Clarity and Openness in Reporting: E3-based

News Summary

January 2025

Welcome to our first News Summary of 2025

From January 2025, the CORE Reference Project is moving away from email and onto LinkedIn to streamline our distribution of educational materials, including our monthly News Summaries. We hope you enjoy our new look.

To continue to receive CPD from our team, follow us on our new LinkedIn page: www.linkedin.com/in/core-reference-57196a348

Once you are a Follower, we will invite you to the 'CORE Reference Project' business page. This is where we will be posting our monthly News Summaries and other resources to support you - as email distribution is no longer possible.

MEDICINES AND VACCINES

ICH

1. A joint US FDA – Health Canada ICH Public Meeting is to be held on 11 Feb 2025. Details of the meeting here. FDA and Health Canada will be co-hosting a regional public meeting to provide information to stakeholders and solicit input prior to the next International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Biannual Assembly meeting scheduled for May 13-14, 2025. This Joint US FDA – Health Canada ICH Public Meeting will include presentations by FDA, Health Canada, and PhRMA experts on ICH guidelines recently reaching significant ICH milestones.

2. The final ICH E6(R3) **Good Clinical Practice** Guideline was finalised on 06 Jan 2025 and is available now. There is also an ICH presentation to accompany this guideline Please also note that training materials are planned to be developed that will clarify or provide supplementary explanation to the application of the GCP guideline.

- For those interested Shaun Hastings has published a comparison of changes between ICH E6 (R3) Step 2 and E6 (R3) Step 4 using the Compare tool in Word. See his post/comparison on Linked In here.
- The Institute of Clinical Research has written a post about the potential impact of ICH GCP E6(R3) updates which can be read here.

CTR and CTIS

1. December 2024 CTIS Release Notes - Release v2.1.2 of CTIS public portal outline improvements made for publication of correct end of trial date, notification of restart of trial and user interface changes.

2. The latest CTIS Newsflash, dated 14 and 28 January 2025, are now available. They provide key updates on CTIS and links to useful reference materials.

3. EMA is offering a virtual training programme, organised by DIA, to support sponsor user preparedness concerning the new way of submitting Clinical Trial Applications in the EEA via the new Clinical Trial Information System and in compliance with the Clinical Trial Regulation No. 536/2014. This will take place on Tue 25-28 March 2025, 08:00-12:30 GMT. Register here.

4. EMA has released a survey for academia and SMEs to share their clinical trial training needs. The survey will be open until 11 February 2025. The identified training needs will be matched with available training and potential gaps, an overview of which will be published later in 2025.

5. On 15 Jan 2025 EMA published Version 7 of EMA CTR Q&A document. Changes within Annex II and Annex III are noted in the document history (this new version supersedes v6.9).

6. EMA is hosting a CTIS walk-in clinic on 29 January 2025, where sponsors can raise questions about any CTIS functionality and receive advice from CTIS experts.

7. As of 31 January 2025, Clinical Trials Regulation (CTR) has become fully applicable. Hence, all clinical trials in the EU, including ongoing trials that were approved under the previous legal framework, the Clinical Trials Directive (CTD), are now governed by the CTR. Remaining trials that were ongoing after 30 January and that were not moved to the new system may be subject to corrective measures applied by EU Member States. Transition procedures are no longer available and sponsors of ongoing CTD trials are required to submit a new application via CTIS. See the EMA news release here.

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EU Regulatory

European Health Data Space (EHDS) News

The Council of the EU has adopted a new law that will make it easier to exchange and access health data at EU level, paving the way for it to come into force.The regulation will now be formally signed by the Council and the European Parliament. It will enter into force 20 days after publication in the EU's

Official Journal. Read the 21 Jan 2025 press release here. The 8 Jan 2025 regulation can be accessed here.

UK and MHRA News

Blog post "MHRA Good Clinical and Laboratory Practice Symposia (11 and 12 February 2025)" has just been published on the MHRA Inspectorate blog. Join the next MHRA Symposia in February 2025 and hear the latest on Good Clinical Practice (GCP) in the UK from MHRA inspectors and regulators. Book the GCP Symposia on 11 Feb 25 here.

FDA Guidance and News

1. The FDA issued a draft guidance to provide recommendations on the use of artificial intelligence (AI) intended to support a regulatory decision about a drug or biological product's safety, effectiveness or quality. This is the first guidance the agency has issued on the use of AI for the development of drug and biological products. The FDA is seeking public comment on the draft guidance, Considerations for the Use of Artificial Intelligence to Support Regulatory Decision-Making for Drug and Biological Products, within 90 days. In particular, the FDA is asking for feedback on how well this draft guidance aligns with industry experience and whether the options available for sponsors and other interested parties to engage with the FDA on the use of AI are sufficient. The agency will review and consider comments received before finalizing this guidance.

2. FDA issued Draft Guidance on 06 Jan 2025 on Including Tissue Biopsies in Clinical Trials that when finalised will provide recommendations for including tissue biopsies as part of clinical trials. The draft guidance is intended, when finalized, to assist industry, clinical investigators, institutions, and institutional review boards in understanding considerations for tissue biopsies in adults and children as part of clinical trials that evaluate investigational medical products and/or that are conducted or supported by the U.S. Department of Health and Human Services (HHS). Submit comments by 10 Mar 2025.

3. FDA issued Draft Guidance on 06 Jan 2025 on Study of Sex Differences in the Clinical Evaluation of Medical Products. Differences in physiology between females and males can lead to differences in disease manifestation, pharmacokinetics, pharmacodynamics, and response to treatment. Analysing sex-related differences in medical product response is an important component of assessing product safety and effectiveness and can inform what goes into product labeling. Topics addressed in this guidance include:

- Practices to improve the recruitment, enrollment, and retention of females in clinical trials, to help ensure the generalisability of research results to intended patient populations
- Statistical considerations for analysing sex differences
- Reporting results based on analyses of sex differences.

Comment under docket number FDA-2024-D-4245 by 07 Apr 2025.

4. The US Health and Human Services Department has issued a technical amendment to the Final Rule which changes the internet web address for obtaining information about formatting of information for submission, procedures, and tools as specified in the regulation, by replacing the URL "https://prsinfo.clinicaltrials.gov" with "https://clinicaltrials.gov or successor site.

5. Modernised PRS updates: Modernised PRS now includes the ability to create results for specific study types. In addition, users can view and edit data in the newly added Baseline Characteristics module. The remaining Results modules, "Outcome Measures" and "Adverse Events," are still under development. Read more in the Release Notes.

6. US FDA officials have clarified how sponsors can achieve agency diversity action plan goals within multiregional clinical trials (MRCTs) in an article published in the New England Journal of Medicine

entitled "When Diversity Goals Meet Multiregional Trials". A summary of this paper can be found here.

EMA Guidance and News

1. A short article by EMA and HMA on their Data Transparency page describing the overhaul of their guidance on the identification of commercially confidential information (CCI) and personal data in marketing authorisation applications for human medicines.

2. A revised workplan for the Accelerating Clinical Trial in the EU (ACT EU) initiative is now available on the ACT EU website and outlines deliverables for 2025-2026.

3. EMA and the Heads of Medicines Agencies are launching a European platform for regulatory science research. It will bring together academia and regulators as well as other stakeholders with the aim of accelerating regulatory science research solutions. The call for expression of interest can be found here.

4. The European Medicines Regulatory Network (EMRN) aims to support academia as well as micro, small and medium-sized enterprises (SMEs) by sharing good regulatory practices that support the planning, set up and conduct of clinical trials. To help meet this aim, relevant stakeholders are asked to fill in a survey with their clinical trial training needs. The survey is open until 11 February 2025.

5. The EMA released the ICH E6(R3) Guideline for good clinical practice (GCP) - Step 5 (dated 23 Jan 2025). The date for coming into effect is 23 July 2025. The document can be viewed here.

Real-World Data

1. PHUSE Real World Data Spring Event 2025 takes place on 9–10 April 2025, 14:00-16:30(GMT) / 9:00-11:30(EST) / 15:00-17.30(CET). Registration opens 17 February. This is a new PHUSE Event that will build upon the engagement in the RWE Projects, Community Forums, and PHUSE CSS break-out sessions. It will bring together engaged speakers from the field ranging from data vendor and data registry representatives to pharmaceutical and biotech industry representatives who are sharing their knowledge and ideas around Real World Data utilisation in a fast-moving and challenging environment.

2. The recording and slides of the CIOMS Webinar introducing the CIOMS Working Group XIII consensus report on RWD and RWE in regulatory decision making are available. Note that these materials are behind a paywall.

- Recording Vimeo: https://lnkd.in/dPXDFMzX
- CIOMS consensus report: https://lnkd.in/d_U2iU_Z.

3. The US Centers for Medicare & Medicaid Services (CMS) has opened for public consultation the Proposed Guidance Document: Study Protocols that Use Real-World Data. The guidance draws heavily from the HARPER (HARmonized Protocol Template to Enhance Reproducibility of hypothesis evaluating real-world evidence studies on treatment effects) template jointly developed by ISPE and ISPOR. Blank HARPER templates and instructions can be found here.

Transparency and Disclosure Resources and News

1. On 17 Jan 2025, the European Data Protection Board published guidelines on pseudonymisation which clarifies the use and benefits of pseudonymisation for controllers and processors. The guidelines further look into some technical and organisational aspects of data transformation and pseudonymisation, including a useful list of considerations when determining the means for processing. Submit feedback here. Guideline can be downloaded from here.

2. A recent blog post by Honz Slipka, entitled “Anonymization vs. Redaction of Clinical Trial Data” can be accessed here.

3. ‘How Canadian Regulators Approach De-Identification: An Interview Study’ will be presented by Lisa Pilgrim and Khaled El Emam on 11 Feb 2025 11.00-12.00 EDT. The results of an interview study with Canadian privacy regulators to understand their perspectives on anonymisation will be presented. This Webinar is free to attend. Sign up for tickets here.

4. Continuing on from the September 2024 issue of the #EMWA journal dedicated to clinical trial transparency and disclosure, an additional T&D article is published in the December 2024 edition of MEW. Bina Mehta and co-authors explore the growing complexity of clinical trial disclosure and transparency in their article entitled "Transparency through the lens of data protection and privacy: A clinical research organisation medical writing perspective."

Development Strategy News

1. The Inter-Association Taskforce (IATF) on electronic Product Information (ePI) is a collaboration between the industry associations AESGP, EFPIA and Medicines for Europe. The IATF have launched a new series of position papers advocating for the implementation of ePI and improvement of the patient leaflet content. The position papers can be accessed here and the related IATF announcement can be accessed here.

2. The US FDA recently published a new draft guidance to provide sponsors with answers to FAQs and commonly faced issues that arise during the development of cellular and gene therapy products. The FAQs span multiple disciplines, including regulatory review, chemistry, manufacturing, and controls (CMC), pharmacology/toxicology (PT), clinical, and clinical pharmacology. You can review the guidance and submit comments until 18 Feb 2025.

3. FDA draft guidance was released on 30 Dec 2024 titled ‘M15 General Principles for Model-Informed Drug Development’. Developed under the auspices of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), this draft guidance discusses the multidisciplinary principles of model-informed drug development (MIDD) and provides recommendations on MIDD planning, model evaluation, and evidence documentation. Submit comments here by early March 2025.

4. This AMWA blog shares best practices for protocol writing.

5. The European Pharmacopoeia Commission has approved three new general standards addressing the production and quality control of monovalent messenger ribonucleic acid (mRNA) vaccines and their components. The new Ph. Eur. texts will support developers and manufacturers, and also regulatory agencies and national control laboratories worldwide that regulate them. They provide a framework of requirements for the production and control of mRNA vaccines. The new texts will be published in the Ph. Eur. in July 2025. See the full announcement here.

6. TransCelerate is hosting a webinar on Vulcan UDP (Utilizing the Digital Protocol): Complementing ICH M11 with an Interoperable Schedule of Activities (SoA) on Tuesday 11 February 15:00-16:15 CET. In this webinar, they will give insight into the UDP connectathons, discuss SoA testing, and address the pathway to further digitisation.

Artificial Intelligence/Machine Learning

1. Center for Information and Study on Clinical Research Participation, Inc.’s (CISCRP) has released a draft considerations document for the use of AI in the creation of lay summaries of clinical trial results. Download the document from here. The draft document is open for public consultation until 14 Feb 2025.

2. A paper by Inger Ødum Nielsen, Vanessa de Langsdorff, and John April entitled "How Medical Writing and Regulatory Affairs Professionals Can Embrace and Deploy Generative AI at Scale" has been published in Applied Clinical Trials (online dated 7 Jan 2025). The authors describe the CSR as a use case for automation through the use of generative AI.

3. An article published by the World Economic Forum entitled "Intelligent Clinical Trials: Using Generative AI to Fast-Track Therapeutic Innovations" discusses the potential of Generative AI in revolutionising clinical development.

News from Asia Regulators

1. The Indonesia Clinical Research Registry (INA-CRR) will transition to a new website for clinical research registry submissions. Their existing website (https://ina-crr.id/) will continue to accept new clinical research registry submissions until 30 June 2025. Until then, new submissions can also be made through the new website https://ina-crr.kemkes.go.id/id. Starting 01 July 2025, all new clinical research registry submissions must be made exclusively through https://ina-crr.kemkes.go.id/id.

2. The Health Sciences Authority (HSA) of Singapore has initiated a new regulatory pathway – Change Management Program (CMP), specifically for Software as a Medical Device (SaMD) application. The current regulatory framework does not support the rapid iterative nature of SaMD, eg. obtaining regulatory approvals for software changes, which can impact the timeliness of implementing SaMD updates. This guidance is intended for stakeholders who are involved in SaMD development and/or the Registrant of such devices in Singapore. It outlines the regulatory requirements and procedures for submitting a CMP application, either during initial SaMD Product Registration or as part of a Change Notification application.

3. This article by Sharma et al. "The Evolving Regulatory Framework in India: Impact on the Pharmaceutical Industry" reviews the recent key regulatory changes that have particular significance to the pharmaceutical industry and a general, global industry impact assessment, such as the key updates in the 2019 New Drugs and Clinical Trials (NDCT) Rules, the revised guidance for the submission of CTA for biological products, post-approval changes and monitoring guidance, and the ongoing regulatory development in India.

4. Asano et al. published an open-access article "PMDA Perspective on Use of Real-World Data and Real-World Evidence as an External Control: Recent Examples and Considerations". The authors present their recent review experience focusing on efficacy evaluations with an external control based on RWD/RWE that were submitted as a part of new drug applications in Japan, and describe the regulatory consideration of the utilization of RWD/RWE for drug evaluation and approval.

MEDICAL DEVICES

This subsection covers transparency in relation to medical devices, and the emerging intersection of the regulatory medical devices and the regulatory drugs spaces. Devices information or regulations that impact the reporting of device studies are also covered. Context is provided, where possible, to help readers understand how the information could be used.

General Updates

IMDRF Updates

The International Medical Device Regulators Forum (IMDRF) is a voluntary group of medical device regulators from around the world who have come together to build on the strong foundational work of the Global Harmonization Task Force on Medical Devices (GHTF) and aims to accelerate international medical device regulatory harmonization and convergence. The following IMDRF guidance has been finalised this month.

- Technical document (IMDRF/SaMD WG/N81 FINAL:2025) on Characterization Considerations for Medical Device Software and Software-Specific Risk.
- Technical document (IMDRF/AIML WG/N88 FINAL:2025) on Good Machine Learning Practice for Medical Device Development: Guiding Principles.

MDCG Updates

Several MDCG forms and templates related to conformity assessments were updated in early 2025.

- Application form (MDCG 2021-15 Rev1) to be submitted by a conformity assessment body when applying for designation as notified body under the medical devices regulation (MDR), with corresponding preliminary assessment review (PAR) template and Annex with list of documents submitted with the application.
- Application form (MDCG 2021-16 Rev1) to be submitted by a conformity assessment body when applying for designation as notified body under the in vitro diagnostics regulation (IVDR), with corresponding preliminary assessment review (PAR) template and Annex with list of documents submitted with the application.
- Several guidance documents on the European Medical Device Nomenclature (EMDN) have also been updated, including the FAQ on EMDN.

Updates from EU Notified Bodies

Check the following updates from the Notified Body BSI:

- Guidance on Software as a Medical Device
- Best practice guidance on MDR Article 117 - Drug-device combination products application process
- Guidance on Microbiology and Sterile Medical Devices

Updates from TGA Australia

- Guidance on the use of market authorisation evidence from comparable overseas regulators and assessment bodies for medical devices (including IVDs) v2.0 Jan 2025. This Guidance explains how overseas assessments can support our medical device certification and registration processes.
- Guidance on Transitioning to new manufacturer evidence for in-vitro diagnostic medical devices (IVDs) rev Jan 2025. This guidance is to help sponsors and manufacturers of IVD medical devices transition to new manufacturer evidence requirements.

Updates from the UK

MHRA has released an infographic showing the timelines for placing CE marked IVDs on the Great Britain market.

News

1. The US FDA has published draft guidance on developing and managing medical devices with artificial intelligence (AI). It includes recommendations regarding the contents of marketing submissions for devices that include AI-enabled device software functions including documentation and information that will support FDA's evaluation of safety and effectiveness. The recommendations

reflect a comprehensive approach to the management of risk throughout the device total product life cycle (TPLC). To support the development of appropriate documentation for FDA's assessment of the device, this draft guidance also proposes recommendations for the design, development, and implementation of AI-enabled devices that manufacturers may wish to consider using throughout the TPLC. Stakeholders can comment on the draft guidance on under docket no. FDA-2024-D-4488 until 7 April 2025.

2. MedTech Europe has released the 2024 Regulatory Survey: key findings and insights. The document presents the results of the 2024 Regulatory Survey, highlighting challenges manufacturers face with the In Vitro Diagnostic Regulation (IVDR) and Medical Device Regulation (MDR). The findings reveal increasing concerns around costs, timelines, and regulatory predictability.

3. On 29 Jan 2025, the International Medical Device Regulators Forum (IMDRF) AI/ML-enabled Working Group published final guidance on 'Good machine learning practice for medical device development: Guiding principles'. The document outlines 10 guiding principles to ensure safe, effective, and high quality development of AI/ML-enabled medical devices.