



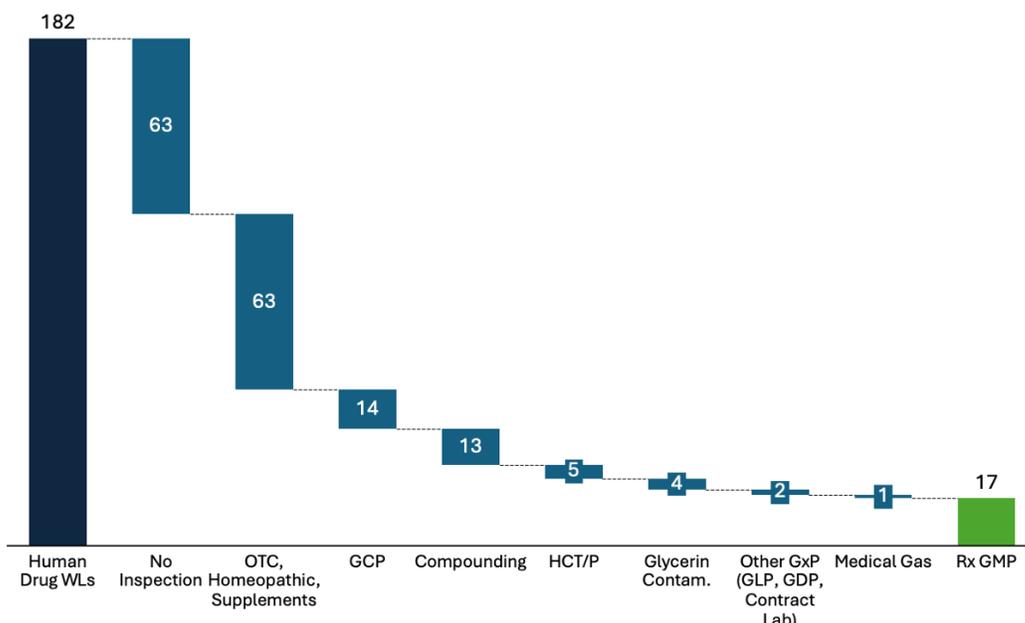
# Key Insights from CDER Warning Letters: Hot Topics and Trends

In a recent Redica Systems webinar, Marie Mathews, former FDA CDER Compliance Officer and current Principal at Franklin Mathews Group joined us to unpack the key trends, hot topics, and regulatory expectations emerging from 2024 CDER Warning Letters. Drawing on Redica's data-driven analysis and Marie's decades of agency experience, the session revealed serious compliance pitfalls in sterile manufacturing, persistent data integrity lapses, and emerging enforcement focus areas, including APIs and supply chain quality. Below is a distilled summary of the discussion, complete with visual data highlights and actionable takeaways.

## METHODOLOGY

Redica analyzed FDA Warning Letters issued between January and December 2024, filtering out non-Rx product types (e.g., OTC, HCT/P), non-GMP scopes (e.g., GCP, GLP), and irrelevant content (e.g., glycerin contamination). The final data set focused on 17 Rx GMP warning letters across finished dosage form (FDF) and active pharmaceutical ingredient (API) manufacturers (**Figure 1**). Letters from early 2025 were also analyzed for emerging signals.

**Human Drugs Warning Letters Jan 2024 - Dec 2024,  
# Warning Letters**



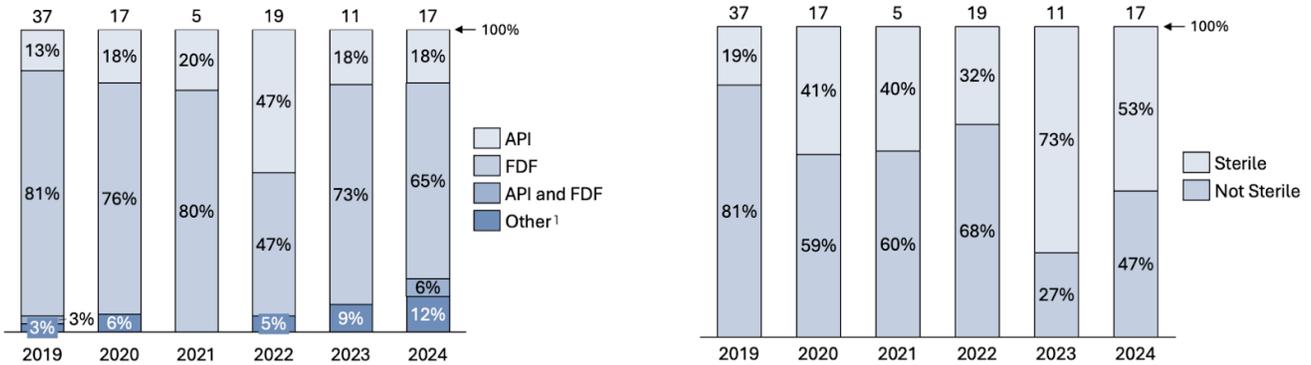
**FIGURE 1 | HUMAN DRUG GMP WARNING LETTERS JAN 2024 - DEC 2024**

## CORE FINDINGS FROM 2024 WARNING LETTERS

### 1. Continued Focus on Sterile Products and FDFs

Sterile manufacturing remained a key FDA priority due to its high-risk profile. With inspection backlogs lingering post-COVID, FDA focused its limited resources on higher-risk operations. Sterile FDFs accounted for the majority of 2024 warning letters.

**Human Drugs Rx GMP Warning Letters by Facility and Product Type Jan 2019 - Dec 2024, % Warning Letters**



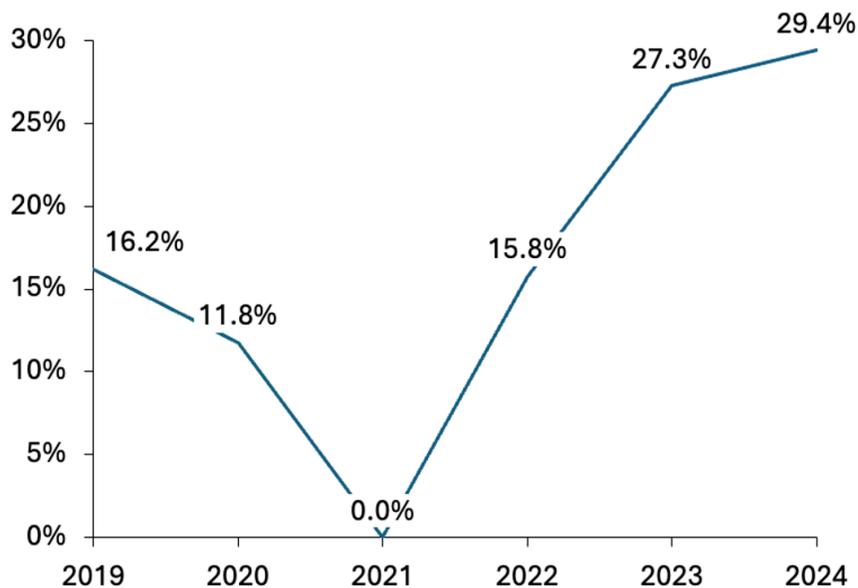
<sup>1</sup>Other includes Combination Product, CGT, Excipient

**FIGURE 2 | HUMAN DRUG GMP WARNING LETTERS BY FACILITY AND PRODUCT TYPE**

### 2. Rise in Import Alerts

Import Alert 66-40 was issued to five Indian manufacturers in 2024 for serious GMP deficiencies. Expect continued scrutiny of overseas facilities, especially with the new U.S. policy that calls for expanded unannounced foreign inspections.

**Human Drugs Rx GMP Warning Letters with Import Alert, Jan 2019 - Dec 2024, % Warning Letters**



**FIGURE 3 | HUMAN DRUG GMP WARNING LETTERS WITH IMPORT ALERT**

## TOP CITED DEFICIENCIES

Redica's heatmap and tagging ontology (**Figure 4**) revealed the following top categories across the 2024 warning letters:

- **Quality Unit:** 23 deficiencies
- **Production (including aseptic technique and interventions):** 20 deficiencies
- **Laboratory:** 16 deficiencies
- **Data Integrity:** Present in 12 out of 17 warning letters

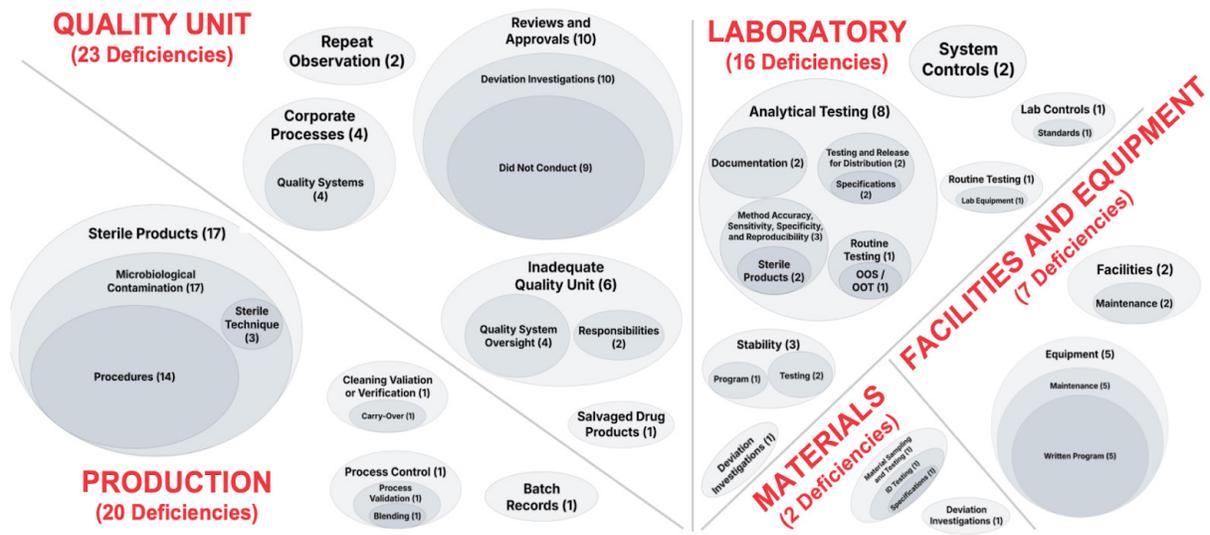


FIGURE 4 | REDICA'S HEATMAP AND TAGGED ONTOLOGY

Human Drugs Rx GMP Warning Letters with Data Integrity Issues, Jan 2019 - Dec 2024, % Warning Letters

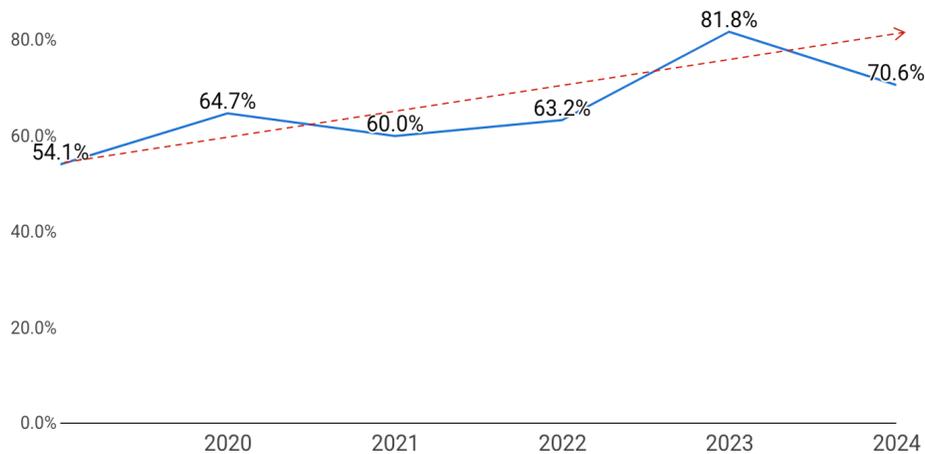


FIGURE 5 | HUMAN DRUG GMP WARNING LETTERS WITH DATA INTEGRITY ISSUES

**Takeaway:** FDA sees the Quality Unit as ultimately responsible when issues recur across multiple systems. Quality Unit resource constraints, ineffective oversight, and a lack of floor presence were commonly cited root causes.

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## SPOTLIGHT #1: STERILE PROCESSING AND ASEPTIC CONCERNS

Sterile production failures dominated 2024 citations. The most egregious issues included:

- Operators disrupting first air, reaching over vials/stoppers, and touching critical surfaces
- Inadequate gowning and media fill oversight
- Unjustified interventions and failure to remove impacted vials
- Transfer cart turbulence, failing to protect product in Grade A/B transitions

**Tip:** Excessive aseptic line interventions or improper RABS handling must trigger formal investigation and CAPA. Don't justify risks based on passing media fills or smoke studies alone.

“These letters show us what FDA sees as inexcusable—like allowing contamination vectors through basic design flaws.”

— Marie Mathews

## SPOTLIGHT #2: FACILITIES AND EQUIPMENT DESIGN FAILURES

Multiple warning letters cited poor aseptic line design, including:

- Manual interventions and poor RABS setup
- Differential pressure reversals
- Incomplete airflow studies
- Improperly secured panels and exposed wiring
- Lack of HEPA filtration verification

**Insight:** Firms were urged to conduct independent expert evaluations and comprehensive redesign assessments where systemic risks were found.

## SPOTLIGHT #3: DATA INTEGRITY, A PERSISTENT AND ESCALATING CONCERN

From falsified environmental monitoring logs to backdated batch records, data manipulation continues to be a top issue. Serious deficiencies included:

- Routine fabrication of microbiology and EM results
- Editing of third-party COAs and document destruction
- Unauthorized access to blank production records
- CGMP records found in trash bags or rooftops
- Critical test records created by analysts not on-site

**Warning:** Revoking access or firing staff is not sufficient. Expectation includes:

- Third-party DI investigations
- Retrospective batch impact assessments
- Employee interviews (including former staff)
- Implementation of a Chief Integrity Officer

## SPOTLIGHT #4: RARE BUT SIGNIFICANT CELL & GENE THERAPY WARNING LETTER

One rare warning letter was issued to a CAR-T manufacturer due to:

- Fly infestations in cleanrooms
- Poor environmental monitoring
- Lack of viable and non-viable particulate control
- Failure to conduct cleaning validation

**Implication:** Warning letters may be rare in this space, but when issued, they cause severe business disruptions. Supply chain partners should be audited rigorously.

## EARLY 2025 TRENDS: RISE IN API ENFORCEMENT

Six of seven warning letters issued in Q1 2025 were to API firms.

Site Display Name	Facility Type	Product Type	Import Alert	Inspection End
			Issued	Date
Shree Jaya Laboratories Private Limited [Choutuppal / India]	Generic	API	--	9/12/24
Wuhu Nuowei Chemistry Co., Ltd [Wuhu / China]	--	API	Yes	9/6/24
Granules India Limited [Qutubullapur / India]	Generic	FDF	--	9/6/24
TYCHE INDUSTRIES LIMITED [Kakinada / India]	--	API	Yes	8/16/24
GLOBAL CALCIUM PRIVATE LIMITED [Hosur / India]	Generic	API	Yes	8/2/24
Genzyme Corporation [Framingham / USA]	--	API	--	7/9/24
Jagsonpal Pharmaceuticals Ltd [Bhiwadi / India]	--	API	Yes	4/3/24

FIGURE 6 | WARNING LETTERS ISSUED TO API FIRMS

Top deficiencies include:

- Unvalidated cleaning and equipment maintenance
- Falsified lab results
- Lack of stability programs
- Incomplete documentation and unqualified methods

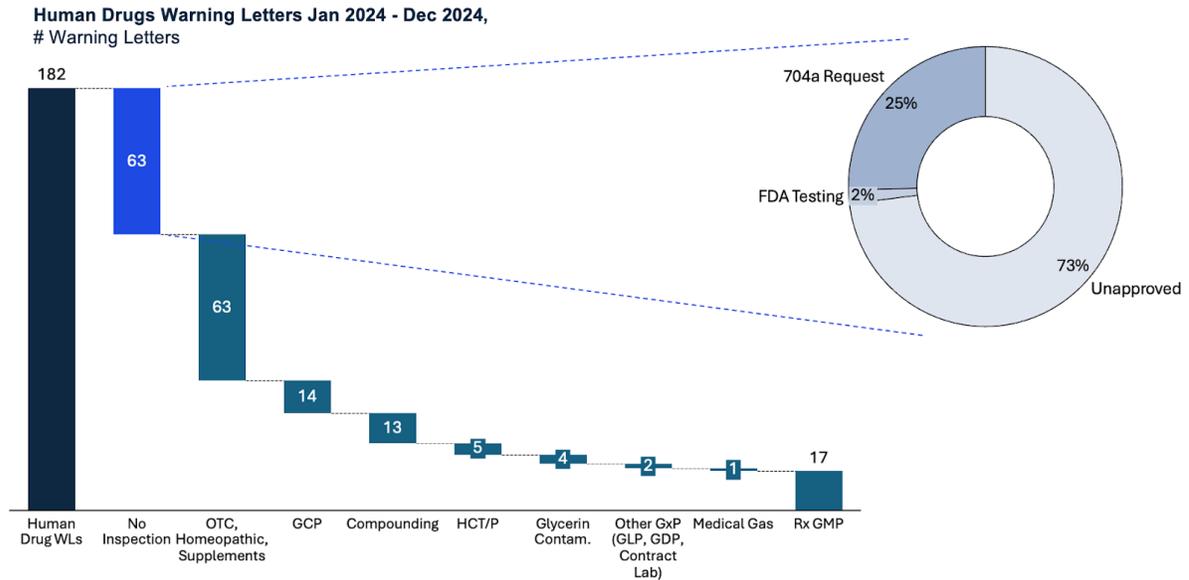
**Advice:** Never assume a PAI clearance guarantees quality. Many API sites lacked control over critical process parameters (CPPs).

## WARNING LETTERS WITHOUT INSPECTION

Several 2024 warning letters were issued without an on-site inspection, highlighting the use of remote assessments, sample test results, and voluntary disclosures as triggers.

“I don’t think these are going away—especially with ongoing travel challenges and inspection backlogs. Expect to see more remote assessments moving forward.”

— Marie Mathews



**FIGURE 7 | HUMAN DRUG GMP WARNING LETTERS JAN 2024 - DEC 2024**

## ACTIONABLE TAKEAWAYS

- Proactively audit aseptic behaviors and operator practices
- Perform design reviews of sterile lines and document airflow patterns
- Embed independent QA reviews, especially in media fills and gowning
- Implement robust DI remediation, including root cause protocols
- Strengthen your supplier quality agreements and proactively monitor your suppliers
- Benchmark against Redica-tagged warning letters to spot systemic risks early

## LOOKING AHEAD

With new White House directives pushing for unannounced foreign inspections, ongoing inspectional backlog recovery, and renewed focus on supplier integrity, 2025 is shaping up to be a high-stakes year for pharmaceutical quality systems.

To dive deeper into these insights or to request access to Redica’s complete warning letter database and tagging system, contact our team to [request a demo](#).

## ABOUT THE SPEAKER

Marie Mathews is Principal at Franklin Mathews Group and a former CDER Compliance Officer. With over 18 years of experience at FDA spanning inspections, enforcement, and regulatory strategy, she now advises global life sciences companies on remediation, inspection readiness, and strategic compliance.