# Regulatory Public Disclosure

SECTION EDITOR

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**Editorial**

**EU CTR and CTIS**

Since the EU Clinical Trials Regulation (CTR) 536/2014 came into force on January 31, 2023, the platform supporting it – the Clinical Trials Information System (CTIS) – and the underlying transparency rules were updated with a site relaunch on June 18, 2024. In brief, the aim of the relaunch is to strike a balance between transparency of information and protection of commercially confidential information. As well as the publication deferral mechanism being removed for all documentation, the number of documents published has been streamlined. For example, the Investigator's Brochure is no longer published (as is now specifically mentioned in Annex 1, Table VI of Version 2 of the EMA Guidance document on how to approach the protection of personal data and commercially confidential information while using the CTIS, June 18, 2024). The welcome overall outcome is a rationalisation of the published documents to reduce complexity and workload for users engaged in redactions.

Furthermore, there is alignment between the requirements for publication of clinical data under the CTR – when documents and data are submitted in a clinical trial application (CTA) in CTIS – and when documents and data are submitted in the context of a marketing authorisation application under Policy 0070. Thanks to Alison McIntosh for nicely summarising the detail in Table 1 "A bitesize guide to clinical data publication under Policy 0070 and the CTR".

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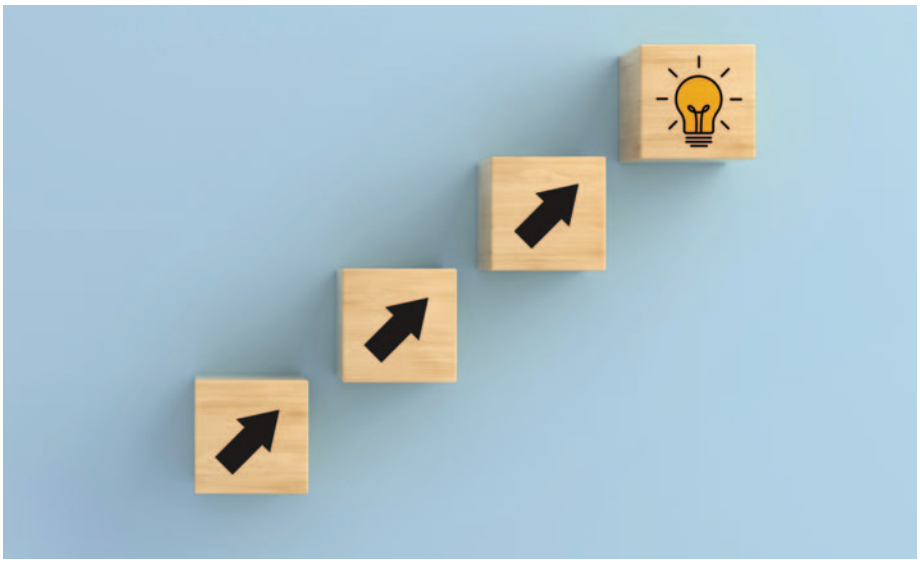
## Continuing professional development for regulatory medical writers

At the May 2024 EMWA Valencia conference, the CORE Reference Team presented a live update on the project, its aims, and its recent resources. We repeated the presentation in a well-attended open webinar soon afterwards in June 2024. Topics covered were:

- Value of CORE Reference for disclosure-ready clinical study reports and Continuing Professional Development (CPD) resources
- A real-life Policy 0070 submission, including a planned versus actual timeline
- Policy 0070 relaunch: Anonymisation Report (AnR) template and insights on its completion
- Medical devices CPD, including the devices and drugs spaces intersection
- An overview of the CORE Reference 2023 Utility Survey results
- Breaking news in the public disclosure arena.



The full recording of the presentation and the slides are available here: https://www.core-reference.org/news-summaries/core-reference-seminar-emwa-valencia-may-2024-and-webinar-07-june-2024/ Do feel able to share them widely.

Although we cover the survey results in our slides and presentation, I encourage you to read the full feature article "The 2023 CORE Reference Utility Survey: Perceptions on a best practice tool for globally applicable clinical study reporting and provision of continuing professional development resources for the regulatory medical writing community" on page 38. As well as reporting on the community's perception of the usefulness of the original CORE Reference manual 7 years after its publication, we share how you perceive the value of the CPD that we disseminate monthly. As we go into an era that includes AI-generated clinical study report texts, the need for regulatory medical writers to fully understand the content requirements of CSRs and keep up to date with evolving requirements is more important than ever. CORE Reference's original resources and ongoing CPD support you to critically review those AI-generated texts that you may now be seeing more frequently. The medical writer's role is undoubtedly evolving from pure de novo content creator to encompass curious and robust content interrogator – both of which need a sharp regulatory eye.

Finally, the RPD section would be incomplete without a handy tabulation (see Table 2) of the most relevant information in the world of RPD in the last few months. Thanks to Vivien Fagan for compiling it.

*Table 1. A bitesize guide to the publication of clinical data in the EU: Policy 0070 versus EU CTR*[a]

| | EMA Policy 0070 | EU CTR |
|---|---|---|
| **Medicinal products covered** | Centrally authorised products only | Investigational medicinal products regardless of whether they have a marketing authorisation |
| **Clinical studies covered** | Clinical studies submitted to the agency in the context of a MAA, Art 58 procedure, line extension or new indication, *regardless of where the study was conducted* | Clinical trials conducted in the EU and paediatric trials conducted outside the EU that are part of paediatric investigation plans |
| **Documents published** | Includes publication of:<br>• Clinical overview (Module 2.5)<br>• Clinical summaries (Module 2.7)<br>• Module 5 – Individual CSRs (Sections 1-15) with a limited number of CSR appendices:<br>16.1.1 Protocol/amendment(s)<br>16.1.2 Sample CRF<br>16.1.9 Documentation of statistical methods including SAP | Includes publication of clinical trial-related information generated during the life cycle of a clinical trial, e.g. protocol, synopsis, patient-facing documents, final summary of trial results, lay summary of results, CSRs<br><br>Following revised CTIS transparency rules, the focus is now on publishing key documents of interest.<br>Applicable to all trials submitted post June 18, 2024 |
| **Publication channel** | EMA Clinical data website<br>https://clinicaldata.ema.europa.eu/web/cdp/home | Clinical trials website<br>https://euclinicaltrials.eu/ |
| Uploads are made independently but make use of the same data protection and CCI rules [b,c,d] | | |

Abbreviations: EMA, European Medicines Agency; EU CTR, European Union Clinical Trial Regulation; MAA, marketing authorisation application; CSR, clinical study report; CRF, case report form; SAP, statistical analysis plan; CTIS, Clinical Trials Information System; CCI, commercially confidential information

**Sources**

[a] https://www.ema.europa.eu/en/human-regulatory-overview/ marketing-authorisation/clinical-data-publication (last accessed -25 Jun 2024)

[b] https://accelerating-clinical-trials.europa.eu/system/files/2023-07/ guidance-document-how-approach-protection-personal-data-commercially-confidential-information-while–.pdf (last accessed June 25, 2024)

[c] https://www.ema.europa.eu/system/ files/documents/other/ wc500174796 –en–0.pdf (last accessed June 25, 2024)

[d] https://www.ema.europa.eu/system/ files/documents/report/ wc500174378– en.pdf (last accessed June 25, 2024)

*Table 2. Selected regulatory information shared via CORE Reference (April 2024 – July 2024)*

| April 2024 highlights | Brief description | Link |
|---|---|---|
| HMA/EMA draft guidance for public consultation: "HMA/EMA guidance document on the identification of personal data and commercially confidential information within the structure of the marketing authorisation application (MAA) dossier" | An update to the guidance adopted in 2012 defining the common approach on what should be considered as PD and CCI in the MAA dossier of medicinal products for human use. | https://www.ema.europa.eu/en/documents/other/draft-revised-heads-medicines-agency-european-medicines-agency-guidance-document-identification-personal-data-commercially-confidential-information-within-structure-marketing-authorisation-application_en.pdf?trk=article-ssr-frontend-pulse_little-text-block |
| PHUSE's EU Clinical Trial Regulation (CTR) Implementation project within the Data Transparency Working Group | Blog gives a summary of Year 2 of implementation of the EU CTR from a sponsor perspective, with a focus on transparency aspects. | https://advance.phuse.global/display/WEL/EU+CTR+Implementation<br>https://phuse.s3.eu-central-1.amazonaws.com/Deliverables/Data+Transparency/EU+CTR+Update+%E2%80%93+Year+2.pdf |

| April 2024 highlights | Brief description | Link |
|---|---|---|
| ICMJE Recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals | Key updates to the ICMJE recommendations include guidance on the use of AI by authors, editors, and reviewers.<br>Other important updates include statements on fair authorship assignment, sustainability goals, funding support declarations, and protection of research participants. | https://thepublicationplan.com/2024/04/02/icmje-recommendations-update-2024-whats-new-and-whats-next/ |
| Best practices in clinical study protocol writing | Blog provides an outline/guide on how to approach protocol development. Key points for different functions include knowing your scope, developing a study outline (synopsis) with a schedule oactivities (schedule of events) early, clearly defining objectives and endpoints, and keeping the end user (i.e., investigators, site staff, regulators, study personnel) in mind when writing and structuring content. | https://www.allucent.com/resources/blog/best-practices-clinical-study-protocol-writing |
| A cost-effective approach to EU Medical Device Regulations (MDR) compliance | Article focusing on being cost-effective in the face of the cost of compliance as it pertains to maintaining EU MDR activities. | https://www.meddeviceonline.com/doc/a-cost-effective-approach-to-eu-mdr-compliance-0001 |
| **May 2024 highlights** | | |
| CTIS newsflash –May 17, 2024 | For all clinical trial applications submitted on or after June 18, 2024:<br>• it will no longer be possible to defer the publication of data and documents<br>• data and documents will be published according to the established timelines for the trial category, population age and trial phase<br>• publication of documents will be focused on key documents of interest.<br>Data on all clinical trial applications submitted before June 18 2024 will be made publicly available in line with the principles and timelines defined in the revised transparency rules. | https://www.ema.europa.eu/en/documents/newsletter/ctis-newsflash-17-may-2024_en.pdf |
| Guidance for the transition of clinical trials from the Clinical Trials Directive to the Clinical Trials Regulation, Version 4 | What has changed compared to Version 3, dated March 2024:<br>• Clarification of consequences of non-compliance with transition requirements<br>• Addition of Annex II (Decision tree administrative transition clinical trial)<br>• Clarification on the interface with medical devices and in vitro diagnostic<br>• Clarification on active sites<br>• Minor amendments to elements related to the CTIS transparency rules. | https://health.ec.europa.eu/document/download/10c83e6b-2587-420d-9204-d49c2f75f476_en?filename= transition_ct_dir-reg_guidance_en.pdf |
| MHRA policy paper | Considers the impact of AI on the regulation of medical products, which also considers the opportunities and risks of AI and is the MHRA's response to the letter from the UK Department of Science, Innovation & Technology and Department of Health & Social Care Secretaries of State to the MHRA. | https://assets.publishing.service.gov.uk/media/662fce1e9e82181baa98a988/MHRA_Impact-of-AI-on-the-regulation-of-medical-products.pdf<br>https://www.gov.uk/government/publications/request-for-regulators-to-publish-an-update-on-their-strategic-approach-to-ai-secretary-of-state-letters/letter-from-dsit-and-dhsc-secretaries-of- state-to-the-medicines-and-healthcare-products-regulatory-agency-html |

| Disseminated Information | Brief description | Link |
|---|---|---|
| **May 2024 highlights** | | |
| Council for International Organizations of Medical Sciences (CIOMS) consensus report | This freely available report describes the potential use of RWE for decision making; RWD and data sources; key scientific considerations in the generation of RWE; and ethical and governance issues in using RWD. It reflects the opinions of the CIOMS Working Group XIII on RWD and RWE in regulatory decision making and was finalised after considering comments received during a public consultation. | https://cioms.ch/publications/product/real-world-data-and-real-world-evidence-in-regulatory-decision-making/#description |
| EMA Policy 0070 relaunch | EMA has released the new anonymisation report form template together with the anonymisation report form instructions. The new template was developed jointly by EMA and the Health Canada PRCI team. The guidance document contains instructions and a set of definitions to guide applicants on how to complete the anonymisation report form for the clinical document package. | https://www.ema.europa.eu/en/human-regulatory-overview/marketing-authorisation/clinical-data-publication/support-industry-clinical-data-publication |
| **June 2024 highlights** | | |
| EMA CTIS relaunch, June 18, 2024 | Clinical Trials Information System (CTIS) – and the underlying transparency rules were updated with a site relaunch on 18 June 2024 | https://www.ema.europa.eu/en/human-regulatory-overview/research-development/clinical-trials-human-medicines/clinical-trials-information-system |
| EMA Guidance document on how to approach the protection of personal data and commercially confidential information while using the Clinical Trials Information System (CTIS) Version 2, June 18, 2024 | This document provides guidance to users on the revised Clinical Trials Information System (CTIS) transparency rules and on the protection of personal data and commercially confidential information (CCI) submitted to CTIS. Changes include alignment with revised CTIS transparency rules, including removal of chapter 5 (no longer applicable), new sections on the 'historical trials' publication principles and on transition trials. Principles of protection of personal data and CCI remained unchanged compared to the former versions.<br><br>It should be read in conjunction with its Annex I<br><br>A Questions and Answers (Q&A) document is also available | **EMA Guidance on how to approach protection of PD and CCI while using the CTIS, Version 2, 18 June 2024:** https://accelerating-clinical-trials.europa.eu/system/files/2023-07/guidance-document-how-approach-protection-personal-data-commercially-confidential-information-while_.pdf<br>**Revised CTIS Transparency Rules:** https://www.ema.europa.eu/en/documents/other/revised-ctis-transparency-rules_en.pdf<br>**Annex 1:** https://accelerating-clinical-trials.europa.eu/document/ download/824905dd-3033-41e6-a871-67b20c4f4c94_en? filename=annex-i-guidance-document-how-approach-protection-personal-data-commercially-confidential_.pdf<br>**Questions and Answers (Q&A):** https://accelerating-clinical-trials.europa.eu/document/ download/33702a5d-13be-4c4f-936d-3627dd73085b_en? filename=ACT%20EU_Q%26A%20on%20protection%20of%20Commercially%20Confidential%20Information%20and%20Personal%20Data%20while%20using%20CTIS_v1.3.pdf |
| EMA CTIS Information Day, October 17, 2024 | To be held the day after the closure of the window for expedited transition of clinical trials, join this information day for comprehensive guidance and practical insights, covering both the transition and the subsequent steps. Your questions will be answered live by EMA, NCA, and industry representatives during the Q&A session. | **Register here:** https://www.diaglobal.org/en/ema/conference-listing/2024/10/ema-clinical-trial-information-system-ctis-information-day?utm_source=Social+Media&utm_medium=LinkedIn&utm_campaign=24526#showcontent<br>**Submit questions here:** emaevents@diaglobal.org |

| Disseminated Information | Brief description | Link |
|---|---|---|
| **June 2024 highlights** | | |
| FDA updated the Top Questions and Answers about the Transition to the Modernised ClinicalTrials.gov and Modernised PRS document along with a series of short videos | The Q&A document has been updated to include new information about the retirement of the classic version of ClinicalTrials.gov and additional questions on PRS modernisation while the series of short videos describe how to complete basic tasks on the modernised website. | **Q&A:** https://cdn.clinicaltrials.gov/documents/Modernization_Transition_Top_Questions_RELEASE_508.pdf?utm_medium=email&utm_source=govdelivery **Videos:** https://www.nlm.nih.gov/oet/ed/ct/demo_videos.html?utm_medium=email&utm_source=govdelivery |
| ACT-EU has launched two advice pilots to improve the quality of applications for clinical trials in Europe | Pilot 1 offers scientific advice on clinical trials and on requirements for MAA.Pilot 2 is coordinated by the Clinical Trials Coordination Group and provides technical and regulatory support on the dossier of a CTA prior to its submission through the CTIS. | https://www.ema.europa.eu/en/news/two-new-advice-pilots-improve-clinical-trials-europe **Pilot 1 Guidance:** https://accelerating-clinicaltrials.europa. eu/document/download/13c622d1-6aef-4d54-b41d-b60dd2e 1e0a9_en?filename=Guidance%20for%20applicants%20S AWP%20CTCG%20pilot%20on%20scientific%20advice.pdf **Pilot 2 Guidance:** https://accelerating-clinical-trials.europa. eu/ document/download/741d2c8d-3a99-48e1-ab51-2bec3e cf3277_en?filename=Guidance%20for%20applicants %20pre-CTA%20advice%20pilot.pdf |
| Phase 2 of the Declaration of Helsinki Revision Process | To maximise input by all stakeholders and the public, two separate public comment periods are held. Phase 1 public comment period was held earlier in 2024, and a Phase 2 comment period was open June 4–24, 2024. | https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/public-consultation-on-a-draft-revised-version-of-the-declaration-of-helsinki-2/ |
| **July 2024 highlights** | | |
| EMA released an ICH reflection paper on pursuing opportunities for harmonisation in using real-world data to generate real world evidence, with a focus on effectiveness of medicines. | The paper outlines a strategic approach to address challenges and discusses how to enable the integration of RWE into regulatory submissions and timely regulatory decision-making. The authors state that the reflection paper represents the initial step of an incremental approach towards harmonisation of regulatory RWE guidance. | https://www.ema.europa.eu/en/documents/other/ich-reflection-paper-pursuing-opportunities-harmonisation-using-real-world-data-generate-real-world-evidence_en.pdf |
| FDA released finalised guidance "Real-World Data: Assessing Electronic Health Records and Medical Claims Data to Support Regulatory Decision-Making for Drug and Biological Products" | The guidance offers clarification of study design elements including on selecting study variables and validation. | https://www.fda.gov/regulatory-information/search-fda-guidance-documents/real-world-data-assessing-electronic-health-records-and-medical-claims-data-support-regulatory |
| Webinar "Utilizing the Digital Protocol): Collaborating to Accelerate ICH M11 and End User Value | This provides an update to the challenge of defining, adapting, and releasing a fully utilisable digital protocol template. The Webinar included representatives from FDA, EMA, CDISC, TransCelerate and Vulcan. **Of note, ICH M11 Step 4 is planned for autumn 2025.** | **Recording**: https://www.youtube.com/watch?v=E72Dc6ib7Q **Slides**: https://www.transceleratebiopharmainc.com/wp-content/uploads/2024/07/TCB-CDISC-and-Vulcan-Webinar_July24.pdf |

| Disseminated Information<br><br>July 2024 highlights | Brief description | Link |
|---|---|---|
| The WHO has introduced an online platform called MeDevIS (Medical Devices Information System), the first global open access clearing house for information on medical devices. | A webinar was held on July 8 titled "Nomenclature of medical devices: EMDN & GMDN" | **Recording and slides:** https://www.who.int/news-room/events/detail/2024/07/08/default-calendar/webinar—nomenclature-of-medical-devices—emdn—-gmnd **The WHO announcement:** https://www.who.int/news/item/08-07-2024-medevis-platform-announced-to-boost-access-to-medical-technologies-and-devices#:https://www.raps.org:text=The%20MeDevIS%20platform%20became%20operational,00%2D15%3A00%20CEST. |

Abbreviations: ACT-EU, Accelerating Clinical Trials in the EU; AI, artificial intelligence; CCI, commercially confidential information; CIOMS, Council for International Organizations of Medical Sciences; CTA, clinical trial application; CTIS, Clinical Trials Information System; CTR, clinical trial regulation; EMA, European Medicines Agency; FDA, Food and Drug Administration; HMA, Heads of Medicines Agencies; ICMJE, International Committee of Medical Journal Editors; MAA, marketing authorisation application; MDR, Medical Device Regulations; MeDevIS: Medical Devices Information System; MHRA, Medicines and Healthcare products Regulatory Agency; NCA, National Competent Authorities; PD, personal data; PRCI, Public Release of Clinical Information; PRS, Protocol Registration and Results System; RWD, real-world data; RWE, real-world evidence.

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Table 2 (above) provides a selection of key information disseminated by the CORE Reference Project Team between April and July 2024.