Clarity and Openness in Reporting: E3-based

News Summary

February 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. 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. TransCelerate will hold a webinar on 4 March 2025 to discuss the latest tools and resources for understanding the ICH E6(R3) revision and its implementation. Panelists will explain the key changes in the guidelines, discuss the interconnection between ICH E6 and E8, and share more information about the collaboration with ACRO. Registration details here.

2. The presentations and video recordings of the ACT EU Workshop on ICH E6 R3 (Principles and Annex 1), held 19-20 February 2025A have been uploaded and can be accessed here. A short summary of the workshop can be downloaded here.

CTR and CTIS

1. As of 31 January 2025, the Clinical Trials Regulation became fully applicable with the Clinical Trials Information System supporting submission, assessment and oversight of all trials in the EU. See the latest here.

2. At the end of January 2025, the EMA updated the following public documents to include the latest additions:

- CTIS public portal: Full trial information
- CTIS public portal: Trial Documents.

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

- CTIS newsflash - 28 January 2025
- CTIS newsflash - 11 February 2025
- CTIS newsflash - 25 February 2025.

4. The Clinical Trials Coordination Group (CTCG) have published a Best Practice Guide for sponsors who have missed the transition timeline. The sponsor of ongoing Clinical Trial Directive (CTD) 2001/20/EC clinical trials without Clinical Trials Regulation (EU) 536/2014 (CTR) approval must submit a complete new clinical trial application for approval in CTIS according to CTR rules.

5. The next Clinical Trials Information System (CTIS) bitesize talk will be "Change of sponsor in CTIS" on Wednesday, 5 March 2025 - 15:30 - 17:00 (CET). Registration is required and you can submit questions by 19 Feb 2025.

6. Clinical Trials Information System (CTIS) Sponsor end user training programme to be held 25-28 March 2025. This training programme is open to new sponsor users of the CTIS, commercial and non-commercial, as well as Contract Research Organisations. Full information of cost and learning programme here.

7. EMA has published Clinical Trial Highlights issue 23 - February 2025. This issue includes What's next for EU clinical trials along with CTCG updates and CTIS training and events.

8. EMA have released the following updates to the online modular training programme:

- v5.0 of CTIS - Sponsor Handbook, dated February 2025.
- v1.3 of FAQs - Introduction to the Clinical Trials Regulation (EU) No 536/2014. CTIS Training Programme - Module 01, dated February 2025.
- v1.4 of Quick Guide: How to search, view and download a CT and a CTA (Sponsors). CTIS Training Programme - Module 09, dated February 2025.
- v1.4 of Introductory guide: CTIS for SMEs and Academia. CTIS Training Programme - Module 19, dated February 2025.

9. In January 2024, the ACT EU Clinical Trials Analytics Workshop introduced a key deliverable: the integration of a map of clinical trials in the EU, with the CTIS public portal. This map was developed in response to feedback from stakeholders who emphasised the need for a simple, patient-friendly dashboard to help patients and healthcare professionals easily locate clinical trials of interest running in the EU. This trial map will be launched on 3 March 2025. A public webinar will be held on 7 March 2025 at 13:00-14:30 Amsterdam time to provide a live demo of the map's features. During the webinar, participants will be encouraged to submit questions using Slido (code: #TrialMap25).

10. EMA has outlined its data processing activities related to personal data in CTIS, detailing compliance with GDPR, data security measures, and participants rights in Records of data processing activity (public) regarding the processing of personal data in CTIS, dated 13 February 2025.

EU Regulatory

1. The European Data Protection Board welcomes comments on the Guidelines 01/2025 on Pseudonymisation by 28 February 2025 using the form provided.

2. To address the current challenges faced by cross-border participants in clinical trials, the EU-X-CT initiative has developed general recommendations on key aspects of clinical trial management and conduct. The recommendations aim to improve safe and equitable access to cross-border clinical trials within Europe. The draft recommendations are open for public consultation until 10 March 2025, 12.00 PM CET.

3. The EMA has published the "Annual Report of the Good Clinical Practice (GCP) Inspectors' Working Group (IWG) 2023" which was adopted by the GCP IWG on 26 November 2024.

UK and MHRA News

1. The MHRA launched a consultation on its draft guidance for developing individualised messenger ribonucleic acid (mRNA) cancer immunotherapies. These immunotherapies are being developed to use mRNA as a messenger to train a patient's own cells to make specific proteins to fight cancer. The draft MHRA guidance (including clinical aspects) aims to clarify and streamline pathways for bringing these therapies through to patients, without compromising on robust safety principles. The MHRA announcement can be found here.

2. From 21 January 2025, the MHRA will review all new requests for scientific advice meetings against whether the requirements can be addressed with existing guidance, written advice, or a scientific advice meeting. See the full MHRA notice here.

3. UK HRA re-stated in their operational bulletin on 10 February 2025 that from 01 April 2025 sponsors should use the updated General Data Protection Regulation (GDPR) Transparency Wording Template. The template was revised by the HRA in October 2024 to align with the new Participant Information Quality Standards and the Four Principles for meaningful involvement of patients and the public in health and social care research. Sponsors were notified of a transition period which ends on 31 March 2025, and they are expected to use the new GDPR wording in the Integrated Research Application System (IRAS) submissions from 01 April 2025.

4. The MHRA has published the Nanomedicine Decision Tree —a structured tool designed to guide manufacturers, developers, and regulatory professionals in determining the appropriate regulatory pathway for nanomedicines.

5. The UK's Clinical Study Registry, the ISRCTN, was updated February 2025. Details of these updates, aimed to enhance the user's experience, can be found here, and include enhanced reporting and advanced search improvements.

FDA Guidance and News

The US FDA has published an information sheet entitled: "Institutional Review Boards Frequently Asked Questions." The sheet is a compilation of answers to questions asked of FDA regarding the protection of human subjects of research. The final document can be downloaded from here.

EMA Guidance and News

1. EMA has published the latest version of the EudraCT & EU CTR Frequently Asked Questions, dated 31 January 2025. As of 31 January 2025, any EU/EEA trial on Investigational Medicinal Product(s) needs to be conducted under Regulation (EU) 536/2014. The use of the EudraCT database is now limited to the tasks described in question 2 of the FAQ document.

2. EMA has released the Guide to manufacturers on the procedure for requesting advice from Expert Panels on clinical investigations and/or clinical development strategies for high-risk medical devices.

More details are provided below under medical devices.

3. Two guidance documents on consolidated advice on clinical trials (SAWP/CTCG and pre-CTA) have been updated (both dated 4 February 2025) following feedback provided by the applicants and the experience gained since the launch of the two pilots. The latest versions of the documents are available on the ACT EU website here.

4. Arlett et al., have published a perspective entitled "Clinical Evidence 2030." In their publication, the EMA authors outline their six guiding principles for excellent clinical evidence generation.

Health Canada Guidance and News

1. Health Canada has shared insights from the public consultation on the draft guidance on expanded access clinical trials. The public consultation ran from August through October 2024 and the comments have been presented as 5 key themes:

1: Clarifying policy objectives
2: Aligning with other regulators
3: Barriers to update under a clinical trial model
4: Patient participation and engagement
5: Benefits of decentralization.

2. The recording and slides from 11 February 2025 webinar presented by Drs Lisa Pilgram and Khaled El Emam, entitled "How Canadian Regulators Approach De-Identification: An Interview Study" are available to view here. The results of this study were also published in the Journal of International Data Privacy Law in December 2024.

Real-World Data

PHUSE is organising an 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). The full agenda is available together with registration details.

Transparency and Disclosure Resources and News

The PHUSE Data Transparency Winter Event took place from 4-6 February 2025. During this virtual event, presentations were delivered across the three days in bitesize chunks. Each day also hosted a panel discussion and Q&A session focused on the day's themes. The 12 presentations and 3 event recordings have been uploaded and can be accessed here.

Development Strategy News

1. TransCelerate Biopharma's ICH E6(R3) initiative team, in collaboration with ACRO, has developed toolkits to help investigators and sponsors navigate the new data governance section in the ICH E6 guidelines. Resources - which include practical frameworks, templates, and tools designed to support implementation of the new guidelines, data quality, and decision-making in an evolving clinical research landscape - this ICH E6 Asset Library is now available.

2. The fourth installment of the PHUSE video series on data privacy and data sharing in clinical trials has now been released. Entitled "Data Privacy and Data Sharing in Clinical Trials – What Is Clinical Data?" it can be accessed here. Thavarajah and co-authors previously published an article in the special edition of the EMWA Journal on Clinical Trial Transparency and Disclosure. In their EMWA article they describe the process used to create the videos and infographics to support data literacy. Their full EMWA article can be downloaded from here.

3. The World Health Organization (WHO) has released the 2025 edition of the International Classification of Diseases 11th Revision (ICD-11) – a tool that standardises the language used by health professionals worldwide in diagnosing, reporting and monitoring diseases, injuries and causes of death.

4. EU regulatory network vision for clinical evidence by 2030 is presented by Arlett and colleagues in an open access paper entitled "Clinical Evidence 2030" which can be accessed here.

5. The two guidance documents on consolidated advice on clinical trials (SAWP/CTCG and pre-CTA) have been updated following the feedback provided by the applicants and the experience gained since the launch of the two pilots. The latest versions of the documents are available on the ACT EU website.

6. Webinar on 28 March 2025, entitled "Shaping the future of clinical trials: Building an ethical, efficient, and equitable ecosystem" from 13:00 – 14:30 (CET). This builds on World Health Assembly resolution (WHA75.8) on strengthening clinical trials and WHO's Guidance for best practices for clinical trials (2024). Register for the webinar here.

7. An MRCT webinar on entitled "Equitable Access to Clinical Trials: Best Practices for Industry" will be held on Wednesday 5 March 17:00-18:00 CET. Registration details are here.

Artificial Intelligence/Machine Learning

1. EMA announced that from 2 February 2025 the first rules of the Artificial Intelligence Act are now applicable. This includes the AI system definition, AI literacy, as well as a very limited number of prohibited AI use cases outlined in the AI Act that pose unacceptable risks in the EU. Furthermore an Annex entitled "Approval of the content of the draft Communication from the Commission - Commission Guidelines on the definition of an artificial intelligence system established by Regulation (EU) 2024/1689 (AI Act)" was published on 6 Feb 2025. The guidance and announcement can be found here.

2. A special FDA communication by Warraich et al FDA Perspective on the Regulation of Artificial Intelligence in Health Care and Biomedicine was published last year. A response has been released by Jaiswal et al.

3. Painter et al have published the paper Automating pharmacovigilance evidence generation: using large language models to produce context-aware structured query language which looks at how LLMs can enhance the accuracy of pharmacovigilance data retrieval.

4. The article The rise of agentic AI teammates in medicine by Zou and Topol advocates for using AI systems not only as tools but as healthcare teammates.

5. The Center for Information and Study on Clinical Research Participation (CISCRP) has opened the document Considerations for Using AI to Create Lay Summaries of Trial Results for public comment. Deadline is 18 Feb 2025.

6. A recent paper in the BMJ describes a framework and guidance for the development and deployment of trustworthy AI tools in healthcare. Entitled: FUTURE-AI: international consensus guideline for trustworthy and deployable artificial intelligence in healthcare" it can be downloaded from here.

7. The Lancet has recently published an article on publication bias and reporting discrepancies in research on the clinical application of AI: Discrepancies in reported results between trial registries and journal articles for AI Clinical research. This research uncovers concerns with the registration and reporting of AI clinical trial results.

8. Bornet et al have published the article Analysis of eligibility criteria clusters based on large language models for clinical trial design. This study aims to evaluate the effectiveness of LLMs in encoding eligibility criterion information to support CT protocol design.

9. The Swiss Federal Council has decided on a Swiss AI Regulation and intends to ratify the Council of Europe Convention on AI.

10. Busch et al. have published the paper Current applications and challenges in large language models for patient care: a systematic review. The review aims to synthesise current applications and limitations of LLMs in patient care.

11. The Lancet commentary by Boraschi et al. Governing synthetic data in medical research: the time is now calls for the responsible use of synthetic data created by generative AI algorithms.

News from Asia Regulators

1. Post by HSA Singapore on ICH E6 R3 Annex 2 titled 'ICH E6 (R3) GCP Guideline Annex 2 Additional Considerations for Interventional Clinical Trials; Overview of Step 2 draft'

2. MFDS South Korea released the latest update of the Enforcement Decree of the Medical Device Act, effective 07 February 2025. This enforcement decree outlines regulations and procedures related to the Medical Devices Act, including the duties of committee members, dismissal criteria, meeting protocols, subcommittees, research committees, and penalties for violations. The latest update was reflected specifically in Article 13.

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

Europe

1. The European Commission and Member States have launched a pilot coordinated assessment for clinical investigations (CI) and performance studies (PS) under Regulations (EU) 2017/745 (MDR) and (EU) 2017/746 (IVDR). The pilot aims to create a harmonized, predictable process across Member States, reducing administrative burden for sponsors and ensuring high transparency and consistency in coordinated assessments.

2. The European Commission has adopted an implementing regulation (2015/117) establishing the rules for joint scientific consultations on medical devices and in vitro diagnostic medical devices, under the Health Technology Assessment (HTA) Regulation.

3. In collaboration with the EMA, the Commission has established a standard procedure for manufacturers of certain high-risk medical devices to request scientific advice on their intended clinical development strategy and proposals for clinical investigation. Manufacturers of class III devices and class IIb active devices intended to administer or remove medicines can now submit their request for advice via a portal and consult the medical device expert panels at different stages of the clinical development. For transparency, the opinions of the expert panels for different high risk

medical devices provided under the Clinical Evaluation Consultation Procedure (CECP) of the EU MDR are publicly available here. The list of expert views provided and ongoing consultations under the Performance Evaluation Consultation Procedure (PECP) provided under the EU IVDR is also publicly available here.

4. The EU draft guidance on electronic instructions for use for all medical devices intended for exclusive use by healthcare professionals is open for public consultation until 21 March 2025.

4. The MDCG has revised MDCG 2019-6 Rev5 Questions and answers: Requirements relating to notified bodies.

5. The EU Medical Devices Newsletter for February 2025 is available here.

6. EMA has published the latest revised version of the Q&A document with respect to the implementation of the regulations on medical devices and in vitro diagnostic medical devices. The recent updates primarily include the additions made with respect to the MAH's compliance with the general safety and performance requirements (GSPRs) of the regulations as part of the Marketing Authorization Application.

Germany

1. The German Federal Office of Information Security has released the report on Security assessment of wearable devices with medical functionalities (SiWamed).

2. EIT Health has released the report MedTech and Digital Health: A Comprehensive Guide to Market Access in Germany.

UK MHRA

UK MHRA released/updated several guidances in February 2025:

- Digital Mental Health Technology - Regulation and Evaluation for Safe & Effective Products, aimed at supporting manufacturers and safeguarding users of digital mental health technologies, including mental health apps, AI-powered assessments, and virtual reality therapy.
- Guidance on registration of certain in vitro diagnostic devices in the UK, in relation to the extension of certain EU IVDD certificates.
- Updated: Guidance on regulating medical devices in the UK. Updates include guidance for the EU IVDR transition extension under Article 110 for the registration of IVD devices with the MHRA.
- Updated: Guidance on software and artificial intelligence (AI) as a medical device. Updates are focused on outputs of the UK Software Group, responsible for safety of SaMD

Health Canada

Health Canada has published the following:

- Final Pre-market guidance for machine learning-enabled medical devices.
- Draft guidance on managing applications for medical device licences.