GCP Updates

14th December 2021

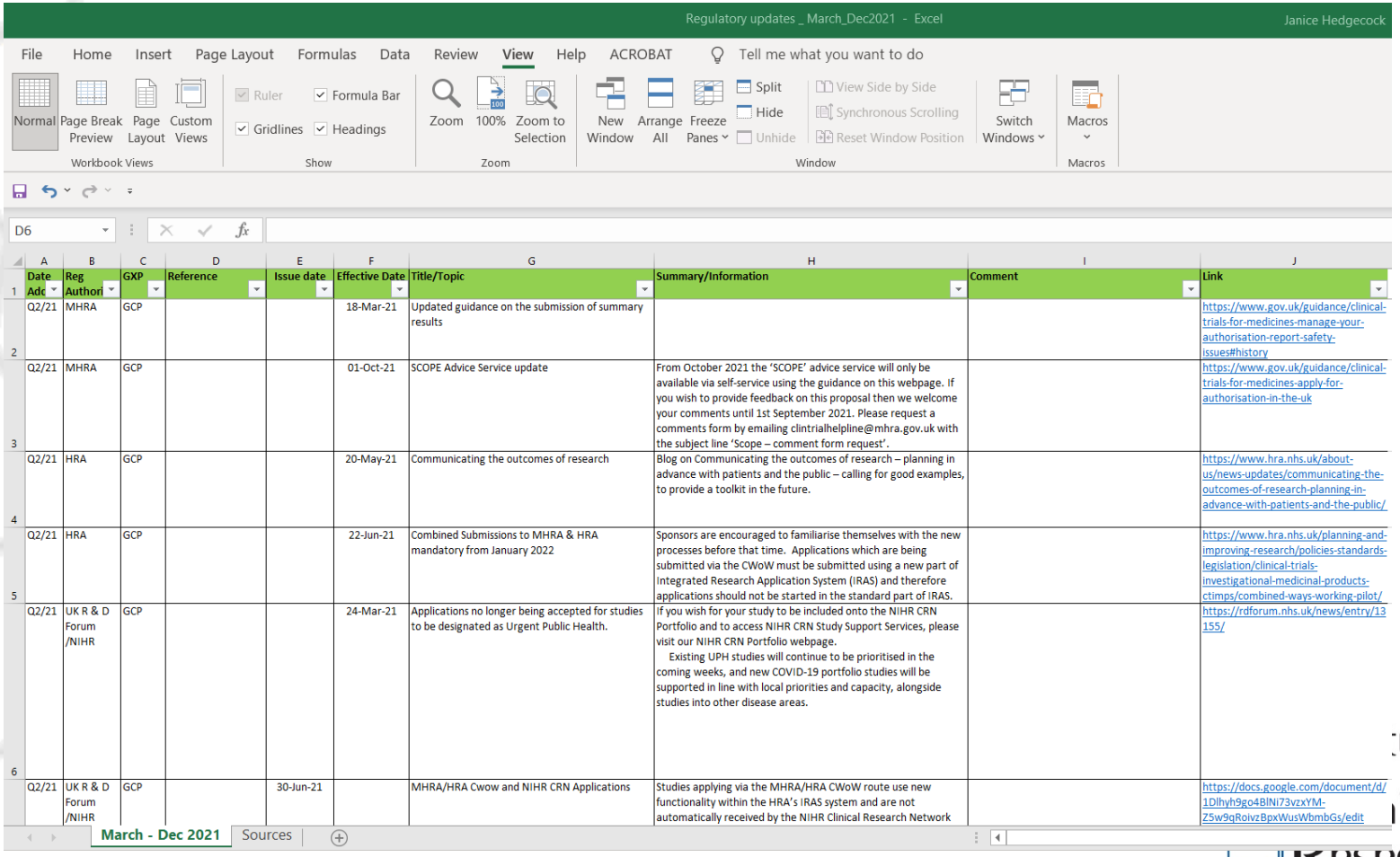
The Institute of Clinical Research

GCP Updates - Agenda

- ICH
- UK
- Europe
- USA

GCP Updates – Supplementary list of updates March - Dec

- Available for download with the presentation slides



	A	B	C	D	E	F	G	H	I	J
1	Date Adc	Reg Authori	GXP	Reference	Issue date	Effective Date	Title/Topic	Summary/Information	Comment	Link
2	Q2/21	MHRA	GCP			18-Mar-21	Updated guidance on the submission of summary results			https://www.gov.uk/guidance/clinical-trials-for-medicines-manage-your-authorisation-report-safety-issues#history
3	Q2/21	MHRA	GCP			01-Oct-21	SCOPE Advice Service update	From October 2021 the 'SCOPE' advice service will only be available via self-service using the guidance on this webpage. If you wish to provide feedback on this proposal then we welcome your comments until 1st September 2021. Please request a comments form by emailing clintrialhelpline@mhra.gov.uk with the subject line 'Scope – comment form request'.		https://www.gov.uk/guidance/clinical-trials-for-medicines-apply-for-authorisation-in-the-uk
4	Q2/21	HRA	GCP			20-May-21	Communicating the outcomes of research	Blog on Communicating the outcomes of research – planning in advance with patients and the public – calling for good examples, to provide a toolkit in the future.		https://www.hra.nhs.uk/about-us/news-updates/communicating-the-outcomes-of-research-planning-in-advance-with-patients-and-the-public/
5	Q2/21	HRA	GCP			22-Jun-21	Combined Submissions to MHRA & HRA mandatory from January 2022	Sponsors are encouraged to familiarise themselves with the new processes before that time. Applications which are being submitted via the CWoW must be submitted using a new part of Integrated Research Application System (IRAS) and therefore applications should not be started in the standard part of IRAS.		https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/clinical-trials-investigational-medicinal-products-ctimps/combined-ways-working-pilot/
6	Q2/21	UK R & D Forum /NIHR	GCP			24-Mar-21	Applications no longer being accepted for studies to be designated as Urgent Public Health.	If you wish for your study to be included onto the NIHR CRN Portfolio and to access NIHR CRN Study Support Services, please visit our NIHR CRN Portfolio webpage. Existing UPH studies will continue to be prioritised in the coming weeks, and new COVID-19 portfolio studies will be supported in line with local priorities and capacity, alongside studies into other disease areas.		https://rdforum.nhs.uk/news/entry/13155/
	Q2/21	UK R & D Forum /NIHR	GCP		30-Jun-21		MHRA/HRA Cwow and NIHR CRN Applications	Studies applying via the MHRA/HRA CWoW route use new functionality within the HRA's IRAS system and are not automatically received by the NIHR Clinical Research Network		https://docs.google.com/document/d/1Dlhyh9go4BINi73vzxYM-Z5w9qRoivzBpxWusWbmbGs/edit

ICH: E8R1
General Considerations for Clinical Studies

First revision since 1997

- Overall introduction to clinical development
- Describes and provides guidance on:
  - Internationally accepted principles and practices
  - Quality in the design and conduct of clinical studies
    - Identification of factors critical to quality of study
    - Management of risks to critical factors
  - Overview of study types, study design elements re.
    - Factors critical to quality
    - Protection of patients
    - Data integrity and reliability f results
    - Ability of studies to meet their objectives
- Adopted: 6 Oct 2021
- Effective: 6 Apr 2022
- https://www.ich.org/page/efficacy-guidelines#8-1

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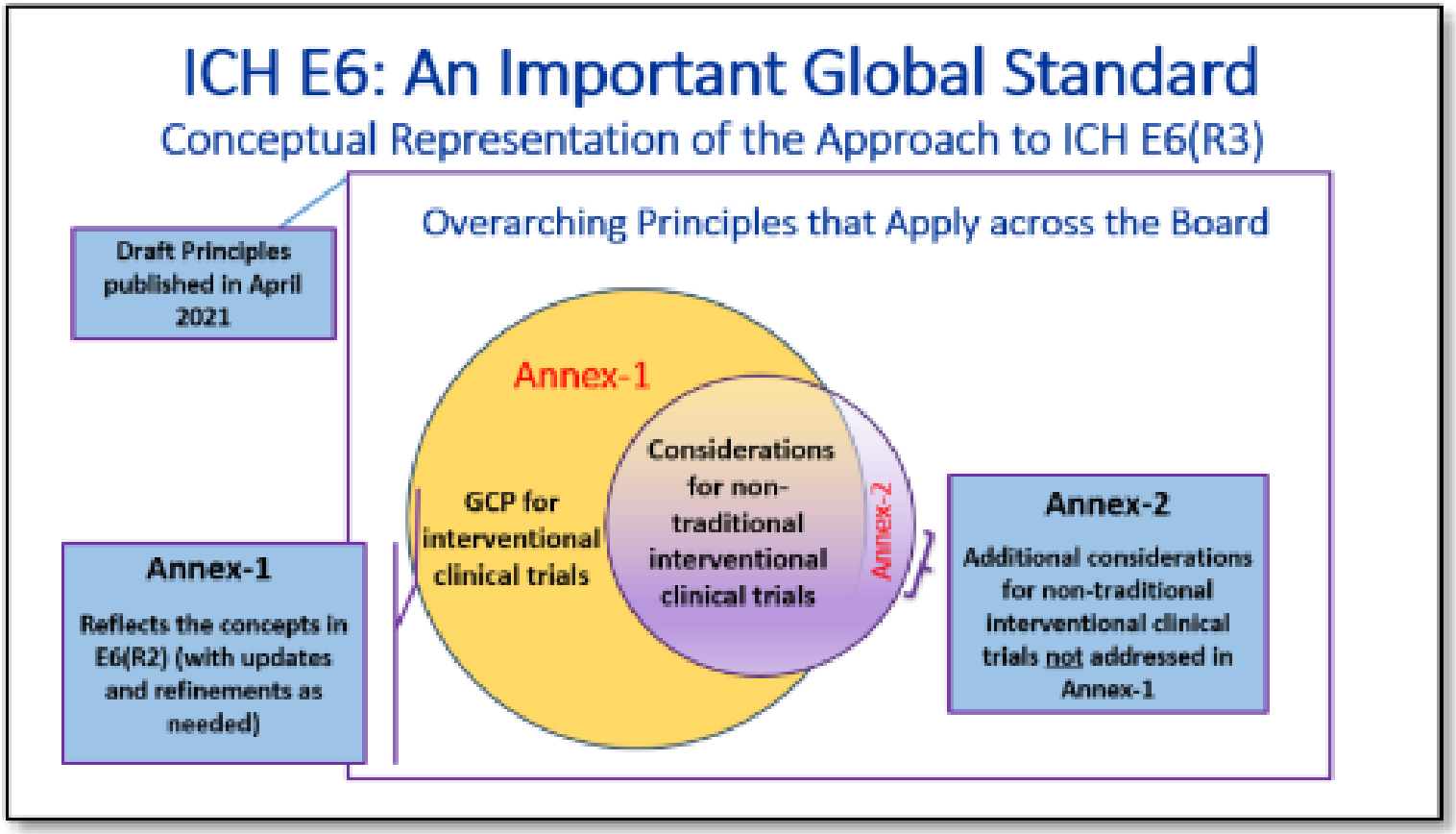
ICH: E6R3 Revision
Web Conference Report



https://www.ich.org/page/efficacy-guidelines

Diagram extracted from ICH E6R3 Web Conference Report

ICH: E6R3
Draft Principles Available for download

- 12 Principles
- 42 clarifying statements to the 12 principles

- Proposed time frames:
- 19 April 2021: Principles published
- Oct 2022: Public Consultation of Principles and Annex I
- March 2023: Begin draft of Annex 2
- August 2023: Planned Adoption of Principles and Annex I
- No time frame published yet for consultation or adoption of Annex 2

- https://www.ich.org/page/efficacy-guidelines

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ABPI

- Code of Practice for the Pharmaceutical Industry Updated July 2021
- Clinical research in the UK: an opportunity for growth

MHRA - Selected Updates

- Clinical trial summary results – Updated guidance
- DSURs: Added guidance on how to increase transparency when presenting safety information in the DSUR
- Managing clinical trials during Coronavirus (COVID-19): updated guidance for remote monitoring for trials
- Reference Safety Information – updated guidance

MHRA/HRA Guidance: Access to Electronic Health Records

- Changing methods of access to medical records for monitoring
- If system cannot restrict access only to specific trial participant records
  - Printouts are not an appropriate safeguard
  - Organisation level Risk Assessment required
  - Mitigating steps required (examples given, including contractual obligations)
  - Examples of inspection findings provided
  - Processes for direct remote access by log-in are discussed
  - Use of internet sharing portals require complete, certified copies
  - Consent considerations
  - System functionality and security considerations
  - Section on Sponsor-implemented controls
- Published Nov 2020. Remote access guidance added Sept 2021
- https://www.gov.uk/guidance/on-site-access-to-electronic-health-records-by-sponsor-representatives-in-clinical-trials

HRA – Selected Updates

- Combined review for all CTIMPs from 1 January 2022
- Make research transparency the norm
- Multi-agency advisory service for developers and adopters of artificial intelligence (AI) (Blog)
- Changes in Radiation Assurance
- Think Ethics
- Transparency partnership
- Parkinson's UK interactive web-based communications toolkit

NIHR CRN Support

English-led CTIMPs Applying via HRA/MHRA Combined Review

English-led studies that do not need HRA Approval in IRAS

- Apply for CRN support through the new Non-Commercial Portfolio Application Service in CPMS

Studies requiring HRA approval but not processed via combined review

- Select 'yes' to question 5b of the IRAS Project Filter
- Key information will automatically be shared with NIHR
- Eligibility will be confirmed by email

If unable to apply via either of these routes, contact your Local CRN for advice on how to proceed

- https://www.nihr.ac.uk/researchers/collaborations-services-and-support-for-your-research/run-your-study/crn-portfolio.htm

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Europe
Clinical Trials Regulation (EU) No 536/2014

31 January 2022

- CTR Comes into application
- Go-live of the Clinical Trials Information System (CTIS)
- Dedicated webpage on CTIS
- Training programme is now available
- 23 training modules

- https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trial-regulation/clinical-trials-information-system-ctis-training-programme
- https://www.ema.europa.eu/en/documents/other/guide-ctis-training-material-catalogue_en.pdf

Europe
Clinical Trials Regulation Implementation

Period 0: Before Go-Live	Period 1: First 12 months	Period 2: Next 24 Months	Period 3: From 3 years after Go-Live
• Any CTA submitted at this time, is still governed by the old Directive until 3 years after Go-Live	• A CTA may still be submitted in EudraCT and governed by the old Directive • A CTA may be submitted in the new EU portal and be governed by the new regulation	• All initial CTAs must be submitted in the new EU portal and be governed by the new regulation	• All Clinical Trials are governed by the new regulation regardless of their date of submission

Slide content courtesy of MHRA

Europe

EMA Guideline on registry-based studies

- Applies to Clinical Trials or Non-interventional studies
  - using the data collection infrastructure or the patient population of one or several patient registries
  - differences in requirements for types, structures and processing of data across existing registries
  - Guideline aims to better define study populations and design study protocols
  - Guidance on data collection, data quality management and data analysis to achieve higher quality evidence
  - includes an annex with good practices in the establishment and management of patient registries and their use
- EMA/426390/2021
- Adopted: 16 Sept 2021
- https://www.ema.europa.eu/en/guideline-registry-based-studies-0

Europe

EMA Assent/ Informed Consent Guidance for Paediatr
Clinical Trials of Medicinal Products in Europe

- Provides general guidance on contents:
  - Principles to consider
  - Case by case design
  - Tabular format to guidance providing recommendations of aspects to include for different age groups

- EMA/671028/2019
- Effective Date: 25 January 2021
- https://www.ema.europa.eu/en/documents/other/assent/informed-consent-guidance-paediatric-clinical-trials-medicinal-products-europe_en.pdf

Europe

EMA Assent/ Informed Consent Guidance for Paediatric Clinical Trials of Medicinal Products in Europe

Table 1. (Cont.): General information for informed consents and assents (agreements)

Age Group in years 0<2	2<6	6<10	10<18	Legal representative(s)	Elements to consider / Information which must be included into the assent/consent document	Questions to be addressed	NOTES and example methods / texts to be used
✖	✖	◎	✓	✓	**Explanation of the concept of a clinical trial and the methodology used.**	• What is a clinical trial? • How does the clinical trial differ from normal routine care? • What is randomisation / double-blind / open label etc.?	NOTE: **Explain only the relevant methodology – a short version - used according to the current protocol. Avoid complex terms and flowcharts with too much detail.**
✖	✓	✓	✓	✓	**Dissent / Refusal / Disagreement / Respect for autonomy** **Voluntariness / Right to refuse / Right to dissent / Free decisions**	• What is the explicit wish of the child / adolescent (capable of forming an opinion and assessing the information)? • Has the child / adolescent understood that they may refuse participation or withdraw at any time during the trial? • Is the child / adolescent's free wish / decision respected (according to the age / maturity) by the investigator / trial personnel?	NOTE: The agreement of a child should be requested systematically, even if the assent is not legally required. **Children should be provided with age-appropriate information (with supplementary visual information where appropriate) and have the opportunity to form an opinion or decision.** Their refusal or dissent should be respected, objections should be analysed (reason), and possible help sought for anticipated burden (fear, distress etc.). **Resistance of very young children should be identified, and discussed with legal representatives.**

USA
Selected Updates from FDA

- Adjusting for Covariates in Randomized Clinical Trials for Drugs and Biological Products
- COVID-19: Master Protocols Evaluating Drugs and Biological Products for Treatment or Prevention
- Sponsor Responsibilities - Safety Reporting Requirements and Safety Assessment for IND and Bioavailability/ Bioequivalence Studies
- Providing Regulatory Submissions in Alternate Electronic Format Guidance for Industry. Final Guidance.
- Nonmetastatic Castration-Resistant Prostate Cancer: Considerations for Metastasis-Free Survival Endpoint in Clinical Trials

USA
More Selected Updates from FDA

- FDA Guidance on Conduct of Clinical Trials of Medical Products During the COVID-19 Public Health Emergency (Final Guidance)
- Investigator Responsibilities – Safety Reporting for Investigational Drugs and Devices (Draft Guidance for comment)
- Data Standards for Drug and Biological Product Submissions Containing Real-World Data
- Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products Guidance for Industry

China
Selected updates from NMPA's CDE

- CDE Announcement No. 2021/52: Issuance of Technical Guidelines of Clinical Trials for Weight Management Drugs

- CDE Notification No.2020/50: Technical Guidelines for Long-term Follow-up Clinical Research of Gene Therapy Products

And Finally…..

- Next meeting – 29 March 2022
- Face to Face at UCL Cruciform Lecture Theatre, London (unless restrictions/guidance prevent Face to Face)
- Please provide feedback on today's webinar to guide the planning of future meetings
- Certificates for today's meeting will then be emailed to all attendees and presenters
- Presentations and recordings will be available to attendees - aim is within 1 week of today's meeting

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Thank You

- Thank you to all our speakers, attendees and those who asked questions
- ICR for logistical support and hosting Zoom

From:

- Ethics Forum: Joan Perou (chair)
- GCP Forum: Janice Hedgecock (outgoing chair)
  Trish Parry & Helen Buck (incoming Co-Chairs)
  Stuart Harris, Julia DeCesare,
  Helen Cadiou, Heidi Chandler,
  (committee members)

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