What's New in Clinical Development Practices & Regulations

Quarter 4 – 2022

REGULATIONS & ICH GUIDELINES

Clinical Trial Regulation (CTR) (EU) 536/2014

End of Transition Period – 31 January 2023

Sponsors who wish to start an interventional clinical trial in Europe from 31-Jan-2023 must make their applications for authorisation using the Clinical Trials Information System (CTIS) and adhere to the requirements of the Clinical Trial Regulation. The European Medicines Agency (EMA) has produced a Quick Guide and FAQ document: *CTTM23 - Quick Guide_Sponsor (europa.eu)*
and *CTTM23_FAQs (europa.eu)*

Accelerating Clinical Trials in the EU (ACT EU)

A 5-year workplan has been released for ACT EU, see Q2 and Q3 Newsletters for further information relating to ACT EU. *act-eu-multi-annual-workplan-2022-2026_en.pdf (europa.eu)*

Future Medical Device Regulations

UK's Medicines and Healthcare product Regulatory Agency (MHRA) has introduced a 12-months extension to the implementation of the upcoming Medical Device Regulations. The new Regulations will come into force by July 2024. *Implementation of the Future Regulations - GOV.UK (www.gov.uk)*

Final GMP Guidance on Manufacture of Sterile Medicinal Products

The European Commission (EC) has finalised its revision of Annex 1 to the EU Good Manufacturing Practice (GMP) guidelines. *20220825_gmp-an1_en_0.pdf (europa.eu)*

Proposal for an EU Regulation on Substances of Human Origin

The EC has published a proposed Regulation on standards of quality and safety for substances of human origin (blood, tissues and cells) for use on or in human recipients. When agreed, the Regulation will replace the current legislation for blood (Directive 2002/98/EC) and tissues and cells (Directive 2004/23/EC). *Proposal for a Regulation on substances of human origin (europa.eu)*

ICH Guidelines

E19 'A Selective Approach to Safety Data Collection in Specific Late-Stage Pre-Approval or Post-Approval Clinical Trials'

The final version was adopted 27-Sep-2022 *ICH_E19_Guideline_Step4_2022_0826_0.pdf*

S1B(R1) 'Testing for Carcinogenicity of Pharmaceuticals'

The final version (R1) has been released and comes into force 16-Mar-2023: *ICH guideline S1B(R1) on testing for carcinogenicity of pharmaceuticals Step 5 (europa.eu)*

Q5A(R2) 'Guideline on Viral Safety Variation of Biotechnology Products'

The draft guideline (R2 revision) reached *step 2* of the approval process on 29-Sep-2022. *ICH Official web site: ICH*

M11 'Clinical Electronic Structured Harmonised Protocol'

This draft version is currently under public consultation: *Microsoft Word - ICH_M11_draft_Guideline_Step2_2022_0904*

FDA GUIDELINES

Final Guidance 'General Clinical Pharmacology Considerations for Neonatal Studies for Drugs and Biological Products'

July 2022: *General Clinical Pharmacology Considerations for Neonatal Studies for Drugs and Biological Products | Guidance for Industry U.S. Department of Health and Human Services July 2022 (fda.gov)*

Final Guidance 'Cancer Clinical Trials Eligibility Criteria: Available Therapy in Non-Curative Settings'

July 2022: *Cancer Clinical Trial Eligibility Criteria: (fda.gov)*

Final Guidance Document 'Submitting Documents Using Real-World Data and Real-Word Evidence to FDA for Drug and Biological Products'

September 2022: *Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drug and Biological Products*

Final Guidance 'Multiple Endpoints in Clinical Trials'

October 2022: *Multiple Endpoints in Clinical Trials - Guidance for Industry (fda.gov)*

Final Guidance 'Human Gene Therapy for Neurodegenerative Disease'

October 2022: *Human Gene Therapy for Neurodegenerative Diseases; Guidance for Industry (fda.gov)*

Draft Guidance 'General Clinical Pharmacology Considerations for Pediatric Studies of Drugs, Including Biological Products'

September 2022: *Draft Guidance: General Clinical Pharmacology Considerations for Pediatric Studies of Drugs, Including Biological Products (fda.gov)*

Various Oncology Guidance

Final Guideline: *Guidance for Industry (fda.gov)*

Draft Guidelines: *Real-Time Oncology Review (RTOR) Guidance for Industry (fda.gov)*, *download (fda.gov)* and *download (fda.gov)*

CLINICAL TRIAL DATA - QUALITY & TRANSPARENCY

EU - Increase Access to and Quality of Clinical Trial Data

The joint Big Data Steering Group set up by the EMA and the Heads of Medicines Agency (HMA) has endorsed two draft documents for public consultation:

- Data quality framework: *data-quality-framework-eu-medicines-regulation_en.pdf (europa.eu)*
- Use of Metadata catalogue of Real-World Data: *real-world-metadata-good-practice-guide-for-public-consultation (europa.eu)*

Europe – Need for a Better Clinical Trial Transparency

A recent evaluation suggests that medical research funders in Europe could do more to accelerate science and reduce research waste and publication bias by improving clinical trial transparency.

- *Adoption of World Health Organization Best Practices in Clinical Trial Transparency Among European Medical Research Funder Policies | Global Health | JAMA Network Open | JAMA Network*
- *Joint statement on public disclosure of results from clinical trials (who.int)*

US – Failings to Report All Clinical Trial Results

The US National Institutes of Health (NIH) is responsible for ensuring clinical trials results are reported on <ClinicalTrials.gov>. A recent audit found that less than half of the trials for which results should have been posted in 2019/2020 met the federal requirements for reporting. *The National Institutes of Health Did Not Ensure That All Clinical Trial Results Were Reported in Accordance With Federal Requirements A-06-21-07000 08-12-2022 (hhs.gov)*

PATIENTS & STUDY PARTICIPANTS IN FOCUS

Patient Involvement in the Development, Regulation and Safe Use of Medicines

The Council for International Organizations of Medical Sciences (CIOMS) has issued a report describing the importance of systematically involving patients throughout a medicine's life. The report provides a comprehensive overview of the current knowledge about the benefits of patient involvement and existing initiatives. *Patient involvement in the development, regulation and safe use of medicines - CIOMS*

Using Patient Preference Information (PPI) in Medical Device Trial Design

This paper, published by the Medical Device Innovation Consortium, describes ways of using PPI when designing medical device clinical trials. *Leveraging Patient Preference Information in Medical Device Clinical Trial Design - PubMed (nih.gov)*

Patient Reported Outcomes (PROs) in Oncology Therapy

Research has shown that, amongst other things, immune checkpoint inhibitors have a favourable effect on patients' quality of life. *Association of Anticancer Immune Checkpoint Inhibitors With Patient-Reported Outcomes Assessed in Randomized Clinical Trials: A Systematic Review and Meta-analysis | Targeted and Immune Cancer Therapy | JAMA Network Open | JAMA Network*

US - Right to Try Act

The Right to Try Act provides a new pathway for study participants to request, and for manufacturers or sponsors to choose to provide, access to certain unapproved investigational drugs. *Right to Try | FDA*

US – Revised Draft Guidance 'Expanded Access to Investigational Drugs for Treatment Use: Q&As'

The final guidance document was published in June 2016 and revised in October 2017. The corresponding Q&A document has been updated: *Expanded Access to Investigational Drugs for Treatment Use: Questions and Answers | FDA*

US – Harmonising Regulations on Study Participants

The FDA has issued two new proposed rules that aim to harmonise regulations on study participants protection and institutional review boards with the revised Common Rule:

- *Federal Register :: Protection of Human Subjects and Institutional Review Boards*
- and *Federal Register :: Institutional Review Boards; Cooperative Research*

MISCELLANEOUS INITIATIVES AND ADDITIONAL GUIDELINES

EC - Labelling Rules: Unauthorised Medicinal Products used in Clinical Trials

This initiative eliminates the obligation to include an expiry date on the immediate packaging of unauthorised medicinal products used in clinical trials in specific circumstances (e.g. on syringes).

The aim is to prevent additional safety and quality risks associated with relabelling procedure and the need for more frequent re-supply, which could potentially lead to delays in clinical trials. *Unauthorised medicinal products used in clinical trials (labelling rules) (europa.eu)*

EMA – Guideline on 'Core SmPC, Labelling and Package Leaflet for Advance Therapy Medicinal Products (ATMPs) Containing Genetically Modified Cells'

Scientific guideline: *Guideline on core SmPC, labelling and package leaflet for advanced therapy medicinal products (ATMPs) containing genetically modified cells - Scientific guideline | European Medicines Agency (europa.eu)*

EMA – Personal Data Protection & CTIS

A draft guidance document on how to protect personal data and commercially confidential information in documents uploaded and published in CTIS is available for public consultation: *Event Summary - Workshop _14-07-2022 (europa.eu)*

UK – Guidance on Pharmacovigilance Procedures

Guidance on pharmacovigilance procedures - GOV.UK (www.gov.uk)

UK – Guidance for Formulating Responses to GCP Inspection Findings

Microsoft Word - Guidance for Formulating Responses to GCP Inspection Findings V2 (25-04-22) (publishing.service.gov.uk)

Thank you for taking the time to read this Industry Update from S-cubed

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