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ICH E8(R1)

Webinar

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Objectives

- C** To provide an overview of the contents of ICH E8(R1).
- 🔧** To Discuss the implications of the changes.
- ⚠️** To provide an update on the status of E6(R3).

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Agenda

- ICH Overview
- ICH E8
 - Structure
 - Contents
- Quality by Design
- Critical to Quality Factors
- Update on E6(R3)

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- International Council on Harmonisation
- US, EU and Japan
- Purpose:
 - Harmonise marketing authorisation requirements
 - Reduce timelines and cost
 - Reduce subject exposure to investigational products


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 **GCP renovation** JoBurmester.com
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- Public Consultation – meetings 2019 and 2020




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- 1 Objectives of this document
- 2 General Principles
- 3 Designing Quality into Clinical Studies
- 4 Drug Development Planning
- 5 Design Elements and Data Sources for Clinical Studies
- 6 Conduct, Safety Monitoring and Reporting
- 7 Considerations in Identifying Critical to Quality Factors
- Annex – Types of Clinical Studies


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 **1. Objectives** JoBurmester.com
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“This document provides guidance on the clinical development lifecycle, including designing quality into clinical studies, considering the broad range of clinical study designs and data sources used.”


-  International principles
-  Quality by Design
-  Types of studies
-  Guide to ICH Efficacy documents

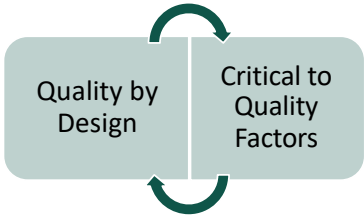
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 **2. General Principles** JoBurmester.com
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- Protection of participants
- Scientific approach (QbD)
 - Design
 - Planning
 - Conduct
 - Analysis
 - Reporting
- Patient input into drug development


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 **3. Designing Quality into Clinical Trials** JoBurmester.com
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Quality by Design Critical to Quality Factors

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4. Drug Development Planning




Quality of IMP 

Non-Clinical studies 

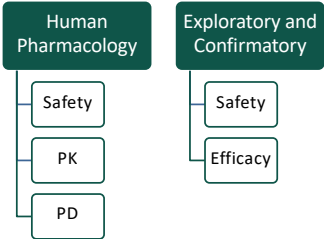
Clinical Studies 

Additional Development 

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4.3 Clinical Studies




Human Pharmacology

- Safety
- PK
- PD

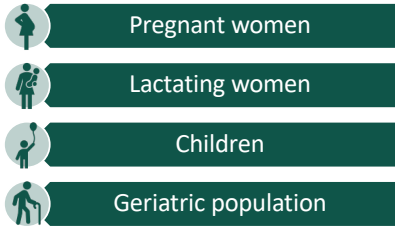
Exploratory and Confirmatory





- Safety
- Efficacy

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Special Populations



-  Pregnant women
-  Lactating women
-  Children
-  Geriatric population

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5. Design Elements and Data Sources


Quality by Design

- Objectives
- Participants
- Minimising bias
- Endpoints

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5.1 Study Population



- Chosen to meet objectives
- Appropriately representative
- Sample size

Feasibility


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5.2 Treatment Description



- Described explicitly and specifically
- Including controls
- Aligned to objectives –
e.g. background treatment

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5.3 Choice of Control Group

- May be:
 - placebo
 - no treatment
 - standard of care
 - other treatments
 - different doses
- Internal or external?



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What factors influence choice of control?

Discussion

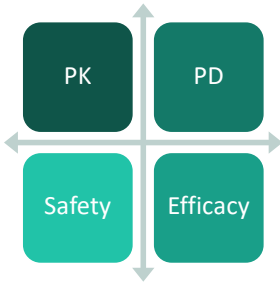


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5.4 Response Variables

- Attribute of interest
 - Primary endpoint – clinically relevant
 - Secondary endpoint – supportive
 - Exploratory endpoints




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5.5 Methods to reduce bias

- Randomisation
- Blinding
- Care with:
 - Interim analysis
 - Observational studies


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5.6 Statistical Analysis

Specified in protocol
Define estimand(s) (ICH E9)
Primary and secondary endpoints
Sensitivity analyses
SAP before unblinding
Deviations from SAP indicated in CSR


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5.7 Study Data

- Primary – generated specifically
- Secondary – obtained from external sources
- Data protection
- Data quality (ALCOA++)


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6. Conduct, Safety Monitoring and Reporting

Conduct	Safety	Reporting
<ul style="list-style-type: none">• Protocol adherence• Training• Data Management• Interim data access	<ul style="list-style-type: none">• Safety monitoring• Withdrawal criteria• DMC	<ul style="list-style-type: none">• ICH E3• Factual summary• Info for participants and PIs• Transparency

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7. Identifying CtQ factors


- Long list of considerations
- Covered in everything above!

“proactive, cross- functional discussions and decision making at the time of study planning”

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Annex – types of clinical studies



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graph TD; A[Human pharmacology] --> B[Exploratory]; B --> C[Confirmatory]; C --> D[Post-Approval];
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ICH E6: An Important Global Standard

Conceptual Representation of the Approach to ICH E6(R3)

Overarching Principles that Apply across the Board

Annex-1
Reflects the concepts in E6(R2) (with updates and refinements as needed)

Annex-2
Additional considerations for non-traditional interventional clinical trials not addressed in Annex-1

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ICH E6(R3) – future

- Step 2 (draft for public consultation) end 2022
- Step 4 (final version) for Principles and Annex 1 Aug 2023
- Annex 2 - ???

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Thank you for coming!

- Certificates
- Feedback forms
- Post-course resources

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