Clarity and Openness in Reporting: E3-based

News Summary

March 2025

The CORE Reference Project has moved away from delivering the monthly News Summary by email. We are now on LinkedIn as this allows us 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:

https://www.linkedin.com/company/the-core-reference-project

As a follower of the 'CORE Reference Project' you will receive notifications of our postings including the monthly News Summaries and other resources to support your self-led CPD. Of note, email distribution is no longer possible. To access the links in the News Summary, view in full screen and then either select 'accessibility mode', or download the News Summary PDF and then access.

CORE Reference at EMWA Conference in Riga, Latvia 6-10 May 2025:
The CORE Reference Foundation Workshop will be presented at the EMWA Conference on Wednesday 7 May 2025, 8.45-12.15 (CET) by Sam Hamilton and Vivien Fagan. Once conference registration opens please register with EMWA to attend the workshop.

The CORE Reference Project will hold a “Learn and Share” face to face session at lunchtime on Thursday 8 May 2025, 12.30-13.15 pm (CET). Bring your lunch along and join in our discussions. More details will be provided as they become available.

MEDICINES AND VACCINES

ICH

1. ICH M11 guideline, clinical study protocol template and technical specifications - Scientific guideline are now available. The updated template (Step 2 draft dated 13 Mar 2025) is provided as reference only for the second round of public consultation of the M11 Technical Specification (document dated 03 Feb 2025). The technical specifications consultation period is open until 22 April 2025. Stakeholders can send in their comments via email to ich@ema.europe.eu using this template.

The ICH M11 Clinical Electronic Structured Harmonised Protocol Template provides comprehensive clinical protocol organization with standardised content with both required and optional components. The Technical Specification (TS) that are acceptable to all regulatory authorities of the ICH regions presents the conformance, cardinality, and other technical attributes that enable the interoperable electronic exchange of protocol content with a view to develop an open, non-proprietary standard to enable electronic exchange of clinical protocol information.

2. An examination of how ICH E6(R3) will impact biospecimen management practices will be the subject of a webinar on 15 April 2025, 11am EST. Details and registration for the webinar entitled "The Impact of ICH E6 R3 on Biospecimen Management" are here.

CTR and CTIS

1. An integrated map of clinical trials in the EU and published within the CTIS public portal is active. The map provides real-time information about clinical trials by geographic area. A public webinar with a demo of the map's features was held on 7 March 2025. A recording of the meeting can be accessed here.

2. The Accelerating Clinical Trials in the EU (ACT EU) initiative launched the pre-CTA advice pilot in 2024 to provide guidance to sponsors/applicants planning to submit a Clinical Trial Application (CTA) to the Clinical Trial Information System (CTIS) under European Regulation (EU) No 536/2014. The Guidance for applicants was updated last month, February 2025. The Pre-CTA advice will involve coordination between assessors from the National Competent Authorities of EU Member States on the regulatory and technical aspects of clinical trials.

3. EMA have released the following update to the online modular training programme:

- v1.8 of FAQs. How to create, submit and withdraw a Clinical Trial Application - CTIS Training Programme - Module 10, dated March 2025.
- v1.2 of FAQs. How to create and submit an annual safety report and respond to related requests for information - Module 18, dated March 2025.

4. The latest CTIS newsflashes, which include key updates and links to reference materials, can be found at the following links:

- CTIS newsflash - 11 March 2025
- CTIS newsflash - 25 March 2025

5. The video recording of the Clinical Trials Information System (CTIS) bitesize talk: Change of sponsor in CTIS, held on 5 March 2025, is now available.

6. In the 11 Mar 2025 CTIS newsflash Sponsor's were reminded to keep CTIS up-to-date, in compliance with articles 36, 37 and 38 of the Clinical Trials Regulation. This is especially important for the recruiting status and contact details of investigators.

EU Regulatory

European Health Data Space (EHDS) News

Regulation (EU) 2025/327 of the European Parliament and of the Council of 11 February 2025 on the European Health Data Space and amending Directive 2011/24/EU and Regulation (EU) 2024/2847 was published on 5 March 2025.

The aim of this Regulation is to "establish the European Health Data Space (EHDS) in order to improve natural persons' access to and control over their personal electronic health data in the context of healthcare." The EFPIA Press Release titled: A Call for Effective Stakeholder Engagement and Capacity Building during the Implementation of the European Health Data Space calls on policymakers to guarantee an actionable process for involvement in this new health data ecosystem. EFPIA position paper on the Regulation on the European Health Data Space (EHDS) can be accessed here. The FAQs document on the European Health Data Space has also been updated.

UK and MHRA News

The UK HRA February 2025 Clinical Trials update included an update on the progress of the UK's new Clinical Trials regulations: a guidance to accompany the new regulations is being developed; however, the draft will not be published online. Instead it will be shared with individuals and organisations that have contacted the HRA and expressed an interest in reviewing it. The first draft guidance should be complete by mid-March. Those of you who wish an opportunity to review should email engagement.team@hra.nhs.uk. This Pharmaforum article describes the work done on the overhaul.

FDA Guidance and News

1. The FDA publication Artificial Intelligence & Medical Products: How CBER, CDER, CDRH, and OCP are Working Together (first published in March 2024) was revised in February 2025.

2. The modernised PRS now includes the Adverse Events module of the Results Section. Users can now create, view and edit all modules in the Results Section of the Modernised PRS and submit the results in the Classic PRS. To learn more, view the latest Release Notes.

3. The FDA has released the final guideline Study Data Technical Conformance Guide - Technical Specifications Document which aims to assist with creating and submitting standardized study data for regulatory submissions.

EMA Guidance and News

EMA and other European National Health Agencies have published Clinical Evidence 2030. "Building on existing practices, our vision is that by 2030, clinical evidence generation will be further guided by the patient voice and informed by existing data and knowledge; study design will be driven by research questions to be addressed; clinical trials will be more efficient and impactful; real-world evidence (RWE) will be enabled and its value fully established; and trust will be built through transparency." This document outlines the 6 guiding principles for generating clinical evidence. Although all principles are important, at a time where diversity is being rolled back, Principle 1 is particularly significant as it reinforces the need for patient representation at every step of evidence generation.

Real-World Data

1. Register for the PHUSE online Real World Data spring event which will be held 9-10 April 2025 (14:00-16:30[GMT]) / 9:00-11:30[EST] / 15:00-17.30[CET]). Access to the full agenda is available together with registration details.

2. EFPIA has released a paper entitled "Harnessing RWE to transform Healthcare Decision-Making in Europe. EFPIA vision on the role and use of RWE in decision-making" Read the EFPIA press release and download the paper here.

3. Zou and Berger have published the paper Real-World Data and Real-World Evidence in Healthcare in the United States and Europe Union. Key highlights include Data Quality Frameworks, criteria for assessing RWD source quality to ensure suitability, Regulatory agencies' role in using RWE for treatment decisions, and addressing data transparency, quality assurance, and sensitive data protection.

4. The paper by Riskin et al. Implementing Accuracy, Completeness, and Traceability for Data Reliability tackles the question "Consistent with FDA Real-World Evidence Program guidance on data reliability, can accuracy, completeness, and traceability of real-world data be measured, and what are the impacts of advanced data and technologies in these dimensions?"

5. The recent report from the Council for International Organizations of Medical Sciences (CIOMS) Working Group XIII on Real-World Data and Real-World Evidence in Regulatory Decision Making has

been summarized in a publication.

Transparency and Disclosure Resources and News

1. The PHUSE data transparency working group with a focus on Rare Disease/Small Population Data Sharing has released a draft White Paper entitled "Rare Disease Clinical Data Sharing" for open consultation and feedback. The working group has investigated key barriers to sharing rare disease data, including the risk of re-identification and privacy concerns as well as providing key recommendations. Closing date for feedback is 7 April 2025 and should be provided by emailing: workinggroups@phuse.global.

2. PHUSE's Webinar Wednesday to be held on 30 April at 15:00 (BST) will include an exploration of a case study on a successful health Canada public release submission. Registration and further details of the webinar here.

3. PHUSE are looking for volunteers to join the Data Transparency Working Group's 'Anonymization of Imaging Data' project. Project members will help develop best practices for anonymising and sharing DICOM images in oncology alongside clinical trial data. If you have experience processing and de-identifying DICOM images in clinical trials contact workinggroups@phuse.global by 25 April to express your interest.

4. The MRCT Center and PHUSE are presenting a webinar entitled "Data Literacy in Clinical Research: Enhancing Trust and Transparency" on 3 Apr 2025; 10-11 am EST. Registration and agenda details here.

5. White Paper titled 'Purposeful Clinical Trial Transparency: Delivering Societal Value Beyond Compliance' available for download.

GDPR and Data transfer Ex-EU

This paper on the EU data transfer pacts explains that EU lawmakers question the viability of the transatlantic data transfer pact between the US and Europe, and is significant because:

- The DPRC is charged with protecting Europeans' privacy from US government surveillance by hearing privacy complaints from EU citizens.
- The DPRC was created by Executive Order to ensure that the US complies with privacy rights obligations under the EU-US Data Privacy Framework. Its existence allows data transfers between the US and Europe to continue happening for now.
- Privacy and Civil Liberties Oversight Board (PCLOB) members have resigned and been fired. This Board oversees the DPRC and acts as a critical safeguard against US surveillance overreach.
- EU lawmakers are pressing the EC to consider suspending the DPF, as they no longer believe that the PCLOB can operate independently.

Development Strategy News

1. A publication in Clinical Cancer Research from the FDA Oncology Center of Excellence (OCE) and the Clinical Trials Transformation Initiative (CTTI), reports how decentralized clinical trial elements were used during the COVID-19 pandemic in cancer trials that supported FDA approval. Read the press release here and access the abstract here.

2. TransCelerate will hold a webinar featuring TransCelerate's Diversity of Participants in Clinical Trials Initiative, the Reagan-Udall Foundation, and the Clinical Trials Transformation Initiative on 24 April 2025 (10 -11 am EST). Titled, "Representation by Design: Enhancing Clinical Trial Access through Multi-Stakeholder Collaboration" full webinar registration details can be accessed here.

3. Califf et al. published The importance of ClinicalTrials.gov in informing trial design, conduct, and results, commenting on the progress of clinicaltrials.gov in clinical trial design transparency, as well as reporting.

4. Thomassen et al. published Handling missing values in patient-reported outcome data in the presence of intercurrent events, which focuses on methodology of handling ICEs in PRO data.

Artificial Intelligence/Machine Learning

1. The WHO has designated the Digital Ethics Centre at Delft University of Technology in the Netherlands as a WHO Collaborating Centre on artificial intelligence (AI) for health governance. Access the press release here.

2. EMA has qualified the first AI tool, called AIM-NASH, which helps pathologists analyse liver biopsy scans to identify the severity of an inflammatory liver disease (MASH) in clinical trials. The tool is expected to help researchers obtain clearer evidence on the benefits of new treatments. This qualification marks a significant step towards integrating AI in medicine development. The tool is trained on more than 100,000 annotations from 59 pathologists who assessed over 5,000 liver biopsies across nine large clinical trials.

3. The WHO has released the policy document Health data governance in the age of artificial intelligence: policy imperatives for the WHO European Region. It highlights urgent considerations for health data governance.

4. Kilian et al. published the paper European AI Standards - Technical Standardization and Implementation Challenges under the EU AI Act, which presents "one of the first systematic analyses of European technical and soon to be harmonized standardization for organizations providing AI systems."

5. The WHO released "Ethics and governance of artificial intelligence for health: Guidance on large multi-modal models". This guidance addresses one type of generative AI, large multi-modal models (LMMs), which can accept one or more type of data input and generate diverse outputs that are not limited to the type of data fed into the algorithm.

News from Asia Regulators

1. China's NMPA released two new guidelines which take effect on 10 March 2025:

- Guideline for Chemical Drug Application Review (page in Mandarin) - the procedures, key documents required, and review and acceptance criteria are provided, including the digital submission requirements, submission of DSUR and SUSAR reports, and provision of the medical device components for drug-device combination products.
- Guideline for Biological Product Application Review (page in Mandarin) - key updates included the digital submission requirements, the provision of quality assessments for biosimilarity in the eCTD and a new review timelines.

2. In recent years, China NMPA released several policies and guidelines on patient-focused clinical trials and the use of real-world data to support regulatory decision-making for medical products and drugs. The article by Hu et al. "Patient-focused drug development and real-world study" discusses patient-focused drug development and real-world study in China as well as the associated guidelines.

3. Singapore HSA has released for public consultation Best Practices Guide for Medical Device Cybersecurity.

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. Combination products, including pharmaceutical and medical device components, may need to be reported under pharmaceutical legislation, depending on what the product is, and how regulatory authorities in different global regions assess combination products. Contextualisation is provided, where possible, to help readers navigate the information.

Medical Devices General Updates and News

Europe

1. The European Commission has authorised the first GenAI-enabled medical device in the EU. Prof. Valmed® is now officially CE-certified (class IIb) for support of diagnosis and treatment as the medical co-pilot. It is designed to assist healthcare professionals and medical personnel by providing recommendations for the diagnosis or therapy of human diseases.

2. EFPIA has released the reflection paper The challenges of integrating Medical Devices (MDs) into medicinal product clinical trials - CTA Documentation. It focuses on the technical documentation requirements for medicinal product Clinical Trial Applications with MDs.

3. The Belgian Federal Agency for Medicines and Health Products (FAMHP) has released the Guideline Submission Processes of Clinical Investigations according to MDR.

4. The Medical Device Coordination Group has released Revision 4 of MDCG 2020-16 Guidance on Classification Rules for in vitro Diagnostic Medical Devices under Regulation (EU) 2017/746, incorporating the Expert Panel's view from January 29, 2024.

5. The EMA has released the interim report Pilot on the Advice from the Expert Panels to Manufacturers of High Risk Medical Devices which provides an overview of applications received from Feb 23 to Dec 24.

6. Keane et al. have published the review Worldwide trends in the quality and breadth of clinical investigations of medical devices over the past decade. This scoping review maps published clinical investigations of medical devices by device type and clinical specialty and summarises key trial design aspects.

Updates from MedTech Europe, the European trade association representing the medical technology industries

1. Position paper on Digitalisation of Technical Documentation. The document discusses the changes in the regulatory landscape for MDs and IVDs, which has increased the volume of technical documentation required for marketing authorisation. It proposes transitioning to a more advanced, standardised digital framework.

2. Joint discussion paper Future governance of medical technologies in Europe, together with other medical technology groups. It makes the case for a reform of the way that European regulatory system for medical technologies is governed.

3. Reflection paper on the Submission of vigilance reports to Notified Bodies under EU MDR & IVDR. It calls for streamlining vigilance data evaluation processes and enabling a systematic and integrated post-market surveillance system.

4. Report on Administrative Burden under the IVDR and MDR. It maps out necessary vs unnecessary burden to enable a robust, transparent, predictable, and sustainable regulatory framework for IVDs and MDs in Europe.

EU Combine Initiative

1. The European Organization for Research and Treatment of Cancer (EORTC) published Navigating EU Clinical Trials: Adapting to a New Era of Regulations that outlines challenges between the EU's separate regulations. For example, drug-device protocols that have an IMP and medical device require submission under EU-CTR and MDR/IVDR - one (EU-CTR) requiring a centralised submission and the other requiring separate Member State submissions. This process is further complicated if an AI component is involved.

2. The EU 'COMBINE' programme strategy envisions "a clear and smoothly functioning regulatory environment for combined studies through broad involvement of regulators, ethics committees and all impacted stakeholders, with the ultimate goal to support availability of innovative treatments for patients." The programme has been approved by the EU member states.

UK MHRA

The UK Department of Health and Social Care has released the policy paper on The Regulation of Artificial Intelligence as a Medical Device: Government Response to the Regulatory Horizons Council.