iFeed | WEEKLY SIGNALS · W28 · 6 – 12 JUL 2026

Trials modernise while enforcement holds the line

This week the FDA moved to implement real-time clinical trials and opened comment on a reset evidence standard, while enforcement stayed active: a data-integrity warning letter to a major EU fill-finish site and the EMA held its mid-year pharmacovigilance review.

Nine signals • traced to primary sources • selected by iFeed

1 CT Clinical trials 2026-07-24

FDA draft guidances on Substantial Evidence, QSP/MABEL dosing and Master Protocols, comment window closes 24 July

FDA published three draft guidances in the Federal Register on 24 June: a revised Substantial Evidence of Effectiveness draft stating that programs "can rely on one scientifically rigorous adequate and well-controlled clinical investigation with confirmatory evidence to satisfy the substantial evidence of effectiveness standard"; a QSP-based MABEL dosing draft recommending a "model-based approach that considers all available data" to set first-in-human starting doses; and a Master Protocols draft covering trial designs intended "to contribute to a demonstration of safety and substantial evidence of effectiveness." The comment windows don't line up: QSP/MABEL closes 24 July, Master Protocols 24 August, Substantial Evidence 22 September.

WHY IT MATTERS

The QSP/MABEL comment window is the tightest of the three and closes first, on 24 July, sponsors with an FIH dose-selection strategy built on NOAEL should get comments in now rather than treating all three drafts as one deadline. The Substantial Evidence draft has the longest runway (22 September) but the bigger strategic stakes: it reopens how many pivotal trials a program actually needs.

WHAT TO CHECK

Assign each draft to an owner and track its own deadline separately, QSP/MABEL (24 July), Master Protocols (24 August), Substantial Evidence (22 September). File comments while the drafts are still open; this is the cheapest moment to influence the bar you'll be held to. Have your modelling group pressure-test FIH starting doses under the QSP/MABEL approach against your current NOAEL-based method, and re-model your pivotal and confirmatory-evidence plan against the Substantial Evidence draft ahead of its later close.

Source · FDA / Federal Register ↗

2 QMS Quality 2026-07-03

FDA warning letter to Sanofi Genzyme (Waterford, Ireland) cites discarded lab review records and untraceable data changes

FDA sent Genzyme Ireland Limited a warning letter dated 22 June, following a January inspection of its Waterford site. The letter states that "quality control personnel used uncontrolled Review Checklists to unofficially document laboratory record reviews, which were subsequently discarded," and that "updates to your records were not always traceable or attributable to a specific person." FDA's conclusion: "the existence of the above-noted violations despite your described controls demonstrates that your data integrity program was not functioning as represented."

WHY IT MATTERS

Genzyme had a documented QC review process on paper; the letter shows staff working around it with off-system checklists that got thrown away, and edits nobody could trace to a name. Quality units elsewhere should read the letter as a checklist of exactly what to look for in their own labs, not a general warning to be more careful.

WHAT TO CHECK

Pull a sample of QC review records this quarter and check for two specific failure modes named in the letter: working checklists or worksheets that live outside the controlled document system, and electronic changes in CDS or LIMS that lack a named user and reason. Where you find either, fix the form and enforce attributable audit trails before the next inspection, and be ready to walk an inspector through one result's full lifecycle end to end.

Source · FDA ↗

3 QMS Quality 2026-07-07

EMA publishes 2026–2028 GMP work plan, planned revisions to GMP chapters, annexes and inspection frameworks

EMA's 2026-2028 GMDP Inspectors Working Group work plan sets target dates for specific chapter revisions: Chapter 1 (Pharmaceutical Quality System) and Chapter 4 (Documentation) are due Q4 2026, the latter to "assure data integrity in the context of GMP," alongside a matching update to Annex 11 (Computerised Systems). A new Annex 22 on artificial intelligence is also targeted for Q4 2026, to "assure use of artificial intelligence in the context of GMP." Chapters 3, 5, 7 and 9 and Annexes 3, 6 and 14 follow on a longer Q4 2028 timeline.

WHY IT MATTERS

Annex 22 is new, EU GMP doesn't currently have a dedicated AI annex, and this work plan puts a Q4 2026 date on writing one. Any manufacturer already using AI/ML in manufacturing or quality decisions has roughly 18 months before that annex lands, and the paired Chapter 4/Annex 11 data-integrity revision on the same timeline means data-integrity and AI governance are being drafted together, not as separate tracks.

WHAT TO CHECK

If you use or plan to use AI/ML anywhere in manufacturing or quality, assign an owner to track Annex 22's drafting now, the Q4 2026 target means a consultation draft could surface well before then, and getting comments in early is cheaper than retrofitting a validated system later. Do the same for Chapter 4 and Annex 11, since they're revising in parallel on data integrity. Chapters 3, 5, 7, 9 and the remaining annexes can go on a longer watch list against the Q4 2028 date.

Source · EMA ↗

4 CT Clinical trials 2026-07-08

MHRA approves nerandomilast (Jascayd) for idiopathic and progressive pulmonary fibrosis, with ongoing safety review

MHRA approved nerandomilast (Jascayd) on 8 July, granting the marketing authorisation to Boehringer Ingelheim Limited International GmbH for an 18mg tablet taken twice daily. The approval notice adds a specific line PV teams should register: "as with any medicine, the MHRA will keep the safety and effectiveness of nerandomilast under close review."

WHY IT MATTERS

That close-review line is boilerplate MHRA includes on new approvals, but it is worth reading literally rather than skimming past, a twice-daily oral drug in a hard, chronic respiratory indication is exactly the profile where post-market signal detection tends to surface issues that a controlled trial population didn't. Boehringer's PV team should assume the bar for a fast, well-evidenced label update is higher than usual here, not lower.

WHAT TO CHECK

Boehringer's PV team should have signal-detection, PSUR and RMP execution live from the 8 July approval date, not phased in, the MHRA's own language commits the agency to close review, and the MAH's monitoring should match that from day one. Other sponsors filing UK approvals in similarly hard indications should read this notice as the template for what MHRA's standard post-approval framing now looks like, and build their PV resourcing plan against it before launch, not after.

Source · MHRA ↗

5 QMS Quality 2026-07-06

FDA CDER publishes 2026 guidance agenda, includes AI/ML pharmaceutical-quality considerations and responding to 483 observations

CDER's 2026 guidance agenda lists "AI and ML Quality Considerations in Pharmaceutical Manufacturing" under Pharmaceutical Quality/CMC, and "Responding to Form FDA 483 Observations at the Conclusion of a Drug CGMP" under Pharmaceutical Quality CGMP. Both are titles on a forward list, not published guidance yet, CDER hasn't attached dates or draft text to either.

WHY IT MATTERS

A dedicated 483-response guidance is the less obvious of the two entries but arguably the more immediately useful: it means CDER is prepared to write down what an adequate response actually looks like, rather than leaving firms to infer it from enforcement history. Quality units that have treated 483 responses as a formality should expect a more defined standard to write to once this publishes.

WHAT TO CHECK

Treat both entries as a planning input rather than a deadline, CDER's agenda lists intent, not a publication date. If you use or plan AI/ML in manufacturing or quality, start building the governance file (intended-use definition, validation evidence, human oversight) now, since a titled agenda item can move to draft text with little notice. Separately, pull your last two years of 483 responses and check whether they were fast, root-cause-focused and evidence-backed, the profile CDER is likely to codify.

Source · FDA CDER ↗

6 QMS Quality 2026-07-06

FDA refreshes multiple drug import alerts (incl. 66-40 CGMP detention-without-physical-exam) on 6 July 2026

FDA last updated Import Alert 66-40, "Detention Without Physical Examination of Drugs From Firms Which Have Not Met Drug GMPs", on 9 June 2026. The alert's own language sets the bar for listing: detention without physical exam applies "when information has revealed that a firm is not operating in conformity with current good manufacturing practice requirements," and release requires the responsible party to "demonstrate that the CGMP violation(s) for the affected product(s) have been adequately corrected."

WHY IT MATTERS

The correction bar in the alert's own text, demonstrating that violations were "adequately corrected", is deliberately open to FDA's judgment, not a fixed checklist. A listed firm's fastest path off the alert is documentation FDA accepts as adequate, and firms that treat this as a negotiation rather than a compliance filing tend to stay listed longer.

WHAT TO CHECK

Check your own sites and every active supplier against the 9 June update to Import Alert 66-40. If you or a supplier appears, assemble the corrective-action documentation now, the alert names this explicitly as the release condition, and map alternative supply for anything exposed in the meantime. Add import-alert screening to supplier qualification on a recurring basis rather than a one-time check at onboarding.

Source · FDA ↗

7 CT Clinical trials 2026-07-07

EMA starts phased (rolling) review of daraxonrasib for metastatic pancreatic cancer, a test case for reformed EU phased reviews

EMA's CHMP started a phased review of daraxonrasib for metastatic pancreatic cancer on 7 July, based on a Phase 3 trial against chemotherapy in previously-treated patients. EMA said directly that "the review of daraxonrasib will serve as an example for some of the provisions of the reformed EU pharmaceutical legislation which is expected to strengthen the use of phased reviews", this isn't a routine rolling review, EMA named it a test case for itself.

WHY IT MATTERS

EMA choosing to publicly flag one specific review as its example case means the daraxonrasib assessment will get more scrutiny of its process, not just its outcome, regulatory teams building a case for phased review on their own high-unmet-need asset should watch how EMA sequences the modules here, since that sequencing is what the reformed legislation's guidance will likely draw from.

WHAT TO CHECK

If you're planning an EU submission for a high-unmet-need medicine, track how EMA sequences the daraxonrasib review specifically, module cadence, what triggers each phase, what CHMP asks for between modules, since EMA has said this case will inform how the reformed legislation's phased-review provisions get applied. Build your own dossier-sequencing capability now so you can deliver assessment-ready modules on a planned cadence rather than assembling one final package.

Source · EMA ↗

8 CT Clinical trials 2026-07-07

Saol Therapeutics resubmits NDA for SL1009 (sodium dichloroacetate) in pyruvate dehydrogenase complex deficiency after August 2025 Complete Response Letter

Saol Therapeutics resubmitted its NDA for SL1009 on 7 July, eleven months after an August 2025 Complete Response Letter that, per the company, "did not identify concerns related to safety or manufacturing, but requested additional evidence to support approval." The resubmission followed a Type A meeting in December and a Type C meeting in March, at which FDA "provided guidance recommending additional survival analyses to support the application", analyses Saol ran on data it already had, including two Phase 3 studies and long-term open-label extension data, rather than through a new trial.

WHY IT MATTERS

The detail worth registering is what the CRL didn't say: no safety or manufacturing concerns, per Saol's own characterization. That narrowed the problem to an evidence-presentation question FDA was willing to resolve through additional analysis of an existing dataset, which is a meaningfully different, and faster, recovery path than a CRL citing safety or CMC deficiencies would allow. CT and regulatory teams facing a CRL on a rare-disease program should push for that same distinction early in their Type A meeting.

WHAT TO CHECK

If you receive a CRL on a rare-disease program, get the Type A meeting on the calendar promptly and ask FDA directly whether the deficiency is evidentiary or a safety/manufacturing finding, Saol's sequence shows an evidentiary-only CRL can be resolved through a Type C meeting on statistical approach (survival endpoints, estimands, open-label extension handling) rather than a new trial. Before resubmitting on re-analysis, confirm your legacy trial data's traceability can withstand another round of review, since re-analysis puts the original dataset back under scrutiny.

Source · Saol Therapeutics / FDA ↗

9 QMS Quality 2026-07-06

MHRA updates labelling & packaging best-practice guidance; adds self-certification route for label/PIL changes

MHRA published updated guidance on 3 July making self-certification the default submission route for label and PIL changes that don't touch the Summary of Product Characteristics, full assessment stays mandatory only for changes falling into categories P1 through P4. Outside those four categories, the sponsor certifies compliance rather than MHRA confirming it before the change goes live.

WHY IT MATTERS

The P1-P4 carve-out is the operative detail: it means the self-certification route isn't a blanket option, it's everything that falls outside four defined exceptions. Regulatory teams need the exact P1-P4 definitions in hand, not just the existence of the route, before they can tell which of their own pending label changes actually qualify.

WHAT TO CHECK

Pull the full P1-P4 category definitions from MHRA's guidance before routing any change to self-certification, the 3 July update makes self-certification the default only for changes outside those four categories, so getting the boundary wrong means certifying something that needed full assessment. Update your change-control SOPs to name who is authorised to certify and what evidence file has to exist behind each certification, since MHRA can still inspect the record after the fact even though it didn't review the change up front.

Source · MHRA ↗