Regulatory Round-up

November 2025

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United Kingdom

Medicines and Healthcare products Regulatory Agency (MHRA)

Insurance Review in Phase 1 Clinical Trials

On 28 April 2026, new UK clinical trial regulations — the most significant in 20 years — will take effect. To support industry, the MHRA and HRA have issued guidance clarifying insurance requirements for Phase 1 trials.

For Clinical Trials of Investigational Medicinal Products (CTIMPs), insurance or indemnity must cover the liability of the investigator and sponsor. This requirement is set out in:

- UK Statutory Instrument 2004/1031 – The Medicines for Human Use (Clinical Trials) Regulations (Part 2, Schedule 1, Regulation 14).
- UK Statutory Instrument 2025/5 (Part 2, Schedule 1), effective 28 April 2026).
- UK Statutory Instrument 2025/538 (Schedule 3, Part A1(f), effective 28 April 2026).

Responsibilities:

- Sponsors must provide proof of insurance, a guarantee, or similar arrangement with the Research Ethics Committee (REC) application.
- Research sites must ensure insurance or indemnity covers liabilities from their conduct of the trial.
- Non-NHS Phase 1 sites (e.g., CROs) must not rely solely on REC approval but independently verify cover, check exclusions, and document reviews in the Trial Master File (TMF).
- NHS organisations will rely on the UK study wide review, which checks sponsor insurance for appropriateness and exclusions.

Major change for rare disease treatments on way, signals MHRA

On 2 November 2025, the MHRA published a paper committing to a major reform of the UK's regulatory framework for rare disease therapies. The new pathway, set for release next year, aims to accelerate the journey from discovery to delivery of treatments.

The scope spans:

- Risk appropriate evidence generation for non-clinical and clinical studies, quality, and GxP compliance.
- Licensing and regulatory assessment, including ongoing patient access.
- Enhanced post-market data collection and surveillance.

This initiative signals a transformative shift in how the UK supports innovation and access in rare disease treatment. Please find further information here.

NHS England

Personalised 'living drug' to offer "hope of cure" for aggressive leukaemia on NHS

On 25th November 2025, NHS England announced that the personalised therapy obecabtagene autoleucel (known as obe-cel, brand name Aucatzyl) will be available on the NHS within weeks through specialist centres. This CAR T-cell treatment reprograms a patient's immune cells to fight aggressive leukaemia and has been approved by NICE for adults aged 26+ with relapsed or refractory B-cell acute lymphoblastic leukaemia. Patients will receive two intravenous doses, ten days apart, at specialist CAR-T centres. The treatment – which has been researched, developed and manufactured in the UK – was found to have lower toxicity and was less likely to cause serious side effects than other CAR (chimeric antigen receptor) T-cell therapies.

EUROPE

European Medicines Agency (EMA)

First gene therapy to treat rare disease Wiskott-Aldrich syndrome

The EMA has recommended EU approval of Waskyra (etuvetidigene autotemcel), a gene therapy for patients aged 6 months and older with Wiskott-Aldrich syndrome (WAS) who lack a suitable stem cell donor. WAS is a rare inherited disorder, mainly in males, that impairs blood and immune cells, causing bleeding, infections, and increased cancer risk.

Waskyra is made from a patient's own stem cells, genetically modified to produce functional WAS protein. After infusion, these cells restore healthy blood and immune function. In clinical studies involving 27 patients, Waskyra significantly reduced severe infections (from 2.0 to 0.12 events annually) and bleeding episodes (from 2.0 to 0.16).

Side effects were mostly linked to pre-treatment and infusion procedures. EMA's expert committees concluded that Waskyra's benefits outweigh its risks for patients without a donor. The recommendation now goes to the European Commission for final approval, after which pricing and reimbursement will be decided by individual EU Member States. Please find further information here.

European Medicines Agency post-authorisation procedural advice for users of the centralised procedure

The latest revision of the EMA's Post-authorisation procedural advice for users of the centralised procedure (updated November 2025) introduces clarifications and new requirements for post-authorisation changes, renewals, and pharmacovigilance obligations. These revisions are the most comprehensive update in years, ensuring consistency with new EU legislation, improving clarity for industry, and strengthening pharmacovigilance oversight.

Guideline on non-inferiority and equivalence comparisons in clinical trials

The EMA draft guideline on non-inferiority and equivalence comparisons in clinical trials provides methodological and regulatory recommendations for designing, conducting, and interpreting non-inferiority and equivalence clinical trials, ensuring that such studies are scientifically valid, ethically sound, and capable of supporting reliable conclusions about whether a new treatment is not worse than (non-inferior) or essentially the same as (equivalent to) an established comparator. The draft guideline is open for public consultation until 31 May 2026.

USA

Food and Drug Administration (FDA)

FDA approves gene therapy for treatment of spinal muscular atrophy

The FDA has approved Itvisma (onasemnogene abeparvovec-brve), an adeno-associated virus (AAV) vector-based gene therapy, for the treatment of spinal muscular atrophy (SMA) in adult and pediatric patients aged two years and older with a confirmed mutation in the SMN1 gene.

Spinal muscular atrophy (SMA) is a rare autosomal-recessive disorder caused by SMN1 gene mutations, leading to progressive motor neuron loss, muscle weakness, and, in severe cases, paralysis and death. Affecting about 4–10 per 10,000 live births, SMA was once a leading genetic cause of infant mortality in the U.S. before effective treatments became available.

The active ingredient (drug substance) in Itvisma is identical to Zolgensma, but they differ in formulation and delivery: Zolgensma is given intravenously in a weight-based dose to children under two years with SMA, while Itvisma is a concentrated formulation administered as a single intrathecal injection, independent of patient weight, expanding treatment options to patients aged two years and older. Please find further information here.

FDA takes action on new boxed warning for acute serious liver injury and acute liver failure following treatment with elevidys and revised indication that is limited to ambulatory duchenne muscular dystrophy (DMD) patients

In June 2025, the U.S. FDA issued a safety communication in response to two reported fatalities involving non-ambulatory pediatric male patients treated with Elevidys (delandistrogene moxeparvovec-rokl). These cases, along with additional serious

liver-related adverse events, prompted the FDA to identify hepatotoxicity-associated fatalities as a potential safety signal in its January–March 2025 FAERS quarterly report.

Following these developments, the manufacturer voluntarily suspended U.S. distribution of Elevidys for non-ambulatory DMD patients. Elevidys, an adeno-associated virus vector-based gene therapy, was subsequently subject to a comprehensive FDA safety review. As a result, the FDA approved significant revisions to the product's labeling, including the addition of a Boxed Warning and updates across multiple sections of the prescribing information. The revised indication now restricts use to ambulatory patients aged four years and older with a confirmed DMD gene mutation; use in non-ambulatory patients is no longer authorized under the Biologics License Application (BLA).

To further evaluate the identified risks, the FDA has imposed a postmarketing requirement under section 505(o) of the FDCA. This entails a prospective observational study involving 200 DMD patients, monitored for at least 12 months post-treatment, with structured hepatotoxicity assessments. Please find further information here.

Public consultations

European Medicines Agency (EMA)

	Title	Consultation Period	Category
1.	*ICH Q3E Guideline for extractables and leachables*	*End date: 18 December 2025*	*Public consultation*
2.	*Guideline on quality aspects of phage therapy medicinal products*	*End date: 30 Apr 2026*	*Public consultation*
3.	*Guideline on non-inferiority and equivalence comparisons in clinical trials*	*End date: 31 May 2026*	*Draft guidance*