Regulatory Round-up

August 2025

Also available on our new online news hub at

https://ct.catapult.org.uk/news-hub

UNITED KINGDOM

Medicines and Healthcare Products Regulatory Agency (MHRA)

Consultation on the revised international council for harmonisation guideline M4Q(R2)

The MHRA is consulting with UK stakeholders to gather feedback and comments on a revised international guideline, M4Q(R2). The new International Conference on Harmonisation (ICH) M4Q(R2) guideline will revise and update the current ICH M4Q(R1) guidelines.

The introduction of the M4Q(R1) guidelines on the Common Technical Document (CTD) in 2002 harmonised the format of quality information for registration of pharmaceuticals for human use. M4Q(R1) is now due for revision to further improve registration and lifecycle management efficiency, use of digital technologies, and accelerate patient and consumer access to pharmaceuticals.

The focus of M4Q(R2) is the revision of CTD Quality sections in Modules 2 and 3 to capture quality information for the registration and lifecycle management of pharmaceuticals for human use. The M4Q(R2) guideline would speed up patients and consumers' access to pharmaceuticals as well as provide benefit to the industry and regulatory agencies.

Patients will receive medicines 3-6 months faster under 10-Year Health Plan, as regulators set out plans

Under a joint information sharing agreement, pharmaceutical companies will be invited to register early with the MHRA and National Institute for Health and Care Excellence (NICE) to allow parallel decision making over licencing and value. As a result, patients in England are expected to receive the newest medicines 3-6 months earlier as more medicines get approval for use on the NHS in England at the same as they are licensed for use in the UK. Please find further information here.

Medicines and medical devices act 2021 - Survey

The MHRA, in collaboration with the Department of Health and Social Care, is conducting a review of the UK's medicines and medical device regulatory framework, and is seeking input from stakeholders across the sector, including patients and the public. It is being conducted in accordance with Part 6, Regulation 48 of the Act, which requires the government to assess the operation and impact of the legislation at least once every five years. The focus of the review are the regulations that govern the

Cell and Gene Therapy Catapult is a trading name of Cell Therapy Catapult Limited, registered in England and Wales under company number 07964711, with registered office at 12th Floor Tower Wing, Guy's Hospital, Great Maze Pond, London SE1 9RT. VAT number 154 4214 33. +44(0)20 3728 9500 ct.catapult.org.uk

development, authorisation, supply, and oversight of medicines and medical devices in the UK which include:

- Human Medicines Regulations 2012 (HMRs): which set out the regime for the manufacture, authorisation, supply, and pharmacovigilance of medicines.
- Medical Devices Regulations 2002 (MDRs): which provide the regulatory framework for medical devices, including requirements for safety, performance, and conformity assessment.
- The Medicines for Human Use (Clinical Trials) Regulations 2004: which govern the conduct of clinical trials of medicinal products.
- Medicines and Medical Devices (Fees) Regulations: which outline the fees payable to the MHRA in relation to regulatory.

The deadline for completing the questionnaire is 19th September 2025. Please find further information here.

MHRA designated as WHO-Listed Authority: a milestone for UK life sciences and global health

The MHRA has announced its designation as a WHO-Listed Authority (WLA) by the World Health Organization (WHO), joining the ranks of the world's most trusted regulatory bodies. This recognition affirms MHRA's commitment to the highest international standards in the regulation of medical products and marks a significant milestone for the UK's leadership in global health.

The designation places MHRA alongside Health Canada and Japan's MHLW/PMDA as newly appointed WLAs announced by the WHO on 8th August 2025, reinforcing a growing network of 39 authorities whose work underpins faster, broader access to quality-assured medical products, especially in low- and middle-income countries.

While this appointment does not offer new regulatory pathways for developers in the UK, it underlines the ambitions set out in the Government's Life Sciences Sector Plan and highlights the efficient, mature, and transparent regulatory processes in country as well as its already substantial involvement in international regulatory review programmes, e.g. its membership in the Access Consortium as well as the UK International Recognition Procedure. The UK remains a global hub for innovation, cutting-edge science, and regulatory excellence. Please find further information here.

MHRA pilots new "Route B" for substantial modifications

The MHRA has presented a shift in how it handles substantial modifications to clinical trials. A new pilot program for "Route B" substantial modifications is set to launch on 01st October 2025. It will offer a more streamlined and risk-proportionate review process. This initiative is a crucial step in preparing for the implementation of new clinical trial regulations, which will come into force on 28th April 2026.

A "Route B" substantial modification refers to a specific category of changes to a clinical trial that, while considered "substantial," do not introduce significant new safety concerns. The key criteria for a modification under Route B will require the sponsor to

Cell and Gene Therapy Catapult is a trading name of Cell Therapy Catapult Limited, registered in England and Wales under company number 07964711, with registered office at 12th Floor Tower Wing, Guy's Hospital, Great Maze Pond, London SE1 9RT. VAT number 154 4214 33.

+44(0)20 3728 9500 ct.catapult.org.uk

be confident that there are no significant safety concerns with the modification or any of the investigational medicinal products involved.

In addition, the modification must meet at least one of the following conditions:

- Condition A: The trial does not involve a first-in-human product, and the modification has already been approved by a recognised authority (EU, EEA, or USA).
- Condition B: The modification is limited to a specific set of changes to the trial protocol (e.g., study design, objectives, measurements).

The introduction of Route B is a welcome development for the clinical trials community. It represents a significant step towards a more agile and efficient regulatory landscape in the UK. The MHRA has committed to a 14-day turnaround time for a decision on Route B modifications. Within this period, sponsors will either receive approval or be notified that a full assessment is required. It is important to note that the automatic approval process will not be in place during the pilot. Instead, the MHRA will actively communicate its decision within the 14-day window.

By streamlining the process for lower-risk modifications, the MHRA is reducing the administrative burden on sponsors. Furthermore, the clear eligibility criteria for Route B will provide greater predictability for sponsors when planning and submitting substantial modifications.

The MHRA is encouraging all eligible sponsors to participate in the pilot to help test and refine the process. This is a chance to be at the forefront of regulatory change and to contribute to a more efficient and effective clinical trials environment in the UK.

Interested sponsors can register for the pilot using the Route B Pilot registration form.

Health Research Authority

New report published on simplified arrangements for consent in clinical trials

The Health Research Authority (HRA) ran an online survey from November 2024 to January 2025 to help them get a better understanding of people's views on simplifying the arrangements for obtaining and evidencing consent. Invitations to provide feedback were sent to the public, researchers, research participants, and Research Ethics Committee members. The response rate for research participants was 57%. The findings are summarised below:

- Researchers appreciated the potential for simplified arrangements to make the process simpler and less intimidating for participants, which could widen participation.
- 55% of those who completed the survey did not support the proposal. Members of the public cited concerns about a perceived absence of information about the clinical trial and physical proof that consent had been given.
- 53% of researchers who completed the survey responded positively to the proposal, however some were concerned that verbal consent could become overly brief, and the participant could be less informed as a result.

Cell and Gene Therapy Catapult is a trading name of Cell Therapy Catapult Limited, registered in England and Wales under company number 07964711, with registered office at 12th Floor Tower Wing, Guy's Hospital, Great Maze Pond, London SE1 9RT. VAT number 154 4214 33.

+44(0)20 3728 9500 ct.catapult.org.uk

Please find the published findings here.

Supporting the UK Standards for Public Involvement

Through the Shared Commitment to Public Involvement, which was launched three years ago with the HRA and leading health and social care organisations, the HRA are now calling for public involvement to be delivered in line with the UK Standards for Public Involvement. Members of the Shared Commitment have met with the UK Standards for Public Involvement oversight group to discuss how to support and promote the standards. Said standards set out what good public involvement looks like and are designed to improve the quality and consistency of public involvement across the health and social care sector.

The standards are:

- a framework for what good public involvement in research looks like and are adaptable to different situations
- designed to encourage reflection and learning, including where lessons have been learned when public involvement has failed to lead to expected outcomes
- a tool to help people and organisations identify what they are doing well, and what needs improving
- intended to be used with any method or approach to public involvement in research

Suggestions were made that all the Shared Commitment partners could do more to promote these standards, provide case studies and sector specific examples of their use, add to a library of resources and living updates in the Learning for Involvement website and consider updates relating to safeguarding, accountability and care for people involved. The UK Standards oversight group is seeking feedback on case study examples and experiences using the UK Standards and Public involvement. Please find further information here.

EUROPE

European Directorate for the Quality of Medicines (EDQM)

The Pharmacopeial Discussion Group releases major revision to general chapter Q-09: Particulate Contamination

The revised general chapter “Particulate Contamination (Q-09)” was signed-off by the Pharmacopeial Discussion Group (PDG) on 2nd May 2025. The PDG brings together the European Pharmacopoeia (Ph. Eur.), the Indian Pharmacopoeia Commission (IPC), the Japanese Pharmacopoeia (JP), and the United States Pharmacopeia (USP).

The revision of Q-09 represents a significant step forward in standardised testing procedures for sub-visible particulate matter in all injectable products applied in the

Cell and Gene Therapy Catapult is a trading name of Cell Therapy Catapult Limited, registered in England and Wales under company number 07964711, with registered office at 12th Floor Tower Wing, Guy’s Hospital, Great Maze Pond, London SE1 9RT. VAT number 154 4214 33.

+44(0)20 3728 9500 ct.catapult.org.uk

PDG regions. This update makes the process more robust and adaptable to different product types, including biologicals. Major changes include:

- Definition clarification
- Guidance on sample preparation, especially for formulations with a volume of 25 mL or less
- Method 1 (light obscuration particle count test) updates
- Method 2 (microscopic particle count test) updates

These revisions provide comprehensive standards aligned with current scientific and regulatory expectations, contributing to improved drug development. Please find further information here.

European Medicines Agency (EMA)

First webinar on new approach methodologies (NAMs) in ecotoxicology: State of the science for bioaccumulation

As part of a webinar series on NAMs in ecotoxicology, this first online session taking place on 10th September 2025 explores the state of the science for bioaccumulation with a focus on an integrated weight of evidence approach.

The webinar series on the use of NAMs in ecotoxicology is co-organised by the EMA, the Health and Environmental Sciences Institute (HESI), the National Institute for Environmental Studies (NIES, Japan), PETA Science Consortium International e.V., the US Environmental Protection Agency (EPA), and the Food and Drug Administration (FDA). Please find further details here.

USA

Food and Drug Administration (FDA)

FDA proposes guidance on using overall survival endpoints in cancer drug trials

The FDA has issued a draft guidance to provide recommendations to sponsors on the assessment of overall survival (OS) in randomised oncology clinical trials conducted to support marketing approval of drugs and biological products, with an emphasis on the analysis of OS as a pre-specified safety endpoint. While the guidance discusses scenarios in which it is appropriate to consider overall survival as primary endpoint, this guidance primarily focuses on statistical or design considerations when OS is not the primary endpoint.

The FDA's focus on appropriate statistical methods and trial designs for analysing OS in these scenarios helps sponsors design more efficient and informative studies, ensuring that the evidence for both safety and efficacy is as strong as possible, even with limited patient numbers. This is particularly important for Advanced Therapy Medicinal Products (ATMPs) as they are often innovative, novel therapies, particularly in oncology, with a unique and long-lasting effect that is not fully captured by traditional trial endpoints.

Cell and Gene Therapy Catapult is a trading name of Cell Therapy Catapult Limited, registered in England and Wales under company number 07964711, with registered office at 12th Floor Tower Wing, Guy's Hospital, Great Maze Pond, London SE1 9RT. VAT number 154 4214 33.

+44(0)20 3728 9500 ct.catapult.org.uk

The deadline for comments is 20th October 2025.

FDA approval: Papzimeos

The FDA has approved Papzimeos (zopapogene imadenovec-drba), a first-of-its-kind non-replicating adenoviral vector-based immunotherapy for the treatment of adult patients with recurrent respiratory papillomatosis (RRP). RRP is a rare, chronic disease caused by persistent human papillomavirus (HPV) 6 or 11 infection, leading to the growth of benign tumours in the respiratory tract, most commonly the larynx. The disease is associated with significant morbidity, including voice changes, breathing difficulties, and airway obstruction. Please find further information here.

INTERNATIONAL

International Conference on Harmonisation (ICH)

ICH Q3E Guideline for extractables and leachables

EMA has endorsed the document titled 'ICH Q3E: Guideline for Extractables and Leachables' and released it for public consultation on 1st August 2025. This guideline provides a holistic framework and process for the assessment and control of leachable impurities to further expand the existing ICH guidelines on impurities, including impurities in new drug substances (ICH Q3A) and new drug products (ICH Q3B), residual solvents (ICH Q3C), and elemental impurities (ICH Q3D), as well as DNA reactive (mutagenic) impurities (ICH M7). The framework of this guideline follows the principles of risk management as described in ICH Q9.

Public consultations

Medicines and Healthcare Products Regulatory Agency (MHRA)

	Title	Consultation Period	Category
1.	*ICH E20 guideline on adaptive designs for clinical trials*	*End date: 30 November 2025*	*Public Consultation*
2.	*ICH M4Q(R2) Public Consultation (UK)*	*End Date: open*	*Public consultation*

Health Research Authority (HRA)

	Title	Consultation Period	Category
1.	*UK Standards for Public Involvement*	*End Date: open*	*Public consultation*

Cell and Gene Therapy Catapult is a trading name of Cell Therapy Catapult Limited, registered in England and Wales under company number 07964711, with registered office at 12th Floor Tower Wing, Guy's Hospital, Great Maze Pond, London SE1 9RT. VAT number 154 4214 33.

+44(0)20 3728 9500 ct.catapult.org.uk

European Commission (EC)

	Title	Consultation Period	Category
1.	*EudraLex Volume 4 - Good Manufacturing Practice Guidelines: Chapter 4, Annex 11 and New Annex 22*	*End Date: 07 October 2025*	*Stakeholder Consultation*

European Medicines Agency (EMA)

	Title	**Consultation Period**	**Category**
1.	*ICH Q3E Guideline for extractables and leachables*	*End date: 18 December 2025*	*Public consultation*

Food and Drug Administration (FDA)

	Title	**Consultation Period**	**Category**
1.	*Unique Device Identifier (UDI) Requirements for Combination Products Guidance for Industry and FDA Staff*	*End date: 24 September 2025*	*Draft guidance*
2.	*Approaches to Assessment of Overall Survival in Oncology Clinical Trials*	*End date: 20 October 2025*	*Draft guidance*

Cell and Gene Therapy Catapult is a trading name of Cell Therapy Catapult Limited, registered in England and Wales under company number 07964711, with registered office at 12th Floor Tower Wing, Guy's Hospital, Great Maze Pond, London SE1 9RT. VAT number 154 4214 33.

+44(0)20 3728 9500 ct.catapult.org.uk