Clarity and Openness in Reporting: E3-based

News Summary

June 2025

CORE Reference Webinar

The slide presentation and recording of the CORE Reference webinar held on 11 June 2025 is available to access. Thanks to external speaker Obaraboye Olude from Privacy Analytics who presented information on the use of anonymisation software for statistical anonymisation and redaction of clinical trial documents under EMA Policy 0070 and HealthCanada Public Release of Clinical Information.

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MEDICINES AND VACCINES

ICH

1. Glossary of ICH terms and definitions: Version 8, 5 June 2025 can be downloaded from here.

2. ICH M4Q(R2) Guideline on the Common Technical Document for the registration of pharmaceuticals for human use: Quality Step 2b was endorsed in May 2025 and it is now released for public consultation until 24 October 2025. This revision is aimed to streamline regulatory processes, especially for complex products, for example by modernising the CTD structure and content, applying science- and risk-based approach regulatory review, using useful tools for lifecycle management, and improving digital readiness.

3. ICH E20 draft Guideline on "Adaptive Design for Clinical Trials" has reached Step 2b of the ICH Process on 25 June 2025 and entered the Step 3 public consultation period. The guideline provides guidance on confirmatory clinical trials with an adaptive design, focusing on principles for the planning, conduct, analysis, and interpretation of trials intended to confirm the efficacy and support the benefit-risk assessment of a treatment.

CTR and CTIS

1. All the presentations from the EMA's CTIS Info Day last month (22 May 2025) can be found here, including an update on the CTIS programme, CTCG updates, CTIS cover letter templates and CTIS tips for the users.
Important Note: EMA clarified that CTIS will be updated to hold structured data for results in the future, but there is no timeline for when this will happen.

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

- CTIS newsflash - 10 June 2025.
- CTIS newsflash - 24 June 2025. This will be the final issue of the CTIS Newsflash. EMA is redesigning the sponsor CTIS training materials to improve navigation and ease of use based on stakeholder feedback. The revised sponsor handbook will be published on the EMA website on 9 July 2025, and the new layout will be explained in a dedicated CTIS bite-size talk on Wed 9 July 2025 at 15:30 CEST. See 'Medical Devices' subsection below for COMBINE Pilot.

  From July 2025, the biweekly CTIS newsflash will be replaced by the Clinical Trial Highlights Newsletter. This newsletter will be released monthly, offering a more comprehensive overview of clinical trial developments and insights. To stay updated, subscribe here.

EU Regulatory

EMA released a new guideline for public consultation, open for comment until 15 Sep 2025. This provides recommendations on how to include and retain pregnant and breastfeeding people in clinical trials. This marks a significant shift in the development of medicines in this population. The initiative aims to generate robust clinical data, enabling informed, evidence-based decisions for patients and healthcare providers.

UK and MHRA News

1. The London-based ISRCTN clinical trial registry is being revamped to provide a comprehensive national overview of the UK's medical research landscape.

Plans include making UK studies registered on other registries available on ISRCTN and a form that will allow researchers to upload tabular summary results directly onto the registry. TranspariMED article here.

2. The HRA is developing new digital services to "make it easier for research applications to be submitted, reviewed and approved in the UK." They are looking for volunteers to help test the new services so if you are a current user of the Integrated Research Approvals System (IRAS), HRA Assessment Review Portal (HARP), or Over-Volunteering Prevention System (TOPS), you can register your interest.

3. MHRA Draft Guidance on using non-investigational medicinal products in a clinical trial was published on 25 June 2025, and comes into force on 28 April 2026. Provide your feedback here.

FDA Guidance and News

1. On 15 January 2025, FDA amended its colour additive regulations to no longer allow for the use of FD&C Red No. 3 in food and ingested drugs; drug manufacturers who use FD&C Red No. 3 in ingested drugs have until 18 January 2028 to reformulate their products. Draft FDA Guidance on Replacing Color Additives in Approved or Marketed Drugs was issued on 30 May 2025. The draft guidance includes recommendations regarding the documentation that should be generated to support a color additive replacement. This draft guidance is included in the CORE Reference News Summary for awareness of possible impact on medical writing-related documents.

2. On 4 June 2025, the latest release notes for the Modernised PRS were published: all modules of the Results Section are now available on the Results Summary page.

3. The FDA has published new priorities for the FDA see: "Priorities for a new FDA" by FDA Commissioner MA Makary, published in JAMA (published Online: June 10, 2025. doi:10.1001/jama.2025.10116). See also below "News from US: Possible Impact on Clinical Trial Ecosystem" for additional information.

4. FDA released the final guidance for industry "Conducting Remote Regulatory Assessments--Questions and Answers". An RRA is "an examination of an FDA-regulated establishment and/or its records, conducted entirely remotely, to evaluate compliance with applicable FDA requirements". This guidance is included to inform the medical writing community as this may include readiness of medical writing deliverables.

EMA Guidance and News

Joint Heads of Medicines Agencies and European Medicines Agency's (HMA/EMA) have published an article highlighting the outcomes of a two-day multi stakeholder workshop organized by EMA in 2024. The workshop explored ways to optimise the EMA qualification procedure for patient registries. The article also provides recommendations from the workshop, and is available to download here.

Transparency and Disclosure Resources and News

1. The recording and presentation slides of the MRCT webinar "A Shared Language for Clinical Research: How Technical Organizations are Implementing the Clinical Research Glossary", originally held on 08 May 2025, is available on the MRCT website.

2. WHO has published 'Reporting summary results in clinical trial registries: updated guidance from WHO' which is aimed at improving the reporting of summary results in clinical trial registries. The rationale for developing the guidance can be found here.

GDPR and Data transfer Ex-EU

France's data protection authority, the Commission nationale de l'informatique et des libertes (CNIL) issued a guidance detailing the importance of identifying a controller, joint controller or processor. The English version is available in this LinkedIn post.

Development Strategy News

1. The recording and presentation slides of the MRCT webinar "Innovative Approaches for Gene Therapy Long-Term Follow-Up", originally held on 06 May 2025, is available on the MRCT website. This webinar provides insights for designing and writing a protocol for long-term follow-up studies for gene therapies.

2. A paper by Bond et al: "Recommendation Paper on Advancing the Use of Decentralised Elements in Clinical Trials"presents industry views, experiences and positions on the use of DCT elements in clinical trials.

3. FDA will Launch New Websites for Standard Safety Tables and Figures (ST&Fs) and OND Custom Medical Queries (OCMQs). The two new external websites for the Office of New Drugs (OND) will serve as resources for the public, providing comprehensive information and direct links as a part of OND's ongoing efforts to monitor and evaluate drug safety. FDA aims to enhance transparency and foster a better understanding of its regulatory processes through this initiative.

4. TransCelerate have made two additional resources available in the ICH E6(R3) Asset Library to support teams adapting to the updated GCP guidance:

- The Trial Design Start-up Tool aims to help stakeholders operationalise the guidance that applies to the early stages of trial planning.
- The Data Life Cycle Framework highlights key considerations to help ensure data integrity, traceability, and security throughout the trial lifecycle.

5. EMA released the ICH E6(R3) Annex 2 overview of comments on 20 May 2025. Download the 47-page document here. Expected adoption is planned for July 2026.

6. Generating Synthetic Clinical Trial Data with AI: Methods, Challenges, and Insights by Ma, Yang and Ma - was recently presented at the PharmaSUG 2025 conference, winning 'best paper'.

7. The MRCT Center has shared that the Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard (MRCT Center) Center has new Clinical Research Glossary (CRG) definitions for review in the June 2025 CDISC Public Review. Access the survey here. A webinar on how one can participate in the annual Public Review was held on 24 June 2025, access the recording here.

8. The 196-page Report of the Council for International Organizations of Medical Sciences (CIOMS) Working Group XII "Benefit-Risk Balance for Medicinal Products" is out now. Chapter 4: Specificities Of Benefit-Risk Assessment Methods For Special Situations may be of interest. Download from CIOMS web site (free registration needed).

9. Update on revision of the 'Recommendation paper on the use of Auxiliary Medicinal Products' is available on the ACT EU website. Next steps: Endorsement by CTCG and CTAG if no blocking comments; post-endorsement, publication in Eudralex volume 10 together with instructions regarding the impact for ongoing clinical trials.

Artificial Intelligence/Machine Learning

1. Training course on AI and data protection released by the European Data Protection Board: Fundamentals of Secure AI Systems with Personal Data. See the announcement here. Access the open book training here.

2. Fortune article 11 June 2025: 'Exclusive: New Microsoft Copilot flaw signals broader risk of AI agents being hacked' highlights the risks with use f AI Agents.

3. EMA/HMA are hosting an online workshop on AI on Thursday 20 Nov and Friday 21 Nov 2025. The registration process and the outlines of the agenda will be shared in the next few weeks. Preliminary details can be found here.

4. Current Opportunities for the Integration and Use of AI/ML in Clinical Trials: Good Clinical Practice Perspectives – is published in the Journal of the Society for Clinical Data Management (JSCDM). The paper captures the work done in 2020 and 2021 by the Society for Clinical Data Management (SCDM) and GCP Inspectors Working Group (IWG) in organising two foundational workshops dedicated to exploring how Artificial Intelligence and Machine Learning can be responsibly integrated into clinical trials.

5. The European Commission's Joint Research Centre has released the Generative AI Outlook Report that examines the transformative role of GenAI across various sectors including science and healthcare.

6. The paper "The EU project Real4Reg: unlocking real-world data with AI" sheds light on how to fully leverage RWD to inform regulatory decisions and HTA across Europe. Real4Reg is a consortium of ten European institutions which aims to promote the use of RWD (ie, national healthcare registers and claims data) to support the regulatory decisions about medicines.

News from Asia Regulators

1. On 28 May 2025, Japan's parliament passed its first AI-specific statute—the Act on the Promotion of Research, Development and Utilization of Artificial Intelligence Technologies. The Act aims to promote the safe use and development of AI by empowering the government to monitor and investigate misuse and issue guidance to AI providers. The Act does not set out a regulatory framework nor impose penalties. This article summarizes the key takeaways of the Act.

2. China NMPA issued "Implementation Rules for the Special Review of Innovative Medical Devices" (page in Mandarin) in April 2025. This document provides detailed rules on the expert review system for innovative medical devices. One of the rules specifies the expectation of inclusion of Chinese patient data, which is a consideration for trial design. This third-party article provides an overview in English.

3. In May 2025, China NMPA released the revised clinical evaluation exemption list 2025 for medical devices registration in China (complete list from the NMPA website in Mandarin). The new list replaces the 2023 edition. Refer to this third-party news article for the newly added exempted medical devices in 2025.

4. In June 2025, the Medical Device Authority (MDA) of Malaysia released the Third Edition of the "Harmonised Classification of Medical Devices in ASEAN" Guidance Document (MDA/GD/0062). This document aligns with the ASEAN Medical Device Directive (AMDD), providing a harmonized approach to classifying medical devices, including IVD devices.

News from US: Possible Impact on Clinical Trial Ecosystem

1. NOTUS Report on the Make America Healthy Again (MAHA) Report which was released in Feburary 2025.

2. The US Department of Justice (DOJ) Final Rule came into effect on 08 April 2025. The rule prohibits/restricts transfer of bulk sensitive personal data of Americans and government-related data to certain foreign adversaries, including China, Russia, Iran, North Korea, Cuba, and Venezuela. A Compliance Guide and FAQs are provided. This rule will impact the clinical trials industry although certain data from clinical investigations and data for supporting regulatory authorisation are part of the exemption. Sponsors are expected to understand and navigate the complexities of the rule. This article provides further reading.

3. FDA Launches Agency-Wide AI Tool to Optimize Performance. Video here. From the statement: "FDA…launched Elsa, a generative Artificial Intelligence (AI) tool designed to help employees—from scientific reviewers to investigators—work more efficiently… The agency is already using Elsa to accelerate clinical protocol reviews, shorten the time needed for scientific evaluations, and identify high-priority inspection targets".

4. BMJ News article: "Trump's "gold standard science" rule would let political appointees edit government science and punish scientists, critics say".

5. This Nature news article reports NIH grant cuts as a result of the US agency's new policy. Clinical trials of infectious diseases and cancer around the world could be ended abruptly without funding. This Nature news article explains that a US judge has ruled that the NIH must restore funding to hundreds of research projects that were cancelled because they touched on diversity, equity and inclusion (DEI), sexual and gender minorities (LGBT+) and COVID-19.

6. The FDA has laid out new priorities for the FDA in the viewpoint article "Priorities for a new FDA" by FDA Commissioner MA Makary, published in JAMA (published Online: June 10, 2025. doi:10.1001/jama.2025.10116). A summary is also presented in Regulatory Focus here.

7. Vaccinology:

- New York Times: 'Kennedy removes all CDC vaccine panel experts'.
- NPR: New members of the CDC vaccine advisory panel announced.
- Nature News article: 'Who is on RFK Jr's new vaccine panel — and what will they do?'
- BMJ news article: Independent US vaccine body is planned after RFK Jr's mass firing of CDC advisory panel

8. On 17 June 25, the FDA announced its Commissioner's National Priority Voucher (CNPV) program. The new voucher may be redeemed by drug developers to participate in a novel priority program that shortens its review time from approximately 10-12 months to 1-2 months following a sponsor's final drug application submission.

9. FDA Statement 18 Jun 25: FDA halts new clinical trials that export Americans' cells to foreign labs in hostile countries for genetic engineering.

10. Nature News 23 June 2025: Will Gates and other funders save massive public health database at risk from Trump cuts?

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

1. MRCT released the framework "Post-trial, Continued Access Responsibilities to Investigational Significant-Risk Devices – Scenarios that require further consideration" in April 2025. It outlines 5 key milestones, specific scenarios, and considerations to support organisations in making equitable and transparent decisions regarding continued access to investigational significant-risk devices after a trial.

2. A summary on coverage of designation codes for Notified Bodies designated under MDR / IVDR (dated June 2025) can be accessed here.

3. The Medical Device Coordination Group has released new guidance documents as well as updated existing ones, several of which revolve around medical device software (MDSW) and AI.

- (NEW) MDCG 2025-4 Guidance on the safe making available of medical device software (MDSW) apps on online platforms has been released. The guidance covers Apps that meet the definition of medical device software (MDSW) under EU law. It explains that App platforms like Apple or Google could now be classified as MD distributors or importers if they host an MDSW App for Sponsors based outside the EU. This means they must also verify MDR/IVDR compliance.
- (NEW) MDCG 2025-5. Q&A regarding performance studies of in vitro diagnostic medical devices under regulation (EU) 2017/746. This document provides clarifications on performance studies for IVDs. A performance study is defined as a study undertaken to establish or confirm the analytical or clinical performance of an IVD.

- (NEW) MDCG 2025-6 Interplay between the Medical Devices Regulation (MDR) & In vitro Diagnostic Medical Devices Regulation (IVDR) and the Artificial Intelligence Act (AIA) also known as AIB 2025-1. This document has been endorsed by the Artificial Intelligence Board (AIB) and the MDCG established by Article 65 of Regulation (EU) 2024/1689 and Article 103 of Regulation (EU) 2017/745. Both groups are composed of representatives of all Member States and are chaired by a representative of the European Commission MDCG and AIB.
- (UPDATED) MDCG 2019-11. Qualification and classification of software - Regulation (EU) 2017/745 and Regulation (EU) 2017/746 (now R1). Changes to the revised version include clarifications on modular MDSW and health apps.

4. The European Commission conducted a public consultation from 12 December 2024 - 21 March 2025 on EU rules for MDs and IVDs. The results are described in "Factual summary report on the public consultation for the targeted evaluation of the EU rules on medical devices and in vitro diagnostics" which can be downloaded from here.

5. The Head of Clinical Investigations at MHRA has posted on LinkedIn the large proportion of invalidated clinical investigations applications submitted to MHRA. He urges applicants to review the MHRA guidance carefully to ensure all requirements are met and avoid unnecessary delays.

6. The amending Implementing Regulation (EU) 2021/2226 as regards the medical devices for which the instructions for use may be provided in electronic form was published on 25 June 2025.

AI/ML

1. 'AIB 2025-1, MDCG 2025-6 Interplay between the Medical Devices Regulation (MDR) & In vitro Diagnostic Medical Devices Regulation (IVDR) and the Artificial Intelligence Act (AIA)' June 2025 guidance describes how the AI Act (AIA) interacts with the MDR and IVDR.

2. FDA released in June 2025 the final guidance document "Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions". The major changes include the new Section VII for cyber devices and quality system regulation alignment.

EU Combine Initiative

The COMBINE PILOT on coordinated assessment is being launched to streamline the review process for multinational clinical trials with a simultaneous performance study by synchronising competent authority and ethics committee reviews. More information on the COMBINE Programme is available on the European Commission website.

- Under this overall strategic programme, the COMBINE Project 1 – pilot "all-in-one" coordinated assessment is now live. As part of the COMBINE programme, the pilot is testing a new, more efficient way of approving combined studies, ie, studies that involve both clinical trials of medicines and performance studies of medical devices. This pilot is designed to allow sponsors of combined studies to submit a single application, ensuring more harmonised interactions with the Member States involved. This approach is expected to reduce the administrative burden for sponsors and promote transparency and consistency in the assessment process. Read the press release here. This pilot phase will accept a limited number of combined study applications and sponsors are asked to express their interest by 31 Aug 2025.