ISSUE 24

NEWSLETTER

Q2 2025

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CONTENTS

Welcome to our regular newsletter, which provides a digest of some of the latest EU/UK and some of the worldwide regulatory news. As ever, Q2 2025 has been another very busy time for new emerging guidelines from the regulatory agencies of the world.

Feel free to contact us on: smt@espl-regulatory.com if you have any questions on the information provided.

MEDICINES

EUROPEAN-WIDE NEWS

EUROPEAN MEDICINES AGENCY (EMA)

NEW **EMA Guidance on Regulatory Acceptance of New Approach Methodologies (NAMs)**

The European Medicines Agency has published a new overview explaining how regulators accept non-animal testing methods for human medicines. The page outlines the scientific and legal basis for using NAMs, lists EMA and EU guidance that already allow in vitro, in silico and other alternative approaches, and points sponsors to procedures for seeking scientific advice on replacing or reducing animal studies in development and quality testing.
https://www.ema.europa.eu/en/human-regulatory-overview/research-development/ethical-use-animals-medicine-testing/regulatory-acceptance-new-approach-methodologies-nams-reduce-animal-use-testing

EUROPEAN COMMISSION (EC)

NEW **EU Pharmaceutical Reform: European Council Adopts Position – June 2025**

The European Council has adopted its first position on the EU's new pharmaceutical legislation, marking a key step toward finalising the reform. This version differs in several areas from the European Parliament's April 2024 text, and Trilogues with the Commission and Parliament will now begin. Key Points:

- Orphan Medicines: Removes the "high unmet medical need" category; proposes 5–10 years of market exclusivity depending on the product type.
- PRIME Criteria: Expanded to include products addressing public health needs, neglected tropical diseases, or antimicrobial resistance.
- Rolling Reviews: Limited to products intended for public health emergencies.
- Unmet Medical Need Definition: Revised and aligned with clinical benefit or absence of existing therapies.
- Shortages: Member states may request marketing and reimbursement action from MA holders.
- Exclusivity: 8 years of data exclusivity + 1 year of market protection, with possible extensions.
- PSURs: Required annually for 5 years, then less frequently.

https://data.consilium.europa.eu/doc/document/ST-10066-2025-INIT/en/pdf

EMA NEWSLETTERS

The EMA publishes monthly newsletters to provide updates on various topics to patients, healthcare professionals and the pharmaceutical industry. The latest newsletters are:

Human Medicines Highlights

Key information on human medicines and changes to regulatory processes each month:

- April: https://ec.europa.eu/newsroom/ema/newsletter-archives/59179
- May: https://ec.europa.eu/newsroom/ema/newsletter-archives/63440
- June: https://ec.europa.eu/newsroom/ema/newsletter-archives/64480

Veterinary Medicines Highlights

Q2 2025 highlights from the EMA Veterinary Medicines Division:
https://ec.europa.eu/newsroom/ema/newsletter-archives/64017

INTERNATIONAL COUNCIL FOR HARMONISATION (ICH)

NEW ICH Announces Key Updates – June 2025

The ICH has released new priorities and draft guidelines, including:

- Drafts for consultation:
  - E21 on including pregnant/breastfeeding individuals in trials
  - Q1 on revised stability testing
- Adopted: E6(R3) – updated Good Clinical Practice
- Draft updates: M4Q(R2) (CTD), M11 (harmonised protocol), and M7 addendum on mutagenic impurities
- Expansion: New observers from Paraguay, Kuwait, and El Salvador
- Training: MedDRA LMS launching in 2025 in 24 languages

https://admin.ich.org/sites/default/files/inline-files/ICH_2024_AnnualReport_2025_0428_ApprovedbyAssembly_2025_0513.pdf

NEW ICH E20 Draft Guideline on Adaptive Clinical Trials – June 2025

ICH has released the draft E20 guideline, providing global principles for the design, analysis, and reporting of adaptive clinical trials in drug development.

Key points:

- Supports prospectively planned adaptive designs (e.g. interim analyses, sample size adjustments)
- Aims to maintain scientific and regulatory rigor while allowing greater trial flexibility
- Open for public consultation until 30 November 2025

Draft guideline (PDF): https://www.ema.europa.eu/en/documents/scientific-guideline/ich-e20-guideline-adaptive-designs-clinical-trials-step-2b_en.pdf

HEADS OF MEDICINES AGENCIES (HMA)

Updated National Information on MAH Transfers (Rev 4, May 2025)

The Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) has issued Revision 4 of its linking document on national requirements for Marketing Authorisation Holder (MAH) transfers. The update consolidates current links, contacts, and specific guidance from each EU/EEA medicines authority, helping companies navigate MAH transfer procedures more efficiently.
https://www.hma.eu/fileadmin/dateien/Human_Medicines/CMD_h_/BREXIT/CMDh_374_2018_Rev4_2025_05_-_National_Links_for_MAH_transfers_required.pdf

DON'T FORGET

A reminder that the new variation guidance and framework are expected to be implemented from 15 January 2026!
https://www.hma.eu/human-medicines/cmdh/procedural-guidance/variation/revised-variations-framework.html

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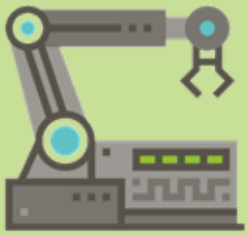

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EUROPEAN DIRECTORATE FOR THE QUALITY OF MEDICINES & HEALTHCARE (EDQM)

NEW EDQM Launches All-Digital 12th Edition of the European Pharmacopoeia

On 18 June 2025, the EDQM officially launched the 12th edition of the European Pharmacopoeia (Ph. Eur.), now available exclusively in digital format. This marks the end of printed editions and the beginning of a fully online platform, reflecting a shift toward greater innovation, accessibility, and international collaboration in medicines quality control.

The launch event took place in Strasbourg, France, and was also livestreamed for public access.

https://www.edqm.eu/en/news/step-into-the-future-edqm-launches-all-digital-12th-edition-of-the-european-pharmacopoeia

Revised EDQM Guide Explains How to Read a CEP

The European Directorate for the Quality of Medicines & HealthCare (EDQM) has published an updated guideline titled “How to Read a CEP”, providing detailed explanations on the content and format of Certificates of Suitability (CEPs) to the European Pharmacopoeia.

The document clarifies common statements found in all CEPs and explains the three current CEP formats: CEP 2.0, Hybrid CEP, and legacy CEP, following content updates introduced in September 2023. It is intended for both industry stakeholders and regulatory authorities and should be used alongside other EDQM certification policies.

https://www.edqm.eu/en/-/-how-to-read-a-cep-revised-guideline-now-available-

INDIVIDUAL AGENCY NEWS

MHRA - UK

‘UK Only’ Sticker Deadline: Printing Required After 30 June 2025

Under the Windsor Framework (in force since 1 January 2025), medicines for the UK market may carry the “UK Only” statement on a sticker only until 30 June 2025. From 1 July 2025, the wording must be printed directly on the pack. Products already stickered and QP-certified before that date may remain on the market until their expiry. Parallel-import (PLPI) packs are not affected and may continue to use over-labelling.gov.uk

https://www.gov.uk/government/publications/labelling-and-packaging-of-medicinal-products-for-human-use-following-agreement-of-the-windsor-framework/labelling-and-packaging-of-medicinal-products-for-human-use-following-agreement-of-the-windsor-framework

NEW MHRA Guidance on Risk Minimisation Measures for Medicines – 9 June 2025

- Introduces additional tools to support safe and effective medicine use by healthcare professionals, patients, and carers.
- Key measures include:
  - Patient guidance (leaflets, checklists, patient cards)
  - Healthcare professional guidance (brochures, posters, prescribing checklists)
  - Access/Distribution Programmes
  - Pregnancy Prevention Programmes

https://www.gov.uk/government/publications/risk-minimisation-measures-for-medicines/risk-minimisation-measures-for-medicines

Updated MHRA Guidance on National Assessment Procedure for Medicines

MHRA has revised its national assessment process (April 2025) to give applicants clearer timelines and greater predictability for innovative and established medicines. An accompanying May 2025 webinar explains the new pathway, including key decision points (first CHM meeting, RFIs), how dossier quality affects timelines, and the value of Scientific Advice and Pre-submission Meetings. The recording is now available.

https://www.gov.uk/guidance/national-assessment-procedure-for-medicines

MHRA Webinar Summary – Point of Care & Modular Manufacture (17 June 2025)
The MHRA has clarified its approach to Decentralised Manufacturing, introducing formal pathways for Point of Care (POC) and Modular Manufacture (MM) under new UK regulations (170A and 170B). Key Points:

- POC: Manufacture must be justified as only possible near the point of use (including mobile units).
- MM: Designed for broader deployment needs (e.g. mobile MRI, pandemic vaccines) based on operational requirements.
- A 60–90 day designation process determines whether a product qualifies as POC or MM, similar to MHRA's scientific advice timelines.
- A Decentralised Manufacture Master File (DM MF) is required to be product-specific, updated annually and is subject to MHRA inspection upon submission with an MIA/MS/mIMP
- Risk Management Plans (RMPs) are required for authorised products, considering the healthcare setting and manufacturing variability.
- Non-serious ADRs must be reported for specials under this framework.

The MHRA has launched a central Decentralised Manufacture Hub providing guidance, templates, and resources to support implementation.
https://www.gov.uk/government/collections/decentralised-manufacture-hub

AIFA - ITALY

Italian Decree Implementing Anti-Doping Law – GU Serie Generale 126 (3 June 2025)
Decree 27 March 2025 lays down detailed rules for applying Article 7 of Law 376/2000 on the health protection of sporting activities and anti-doping controls.
Article 6 obliges Marketing Authorisation Holders (AIC) to comply with new requirements (set out in paragraph 3) for all batches produced 90 days after the decree's entry into force; packs manufactured earlier may be distributed until their normal expiry date.
https://www.gazzettaufficiale.it/atto/serie_generale/caricaDettaglioAtto/originario?atto.codiceRedazionale=25A03201&atto.dataPubblicazioneGazzetta=2025-06-03

HEALTH CANADA

NEW **Health Canada Draft Guidance on Biosimilars – June 2025**
Health Canada has released a draft guidance to streamline biosimilar approvals, open for consultation until September 8, 2025.Key changes:Phase III trials no longer required; focus shifts to comparative pharmacokinetic/pharmacodynamic studies. Applies to well-characterized biologics with high similarity to a Canadian Reference Biologic Drug. Labelling and post-market surveillance requirements remain unchanged. Aims to reduce development time and cost, while maintaining safety and regulatory standards.
Full draft and consultation info: https://www.canada.ca/en/health-canada/programs/consultation-information-submission-requirements-biosimilar-biologic-drugs.html

FDA - USA

FDA Final Guidance: Pre-Submission Facility Correspondence for Priority ANDAs
The FDA has finalized guidance on the Pre-Submission Facility Correspondence (PFC) process for priority generic drug applications, under GDUFA III. Key points:

- A complete PFC must be submitted at least 60 days before the ANDA to qualify for the 8-month priority review.
- PFCs allow the FDA to assess facilities early and plan inspections in advance.
- Applies to all manufacturing, testing, and bioequivalence sites.

https://www.fda.gov/media/163643/download

NEW **Draft Guidance on Replacing Colour Additives in Approved or Marketed Drugs**
The FDA has released draft guidance outlining the recommended approach for replacing colour additives in drugs that are already approved or on the market. The document details how to assess when a change is a minor variation versus requiring a formal supplement or new application. Topics include data requirements, safety assessments, labelling updates, timelines, and regulatory pathways.
https://www.fda.gov/media/186692/download

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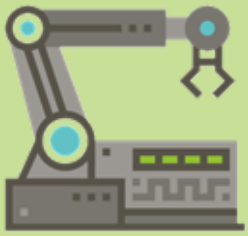

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MEDICAL DEVICES

EUROPEAN-WIDE NEWS

EUROPEAN COMMISSION (EC)

EU eIFU Regulation Update – (EU) 2025/1234

The European Commission has updated its regulation on electronic Instructions for Use (eIFUs) for medical devices. Key changes:

- More devices now qualify for digital-only IFUs, including all professional-use devices and those under MDR transitional rules.
- Devices intended for layperson use must still include paper IFUs.
- Manufacturers will need to register eIFU web links in EUDAMED once UDI registration becomes mandatory.
- The requirement for Notified Body review of eIFUs has been removed.
- Several redundant provisions have been deleted to simplify compliance.

https://eur-lex.europa.eu/eli/reg_impl/2025/1234/oj

EUDAMED Production Deployment – 27 June 2025 (v2.15.0)

The latest EUDAMED production update (v2.15.0) is now live. This may be the final release before EUDAMED becomes mandatory, so stakeholders should familiarise themselves with the updated guidance. Updated User Manuals:

- Regulation Devices: https://health.ec.europa.eu/system/files/2024-06/eudamed-regulation-devices-user-manual_en.pdf
- Legacy Devices: https://health.ec.europa.eu/system/files/2024-06/eudamed-legacy-devices-user-manual_en.pdf
- Notified Bodies & Certificates: https://health.ec.europa.eu/system/files/2024-06/eudamed-nb-certificates-user-manual_en.pdf

MDCG 2025-6: EU Guidance on AI in Medical Devices

The European Commission has published MDCG 2025-6 (19 June 2025), providing key guidance on how the AI Act aligns with the Medical Device Regulation (MDR) and In Vitro Diagnostic Regulation (IVDR). Key Highlights:

- Defines when an AI system in a medical device is classified as high-risk under the AI Act.
- Confirms that compliance with both AI Act and MDR/IVDR is mandatory and cumulative.
- Explains how to align quality, risk management, data governance, and transparency requirements across both regulations.
- Provides updated guidance on post-market monitoring for adaptive ("learning") AI systems.
- Covers expectations for conformity assessment, technical documentation, and human oversight.
- Encourages integration of AI-specific processes into existing MDR/IVDR systems.

https://health.ec.europa.eu/document/download/b78a17d7-e3cd-4943-851d-e02a2f22bbb4_en?filename=mdcg_2025-6_en.pdf

NEW EMDN Helpdesk Now Live to Support Medical Device Classification

The European Commission has officially launched the EMDN Helpdesk to support users of the European Medical Device Nomenclature (EMDN). The helpdesk provides guidance on selecting the correct nomenclature codes for MDR/IVDR compliance and EUDAMED registration. It includes a user manual, contact support, and training resources to assist manufacturers, notified bodies, and regulators.
https://health.ec.europa.eu/medical-devices-topics-interest/european-medical-devices-nomenclature-emdn_en#emdn-helpdesk

TEAM NB

Team-NB Code of Conduct for Notified Bodies – Version 5.1 (25 June 2025)
Minor but meaningful updates to align with newly published EU guidance

- Obsolete legislation references (MDD/AIMDD/IVDD) removed
- Wording refined to reflect latest IAF & MDCG standards
- Enforced discontinuation of peer assessments, with emphasis on MDR/IVDR joint assessments
- Audit duration and technical documentation review methods are now standardized for consistency
- Stronger push for harmonisation through active involvement in NBCG-Med and Team-NB initiatives

https://www.team-nb.org/code-of-conduct-5-1/

Team-NB Best Practice Guidance for MDR Technical Documentation – Version 3
Team-NB has released Version 3 of its Best Practice Guidance (BPG) for compiling Technical Documentation under EU MDR 2017/745, building on and expanding Version 2. It sets clearer expectations for Notified Bodies (NBs) and manufacturers alike. Key Updates:

- Streamlined structure and updated content
- Enhanced pre-submission dialogue with NBs
- Detailed guidance on submission folder structure, hyperlinking, etc.
- Expanded specifications for device descriptions
- New requirements for electronic Instructions for Use (eIFU)
- Highlighted common pitfalls observed by NBs
- Fully revised Clinical Evidence and Post-Market Surveillance (PMS) sections

https://www.team-nb.org/wp-content/uploads/2025/04/Team-NB-PositionPaper-BPG-TechnicalDocEU-MDR-2017-745-V3-20250409.pdf

INDIVIDUAL AGENCY NEWS

MHRA - UK

MHRA Updates Clinical Investigation Guidance for Medical Devices
The MHRA has updated its guidance for manufacturers on conducting clinical investigations on Medical Devices in the UK:

- Great Britain: Must follow UK MDR 2002.
- Northern Ireland: Must follow EU MDR, per the Northern Ireland Protocol.
- For investigations spanning both regions, EU MDR rules apply and a single submission to MHRA is sufficient.

Text boxes in the guidance highlight where NI-specific rules differ.
https://www.gov.uk/government/publications/clinical-investigations-of-medical-devices-guidance-for-manufacturers

Statutory Instrument Retains Key EU-Derived Medical-Device Rules in Great Britain
A new regulation — The Medical Devices (Amendment) (Great Britain) Regulations 2025 (S.I. 2025/591) — entered into force on 24 May 2025. It removes the expiry dates for four pieces of "assimilated" EU law so that they remain part of the UK framework until a full domestic replacement is ready. The retained provisions are:

- Reg. 4H – common technical specifications for certain in-vitro diagnostic devices
- Reg. 4J – requirements for electronic instructions for use
- Reg. 4K – rules for devices manufactured with tissue of animal origin
- Reg. 4L – designation and supervision of approved bodies

The decision follows a public consultation in which a majority of respondents supported retention to avoid regulatory gaps that could compromise patient safety.
https://www.legislation.gov.uk/uksi/2025/591/contents

NEW **MHRA Post-Market Surveillance (PMS) Rules Active from 16 June 2025**

- Mandatory PMS requirements now apply to all UKCA- and CE-marked medical devices marketed in Great Britain.
- Manufacturers must implement a risk-based PMS system, including:
  - Written PMS Plans
  - Periodic safety reporting (PMSR or PSUR)
  - Speedier incident reporting (within 15 days)
  - Availability of PMS documentation (within 3 working days upon MHRA request)
- These reforms aim to enhance real-world safety tracking, identify hazards earlier, and improve public protection.

https://www.gov.uk/government/publications/medical-devices-post-market-surveillance-requirements

UK Joins Global AI Regulator Network, Expands AI Airlock Programme

The UK is the first country to join a new global network of health regulators focused on the safe use of AI in healthcare. At the centre of this effort is the AI Airlock — the MHRA's regulatory sandbox for AI as a Medical Device (AIaMD).

Key AI Airlock Features:

- Provides a controlled testing environment for AI tools used in healthcare.
- Enables collaboration between MHRA, NHS, and developers to evaluate real-world performance and regulatory needs.
- Helps identify safety risks early and informs future AI regulation.

Phase 2 Now Open:

- Launched June 2025 with £1 million in funding.
- Welcomes new AI developers to pilot tools like generative AI and clinical decision support.
- Designed to support faster, safer adoption of AI in UK healthcare and guide global standards.

https://www.gov.uk/government/collections/ai-airlock-the-regulatory-sandbox-for-aiamd

FDA - USA

FDA Final Rule: ISO 13485 Required for US Medical Devices – Effective Feb 2026

The FDA has finalized its Quality Management System Regulation (QMSR), aligning with ISO 13485:2016 starting February 2, 2026.

Key points:

- ISO 13485:2016 compliance will replace most of 21 CFR Part 820.
- FDA-specific requirements still apply, including labelling, complaint handling, UDI, and traceability.
- Certification isn't required, but FDA inspections will assess full QMSR compliance.

Full details and FAQ:

https://www.fda.gov/medical-devices/quality-systems/quality-management-systems-qms-regulation-international-standard-iso-13485-and-its-role-fda-regulatory-requirements

THE ESPL REGULATORY TEAM WISH YOU ALL A LOVELY SUMMER BREAK!

ENJOY THE SUMMER