What's New in Clinical Development Practices & Regulations Quarter 3 – 2023

EU PHARMACEUTICAL LEGISLATION & ICH GUIDELINES

Proposal to Revise the EU's Pharmaceutical Legislation

As detailed in our Q2 Newsletter, the European Commission (EC) proposes to reform the current pharmaceutical legislation with a new Regulation and a new Directive to establish an EU regulatory framework for all medicines (including medicines for rare diseases and children). The EC has generated a Q&A document: *Q&A: Revision of the Pharmaceutical legislation (europa.eu)*

ICH E6 and E8

The planned date for implementation of ICH E6(R3) 'Good Clinical Practice' is Q3 2024. ICH E8(R1) 'General Considerations for Clinical Studies' was implemented in the EU and US during April 2022 (and is yet to be implemented in the UK). E6(R3) and E8(R1) will jointly provide quality guidelines which will follow key aspects:

- Proactively designing quality into clinical trials and drug development planning
- Identifying factors that are critical to trial quality
- Using proportionate risk-based approach and engaging stakeholders, as appropriate

The 'Principles' section in ICH E6(R3) will be expanded, the essential documents section reformed and a new section on data governance added. *ICH-E6(R3)*

Proposal for Three New ICH GCP Guidelines

During the ICH Assembly meeting in June 2023, the following new ICH guidelines were proposed:

- General Consideration for Patient Preference Studies
- Nonclinical Safety Studies for Oligonucleotide-based Therapeutics
- Bioequivalence for Modified-Released

The full press release from the meeting: *ICH Official web site : ICH*

GUIDANCE DOCUMENTS, INITIATIVES & PROPOSALS

Guidance on Transitioning Trials from the CTD to the CTR

Guidance for transitioning clinical trials from the Clinical Trials Directive (CTD) to the Clinical Trials Regulation (CTR): *transition_ct_dir-reg_guidance_en.pdf (europa.eu)*

Points to Consider for Clinical Trials Impacted by Major Disruption

The European Medicines Agency's (EMA's) GCP Inspectors Working Group has adopted a 'Points to Consider' document on the management of ongoing clinical trials impacted by political conflicts, natural disasters or other major disruptions. *EMA GCP IWG points to consider regarding the management of ongoing clinical trials impacted by political conflicts, natural disasters or other major disruptions (europa.eu)*

Real -World Data (RWD) and Real -World Evidence (RWE)

The EMA has produced a report on the experience gained with regulatory-led studies from September 2021 to February 2023. *real-world-evidence-framework-support-eu-regulatory-decision-making-report-experience-gained_en.pdf (europa.eu)*

OPEN Initiative

The EMA has expanded the scope of the OPEN initiative from COVID-19 vaccines and treatments to a wider range of medicines. *OPEN framework extended to a wider range of medicines | European Medicines Agency (europa.eu)*

Guidance on Clinical Trial Electronic Data

The EMA's 'Guidance on Computerised Systems and Electronic Data in Clinical Trials' *Guideline on computerised systems and electronic data in clinical trials (europa.eu)* and the UK's 'Access to Electronic Health Records by Sponsor representatives in clinical trials' *Access to Electronic Health Records by Sponsor representatives in clinical trials - GOV.UK (www.gov.uk)* imply that printouts of electronic medical records may no longer be acceptable for monitoring, auditing or inspections.

Centralised Procedure - Authorisation Advice

The EMA has issued advice (pre-authorisation and post-authorisation) for users of the centralised procedure. Here, there is a single application, a single evaluation and a single authorisation throughout the EU but only certain medicines qualify for the centralised procedure. *European Medicines Agency pre-authorisation procedural advice for users of the centralised procedure (europa.eu)* and *European Medicines Agency post-authorisation procedural advice for users of centralised procedure (europa.eu)*

New Collaboration between World Health Organisation (WHO) and ICH

The collaboration aims to establish a unified language by connecting WHO's International Classification of Diseases (ICD-11) with ICH's Medical Dictionary for Regulatory Activities (MedDRA). In addition, it will offer vital insights into the scope, causes and consequences of diseases and mortality worldwide. *ICH Press Release*

Proposal for Easy-to-Read Medication Guide

US Food and Drug Administration (FDA) has announced a proposed amendment to its human prescription drug labelling regulations. The proposal would mean a new requirement for an easy-to-read medication guide for out-patient medication. Non-adherence to medicine in the US causes an estimated 50% treatment failures and in addition contributes to 25% of hospital admissions and several deaths. *Patient Medication Information | FDA*

Miscellaneous Draft Documents:

- WHO guidance for best practices for clinical trials *Public consultation on WHO guidance for best practices for clinical trials* End of consultation: 15 September 2023.
- EMA reflection paper on establishing efficacy which is based on single-arm trials submitted as pivotal evidence in marketing authorisation *reflection-paper-establishing-efficacy-based-single-arm-trials-submitted-pivotal-evidence-marketing_en.pdf (europa.eu)* End of consultation: 30 September 2023.
- FDA Draft Guidance for Industry, Investigators and Other Stakeholders "Decentralised Clinical Trials for Drugs, Biological Products and Devices" *Decentralized Clinical Trials for Drugs, Biological Products, and Devices Draft Guidance for Industry, Investigators, and Other Stakeholders (fda.gov)*
- FDA Draft Guidance for Industry "Paediatric Drug Development Under the Paediatric Research Equity Act and Best Pharmaceuticals for Children Act" *Pediatric Drug Development Under the Pediatric Research Equity Act and the Best Pharmaceuticals for Children Act: Scientific Considerations (fda.gov)*

ARTIFICIAL INTELLIGENCE (AI) AND MACHINE LEARNING (ML)

Developers, manufacturers, regulators, academic groups and other stakeholders are working to develop a shared understanding of how AI and ML can be best utilised throughout the drug development process. Here are some examples:

- FDA - *Using Artificial Intelligence & Machine Learning in the Development of Drug and Biological Products (fda.gov)* and *Artificial Intelligence Discussion Paper (fda.gov)*
- EMA - *Draft Reflection paper on the use of Artificial Intelligence (AI) in the medicinal product lifecycle (europa.eu)*
- Health Research Authority (HRA) - *One-stop-shop for artificial intelligence and digital regulations for health and social care launched - Health Research Authority (hra.nhs.uk)*

MEDICAL DEVICES

EC Guidance on Summary Report for Medical Device Studies

The European Medical Devices Regulation (MDR) requires the sponsor to submit a report and a separate summary within 1 year of the end of the clinical investigation or within 3 months of its early termination. The EC has issued a short guidance document on the content and structure of the summary. *Publications Office (europa.eu)*

UK – Medical Devices and In Vitro Diagnostic Medical Devices (IVDs)

- Transitional Arrangement for CE Marking - The UK government has put in place legislation that amends The Medical Device Regulations 2002 (SI 2002 No 618, as amended) (the "UK MDR") to extend the acceptance of CE marked medical devices for Great Britain's market. *Implementation of the Future Regulations - GOV.UK (www.gov.uk)*
- Unless exempt, IVDs require a relevant mark of conformity (UKCA, CE or CE UKNI) to be placed on the UK market. *Guidance on the regulation of IVD medical devices in GB (publishing.service.gov.uk)*
    - There is a new section on IVDs in the Medicines and Healthcare products Regulatory Agency's (MHRA's) guidance on applying for authorisation in the UK. *Clinical trials for medicines: apply for authorisation in the UK - GOV.UK (www.gov.uk)*

US – Medical Devices

- The Centre for Devices and Radiological Health (CDRH) now enable users to track premarket submissions of their medical devices. *Send and Track Medical Device Premarket Submissions Online: CDRH Portal | FDA*
- The CDRH has asked for feedback from patients and others on facilitating access to medical devices designed for use outside the traditional clinical settings, including the use of medical devices in the home. *CDRH Seeks Public Comment: Increasing Patient Access to At-Home Use Medical Technologies | FDA*

UK SPECIFIC INITIATIVES

Introduction of New Recognition Routes

When the UK left the EU, the MHRA introduced temporary routes to market for products approved in EU countries. The temporary routes expire at the end of 2023.

The MHRA has now introduced seven new recognition routes which means that medicines approved in Australia, Canada, EU, Japan, Switzerland, Singapore and the US can be used by UK patients. For further information: *MHRA announces new recognition routes to facilitate safe access to new medicines with seven international partners - GOV.UK (www.gov.uk)*

The Innovative Device Access Pathway (IDAP)

A new regulatory pathway (IDAP), set to launch before the end of 2023, will support safe patient access to innovative medical technologies. IDAP will be operated by the MHRA, the National Institute for Health and Care Excellence (NICE), Health Technology Wales (HTW) and Scottish Health Technology Group (SHTG). *New regulatory pathway set to support safe patient access to innovative medical technologies - GOV.UK (www.gov.uk)*

DATA TRANSPARENCY & DATA PROTECTION

Clinical Trials Information Systems (CTIS)

The EMA has undergone a public consultation on the transparency rules for the publication of clinical trials information submitted through CTIS. There is a need for a balance between clinical trial transparency and confidential obligations. *Review of transparency rules for the EU Clinical Trials Information System (CTIS) | European Medicines Agency (europa.eu)*

The interim guidance on the protection of personal data and Commercially Confidential Information (CCI) has been modified. *Guidance document on protection of personal data and commercially confidential information (CCI) in CTIS (europa.eu)* and *Annex I to the guidance document (europa.eu)*

CTIS is now a registered data provider for WHO. *CTIS newsflash - 26 May 2023 (europa.eu)*

US – Publication of Clinical Trial Results

The National Institute of Health (NIH) seeks help to improve compliance of clinical trial results published on the ClinicalTrials.gov website. *NIH Clinical Trials Reporting Compliance: A Shared Commitment – NIH Extramural Nexus*

New EU Ruling on Anonymisation and Pseudonymisation of Data

A recent EU legal judgement stated that pseudonymised data will not be considered as personal data for the purposes of EU data protection law when transferred to a recipient who is unable to link the pseudonyms to identifiable individuals. *EU General Court examines data anonymisation and pseudonymisation | Dechert LLP - JDSupra*

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

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