Clarity and Openness in Reporting: E3-based

News Summary

April 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:

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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. 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

Transcelerate has developed an ICH E6 Asset Library. The tools are designed to help with the adoption of the latest good clinical practice (GCP) guidance, focusing on key areas of change including data governance, risk-based quality management, stakeholder collaboration, and risk proportionality. A webinar was held on 4 March 2025 to discuss TransCelerate's new tools and resources for understanding ICH E6(R3) revision and its implementation. The webinar content can be accessed here.

CTR and CTIS

1. EMA latest version of Clinical Trials Regulation (EU) No. 536/2014 Questions and Answers was released in March 2025, Version 7.1. This version includes updates to Annex II: Language requirements for part I documents.

2. The EMA will host a Clinical Trials Information System (CTIS): Information Day on 22 May 2025, 12:30 to 17:30 CET. The aim of the webinar is to provide an in-depth overview of CTIS, its optimisations, best practices, and upcoming developments. The event will be broadcast live. A video recording will be made accessible.

3. The latest CTIS newsflash, which includes key updates and links to reference materials, can be found at the following link:

- CTIS newsflash - 8 April 2025. CTIS has been designated as a primary registry by the World Health Organisation (WHO) within the International Clinical Trials Registry Platform (ICTRP).
- CTIS newsflash - 29 April 2025. Includes reference to the updated cover letter template for the submission of initial clinical trial applications in CTIS.

The 8 April 2025 Newsflash also has Tips for Sponsors including a reminder that the first document uploaded in CTIS is the one 'for publication.' For all those documents subject to publication see table II of Annex I: Guidance document on how to approach the protection of personal data and commercially confidential information while using the Clinical Trials Information System (CTIS). Sponsors should therefore make sure that the first document uploaded in each of the 'for publication' placeholders is redacted of commercially confidential information (CCI) and that personal data are anonymised as per the relevant guidance.

4. The Clinical Trials Information System (CTIS) officially joined the Primary Registry Network of International Clinical Trials Registry Platform (ICTRP). According to the WHO "Primary Registries in the WHO Registry Network meet specific criteria for content, quality and validity, accessibility, unique identification, technical capacity and administration. Primary Registries meet the requirements of the ICMJE." The EMA news release can be accessed here.

5. Parexel's LinkedIn article 'Biotech development in the EU: Streamlining CTA submissions' summarises highlights from their recently developed playbook for streamlining CTA submissions.

6. EMA is hosting CTIS training for sponsor users, organised by DIA, 23-26 June 2025. A hands-on approach will be used to explain and demonstrate the functionalities of the system. The training programme will also address how to manage the clinical trial transparency and respond to a request for information (RFI) along with information on how to submit Annual Safety Reports (ASRs) as well as Clinical Study Reports (CSRs).

7. The latest updates to the CTIS system, including the secure Sponsor and Authority workspaces, and to the Clinical Trials website, were released on 24 April 2025 and can be viewed here.

EU Regulatory

1. EMA will expand its activities under its clinical data publication policy (CDP) Policy 0070 to cover all clinical data submitted under new marketing authorisation applications (MAAs) for medicinal products as well as any applications for line extensions or new indications, or where the MAA results in a negative opinion or is otherwise withdrawn. These expanded activities apply for MAAs submitted from April 2025 onwards. Article here.

2. The final EMA Reflection paper on use of real-world data in non

interventional studies to generate real-world evidence for

regulatory purposes was published on 17 Mar 25. These studies can complement data from clinical trials and fill in knowledge gaps. However, understanding the limitations and overcoming them is key to ensuring reliable evidence. The paper covers legal obligations and regulatory requirements, study design, bias, confounding and effect modification, governance and transparency, data quality and statistical analyses. It is part of the newly published roadmap for regulatory guidance on RWE.

3. EMA and the Heads of Medicines Agencies (HMA) have published their joint EU medicines agencies' network strategy to 2028 (EMANS). The strategy, titled 'Seizing opportunities in a changing medicines landscape', is a comprehensive update of the five-year strategy which was developed to cover the period 2021 to 2025 and can be found here.

4. The quarterly report monitoring the EU clinical trials environment for January – March 2025 has been published on the ACT EU website.

European Health Data Space (EHDS) News

1. The new European Health Data Space regulation was enforced from 26 March 2025. The new regulation aims to facilitate access to and reuse of electronic health data across the EU. There will be a four-year transition period to establish the necessary electronic health data exchange infrastructures. This is significant and aims to revolutionise healthcare data management across the EU by enhancing accessibility, interoperability, and patient control over personal health data. The objectives are:

- Improved Access and Control: Citizens will have easier access to their health data, whether they are in their home country or elsewhere in the EU. They will also have better control over how their data are used
- Interoperability: The regulation ensures that all electronic health record systems will comply with European specifications, guaranteeing interoperability across the EU
- Research and Innovation: Researchers and policymakers will have access to anonymized/pseudonomised and secure health data, paving the way for significant advancements in research and patient care.

2. This 17 Apr 2025 blog post titled 'Preparing for the European Health Data Space — Opportunities and Challenges for Europe's Digital Future' explains how the EU regulation designed to facilitate secondary use of clinical data for research brings benefits for health research also poses challenges for companies.

UK and MHRA News

1. A reminder that all sponsors are now expected to use the new GDPR transparency working template for any new research applications submitted. This includes the leaflet about the use of confidential data in research, designed for patients and participants. If sponsors don't use the templates, they will be expected to demonstrate how their own GDPR wording meets the principles for meaningful involvement of patients and the public in health and social care research.

2. New regulations for running clinical trials in the UK have been signed into law. A 12-month roll-out begins 11 April 2025 and will take full effect from 10 April 2026. The News and Updates page about this makes interesting reading. Of note is that '…for the first time [the regulations will] legally require trial registration on a WHO-recognised public register and the publication of results summaries'.

3. The HRA have published their new clinical trial registration report: the report covers clinical trials that received a REC favourable opinion in 2023 and shows that 92% of clinical trials were registered on

a publicly accessible database, or in the process of being registered. The report also lists the details of trials that weren't registered.

4. Following the government's announcement of a new UK-wide Health Data Research Service. the HRA had a webinar during which they talked about the work they are leading to streamline and reform the set-up and delivery of all clinical trials to rapidly address the delays affecting clinical research.

FDA Guidance and News

1. The FDA has released a very useful summary About the Modernised PRS. This document contains useful links on all the available features of the modernised PRS.

2. The FDA has recently published a Federal Register Notice exploring the potential adoption of CDISC Dataset-JSON v1.1 as a new exchange standard for electronic study data submissions. This notice is up for public comment and the FDA is seeking input regarding the risks and benefits of adopting this new exchange standard along with any integration challenges with existing tools and systems.

EMA Guidance and News

EMA issued updated guidance (dated 11 April 2025) on the anonymisation of protected personal data and assessment of commercially confidential information during the preparation of RMPs (main body and annexes 4 and 6).

Real-World Data

1. EMA published a reflection paper on non-interventional studies that use real-world data to generate real-world evidence for regulatory purposes. This reflection paper covers the aspects of design, conduct, and analysis of non-interventional studies, and focuses on methodological principles that are considered important for the conduct and assessment of non-interventional studies using RWD and used for regulatory decision-making throughout a medicine's lifecycle.

In addition, EMA has published a short document describing the roadmap that reviews existing real-world evidence guidance that regulators have issued and outlines real-world data related areas that could benefit from further guidance development.

2. Bertelsen et al. have published the paper Patient Engagement and Patient Experience Data in Regulatory Review and Health Technology Assessment: A Global Landscape Review which reviewed the use of RWD and patient input in the regulatory process.

3. The presentations and slides from PHUSE – Real World Data Spring Event held 9-10 April 2025 are available to download and view from here. A blog reflecting and summarising the first RWD Spring event is also available.

4. The FDA has published a Federal Register Notice exploring the Health Level Seven (HL7) Fast Healthcare Interoperability Resources (FHIR) for submission of data collected from real-world data (RWD) sources. Comments are sought on these areas amongst others:

- The current challenges for the pharmaceutical industry of submitting clinical study data collected from RWD sources to FDA
- Opportunities and/or challenges for the pharmaceutical industry on reaching a future state of clinical study data submissions collected from RWD sources using HL7 FHIR (e.g., business

processes, technical considerations)?

Read the full notice and submit your comments by 23 June 2025.

Transparency and Disclosure Resources and News

1. The MRCT (Multi-Regional Clinical Trials) Center and PHUSE Data Transparency have collaborated on material to educate the general public on Data Privacy and Data Sharing. The infographics and videos can be found here.

2. To facilitate data collection, sharing and reuse, the World Health Organization has produced a standardised glossary of definitions of terms for 'Public health data, statistics and health indicators'. The glossary is intended for data managers, health analysts, monitoring and evaluation and surveillance specialists and other stakeholders who deal with health statistics, data and public health indicators across the data cycle, from collection to use.

3. The UK Information Commissioner's Office (ICO) have fined Advanced Computer Software Group Ltd, a software supplier to the NHS and healthcare, £3.07 million following a cyber-attack. This is the first time that the ICO has issued a fine to a data processor (not the data controller) and is a reminder that any organisation using or storing personal information has a legal responsibility to protect it. The breach involved failures in basic security and caused disruption to critical healthcare services, including NHS 111.

4. Julie Holtzople has published a white paper entitled "Purposeful Clinical Trial Transparency: Delivering Societal Value Beyond Compliance" which can be accessed and downloaded from here.

5. The UK Information Commissioner's Office has published guidance around anonymisation to help identify the issues that should be considered when using anonymisation techniques effectively.

6. Risk Management Plans (RMPs): On 11 April 2025, EMA published Rev 3 of the guideline "Anonymisation of Personal Data and Assessment of Commercially Confidential Information during the Preparation and Redaction of RMPs." In terms of changes from the previous version that speak to public disclosure considerations, there is stronger guidance on transforming (not just rewording) personal data and clearer expectations for redaction - black boxes without overlay text.

7. On 16 May 2025 the Synthetic Data Summit with contemporary sessions on privacy regulation, and very specific guidance on how to do that will be held in Montreal Canada. Register here.

GDPR and Data transfer ex-EU

1. A summary of the European Commissioner discussions around the EU-US data privacy framework and guidance on EU-US data transfers can be accessed here.

2. Comment on the emerging questions around EU-US data privacy framework can be accessed here.

3. Data Subject Rights - Empowering Participants in Clinical Trials, a youtube video by RD Privacy explains the most common data subject rights in the scope of clinical trials and how to handle them.

4. The European Data Protection Board has published a study on secondary use of personal health data for scientific research. The 92-page paper can be accessed and downloaded from here. A blog summarising information presented in the paper can be accessed here.

5. Euronews article 'Trump White House jeopardises EU-US data deal: German ministry'. Read here.

Development Strategy News

1. PHUSE has released a new Webinar Series: 'At the Intersection of Estimands & Target Trial Emulation (TTE) for RWE'. The 'Estimands for RWD/RWE' project, part of the Real World Evidence Working Group, has launched this resource to explore frameworks like estimands and target trial emulation (TTE) in real-world data (RWD) and real-world evidence (RWE). Discussions will help shape a forthcoming White Paper. The first webinar, 'An Introduction to the Estimands and Target Trial Emulation (TTE) Frameworks', took place on 22 April and provided an overview of how these frameworks intersect, featuring presentations from publication authors and a panel discussion with a regulatory agency representative. Find Out More: https://lnkd.in/ePb9VC_U. The recording can be downloaded here, slides will be available soon.

2. BMJ Feature on 'How Trump's trade war will break global medicine supply chains'. Understand the bigger picture because it will inevitably impact medicines development.

3. WHO has released a glossary of key terms in evidence-informed policy-making. The glossary is important in providing support to WHO and countries worldwide to promote a common understanding and interpretation of the key elements of evidence-informed policymaking. The publication entitled: "Evidence-informed policy-making, A glossary of key terms," can be downloaded from here.

4. The 2025 update of the CONSORT statement was published on 14 April 2025 in multiple journals. The accompanying Explanation & Elaboration paper for reporting results of randomised trials has also been revised and updated to reflect changes in the recommendations, and is full of examples of good reporting.

- "CONSORT 2025 statement: updated guideline for reporting randomised trials" is available here: (BMJ) (Lancet) (JAMA) (Nature Medicine) (PLoS Medicine)
- "CONSORT 2025 explanation and elaboration: updated guideline for reporting randomised trials" is available here: (BMJ).

A couple of recent BMJ Opinion articles are of interest - around CONSORT and guidelines generally. The first is titled 'The legacy of CONSORT and Douglas G Altman' and the second is 'Innovative solutions are needed to overcome implementation barriers to using reporting guidelines'.

5. EMA have launched two public consultations with the aim of reviewing the template for the product information of centrally approved medicines. The review aims to enhance the clarity and usability of package leaflets to make these more understandable and relevant to patients. This is a valuable opportunity for all stakeholders—regulators and industry but also patients and healthcare professionals—to help shape the new product information of medicines. As MWs know, during the development of a product, studies are designed to help support the intended label claims, so from that perspective, it is important for our community to keep an eye on this. Find out more about how to contribute here.

6. IQVIA free webinar: Accelerating clinical research with master protocols: Challenges and benefits to complex trial designs. Thursday 08 May 2025 11.00 ET. Register here.

7. Reminder that a clinical research glossary for plain language with explanations of technical terms is available. The MRCT of Harvard and Brigham Women's Glossary team and the CDISC Glossary group are working together to help study participants and those in the public understand research concepts: Comprehensive information on the CDISC Glossary and Digital Data Flow; plain language glossary.

8. The Spring edition of the EMWA Journal Medical Writing focuses on Rare Diseases. Many of the articles explore challenges associated with writing for rare disease as well as designing and executing clinical trials in this complex area of clinical research.

News from Asia Regulators

1. China NMPA published "Inspection Checkpoints and Judging Principles for Clinical Trial" in March 2025. Overseas medical device companies who are looking to enter the China market should ensure that their clinical trial protocols, participants' information documentation, and data reporting align with NMPA's latest guidelines.

2. The Ministry of Health, Labour and Welfare (MHLW) of Japan has transferred 4 clinical research websites from the National Institute of Public Health (NIPH) to MHLW's servers on 01 April 2025. The URLs of the affected systems—jRCT, JCRB, Ethics Review Committee Reporting System, and Clinical Research Information Portal—will change from *.niph.go.jp to *.mhlw.go.jp. The new URL of jRCT is now https://jrct.mhlw.go.jp/.

3. The Clinical Trials Registry-India (CTRI) is seeking expert input from professionals for suggestions to revamp the web application of clinical trials registration to improve the functionality, usability, and overall experience for trial sponsors and participants. A google form containing questions regarding a number of defined aspects is available for users to provide input.

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

Updates from the Notified Bodies

1. The European Association of Medical Devices Notified Bodies (Team-NB) has released v3 of their position paper on Best Practice Guidance for Technical Documentation under EU MDR. The Technical

Documentation is the dossier submitted to NBs for conformity assessment of MDs, equivalent to the CTD for medicinal product.

2. Team-NB also released v2 of the position paper on European Artificial Intelligence Regulation (also known as the AI ACT).

3. Team-NB members adopted the position paper on IVDR Certification Process, which includes details on the processes for detail the pre-application and application and post application phases.

4. Team-NB 1.5 day for MD manufacturers for 7 May 2025 is fully booked so another session has been scheduled for 27 Aug 2025. This training is intended for members of a manufacturer's clinical team and have experience in creating CERs and/or are involved in CE submission.

5. BSI has published an expert whitepaper, "The EU AI Act meets MDR - Everything AI-enabled medical device manufacturers need to know", authored by Regulatory Leads and the Head of AI Notified Body at BSI. The whitepaper aims to make it "easy to grasp what it (the EU AI Act) means for your business and how it interplays with the MDR".

Updates from IMDRF

The International Medical Device Regulators Forum (IMDRF) has published a new guidance on AI Medical Device Development which highlights key concepts and principles for the development of medical devices that incorporate AI."

UK MHRA

1. The MHRA has published a guidance on how to apply for an Exceptional Use Authorisation (EUA) for MDs, a mechanism that allows non-UKCA/CE marked medical devices to be placed on the UK market in exceptional circumstances, where this is necessary to protect public health.

2. The MHRA has also updated the Guidance on Clinical investigations for medical devices. Changes include clarification of terms, especially the use of "participants" as preferred terminology.