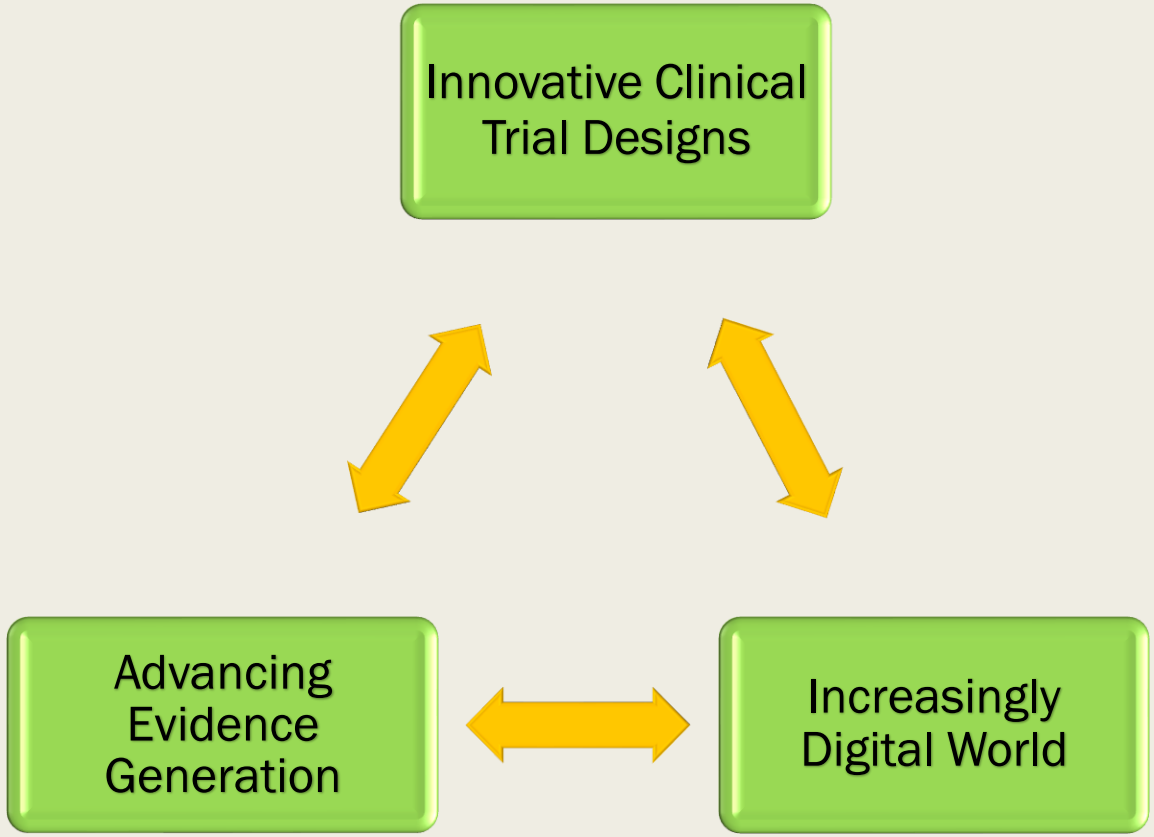
REVIEW | Open Access

Clinical trials for Covid-19: can we better use the short window of opportunity?

Hans-Georg Eichler, Marco Cavaleri, Harald Enzmann, Francesca Scotti, Bruno Sepodes, Fergus Sweeney, Spiros Vamvakas, Guido Rasi

First published:14 May 2020 | https://doi.org/10.1002/cpt.1891

Redesign our approach to enable innovation in a Rapidly Evolving Ecosystem



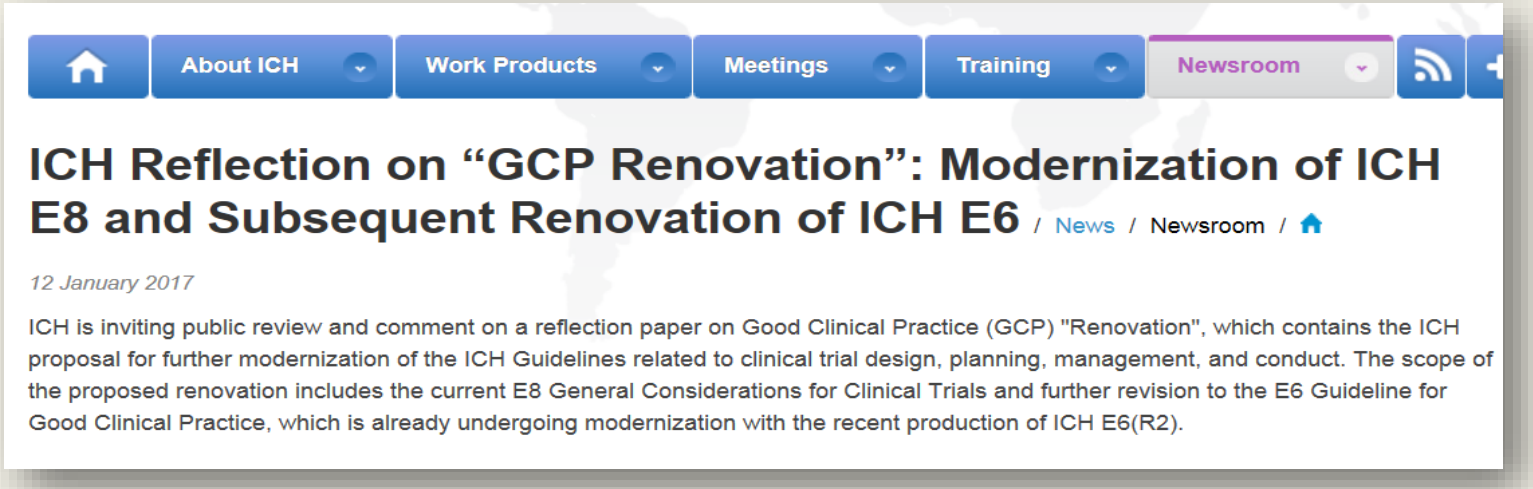
Set the foundations to enable innovation by design and not by reaction:

- the foundation for future
  - medicines,
  - trial designs,
  - technologies,
  - data sources

Stakeholder involvement is essential, informative and enriching

– it will lead to better guidance and better clinical trial designs, with better implementation of the processes and greatly improved results

GCP Renovation: revising how we design and conduct clinical trials



- ICH E8 (R1) General considerations on clinical studies
- ICH E6 (R3) Good Clinical Practice
- Establish a quality continuum through design and conduct,
- Should be read together,
- Design that involves engagement with stakeholders including participants/patients and investigators.

ICH Clinical Trial Guidance Renovation

- The purpose of clinical trials is to generate information to support decision making - their quality must be sufficient to protect participants and generate results that support good decision making
- Focus resources and efforts on what matters most for participant protection and the reliability of trial results – critical to quality factors
- Proportionate management of the risks and controls
- Focus on the intent and goal of GCP, and allow for the many ways these can be achieve

This is about doing things differently – change – We should not just add more to the status quo

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

1 December 2022
EMA/CHMP/ICH/544570/1998 Corr*
Committee for Human Medicinal Products

ICH guideline E8 (R1) on general considerations for clinical studies

Step 5

Transmission to CHMP	25 April 2019
Adoption by CHMP	25 April 2019
Release for public consultation	10 May 2019
Deadline for comments	30 September 2019
Final adoption by CHMP	14 October 2021
Date for coming into effect	14 April 2022

E8 (R1) General Considerations for Clinical Studies Final October 2021

Overview

General Principles

Quality by Design &
Critical to Quality Factors

Drug development planning

Study design, conduct & reporting

Critical to Quality Factor examples

Annex – Study Types

2 GENERAL PRINCIPLES

2.1 Protection of Clinical Study Participants

- "..principles of ethical conduct ..protection of participants, ..origins in the Declaration of Helsinki...all human clinical investigations."

2.2 Scientific Approach in Clinical Study Design, Planning, Conduct, Analysis, and Reporting

- "Quality of a clinical study is .... fitness for purpose."
- "Purpose ... generate reliable information to answer the research questions and support decision making ..quality ....sufficient to support good decision making. "
- "Quality by design .. quality of a study is driven proactively by designing quality into the study protocol and processes... "

2.3 Patient Input into Drug Development

- "Consulting with patients / patient organisations during drug development can help to ensure that patients' perspectives are captured. "
- "Involving patients early in the design of a ..to increase trust in the study, facilitate recruitment, and promote adherence."
- "..provide their perspective of living with a condition, .. supports the development of drugs ...better tailored to patients' needs."

Section 3.3 Approach to Identifying the Critical to Quality Factors

3.3.1 Establishing a Culture that Supports Open Dialogue:

*".. values and **rewards critical thinking and open dialogue** about quality ..**beyond sole reliance on tools and checklists.**"*

3.3.2 Focusing on Activities Essential to the Study:

*".. **essential to the reliability and meaningfulness** of study outcomes for patients…safe, ethical conduct. Consider whether nonessential activities may be eliminated…to simplify conduct…improve efficiency…target critical areas."*

3.3.3 Engaging Stakeholders in Study Design:

*"..**best informed by input from a broad range** of stakeholders, including patients and treating physicians. .. "*

3.3.4 Reviewing Critical to Quality Factors:

"Build on accumulated experience and knowledge with periodic review …"

25 May 2023
EMA/CHMP/ICH/135/1995
Committee for Human Medicinal Products

ICH E6 (R3) Guideline on good clinical practice (GCP)

Step 2b

Transmission to CHMP	25 May 2023
Adoption by CHMP	25 May 2023
Release for public consultation	26 May 2023
Deadline for comments	26 September 2023

Comments should be provided using this template. The completed comments form should be sent to iche6_r3@ema.europa.eu

ICH E6 GCP Principles – headings 1/2

1. Clinical trials should be conducted in accordance with the **ethical principles that have their origin in the Declaration of Helsinki** and that are consistent with GCP and applicable regulatory requirement(s). Clinical trials should be **designed and conducted in ways that ensure the rights, safety and well-being of participants**.

2. **Informed consent is an integral feature of the ethical conduct of a trial.** Clinical trial participation should be voluntary and based on a consent process that ensures participants (or their legally acceptable representatives, where applicable) are well-informed.

3. Clinical trials should be subject to an **independent review by an institutional review board/independent ethics committee (IRB/IEC).**

4. Clinical trials should be **scientifically sound for their intended purpose** and based on robust and current scientific knowledge and approaches.

5. Clinical trials should be **designed and conducted by qualified individuals**.

ICH E6 GCP Principles – headings 2/2

6. Quality should be built into the scientific and operational design and conduct of clinical trials.

7. Clinical trial processes, measures and approaches should be implemented in a way that is proportionate to the risks to participants and to the importance of the data collected.

8. Clinical trials should be described in a clear, concise and operationally feasible protocol.

9. Clinical trials should generate reliable results.

10. Roles and responsibilities in clinical trials should be clear and documented appropriately.

11. Investigational products used in a clinical trial should be manufactured in accordance with applicable Good Manufacturing Practice (GMP) standards and be stored, shipped, handled and disposed of in accordance with the product specifications and the trial protocol.

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ICH E6 GCP – Annex 1

1. INSTITUTIONAL REVIEW BOARD/INDEPENDENT ETHICS COMMITTEE (IRB/IEC)
2. INVESTIGATOR
3. SPONSOR
4. DATA GOVERNANCE – INVESTIGATOR AND SPONSOR

GLOSSARY

Appendix A. INVESTIGATOR'S BROCHURE

Appendix B. CLINICAL TRIAL PROTOCOL AND PROTOCOL AMENDMENT(S)

Appendix C. ESSENTIAL RECORDS FOR THE CONDUCT OF A CLINICAL TRIAL

ANNEX 2 Drafting has started– public consultation may be in late 2024 – watch out for it and be sure to engage and respond

Importance of Clinical Trials Sponsored and run by Academia/public health bodies

- Cancer treatment requires basic research much of it conducted by academia and publicly funded to generate new therapeutic approaches
- Much of cancer therapy is a product of incremental research by academia on treatment protocols
- Academic trials often combine established or new products in comparisons of effectiveness and in exploring new approaches
- Pharmaceutical industry essentially conducts those trials needed to get a new product authorized, or to update labelling. Often the basic research that opened these paths comes from public bodies
- Academic research must be enabled, it is struggling. It has different approaches, priorities and structures and resource (much more constrained), compared to industry.
- Public health, scientific advancement and improvement in therapy of cancer rely on that research. It is essential that it is nurtured and enabled.

ICH GCP Renovation – very welcome

- Enable and facilitate good clinical trials. Focus on the intent and goal of GCP and allow for the many ways these can be achieved.
- Proportionate, efficient approaches – design and resource focussed on what matters most.
- The GCP Principles contain the essential reference for trial conduct
- GCP Principles widely applicable for trials of medicines, the detailed guidelines are, in all their scope, applicable to trials conducted to support marketing authorisation.
- Needs to be made clear - providing European academic/public interest trials with a level playing field with other regions and countries in which Annex 1 detailed guidance is not applied to academic research.
- Academia need to engage with this public consultation, submit written comments – 26 Sep 2023.
- Pay particular attention to potential for unintended consequences.

Accelerating Clinical Trials in the EU (ACT EU)

Joint initiative by European Commission, HMA, EMA

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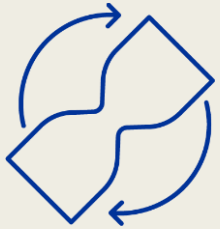
ACT EU Multi-stakeholder platform (MSP)

- Enabling collaboration of all stakeholders for better clinical trials
- Kick-off workshop on 22-23 June 2023
- MSP concept paper published
- Establishment of a MSP Advisory Group by end 2024;
  call for expressions of interest upcoming in October 2023

ACT EU activities on Good Clinical Practice



- Workshop on ICH E6 R3 - Public Consultation on 13-14 June 2023
- Possible follow-up workshop in 2024 on E6(R3)
- Work on mapping EU guidance and impact analysis on current environment
- Communication and change management to support adoption and implementation of the revised guideline

Accelerating Clinical Trials in the EU (ACT EU)

Joint initiative by European Commission, HMA, EMA

ACT EU aims to improve the EU clinical trials environment through:

- Delivery of decisional evidence for unmet medical needs;
- Excellent scientific advice for medicines to reach the market.

Opportunities for oncology research e.g., participation in pilots, consultations, activities under the multi-stakeholder platform.

ACT EU website: https://accelerating-clinical-trials.europa.eu/index_en

Everyone involved in the conduct of clinical trials should read and understand these guidelines. Read them together ICH E8 then ICH E6.

Change the way we all work – don't add more to the status quo.

Change Management is the greatest challenge – every party involved needs to change their approach

– adjusting behaviors, attitudes – away from preconceived ideas and interests – and on to a new, better, way of working.

- "Perfection is achieved not when there is nothing more to add but when there is nothing left to take away" *Antoine de Saint-Exupéry*
- "Everything should be made as simple as possible but not simpler" *Albert Einstein*

Thank you – any questions?

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