Clarity and Openness in Reporting: E3-based

News Summary

September 2025

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MEDICINES AND VACCINES

ICH

1. On 10 October 2025, ICH announced the publication of Step 5 of the ICH M14 Guideline "General Principles on Planning, Designing, Analysing, and Reporting of Non-Interventional Studies that Utilise Real-World Data for Safety Assessment of Medicines". The guideline, which provides recommendations for utilizing real-world data to generate real-world evidence in post-marketing safety submissions of medicines, will come into effect on 18 March 2026.

2. The MRCT Center in collaboration with the ICH E6(R3) Expert Working Group, has designed and developed the first of five eLearning modules to support the interpretation and implementation of the new ICH E6(R3) guideline: Module 1: Introduction and Foundational Concepts. Over the next few months, Modules 2-5 will be released as they become available. Also available to download from ICH training materials website here.

3. ICH Training materials - **Interpretation and Application of ICH E6(R3): Good Clinical Practice Guideline** (Modules 1.1, 1.2, 1.3) - have been published. Links to the recordings and transcripts are in the Training Library.

CTR and CTIS

1. As part of the ongoing work to modernise CTIS, the following improvements are currently under development: increased flexibility for changes via non-substantial modifications (NSM) and publication of NSM. Subject to successful acceptance testing, these improvements are expected to be implemented in the release planned at the end of October. Emails for notices and alerts will be developed in Q4 2025, after email services migrate to the cloud.

2. A new safety module will be launched in CTIS in the first half of 2026 to support the management of annual safety reports and the selection of safety assessing Member State (MS). It will offer a more efficient, user-friendly process, aiming to facilitate the work of MS safety assessors and improve the quality of submissions. Training materials and webinars will be provided to support users, and more details will be shared in upcoming newsletters.

3. The EMA are offering a virtual training programme, organised by DIA, 25 November to 28 November 2025, to support sponsor user preparedness for CTIS. A hands-on approach will be taken to explain and demonstrate the functionalities of the system, such as user management, how to submit an initial application as well as modifications, both substantial and non-substantial.

4. The latest issue of Clinical Trial Highlights (Issue 26) is now available and includes news on the joint Accelerating Clinical Trials in the EU initiative and on the Clinical Trials Information System.

5. EU Trial Map is now accessible in all official EU languages. Patients and healthcare professionals can access information about clinical trials in their own language.

EU Regulatory

European Health Data Space (EHDS) News

1. On 30 Sep 25, TEHDAS2 released 11 guidelines and technical specifications for public consultation (open until 30 Nov 25) as part of European Health Data Space (EHDS). As a reminder - the TEHDAS2 joint action prepares the ground for the harmonised implementation of the secondary use of health data in the EHDS. Read about it here. Details of ongoing public consultation here.

2. On 14 Oct 25, ACT EU's July-September 2025 "Monitoring the European clinical trials environment" report was released. With 10,000 trials now registered in CTIS, the numbers and percentages in this report start to become meaningful.The report findings aim to support the implementation of the EHDS and provide tangible recommendations for enhancing the role of open data in future data spaces.

3. The EHDS Regulation is now in force, which is a major milestone in how health data is accessed and reused across the EU. A new report on the EU Data Portal explores how EHDS and the Open Data Directive (ODD) can work together to innovate in healthcare. The EHDS report titled "The impact of the European Health Data Space Regulation and the Open Data Directive on citizens" shows how open and protected data can be combined to improve outcomes and inform policy.

UK and MHRA News

1. HRA has published its final guidance to accompany The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025, which come into force 28 April 2026. The guidance sets out the changes to the REC and MHRA review process for clinical trials involving investigational medicinal products in the UK, in line with the new clinical trials regulations.

The MHRA has published separate guidance to accompany the The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025, which you can read on their clinical trials hub. The Clinical Trials Hub was updated (01 Oct 2025) with ten new Guidance documents, effective 28th April 2026. The aim of this guidance is to support sponsors in understanding the regulatory changes, covering authorisation processes, safety reporting, and other operational aspects.

To mark the six-month countdown until the update to the UK clinical trials regulations, this Joint commitment from MHRA and HRA is explored further in the Blog: Clinical trials regulations - six month countdown begins.

2. Update 01 Oct 25 from GOV.UK for 'Medicines: clinical trials hub'. The page summary: Guidance on using non-investigational medicinal products in a clinical trial now includes a major update to guidance and diagram attachments.

3. Clinical trials update is a regular round-up of the latest news on the upcoming changes to the UK's Clinical Trials legislation. 1 October issue is available here.

4. HRA have released the recording of their Research transparency webinar - Sharing results with participants which took place earlier this month. The webinar focused on sharing results with participants, and the changes that researchers need to prepare for when the new clinical trials regulations come into effect on 28 April 2026.

5. BMJ News Article 06 Oct 25: "UK considers drug price changes as European leaders warn "unnecessary clinical trials" are sending wrong message to big pharma".

6. In advance of updated clinical trials regulations coming into effect in the UK, HRA and the MHRA have written several articles: Transparency to Ensure Trust in Research: A Key Element of the UK's New Clinical Trials Regulations and Safety in Clinical Trials: Preparing for the UK Legislative Changes.

7. The MHRA is leading three new government-funded projects that will use AI and real-world NHS data to improve medicines safety and speed up access to new treatments. Further details here.

FDA Guidance and News

1. The FDA has announced the availability of a draft guidance for industry entitled Expedited Programs for Regenerative Medicine Therapies for Serious Conditions. The draft guidance provides sponsors engaged in the development of regenerative medicine therapies for serious or life-threatening diseases or conditions with FDA's recommendations on the expedited development and review of these therapies.

2. ClinicalTrials.gov has published a notice on the public website and PRS "Because of a lapse in government funding, the information on this website may not be up to date, transactions submitted via the website may not be processed, and the agency may not be able to respond to inquiries until appropriations are enacted. " We suggest you keep up to date with developments by following the site.

3. The Center for Biologics Evaluation and Research (CBER) published a standard operating policy and procedure (SOPP) for staff on where to find lists of disqualified and restricted clinical investigators, debarred researchers, and companies that are under the application integrity policy available on the agency's website. It also instructs its staff to review the Public Health Service (PHS) list of people who have been debarred or suspended by the Department of Health and Human Services (DHHS) Office of Research Integrity. The SOPP provides links to the relevant lists.

4. FDA released the guidance snapshot for the final guidance Conducting Clinical Trials with Decentralized Elements.The snapshot highlights key points in the guidance document and is not a substitute for the guidance document.

5. FDA has released "Patient-Focused Drug Development: Selecting, Developing, or Modifying Fit-for-Purpose Clinical Outcome Assessments." This final guidance (Guidance 3) is the third in a series of four methodological patient-focused drug development (PFDD) guidance documents that describe how stakeholders (patients, caregivers, researchers, medical product developers, and others) can collect and submit patient experience data and other relevant information from patients, caregivers, and clinicians to be used for medical product development and regulatory decision-making.

6. The FDA has publicly released filing checklists used internally by CDER staff to determine if a submitted application is complete and reviewable.The checklists were published in the latest update

of CDER's MAPP 6025.4 Good Review Practices: Refuse to File. FDA news release here. Filing checklists for Abbreviated New Drug Applications were previously published in MAPP 5200.14 Rev. 1 (3 Oct 2023).

7. FDA published a question-and-answers guidance on expanded access to investigational drugs. FDA expects that the public availability of this guidance will increase awareness and knowledge of the availability of expanded access and the procedures for obtaining investigational drugs for treatment use for patients with serious or immediately life-threatening diseases or conditions who lack satisfactory therapeutic alternatives.

8. FDA has released its final guidance on "Expanded Access to Investigational Drugs for Treatment Use (Oct 22, 2025)", replacing the 2017 edition. This update incorporates the 21st Century Cures Act and FDARA, with a sharper focus on transparency, early planning, and broader patient inclusion. Key updates include reinforced transparency requirements and broader patient definitions. Learn more here in this October 2025 Q&A document.

9. In October 25, FDA released a draft guidance for industry Scientific Considerations in Demonstrating Biosimilarity to a Reference Product: Updated Recommendations for Assessing the Need for Comparative Efficacy Studies. This describes updated scientific considerations regarding a comparative clinical study with efficacy endpoints (comparative efficacy study or CES) intended to support a demonstration of biosimilarity. Docket #. Submit comments here.

EMA Guidance and News

1. On 29 Sep 2025, EMA published 'A path to better include patients' perspectives in the regulation of medicines' - a draft reflection paper on patient experience data (PED) for public consultation, encouraging developers to generate and submit these data as part of new medicine applications. The Reflection Paper sets out how data that directly reflects patients' lived experience - such as patient-reported outcomes, patient preference studies, digital health data, and real-world patient-generated evidence - should be systematically integrated into the development, evaluation and regulatory decision-making for medicines. This paper is open for public consultation until 31 Jan 2026. Comments should be provided using this template and be sent to this email address.

2. The European Medicines Regulatory Network (EMRN) has published its first data strategy, establishing key principles and goals to maximise the value of data shared between medicines agencies, such as regulatory submissions data, master data and healthcare data. You can read the full strategy document here.

3. EMA is holding a workshop on the use of external controls for evidence generation in regulatory decision-making on 3 November 2025. This event will explore opportunities and the potential use of external controls in the regulatory setting and discuss related methodological challenges. Registration is open.

4. EMA updates its guidance document on access to unpublished documents. This version, which is the eighth revision, was updated in line with the full reliance of the Clinical Data Publication (Policy 0070) and complements Policy 43 on access to documents related to medicinal products for human and veterinary use.

Health Canada Guidance and News

1. The new Ontario de-identification guidelines for structured data have been published. These reflect current best practices, are operational, and provide plenty of practical details (checklists) and technical guidance (metrics and thresholds). They are consistent with the ISO/IEC 27559 standard (make it easier to implement the principles-based standard) and consider the elements introduced in the Quebec regulation (i.e., inference). Learn more in this 15 Oct 25 Press Release.

2. Health Canada released a Notice to Stakeholders on 17 Oct 25, regarding the implementation of the ICH E6(R3) guideline. It will be on 01 Apr 26.

Real-World Data

1. This 25 Sep 2025 Regulatory Focus article 'FDA official updates on advancing RWE program, lists common reasons for rejection' explains FDA's main reasons for rejecting applicants from participating in its Advancing Real-World Evidence Program. These include concerns that proposed real-world data studies will use heterogeneous patient populations or that the studies will provide supportive, rather than primary evidence, to support regulatory decisions.

2. The Autumn 2025 issue of EMWA Journal Medical Writing is dedicated to real-world data (RWD) and real-world evidence (RWE). The journal is now fully digital and available online and exclusively to EMWA members.

Transparency and Disclosure Resources and News

1. Per the Draft agenda, the General Data Protection Regulation will be back at EU Parliament 21 Oct 25 for additional procedural rules. Proposal & Legislative Observatory pages here.

2. To rapidly register a clinical trial in the US government shutdown, be aware that the UK's ISRCTN registry accepts registrations. The platform is fully ICJME compliant, forms part of the WHO's global ICTRP network and has a transparency dashboard.

3. HRA and MHRA are writing articles ahead of the updated clinical trials regulations coming into effect in the UK. Read the latest article in DIA Global Forum 'Transparency to Ensure Trust in Research: A Key Element of the UK's New Clinical Trials Regulations'

4. ClinicalTrials.gov requires sponsors who register their trials to indicate if they plan to share trial data; ICMJE has a data sharing statement policy that requires authors to specify a plan to share trial data. Zhang et al. published in BMC Med in September 2025 a cross-sectional study which assessed the concordance between what was registered and what was published in trial publications.

5. The Office of the Information and Privacy Commissioner of Ontario (IPC) released an updated edition of its De-Identification Guidelines for Structured Data. The guidelines were developed in collaboration with the IPC's Scholar-in-Residence, Dr. Khaled El Emam, an expert in de-identification, and further informed by extensive consultations with many interested parties. See 'Health Canada' section above too.

6. Real Life Sciences will hold a free webinar entitled "Streamlining Clinical Transparency: One Workflow for Redaction, Quantitative Anonymization & Confidential Information Management" on 20 Nov 2025. Registration and further details here.

7. EviData is a new Canadian software that verifies whether de-identified, anonymized or synthetic data meets recognized privacy standards, including the latest guidance from the Ontario Information and Privacy Commissioner and ISO, while maintaining data utility. It runs entirely in the client's environment and produces a third-party report with evidence on whether your data is safe to use — something increasingly demanded by oversight partners and regulators and by organizations wanting to demonstrate they follow best practices in de-identification. Khaled El Emam is the CEO and Founder of the company behind this product. Request a demo here on this blog page.

8. PHUSE have published the results of The Patient Data Return project. Based on a cross-industry survey of PHUSE member companies, the blog explores the survey results. The aim is to empower clinical trial participants to gain access to their own data.

GDPR and Data Transfer ex-EU

The recent European Court of Justice ruling (C-413/23 P, 4 September 2025) may quietly become one of the most influential data-governance decisions for health research in years. The Court clarified that not all pseudonymised information is automatically "personal data." This Inside Privacy article explains it. In short, the decisive factor is whether the recipient of the data can realistically re-identify the individual. If not, such pseudonymised data might fall outside the full scope of GDPR — as long as governance, ethics and transparency remain robust, and as long as the data controllers – who still hold the key to re-identification – implement all safeguards that data remains personal and fully subject to GDPR. This "relative identifiability" test could profoundly reshape how we handle survey data, patient experience studies, PROs and preference research, or also retrospective use of clinical trial data. It will be important for patient organisations, researchers, ethics bodies and regulators to interpret and apply the ruling carefully in the coming months.

Development Strategy News

1. On 23 Sep 25, the EC, HMA and EMA jointly developed two new targets for clinical trials, to monitor progress to make the EU a more attractive destination for clinical research and improve timely access to innovative medicines for patients.

2. Transcelerate have released an addendum to the Patient Protocol Engagement Toolkit (P-PET) with additional consideration for engaging patients and caregivers in decentralized clinical trials.

3. The Multi-Regional Clinical Trials Center (MRCT) glossary newly expanded to 216 terms.

4. On 07 Oct 25, WHO launched the Global Clinical Trials Forum (GCTF), a global, multi-stakeholder network to strengthen clinical trial environments and infrastructure at national, regional and global levels. The launch marks a pivotal moment for harmonising clinical trial standards and fostering inclusive, ethical research across borders.

5. UK government Press release 07 Oct 25: 'UK clinical trial approval times twice as fast with AI and reforms'.

6. Transcelerate is revising the CPT to align with ICH M11 Protocol Template (expected to launch later in 2025). To help sponsors with implementation planning, Transcelerate have released a preview draft (September 2025) of the CPT Basic Word edition and supporting materials. Transcelerate expects to release the final version of the CPT in early 2026. Links to the Transcelerate preview draft together with supporting overview and reference materials are available here.

7. Estimand training materials for free. Explore EFPIA's Estimand Academy for Trial Teams series, designed for anyone working in clinical trials and including real-world case studies in diabetes, oncology, cardiovascular health, Alzheimer's, respiratory, and bioequivalence. Access the resource here.

8. Clinical Research Pro is offering free online ICH GCP E6(R3) Training that they state "meets the Minimum Criteria for ICH GCP E6(R3) Investigator Site Personnel Training identified by TransCelerate BioPharma as necessary to enable mutual recognition of GCP training among trial sponsors."

9. On 29 Sep 2025, FDA released the ICH E20 Draft Guidance on Adaptive Designs for Clinical Trials. It has been in public consultation in other countries for some time, with a deadline for comments from September (too late for Health Canada) to the end of November (Europe, UK, China, Saudi Arabia, Switzerland) as seen on ICH Efficacy Guidelines.

Artificial Intellligence/Machine Learning

1. The UK government has launched a new National Commission on the regulation of AI in healthcare, one of the goals of which is to ensure AI integration in healthcare is safe, effective and inclusive.

2. UK Government Press Release 07 Oct 25: 'UK clinical trial approval times twice as fast with AI and reforms'.

3. An interesting BMJ article reports the results of an investigation into the performance of commercially available Clinical Artificial Intelligence Scribes (CAISs). One of the main outcomes reported by the authors is "Clinicians should maintain careful vigilance when using CAISs, especially regarding omitted psychosocial details, medications and plausible-sounding inserted diagnoses or treatments."

4. HMA/EMA multi-stakeholder workshop on artificial intelligence will take place on 20 and 21 Nov 2025. Although delegates are asked to register for virtual participation by 02 Nov 2025, registration is not required to follow the event online via live broadcast. Full details and agenda here.

5. The European Commission has published the official FAQs on the AI Act. The list of FAQs has been compiled based on queries received during the AI Pact webinars as well as submissions from stakeholders. This list will be updated regularly and as needed.

News from Asia Regulators

1. Singapore's Health Sciences Authority (HSA) launched an eCTD Portal for test submission, effective 30 September 2025. The test submission phase will be open for 6 months from 30 September 2025 to 27 March 2026, during which companies could test the new system. Submissions made during this test phase will not be processed for regulatory review - they will be removed from the system at the end of the test period. Actual dossier submission in eCTD format will be accepted from 1 April 2026 onward.

2. Japan's PMDA will proactively utilize AI technologies as a means of enhancing overall operational capabilities. An Action Plan for Use of AI in Operations was developed as a guideline for this initiative.

3. Japan's PMDA published in September 2025 a provisional translation of a document "Early Consideration on Handling of Japanese Data for Confirmation of Comparability of Biosimilars to the Original Biopharmaceuticals". For generic drugs, Japanese data are not mandatory to evaluate the bioequivalence.

4. China's NMPA released an update in September 2025 on optimizing the review and approval of clinical trials of innovative drugs (original page in Mandarin). A 30-day fast-track review channel to accelerate clinical trials for Class 1 innovative drugs, including traditional Chinese medicines, chemical drugs, and biologics. Eligible drugs must show clear clinical value, target pediatric or rare diseases, or be part of global R&D efforts. Sponsors must also commit to initiating clinical trials within 12 weeks of approval.

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6. Malaysia's NPRA released in September 2025 the 2nd Edition "Guidance Document And Guidelines For Registration Of Cell And Gene Therapy Products (CGTPs) In Malaysia". Specifically, Chapter 8.3 Clinical Studies provides the key points of concern in the trial design.

7. Registration has opened for the PHUSE APAC Single Day Event (SDE) in Shanghai, China, on 7 November 2025 on the topic "Human–AI Collaboration: Transforming Clinical Development Through Data-Driven Intelligent Automation and Human Insight". Details and registration here.

News from US: Possible Impact on Clinical Trial Ecosystem

1. BMJ News article 01 Oct 25: 'Trump cuts: Gaps in drug research funding in Europe can't be filled, experts warn'

2. Nature News Explainer 06 Oct 25: Volunteer scientists work … to guide vaccine advice in US.

3. BMJ News Article 15 Oct 25: PubMed is running on autopilot during shutdown, but key independent committee has been abolished.

4. BMJ News Article 22 Oct 25: Antidepressants' effect on weight and blood pressure varies hugely even in short term, study finds.

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.

General Updates and News

1. MedTech Europe published the 4th edition of the clinical evidence e-book titled 'Clinical Evidence Requirements under the EU In Vitro Diagnostics Regulation (IVDR)'. Changes affect the following chapters: Chapter 7 Companion Diagnostics; Chapter 14 Next Generation Sequencing; Chapter 15 Real-World Evidence.

2. ISO 18969 (Stage 30.99) is under development. In brief: The standard is being developed by the technical committee ISO/TC 194 "Biological and clinical evaluation of medical devices." Its objective is to supplement, structure, and harmonise clinical evaluation practices across the entire device lifecycle, and is meant to serve as a bridge between regulatory requirements and practical methods of clinical evaluation, in particular, to help standardize the approach to clinical evidence, before market approval and during real-world use.

3. The European Association of Medical devices Notified Bodies (TEAM -NB) released a position paper in July 2025 on "Orphan In-vitro diagnostics medical devices". This document provides viewpoints to manufacturers, the European Commission, the MDCG and other relevant stakeholders notified bodies on the conformity assessment and performance evaluation aspects pursuant to the IVDR of IVD medical devices, including software and accessories for those devices that qualify as 'orphan devices' (OD) or that have an orphan indication.

4. Medical device and pharmaceutical industry groups in the EU and US are urging significant changes to EU MDR and IVDR. Europe's largest medical device trade group, MedTech Europe, said there are fundamental issues within both regulations that can only be addressed through substantial improvements. Organizations, including MedTech Europe, EfPI), and the US-based Advanced Medical Technology Association (AdvaMed) are advocating for the establishment of a single integrated EU body to ensure a consistent interpretation and application of the MDR and IVDR requirements. Read more in this 09 Oct 25 Regulatory Focus article.

5. The Medical Device Innovation Consortium (MDIC) Medical Device Reporting (MDR) working group collaborated with industry and the U.S. Food & Drug Administration (FDA) to identify ways to improve

the MDR process for product complaints found in scientific literature. They have published a report to provide insight on how to interpret the existing FDA guidance on MDRs for events from scientific literature, specifically, when an individual MDR should be submitted versus when multiple reportable events may be submitted on one MDR. Access the report here.

FDA News

The FDA announced a request for public comment by 01 Dec 2026 on measuring and evaluating the performance of AI-enabled medical devices in the real-world. Further details here. Submit comments to docket/FDA-2025-N-4203.

UK MHRA

MHRA is introducing new international reliance routes that will allow medical devices already approved by the FDA to gain faster access to the UK market. This pathway will apply to products cleared through FDA's 510(k), De Novo, and Premarket Approval (PMA) routes – meaning patients in the UK can benefit from proven innovations sooner while maintaining robust safety standards. Key Timelines: Medtech regulatory reforms entering UK legislation in 2026; new reliance routes opening from 2027. Press Release here.