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Enforcement moves ahead of guidance

This week regulators moved from setting expectations to checking them. A data-integrity audit is now standard on every FDA pre-approval inspection, the MHRA put AI-written compliance responses on notice, and the European Pharmacopoeia became binding across 39 countries.

Nine signals • traced to primary sources • selected by iFeed

1 QMS Quality 2026-06-29

MHRA puts AI-generated inspection responses on notice, unverifiable AI content will be rejected and can escalate to enforcement

MHRA Inspectorate said on 29 June that it has received AI-generated inspection responses citing MHRA guidance that doesn't exist, including one 90-page reply that never addressed the deficiencies raised. The agency's fix isn't a ban on AI drafting, it's a named-accountability requirement: every submission must be accurate, verifiable, technically reviewed, and signed off by someone who owns the answer. A fabricated citation in an AI-assisted response can now trigger rejection or an Inspection Action Group referral.

WHY IT MATTERS

MHRA says it has already seen the failure mode: one inspection response it received "totalled over 90 pages and did not address the deficiencies identified," and other submissions cited MHRA guidance that doesn't exist. The agency's response is procedural, not just a warning, it says it "may reject the response or return it for another attempt," weight it toward "higher risk" in future inspection prioritisation, or refer the firm to the Inspection Action Group. A single invented citation in an AI-drafted response is now a documented path to that outcome.

WHAT TO CHECK

Add an explicit AI-use control to your quality system now. MHRA's stated bar for any submission is three-part: "factually accurate and verifiable," "technically reviewed by appropriately experienced people," and "signed off by someone with authority and accountability." Build that into your SOP for AI-assisted CAPA, deviation and inspection-response drafts, and prohibit unverifiable citations outright. If you have already submitted AI-assisted responses, audit them for fabricated references before your next inspection.

Source · MHRA Inspectorate ↗

2 QMS Quality 2026-06-29

FDA rewrites its Pre-Approval Inspection program (7346.832), a data-integrity audit is now standard on every PAI

FDA's CDER re-issued Compliance Program 7346.832 on 29 June, and Objective 3 now directs every PAI investigator to trace raw data at the facility to "authenticate the data submitted in the CMC section of the application as relevant, accurate, complete, and reliable." That instruction used to apply mainly to for-cause inspections. Now it's standard on every pre-approval visit, which means the question at PAI is no longer just whether you can make the product, it's whether your raw records prove the CMC data are real.

WHY IT MATTERS

CDER's re-issued compliance program instructs investigators to "audit and verify raw data at the facility that are associated with the product" specifically to "authenticate the data submitted in the CMC section of the application as relevant, accurate, complete, and reliable." That's a standing instruction, not a for-cause trigger, every new-application or supplement PAI now includes it. A gap between filed data and source records becomes a first-visit finding that can delay approval.

WHAT TO CHECK

Before any PAI, run your own version of Objective 3: pull the raw chromatograms, notebooks and audit trails behind every result filed in your CMC section and confirm each one is "complete, accurate, and reliable" against the submission, with no orphan or unexplained reprocessed injections. Identify who's accountable for any discrepancy you find and fix it under change control before FDA's investigator runs the same trace.

Source · FDA Compliance Program 7346.832 ↗

3 CT Clinical trials 2026-06-22

FDA’s ‘Operation Trailblazer’, an Expedited IND pilot and a single-pivotal-trial evidence standard reshape early development

HHS and FDA launched Operation Trailblazer on 22 June with two open dockets: an Expedited IND pilot RFI (comments due 22 July) and a revised draft guidance that says a sponsor may rely on "one rigorous, adequate and well-controlled pivotal clinical investigation, plus confirmatory evidence" to show substantial evidence of effectiveness (comments due 22 September, docket FDA-2019-D-4964). Sponsors planning US programmes should model both into protocol and CMC planning now, while the comment window is still open.

WHY IT MATTERS

FDA's revised guidance states sponsors may now rely on "one rigorous, adequate and well-controlled pivotal clinical investigation, plus confirmatory evidence, to demonstrate substantial evidence of effectiveness", language that reframes a two-trial default into an explicit single-trial option. Paired with an Expedited IND pilot built to "shorten the time it takes from drug identification to first-in-human study," the evidence bar and the on-ramp to the clinic are moving on the same timeline. Both dockets are open now, so sponsors can still shape the final text.

WHAT TO CHECK

Assign owners to the two open dockets and file comments: the Expedited IND RFI closes 22 July, and the revised "Demonstrating Substantial Evidence of Effectiveness" draft guidance (docket FDA-2019-D-4964) closes 22 September. Re-examine your pipeline's pivotal-trial and confirmatory-evidence strategy against the single-trial standard. Brief clinical operations and CMC on the Expedited IND pilot and the new Phase 1 IND Navigator.

Source · FDA, Operation Trailblazer ↗

4 BA Bioanalytical 2026-07-01

European Pharmacopoeia 12.3 enters into force across 39 countries, the revised monographs are now the legal standard

EDQM confirmed that European Pharmacopoeia Issue 12.3 became applicable across all 39 Ph. Eur. member territories on 1 July 2026. Any QC or bioanalytical method still built on a superseded monograph is, from that date, out of compliance until it's updated, this is a force date, not a recommendation.

WHY IT MATTERS

EDQM confirmed Ph. Eur. Issue 12.3 became applicable across 39 countries on 1 July 2026. That's a hard force date, not a guidance target, from that date, EU/CEP-facing QC and bioanalytical labs must run methods and hold specifications against the 12.3-revised texts. Any lag between the effective date and method implementation is a live compliance gap an inspector can cite directly against release testing.

WHAT TO CHECK

Confirm that every affected monograph and general chapter in 12.3 is implemented in your methods, specifications and CoA templates as of 1 July, under change control with training records. For CEP holders, action any dossier updates tied to the revised monographs, EDQM's own newsroom post doesn't itemize which CEPs are affected, so check your specific certificate against the 12.3 text rather than assuming. Do not release EU product against a superseded text.

Source · EDQM Newsroom ↗

5 QMS Quality 2026-06-24

FDA warning letter, Wizcure (India): investigators watched sterility plates being swapped, a live data-integrity failure on the fill line

FDA's 24 June warning letter to Wizcure Pharmaa (Bhiwadi, Rajasthan) states that after environmental-monitoring plates showed growth, "the next day, our investigator observed microbial plates with the same identification information with no growth." The same inspection found sterility forms pre-filled before testing, and an ISO 5 fill line where FDA found "the absence of a physical barrier separating the ISO 5 (Grade A) filling zone from the ISO 7 (Grade B) surrounding environment creates an unacceptable risk to product sterility." FDA had already put the firm on Import Alert 66-40 in December 2025, this letter documents why.

WHY IT MATTERS

FDA's investigator didn't infer this failure from records, they watched it happen. The letter states that after plates showed growth, "the next day, our investigator observed microbial plates with the same identification information with no growth." Separately, "investigators also found laboratory forms were pre-filled with microbial testing information", results recorded before testing occurred. FDA had already placed Wizcure's products on Import Alert 66-40 on 23 December 2025, ahead of this 24 June warning letter. For India-based sterile sites serving the US, this is a direct read on what an inspector is trained to catch.

WHAT TO CHECK

Audit your microbiology data chain end to end: are plate reads recorded contemporaneously with a second witness, are results captured before any disposal, is there photographic or system evidence, and is custody traceable? Verify aseptic-zone segregation against your qualification, FDA's letter states that "the absence of a physical barrier separating the ISO 5 (Grade A) filling zone from the ISO 7 (Grade B) surrounding environment creates an unacceptable risk to product sterility." Treat pre-filled forms and any post-hoc plate handling as a critical deviation.

Source · FDA Warning Letter, Wizcure Pharmaa ↗

6 BA Bioanalytical 2026-06-22

FDA draft guidance: model-based (QSP) selection of the first-in-human MABEL starting dose

FDA issued draft guidance on 22 June (docket FDA-2026-D-6539) recommending how sponsors can use a quantitative systems pharmacology approach to set the MABEL starting dose for first-in-human Phase 1 trials. For novel biologics and new modalities, that's a mechanistic alternative to a purely empirical starting dose, but the guidance only supports a model that's built on validated assays and characterised target engagement, so the bioanalytical package behind it carries as much weight as the model itself.

WHY IT MATTERS

FDA's draft guidance (docket FDA-2026-D-6539) sets out "recommendations on the appropriate use of a quantitative systems pharmacology (QSP)-based approach for determining minimum anticipated biological effect level (MABEL) dose in first-in-human (FIH), phase 1 trials." That gives sponsors of first-in-class biologics a mechanistic alternative to a purely empirical starting dose, but a QSP model is only as defensible as the bioanalytical and target-engagement data feeding it. This raises the bar on the data package behind FIH entry, not just the modelling.

WHAT TO CHECK

If you run FIH programmes, map your dose-selection SOPs to the QSP approach in docket FDA-2026-D-6539 and identify where your bioanalytical and target-engagement data would need strengthening to support a model-based MABEL. Ensure assay validation and PK/PD characterisation are fit to feed a QSP model, and document every assumption. File comments while the guidance is in draft.

Source · FDA Draft Guidance (docket FDA-2026-D-6539) ↗

7 BE Bioequivalence 2026-07-01

Revised Ph. Eur. dissolution chapters (2.9.42, 2.9.43) take effect, methods and biowaiver dossiers citing them need review

Ph. Eur. general chapters 2.9.42 (dissolution test for lipophilic solid dosage forms) and 2.9.43 (apparent dissolution) were revised in Issue 12.3 and took effect 1 July 2026 across the 39 member territories. Dissolution methodology sits at the heart of BCS biowaivers, release specifications and in-vitro bioequivalence bridging, any method or dossier still citing the prior text needs to be reconciled to the revised chapters now.

WHY IT MATTERS

Chapters 2.9.42 (dissolution test for lipophilic solid dosage forms) and 2.9.43 (apparent dissolution) were revised and published in Ph. Eur. Issue 12.3, effective 1 July 2026 alongside the rest of the issue. Dissolution methodology underpins BCS-based biowaivers, batch release and in-vitro bioequivalence bridging, so any QC method, release specification or dossier that cites these two chapters needs to be checked against the revised text, and any biowaiver argument built on the prior version may need re-justification.

WHAT TO CHECK

Inventory every method, specification and dossier that references Ph. Eur. 2.9.42 or 2.9.43. Both chapters went through public consultation in Pharmeuropa 36.3 before finalization, confirm your methods match the final 12.3 text rather than the consultation draft, update where needed under change control, and re-check any BCS biowaiver or in-vitro BE argument that relies on them. Prioritise EU/CEP-facing products and anything with a pending filing.

Source · EDQM, Ph. Eur. 12.3 ↗

8 BE Bioequivalence 2026-06-17

FDA approves the first generic of Xofluza (baloxavir), a single-dose oral antiviral sets a bioequivalence reference

FDA approved Norwich Pharmaceuticals' generic baloxavir marboxil tablets on 17 June 2026, the first generic of Xofluza, the single-dose treatment for acute uncomplicated influenza and post-exposure prophylaxis in patients 5 and older. For any ANDA team working single-dose oral products, the bioequivalence design behind this approval is now the reference point to study before your next filing.

WHY IT MATTERS

FDA approved Norwich Pharmaceuticals' generic baloxavir marboxil on 17 June 2026, the first generic of a single-dose oral antiviral. Iilun Murphy, M.D., Director of the Office of Generic Drugs in FDA's Center for Drug Evaluation and Research, called it "a meaningful milestone for the treatment of influenza." First-generic approvals of single-dose products effectively define the accepted bioequivalence pathway for the class: study design, comparator sourcing and endpoint strategy that competing ANDA sponsors will follow into the 2026–27 respiratory season.

WHAT TO CHECK

If baloxavir or single-dose oral antivirals are in your pipeline, review the FDA product-specific guidance and the accepted BE design behind Norwich Pharmaceuticals' approval. For BA/BE units, treat single-dose PK studies of this type as a reference model for design, sampling schedule and statistical approach, and track the product-specific guidance for any revision.

Source · FDA Press Announcement ↗

9 QMS Quality 2026-07-01

New Ph. Eur. chapter 5.38 ‘Quality of data’, a pharmacopoeial data-integrity standard inspectors can cite

New Ph. Eur. general chapter 5.38 'Quality of data' was published in Issue 12.3, the same issue that took effect across 39 territories on 1 July 2026. It covers digital information generated or used by QC laboratories, with a stated focus on the life cycle management of that data, the first time data quality has had a dedicated home in the Pharmacopoeia itself rather than living only in FDA, MHRA or PIC/S guidance.

WHY IT MATTERS

Until now, data-integrity expectations for labs lived in FDA/MHRA guidance and PIC/S documents, persuasive but not compendial. Chapter 5.38 was published in Ph. Eur. Issue 12.3 and, per EDQM's own description reported by industry trade press, addresses digital information generated or used by quality control laboratories, with particular focus on the "life cycle management of digital data." That moves data quality from guidance into an official compendial text an EU inspector can cite directly against chromatography systems and audit trails.

WHAT TO CHECK

Read chapter 5.38 in full, EDQM's own newsroom page was not directly accessible for this review, so verify the final scope text at source before citing specifics. Map its coverage of "life cycle management of digital data" against your laboratory data-governance controls: chromatography data systems, audit-trail review, access control and record retention. Close gaps under change control and update your data-integrity SOPs to reference the new compendial chapter.

Source · EDQM Newsroom ↗