Qualio

Pharmaceutical quality in 2025:
An overview

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2025 will be a big year for pharmaceutical quality professionals.

New technology, fresh legislation, innovative drug and trial delivery formats, and evolving expectations of quality best practice will all shape the profession in the coming year.

This guide breaks down the key drivers and developments you need to be aware of. Forewarned is forearmed – careful preparation now will reap rewards for your business in the months to come.

Meg Sinclair
Quality Operations Manager

Chapter 1

The drivers

We asked our Qualio quality success team of industry experts about the key developments and trends they anticipated impacting the pharmaceutical industry in 2025 and beyond. Here's what they said.

Shortages – and preventing them

Drug shortages are a lingering, damaging threat to both patients and the status quo of the pharmaceutical industry. Responding to them and preventing future shortages is a problem occupying the attention of regulators across the globe.

The FDA noted 111 current drug shortages at the 2024 PDA/FDA Joint Regulatory Conference, with an average resolution time of 5 months each. This isn't a new problem — after all, it was their 2019 Interagency Drug Shortages report which birthed the concept of their upcoming Quality Management Maturity program (more on that below, and in our dedicated QMM guide!) 40-50 new shortages have sprung up in the United States like clockwork for the past 5 years.

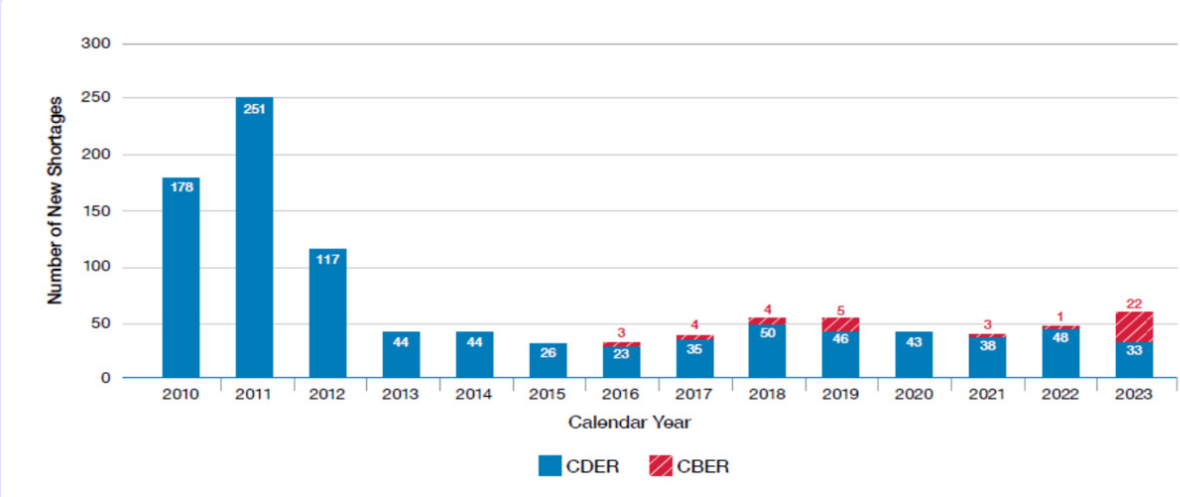


Figure 1. Number of New Drug Shortages Per Calendar Year, (from CY 2010 to CY 2023)

Unsurprisingly, the 2019 report was followed up in 2022 by the FDA's draft guidance: Risk Management Plans to Mitigate the Potential for Drug Shortages. A key requirement of this guidance was the recommendation for stakeholders and key actors in the supply chain to build and collaborate on risk management plans. These supply chain RMPs should consider, evaluate and mitigate supply risks to insulate the broader supply chain from the risk of shortages.

The shortage problem is currently being amplified by low industry engagement with the drug amount reporting required by the 2020 CARES Act. Despite the federal requirement for manufacturers to make an annual report of manufactured product volumes to the FDA, the pitiful engagement levels of around 25% of NDCs in the Act's first year have steadily declined to less than 20% since.

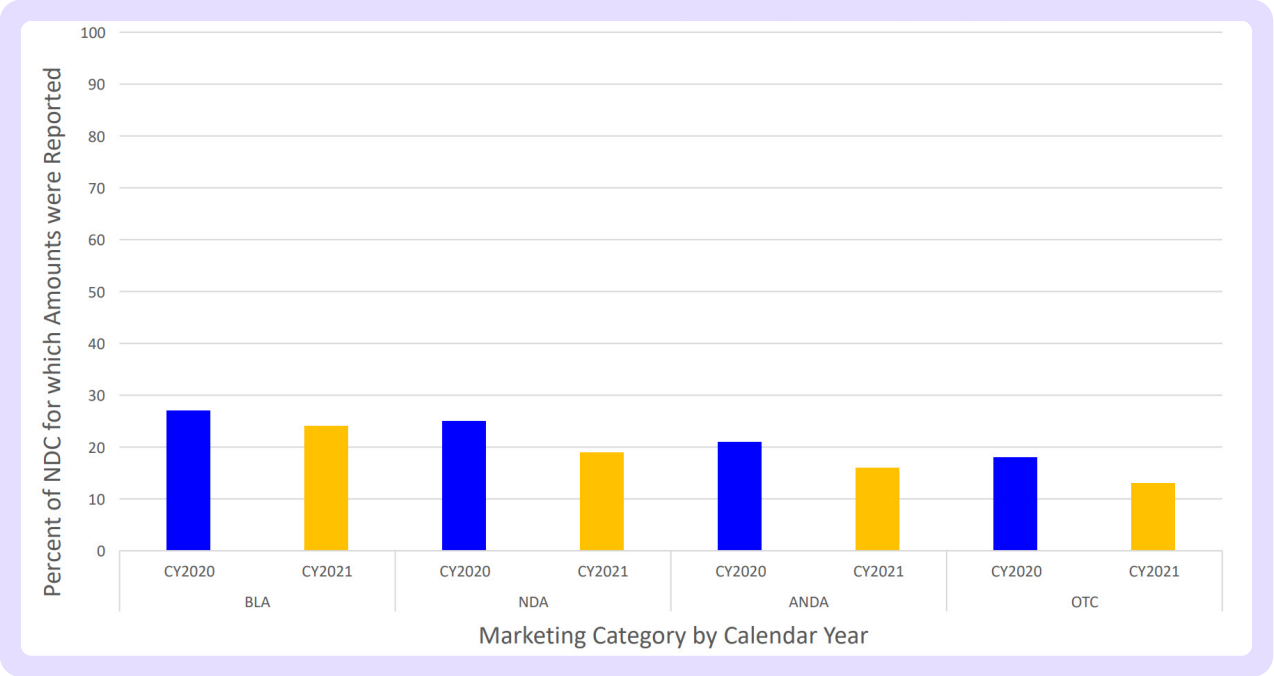


Figure 2: Percent of NDCs for which amounts were reported by marketing category

On top of all this, a key regulatory requirement for American pharmaceutical companies went live in 2024.

The Drug Supply Chain Security Act was originally launched in 2013 by President Obama, mandating end-to-end drug traceability requirements at the package level to further insulate against drug supply disruption. The Act was scheduled for enforcement in

November 2023, before finally going live on November 27, 2024 after the end of the FDA's interim, year-long 'stabilization period'. This recent regulatory nail-biting about supply chain risk isn't restricted to the States. In 2023, the EU proposed its new Human Medicines Regulation. It suggests that future marketing authorization (MA) holders should build and maintain a shortage prevention plan for any product they place on the European market. Keep an eye on this in 2025.

A Critical Medicines Alliance of national authorities, manufacturers, civil society representatives and EU agencies went live in January 2024, but its adjoining Critical Medicines Act, designed to wean Europe off its overreliance on Asian drug imports, has shown no signs of going live any time soon.

And EU Regulation 2022/123, going live in early 2025, gives the EMA a new role to monitor and protect medicinal supplies. A new European Shortages Monitoring Platform (ESMP) will go live simultaneously. All in all, 2025 should prove an especially challenging year for these supply squeezes to be addressed. 2023-4 introduced a host of new obstacles and threats to the fragile quality ecosystem, including:

- Increased patient demand in areas like weight loss drugs, ADHD treatments, and IV fluids and narcotics
- Competition on manufacturing lines for multi-drug manufacturers
- Loss of market capacity due to bankruptcies and plant closures
- Short supplies of key manufacturing components like filters, vials and stoppers
- Hangover from Pfizer's NC tornado in July 2023
- Continued economic uncertainty and high interest rates

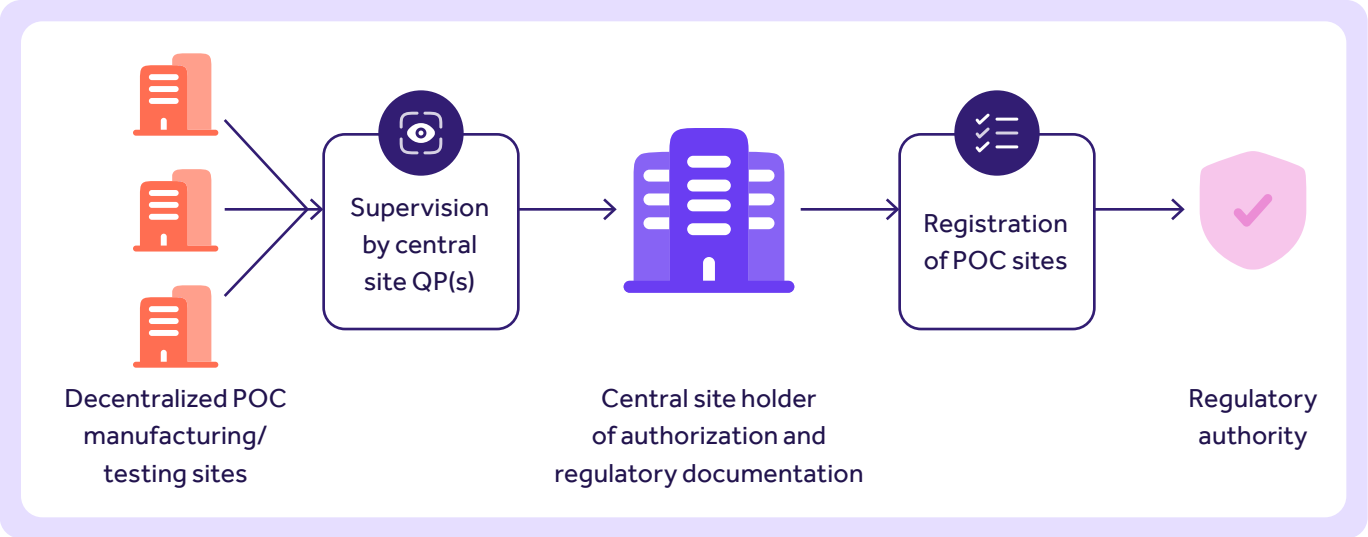
The takeaway: drug shortages continue to rumble on. Regulators are paying attention, and new legislative requirements and expectations will take further shape in 2025. Pay attention to your own output, and focus your quality efforts on consistency as well as quality of supply.

New manufacturing, distribution and clinical trial methods

Between 2021 and 2023, the UK, EU and US all proposed models in that order of a new decentralized point-of-care manufacturing model.

The objective? Build an operational framework for short-life medicines and therapies to be produced at the point of care – such as a hospital or clinic – allowing treatments to be administered rapidly with no delivery and storage phase.

These distributed just-in-time sites would be connected by an overarching 'control site' responsible for regulatory liaison and creation of documents like a master file.



This format has found voice in 3 key ways:

- **The original UK proposal:** August 2021 (94% of surveyed respondents supported the model)
- **US FDA consultation:** October 2022 (part of the FRAME project)
- **EU Human Medicines Directive:** April 2023 (practically identical to the UK model)

Point-of-care manufacturing isn't the only industry innovation gathering pace.

Decentralized clinical trials (DCTs) are also being explored. The FDA has, in recent years, published both its Framework for the Use of Digital Health Technologies in Drug and Biological Product Development and Decentralized Clinical Trials for Drugs, Biological Products, and Devices Guidance for Industry, Investigators, and Other Stakeholders.

But this prospective model is currently being hamstrung in both the USA and EU by the clashing of federal and state requirements.

In the EU, clinical sites are only authorized to deliver experimental trial drugs to patients within the same national territory. While in the States, direct-to-patient trial drug delivery is classed as a pharmacy dispensing activity, forcing trial operators to register as out-of-state pharmacy bodies before DCTs can begin.

This brings a whole slew of pharmacy requirements to integrate into your regular PQS operations, blocking many from being able to realistically take part.

DCTs are one to watch for the future, then, but we expect that the regulatory landscape will require some tweaking to make them realistic operational prospects.

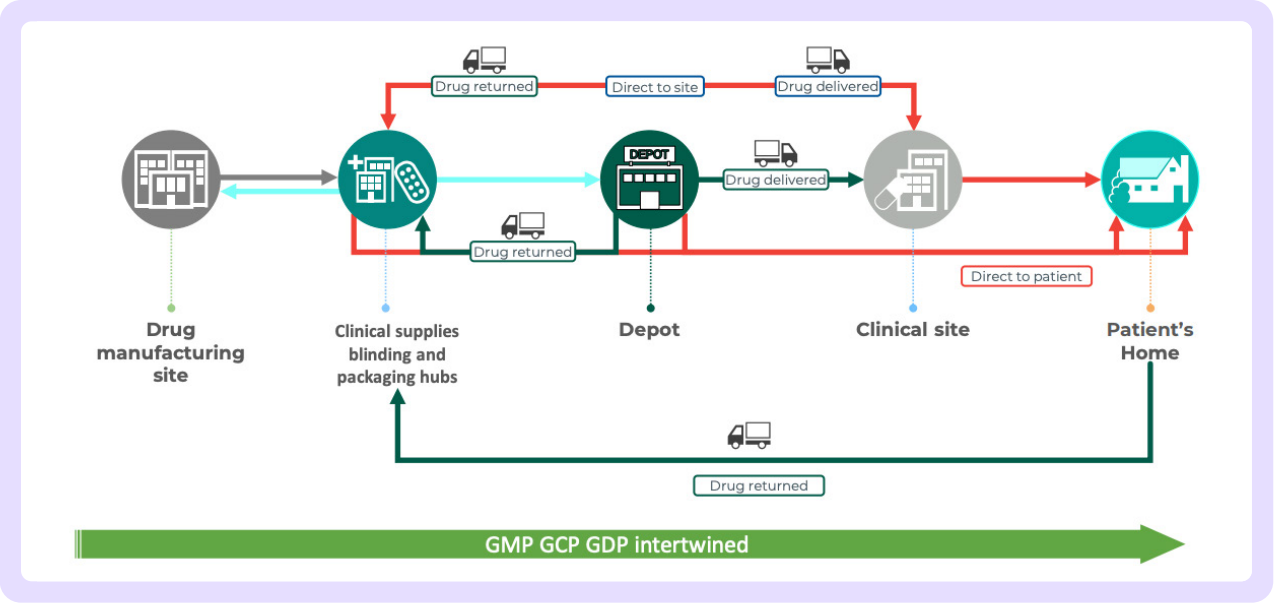


Figure 3: Potential DCT model. Credit: NSF

The takeaway: POC manufacturing and decentralized trials are still in the theoretical stage, but are gradually finding favor in multiple key markets as a way to deliver more agile, personalized therapeutics. Decentralizing operations and moving trial and medicinal delivery closer to the patient, we should imagine, would also help to tackle the supply chain and shortage issues noted above – while bringing new quality challenges to tackle. Keep an eye on developments in this space, particularly if you're involved in especially compatible areas like ATMP production!

Quality management maturity: a new approach to pharmaceutical quality

Arguably the most important industry development for pharmaceutical companies in 2025 is the ever-nearing Quality Management Maturity program from the FDA.

We saw above how it emerged as a response to the continuing drug shortage problem in the US, but its implications go far beyond just insulating drug supply.

A 2019 FDA drug shortage investigation report pitched 3 solutions to the shortage problem:

1 — Cultivating a shared, industry-wide understanding of the impact of drug shortages and the importance of guarding against them

2 — Promoting sustainable private contracts across the pharmaceutical industry to foster consistent supply of pharmaceutical product

3 — Establishing a quality management maturity 'rating' system that rewards companies reaching those 'more advanced levels of quality management'

Of these 3, it's the final point which has formed the heart of the QMM program and generated the most attention.

In short, pharmaceutical companies will be rewarded for the first time for moving beyond the baseline of bare-minimum cGMP compliance. Companies that can demonstrate commitment to continuous improvement, through practices like the adoption of new technology,

quality-cultural initiatives, leading quality metrics and proactive senior management support, will be given a public-facing quality 'score'.

Quality-centric pharma businesses will then enjoy boosted brand equity in front of industry purchasers, regulators and – most importantly – the drug-purchasing American public.

It's unlikely that the program will go live in 2025, but we can expect it to come closer into focus and towards its final form as the FDA finishes its consultation period.

The QMM program represents a dramatic overhaul of industry attitudes to quality management, and we predict international echoes once the FDA has rolled it out. 2025 will be the year when this watershed moment draws nearer.

Read our quality management maturity guide for more details

Chapter 2

Regulatory updates

The past few months have seen the roll-out of a string of new regulatory documents from both the FDA and ICH.

Do your research on all those applicable to your business and ensure you're prepared for evolving regulatory and quality expectations.

New draft guidance documents

May 2024: Platform Technology Designation Program for Drug Development

July 2024: Postapproval Manufacturing Changes to Biosimilar and Interchangeable Biosimilar Products

New final guidance documents

June 2024: Facility Readiness: Goal Date Decisions Under GDUFA

July 2024: Container Closure System and Component Changes: Glass Vials and Stoppers

September 2024: Control of Nitrosamine Impurities in Human Drugs

FDA documents coming soon

Pharmaceutical Quality/CMC – omnibus legislation

Framework for Regulatory Advanced Manufacturing Evaluation (FRAME)

International updates

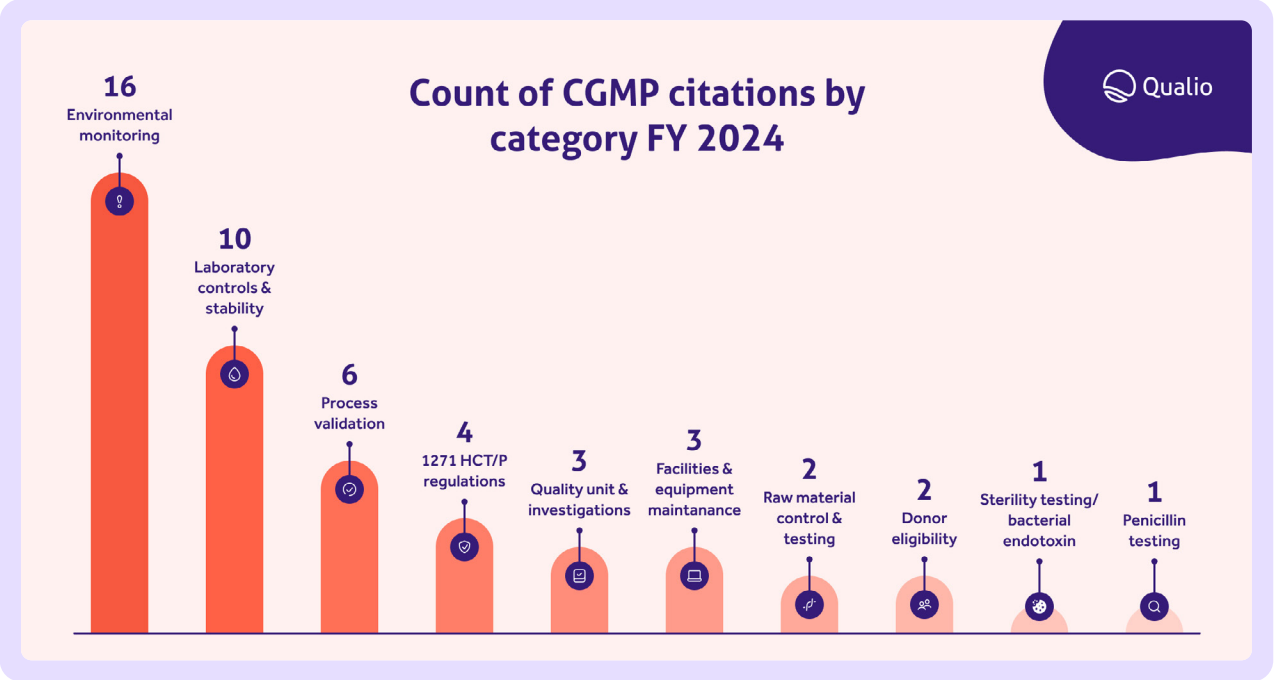
Improved ICH guidelines related to the Common Technical Document (M4Q) and stability (Q1/Q5C).

ICMBRA collaborative pilot: joint FDA-EMA approval system with a mixture of on-site and remote inspections for faster, simultaneous US/EU approvals.

Chapter 3

Quality and regulatory trends

Where are pharmaceutical businesses going wrong with their PQS activities as we head into 2025? A key message from the FDA at the PDA/FDA Joint Regulatory Conference in late 2024 was that lazer focus on manufacturing quality and cGMP adherence is causing other adjacent quality issues to go unnoticed and unfixed. This is borne out in the data:



Environmental monitoring	› 21 CFR 211.113(b): Control of Microbiological Contamination › 21 CFR 211.42(c)(10): Design and Construction Features – Aseptic Processing
Laboratory controls & stability testing	› 21 CFR 211.160: General Requirements › 21 CFR 211.166: Stability Testing › 21 CFR 211.167: Special Testing Requirements
Process validation	› 21 CFR 211.100: Written Procedures: Deviations
Donor eligibility	› 21 CFR 1271.75: Donor Screening › 21 CFR 1271.85: Donor Testing › 21 CFR 1271.80: Donor Testing › 21 CFR 1271.60: Quarantine Requirements for Donor Eligibility
Quality unit & investigations	› 21 CFR 211.192: Production Record Review
Facilities & equipment maintenance	› 21 CFR 211.58: Maintenance › 21 CFR 211.67: Equipment Cleaning and Maintenance › 21 CFR 211.56: Sanitation

Environmental monitoring and control of both raw materials and contamination topped the leading causes of warning letters for the 2015-2024 period.

Contaminations loomed large in recall data too, with three of the five most recalled products for 2016-2020 triggered by nitrosamine and methanol contamination.

What does this mean?

cGMP is important - but so is the environment your drug must pass through on its way to patients. Pay close attention to your adjacent environment, including your supply chain — as supply chains grow in length and complexity, the importance of robust contamination, material and environmental monitoring systems only grows.

The FDA's other key recurring quality concerns as we head into 2025 include:

- Continued marketing of unapproved products without an approved BLA or IND
- Inadequate microbial control
- Lack of adequate aseptic process validation and media fills
- Poor aseptic processes
- Lack of adequate environmental monitoring procedures
- Inadequate cleaning techniques and validation
- Inadequate quality control and screening systems
- Inadequate donor eligibility determination
- Inadequate investigations and material control from QC teams
- Lack of adequate batch and production records
- Inadequate testing programs
- Lack of stability data to support expiration dates
- Lack of appropriate testing for raw materials

If you've not recently reviewed, assured and optimized your quality and compliance in these areas, add them to the top of your internal auditing list. They represent the most common, current weaknesses in pharmaceutical operations.

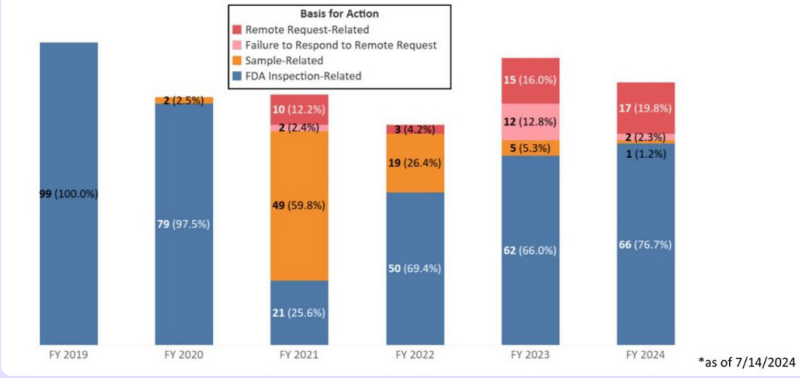


Figure 4: Approach used to identify basis for warning letter: FY19-24*

One final trend to be aware of is the increasing shift towards hybrid inspections, particularly in the US. The shift to 'remote regulatory assessments' and information requests that took place in the pandemic days of 2020-21 doesn't seem to be going anywhere as we head into 2025.

In fact, where physical inspections drove 100% of warning letter triggers before the pandemic in 2019, and where sample requests were heavily relied on to trigger warnings mid-pandemic, a clear preference for remote information requests can now be seen as the COVID years recede behind us.

Remote requests, or a failure to respond to them, accounted for almost a quarter of warning letters issued in FY 2024, while samples have returned to a minimal impact.

The FDA, in short, is relying more and more on remote inspections and record requests to keep tabs on drugmakers. The implication is that remotely accessible, cloud-based and digitized PQS documentation is now expected by default. Organizations that still rely on mountains of paper records will have to be physically inspected, and will therefore miss out on the faster, less burdensome hybrid approach which the FDA is starting to favor.

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Prepare for 2025 with optimized, digitized quality

Learn more