REDICA Systems

Key Insights from CDER Warning Letters: Hot Topics and Trends

May 2025

redica.com

Meet the Speaker!

Marie Mathews

Principal & CEO at
Franklin Mathews Group

Career

- **18+ years at the U.S. FDA**, beginning as an investigator in drugs, devices, and biologics
- **Recipient of the FDA Individual Commendable Service Award** for leading a critical sterile medical device manufacturer investigation
- Served as a **Field Drug and Biologics Compliance Officer**, regularly presenting enforcement findings to senior corporate executives
- Monitored multi-million dollar remediation plans and supported complex inspections as a **strategic advisor**
- Served as a **CDER Compliance Officer**, working with top technical experts on enforcement decisions and drafting warning letters
- Former **Associate Director of GxP External Engagement** at Bristol Myers Squibb

Education & Speaking

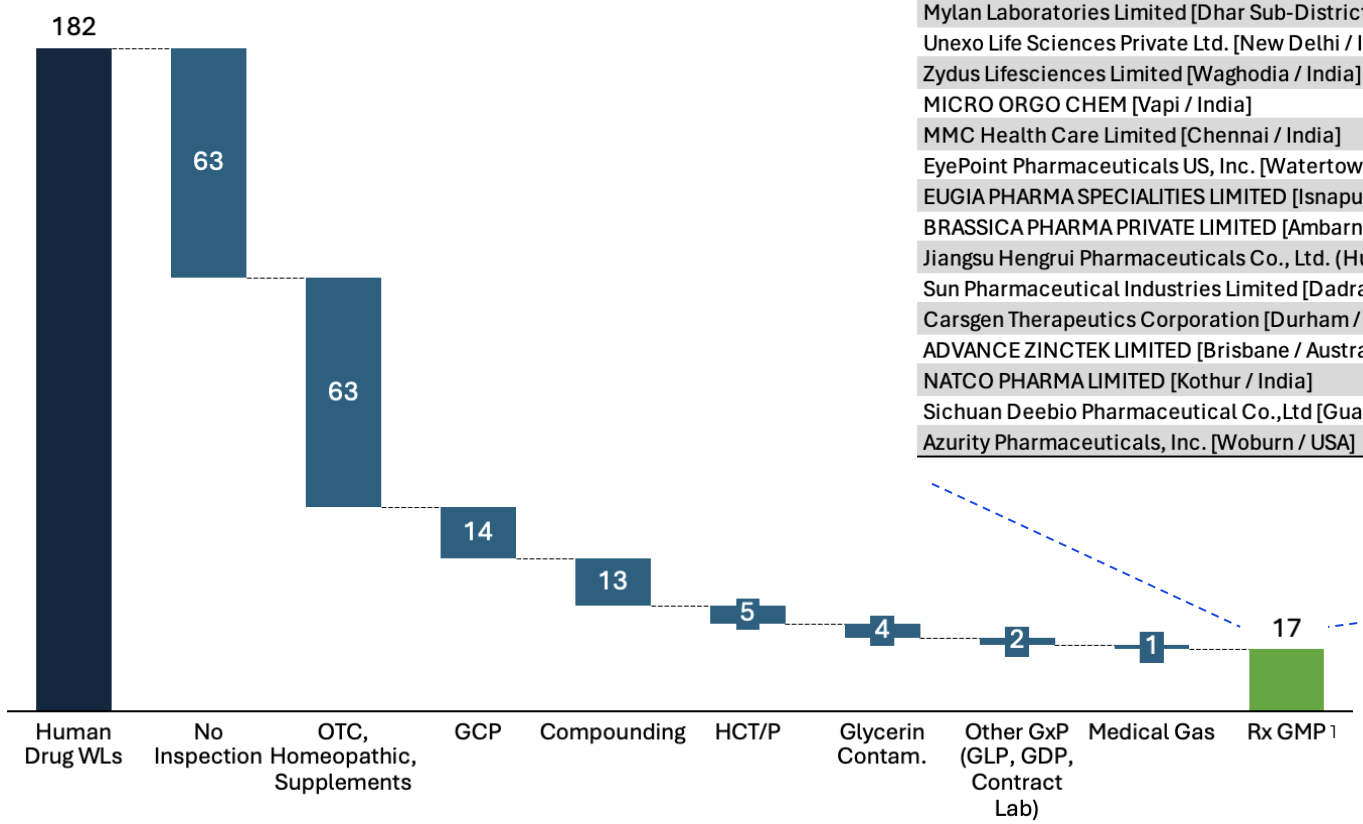
- B.S. & M.S. in Pharmacy/Regulatory Affairs – University of Georgia
- Highly rated speaker at major GxP conferences, most recently at the UGA/FDA International GMP Conference in Athens, GA

Content

- Key Enforcement Trends: 2024 Warning Letters, Affected Facilities, and Common Inspection Findings
- Special Concerns that Lead to Regulatory Action
- Warning Letters Issued Without a Recent Preceding Inspection
- Emerging Trends: Warning Letters Issued in Early 2025

Methodology – 2024 Human Drug Warning Letters

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



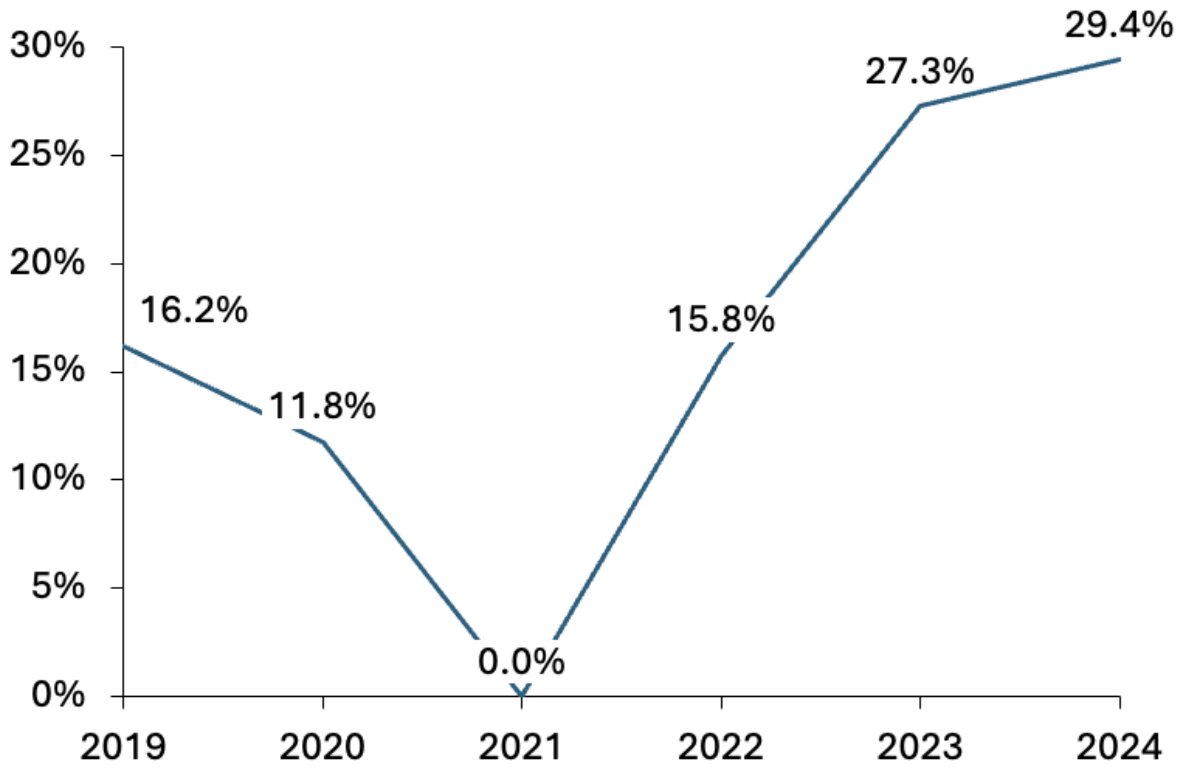
Site Display Name	Facility Type	Product Type	Import Alert Issued	Inspection End Date
INDOCO REMEDIES LIMITED [Mormugao / India]	Generic	FDF, Sterile	--	7/26/24
Bhargava Phytolab Private Limited [Bhiwadi / India]	--	API, FDF, Sterile	Yes	7/26/24
Mylan Laboratories Limited [Dhar Sub-District / India]	Generic	FDF	Yes	6/26/24
Unexo Life Sciences Private Ltd. [New Delhi / India]	--	FDF	--	5/14/24
Zydus Lifesciences Limited [Waghodia / India]	Generic	FDF, Sterile	--	4/23/24
MICRO ORGO CHEM [Vapi / India]	--	API	Yes	4/18/24
MMC Health Care Limited [Chennai / India]	--	FDF	Yes	3/30/24
EyePoint Pharmaceuticals US, Inc. [Watertown / USA]	--	Combination, Sterile	--	2/15/24
EUGIA PHARMA SPECIALITIES LIMITED [Isnapur / India]	Generic	FDF, Sterile	--	2/2/24
BRASSICA PHARMA PRIVATE LIMITED [Ambarnath / India]	--	FDF, Sterile	Yes	1/19/24
Jiangsu Hengrui Pharmaceuticals Co., Ltd. (Huanghe Road Site) [Lianyungang / China]	Generic	FDF, Sterile	--	1/16/24
Sun Pharmaceutical Industries Limited [Dadra / India]	Generic	FDF	--	12/15/23
Carsgen Therapeutics Corporation [Durham / USA]	--	IND, CGT, Sterile	--	12/6/23
ADVANCE ZINCTEK LIMITED [Brisbane / Australia]	--	API	--	11/17/23
NATCO PHARMA LIMITED [Kothur / India]	Generic	FDF, Sterile	--	10/18/23
Sichuan Deebio Pharmaceutical Co.,Ltd [Guanghan / China]	--	API	--	9/8/23
Azurity Pharmaceuticals, Inc. [Woburn / USA]	--	FDF	--	3/2/23

Note: If you are interested in receiving the backup output (i.e. a link to the 17 Rx GMP Warning Letters), please contact your Redica CSM.

[1]Exclusion by Redica Systems product tags (OTC, HCT/P, etc.), scope labels (GCP, GLP, etc.) and content (glycerin contamination)

Warning Letters that Reference Import Alerts on the Rise Since COVID

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

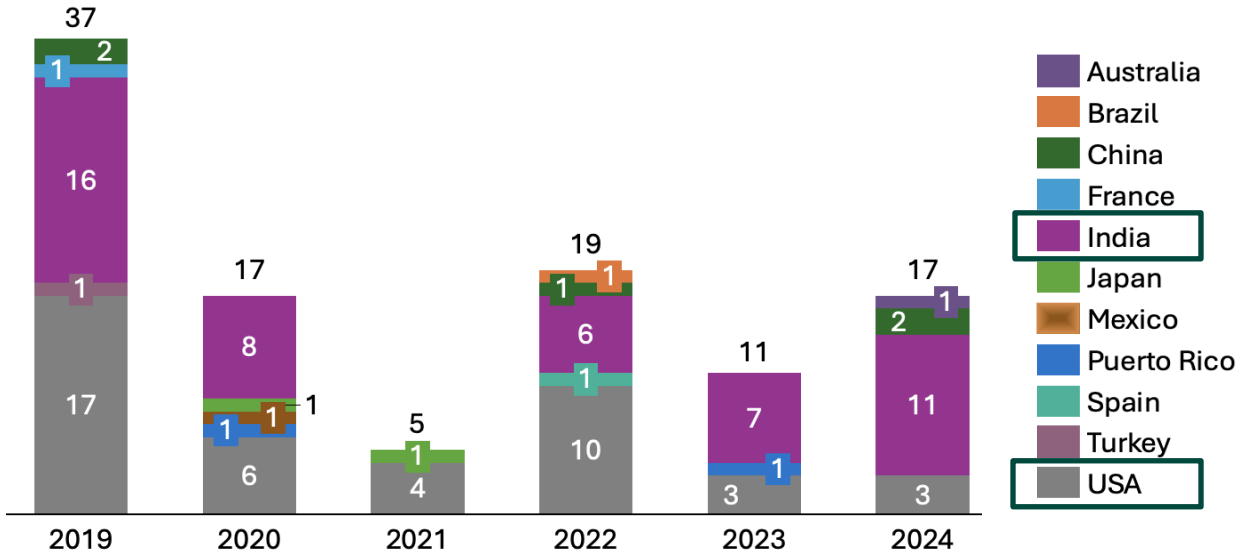


In 2024, **Import Alert 66-40** issued to f**ive API and FDF** manufacturers in **India** for not meeting drug cGMPs.

1. Bhargava Phytolab Private Limited [Bhiwadi / India]
2. Mylan Laboratories Limited [Dhar Sub-District / India]
3. MICRO ORGO CHEM [Vapi / India]
4. MMC Health Care Limited [Chennai / India]
5. BRASSICA PHARMA PRIVATE LIMITED [Ambarnath / India]

Regional Distribution of Warning Letters

Human Drugs Rx GMP Warning Letters by Country Issued Jan 2019 - Dec 2024,
Warning Letters



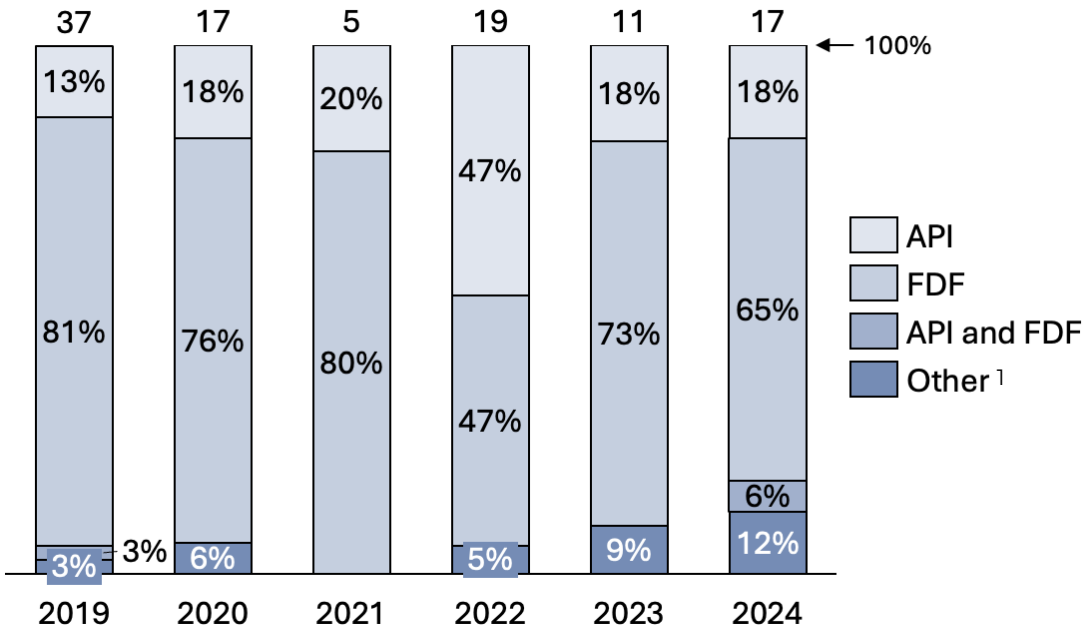
	Rx GMP Warning Letters 2024	Human Drugs GMP Inspections 2024*
Australia	1	6
China	2	196
India	11	245
USA	3	619

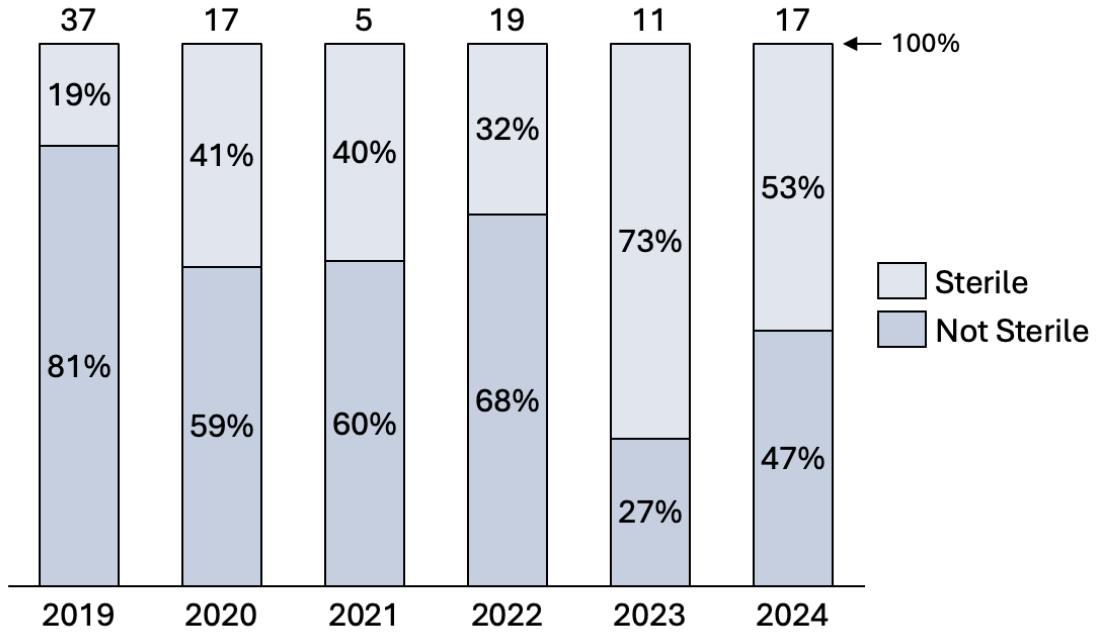
*Human Drugs GMP Inspections 2024 is the total number of inspections conducted across all product types, including Rx, OTC, compounded drugs, and others.

- India and US sites continue to receive majority of WLs.
- Will we see a change in this trend? Possibly…
  - FDA Announces Expanded Use of Unannounced Inspections at Foreign Manufacturing Facilities

Focus Remains on FDF and Sterile Products in 2024

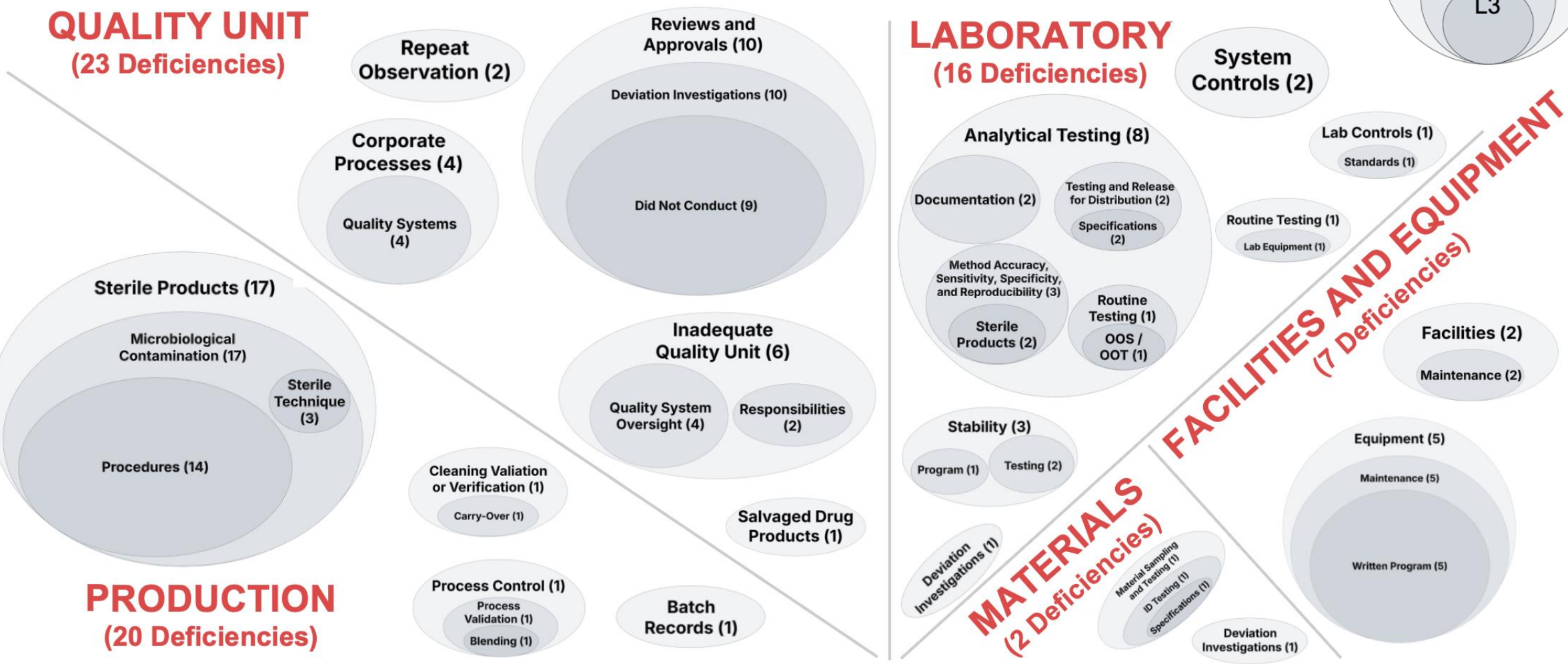
Human Drugs Rx GMP Warning Letters by Product Type Jan 2019 - Dec 2024,
Warning Letters





[1]Other includes Combination Product, CGT, Excipient

What Areas Were Most Cited in 2024 WLs?

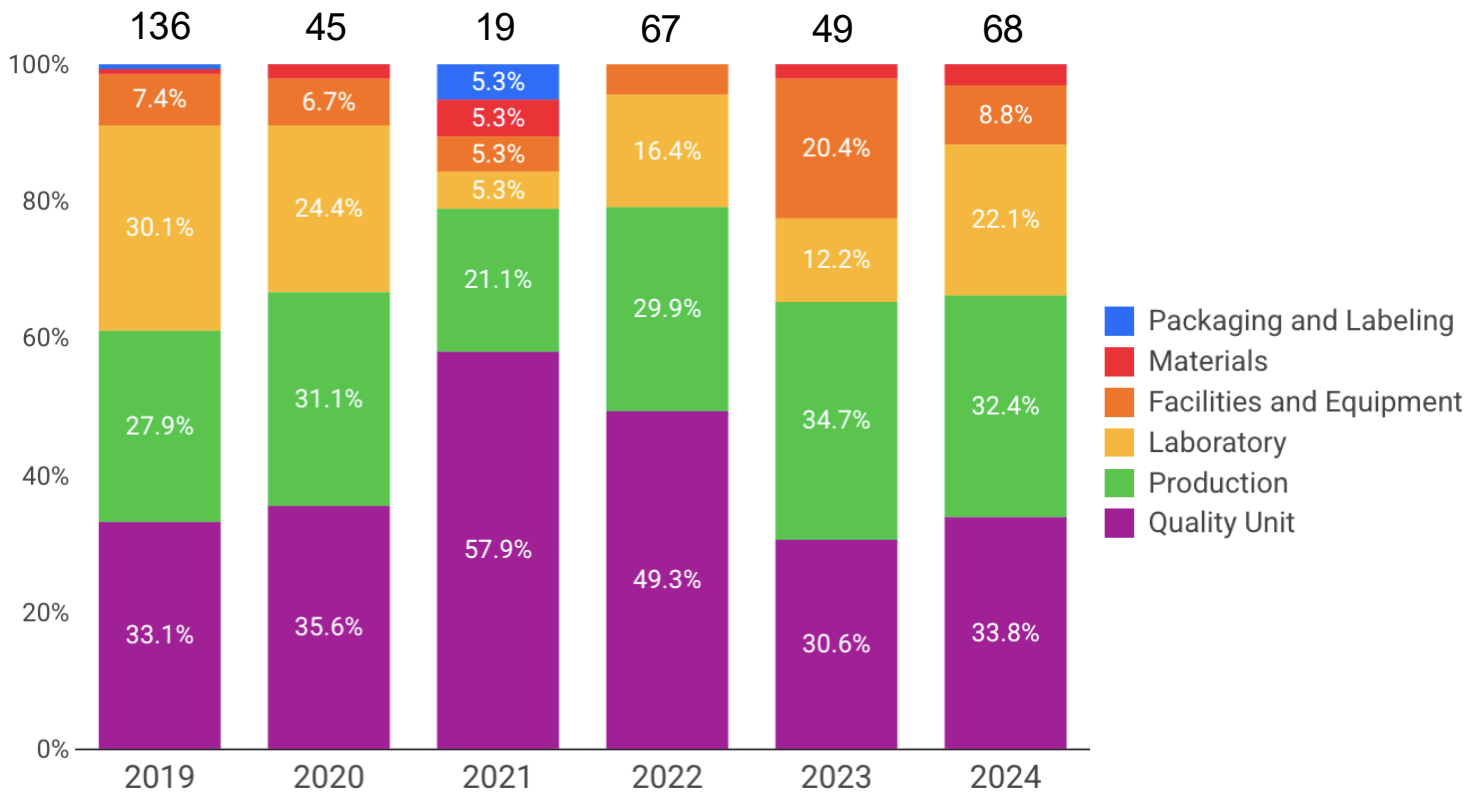


Quality Systems Cited in Rx GMP Warning Letters

Quality Area	# Deficiency
Quality Unit	23
Production	20
Laboratory	16
Facilities & Equipment	7
Materials	2
Total	**68**

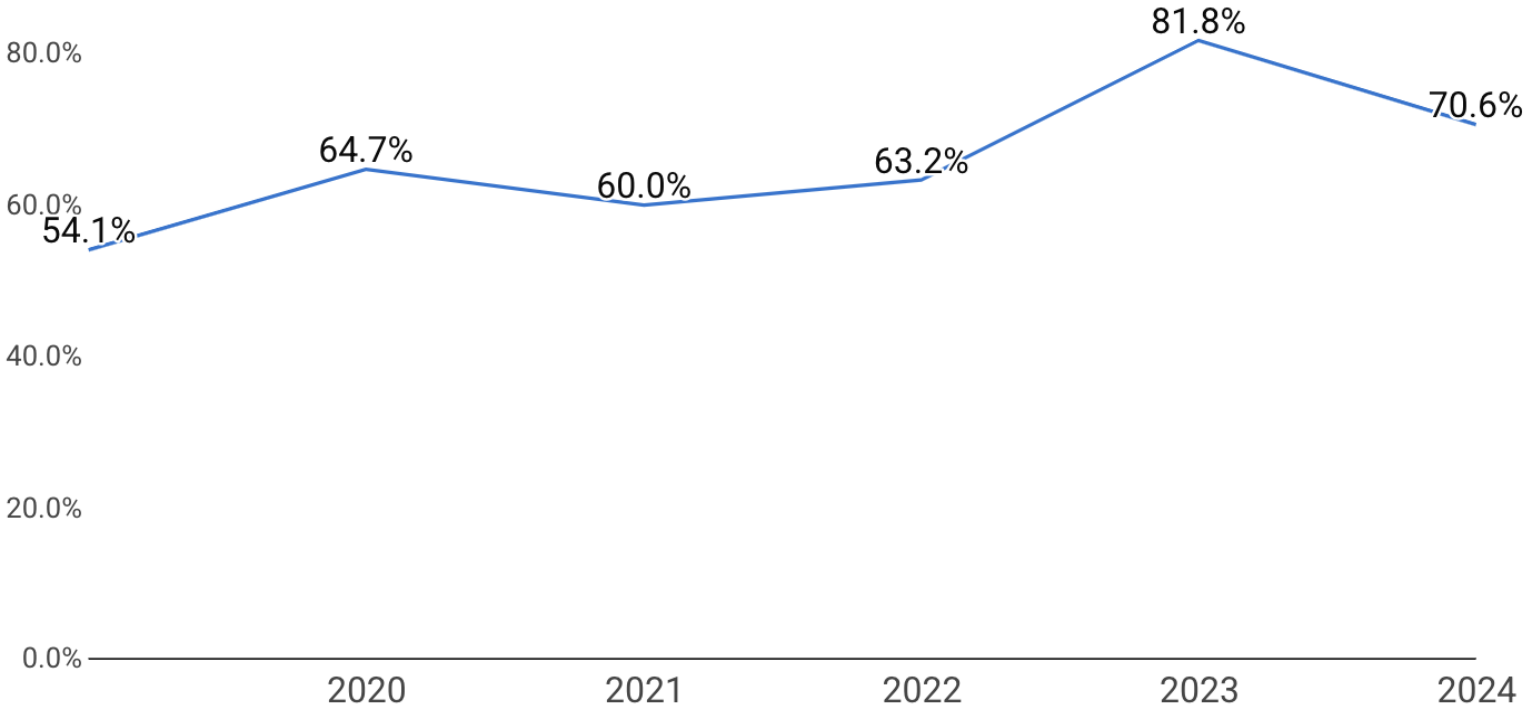
68 deficiencies in the 17 identified WLs **in 2024**

Rx Warning Letters Deficiencies by Quality Area, Jan 2019 - Dec 2024,
% Deficiencies



Data Integrity Compliance Over the Years

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



Data Integrity issues present in **12 out of 17 Rx** Warning Letters in 2024

Deep-Dive into the Content (Selected Topics)

Selected Topics and Special Concerns

1

Sterile Processing and Aseptic Concerns

- Poor Operator Practices
- Facilities and Equipment Design Deficiencies

2

Fraud and Data Integrity

- Data Fabrication and Destruction
- Missing or Inadequate Documentation

3

Rare Cell and Gene Therapy WL

- Inadequate Contamination Control and EM
- Failure to Implement Effective Cleaning and Visual Inspection Controls
- Recurring Microbial Excursions Without Effective CAPA Implementation

4

API Manufacturers[1]

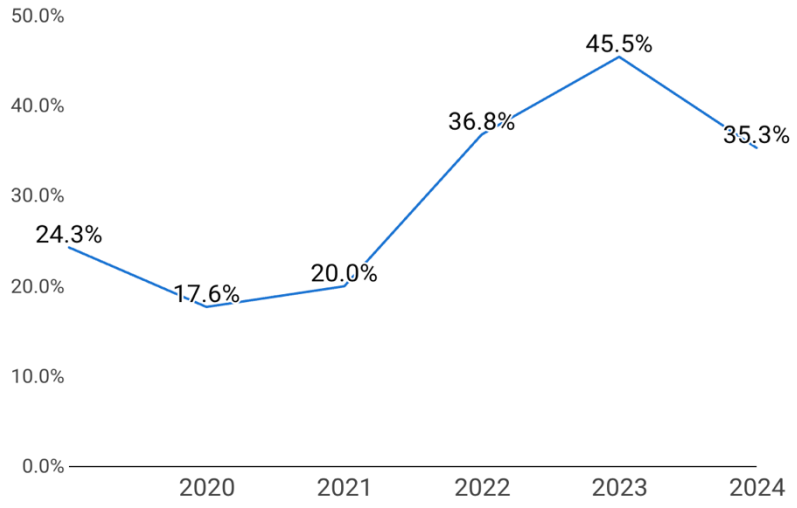
- Inadequate Laboratory Controls
- Lack of Process Validation and Equipment Qualification
- Failure in QU Oversight and Documentation
- Inadequate Testing of Raw Materials

[1]Common deficiencies issued to API manufactures are discussed in the later section under "Warning Letters Issued Start of 2025"

Poor Operator Practices

- *Investigators observed poor aseptic practices, including operators "disrupt[ing] first-air" by reaching over sterile vials and stoppers during interventions without removing affected materials. Operators also touched "(b)(4) stoppers with the (b)(4)-RABS (b)(4)" while aligning equipment during setup*
- *Poor Practices in the Aseptic Processing Areas – operators touching inside of sterile tubes, leaning over the filling line, working in the ISO 5 area with exposed skin*
- *Operators violated aseptic procedures by directly contacting the filling line with gloved hands, blocking airflow over open vials, and failing to remove impacted vials after glass shard incidents.*
- *There was a pattern of inadequate documentation and underreporting of interventions across multiple (b)(4)-RABS filling lines.*
- *Operators violated procedures by wiping (b)(4) dispenser tips without instructions and placing (b)(4) "directly on tables" where implants are manufactured, a repeat violation from the 2021 inspection.*
- *Inadequate Cleaning of Aseptic Processing Line Equipment - "these equipment parts were not observed to be wiped during the set-up or production..*

Rx WLs with "Operator" Deficiencies, 2019-2024
% Warning Letters



Poor Aseptic Practices – What Not To Do

- **Personnel are the Primary Source of Contamination**: Charles Weschler et al found that humans shed at a rate of 500 million cells per day and shed their entire outer layer of skin every 2-4 weeks*.
- Personnel should undergo thorough significant education, including active training, with regular reinforcement of appropriate cleanroom procedures and behaviors.
- Management must play an active role, and they should perform extensive monitoring and observation of operator activities in the critical aseptic processing areas and the associated controlled areas.
- ***Response Tip: Don't Just Say "Retraining"!***
  - Must create a formal plan to implement effective supervision, to include formal audits of operator practices with a defined interval. Likely need enhanced procedures as well, but this is squarely a QU failure (understanding QU could be under resourced). QU needs to be "on the floor" and effective.
  - Warning Letters point this out: "Include steps to better assure routine and effective supervisory oversight for all production batches. Also, describe the frequency of quality assurance oversight (e.g., audit) during aseptic processing and other operations"

Courtesy of Brooke Higgins, FDA CDER OMQ Brach Chief

More Aseptic Operator Behaviors

Re. Frequent opening of RABS doors and not removing potentially impacted vials when interventions occurred:

"Supervisory personnel and the QU are responsible for ensuring operators follow established procedures for manufacturing sterile drugs products (to include monitoring proper procedures around opening RABs doors) and clearing the impacted vials."

TIP: Vials that were exposed to opening of the RABS doors or other intrusive interventions must be cleared when they occur, and both should be documented (both the event and the clearance). See FDA guidance on aseptic processing

Warning: An excessive number of interventions on any aseptic processing line should trigger investigation and CAPA. **Do not try to justify by successful smoke study and/or media fill!**

Facilities & Equipment Design Deficiencies

- *Design of Aseptic Processing Lines - "Basic design deficiencies and manually intensive interventions in your operations compromise your ability to maintain aseptic conditions...investigators observed differential pressure reversals between the (b)(4) and the ISO 5 (b)(4) where filled and (b)(4) exit the line."*

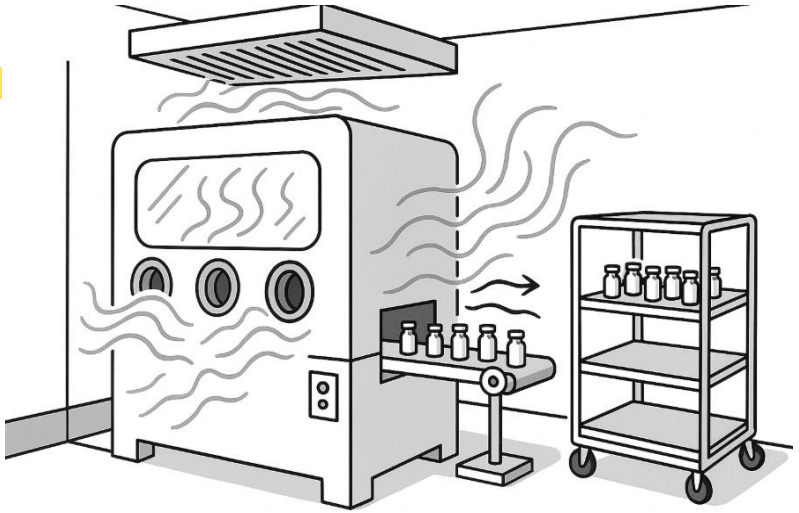
- *Inadequate separation between Grade A and B areas, with only an (b)(4) barrier, compromised sterility during equipment assembly and vial transfer .*
- *Equipment and vials were transferred through an open-air Grade A/Grade B transition without proper airflow studies; smoke study showed visible air turbulence from an open transfer cart.*

- *Non-viable particles were not monitored during vial transfer, relying only on settle plates, further risking product contamination.*

- *In-house media plates lacked smooth surfaces and analysts failed to ensure proper filter contact, both critical for supporting microbial growth detection.*

- *Unsuitable conditions in ISO 5 areas were found, including "rough metal surfaces and an incomplete (b)(4)" on the RABS framework above the stopper loading chute, "(b)(4) or (b)(4) protruding through the interior of RABS (b)(4)," and a "(b)(4) conduit...with exposed wires and not properly secured" in the filtration area.*

- *Your firm produced and distributed sterile drug product without adequate process simulations, as airflow studies showed smoke "flowing outward and upward" during interventions and failed to visibly demonstrate HEPA-filtered air reaching critical areas. The stopper conveyor track design also "appears to block first-air" over (b)(4) stoppers, compromising aseptic conditions.*



Design of Aseptic Processing Lines/Facility

"**Basic** design deficiencies and manually intensive interventions in your operations compromise your ability to maintain aseptic conditions"

- Equipment or parts of the line were observed to be in use without proper protections in place (*make sure guards and panel covers are in place*)
- Aseptic connections for the **transfer** of sterilized bulk drug product to the aseptic processing line were performed for <*product*> under ISO 8 conditions
- (b)(4) was also observed to have connections near the floor that required operators to be close to or touching the ground

TIP: **Don't forget to look at how the design of the line forces operators to move in ways that can contribute contamination vectors to the aseptic core**. Also consider where the operator keypads are located and if vectors for contamination.

Also watch carefully for where their gowns touch – they are frequently a source of problems. Both supervision and training should take this into consideration.

Design of Aseptic Processing Lines/Facility

- The cleaning of all parts on your aseptic processing lines that contact sterile tubes is inadequate. For example, **(b)(4)** contains **(b)(4)** equipment pieces, the **(b)(4)**, that make direct contact with the inside of unfilled sterile tubes and cannot be removed for sterilization.
- "inadequate physical separation between Grade A and Grade B classified areas"

Response Tip: If multiple design problems are found, or one significant design problem in your aseptic line, you should include a comprehensive, independent assessment of the design and control of your firm's manufacturing operations, with a detailed and thorough review of all microbiological hazards.*

FDA will not simply trust that you identified and fixed all the problems and will want proof that an SME did this for you**.** If problems are significant, then you should hire a third party. If you are unsure whether significant, hire a good consultant with significant aseptic experience.

**Refer to warning letters for additional assessments to include in your response.*

Inadequate Design or Controls, Aseptic Processing

- There is inadequate physical separation between Grade A and Grade B classified areas., For example, the “transitional” Grade A areas on either side of the .. conventional filling machine are where production employees transfer …sterile equipment for assembly and …vials of drug products for (b)(4) ., This design does not provide adequate protection and can compromise the sterility of the (b)(4) drug products and the sterile equipment.
- Drug product contact equipment and utensils are sterilized and transferred (b)(4) through this Grade A and Grade B open air transition area which may compromise sterility.
- No smoke studies to demonstrate the airflow in the **transition** between the Grade A and Grade B areas outside of the filling machine.,
- The (b)(4) , is open on both the front and rear sides. Air turbulence was visible in the smoke study video when the **transfer cart** moved through the Grade B area.

Unsuitable Conditions – Aseptic Areas

FDA found unsuitable conditions in ISO 5 areas

- Rough metal surfaces .
- Incomplete < *b4* > on Restricted Access Barrier System RABS framework in the area above the stopper loading chute
- **Multiple WL references to open transfer carts that allow turbulence to reach components**

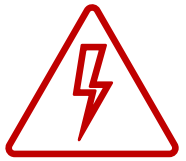
TIP: Transfer carts should be enclosed to protect product from turbulent air flow and contamination. **Air eddies can pick up contamination from the floor and direct towards the shelves if left open.** Carts should also include particle monitoring if transporting open vials or other product contact components or equipment.

RESPONSE: What not to do: "You remediated the Line ...RABS in response to the unsuitable physical condition of Line.. documented in the 2023 inspection of this facility. **Your remediation activities failed to wholistically address the conditions of the Line..."**

When important deficiencies are found in the design of your aseptic line, you need to do a complete assessment of the line to look for other deficiencies. The investigator can't do that for you – you need to have an SME do it. Also, FDA loses trust when a firm doesn't know that a significant issue is present until and the regulator has to point it out.

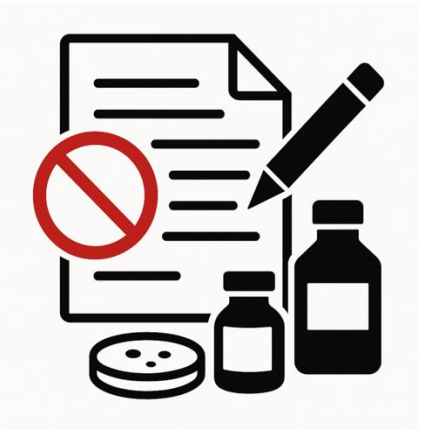
Data Manipulation, Fabrication & Destruction

- *Microbiology Laboratory Data Integrity - Sterility tests were routinely skipped, and records were routinely fabricated by the sole trained analyst; Environmental and personnel monitoring samples were not collected as required - "admitted routine fabrication of environmental monitoring results... no excursions had been documented"*
- Inadequate Media Fill Program - "routine practice not to document interventions... evaluation of media fill vials does not include a review for visual evidence of microbial growth/
- *Environmental monitoring records were falsified by using data "from a different time and place" and altering timestamps, with systemic data integrity breaches growth" involving multiple staff over several months.*
- *Your QC analyst had the ability to manipulate results, dates, and images on third-party component COAs, including duplicating vendor stamp approvals across multiple COAs.*
- *You failed to ensure data integrity during component release testing, as investigators found four worksheets with passing (b)(4) results recorded by analysts who were "not physically present at the facility" during testing.*
- *Operators documented cleaning and sterilization of stopper and cap (b)(4) bowls "without performing these activities" for three sterile injectable batches.*
- *Cleaning activities, including disinfecting the (b)(4), were recorded without properly following procedures or actually completing the operations*
- *Investigators found that your report contained "data added, backdated signatures, and replaced pages," with admissions from senior QA, QC, R&D, and Production managers.*
- *The production manager had "unrestricted access to blank production batch records" and routinely printed uncontrolled documents for employees to "transcribe" corrected data, discarding originals.*



Missing or Inadequate Documentation

- *EM program lacked defined sampling locations, with ISO 5 samples chosen randomly and without documentation*
- *Inadequate Cleaning of Aseptic Processing Line Equipment -.no documentation was provided to show that this cleaning method is adequate to remove potential contamination from the equipment"*
- *Leaks and failures were not properly documented; inadequate monitoring*
- *There was a pattern of inadequate documentation and underreporting of interventions across multiple (b)(4)-RABS filling lines.*
- *You failed to include complete data in laboratory records, such as preparation of solutions and equipment used, relying on "incomplete information" to determine if (b)(4) USP met specifications.*
- *Your response failed to address the "overall lack of traceability" or confirm the validity of previous analytical data, leaving no basic evidence that API batches met release criteria.*
- *Your QC microbiology lab failed to document results contemporaneously, with investigators finding microbiological plates in a waste bin and QC personnel admitting, "I haven't written it yet" and "It's in my head."*
- *You failed to document CGMP manufacturing activities contemporaneously, with investigators finding "numerous unlabeled (b)(4) drums" whose contents and origins personnel could not identify.*
- *You also failed to maintain original batch records, including for (b)(4) batch (b)(4), which was released and shipped to the U.S. without available documentation.*

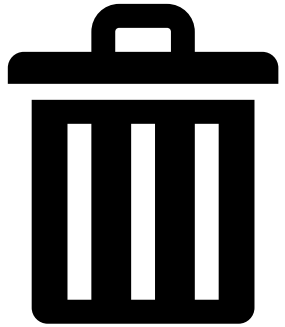


Data Omission & Destruction

- *Original CGMP records were found "stacked in a bag underneath a vehicle and in a nearby trash can," showing severe QA oversight failures.*
- *You failed to maintain complete batch production records, with torn and missing records for U.S.-bound batches found "in plastic bags on your rooftop," including duplicates with identical batch numbers and dates.*
- *Executive management admitted to not having all original records and that batch records were "retrospectively prepared" for investigators.*
- *You lacked raw data for key quality tests on (b)(4) Patch batch (b)(4), including assay, patch weight, peel strength, and rolling ball analysis.*
- *Quality management admitted they had no data for peel strength and rolling ball tests and gave "no explanation" for how the batch was released without it.*
- *"Critical manufacturing steps were recorded 25 days after production" and missing sample weight printouts led to sample weights being "changed 22 days after analysis," both attributed to "inattention" or "analyst error" without evidence.*
- *The inspection also found "questionable practices regarding the disposition and destruction of CGMP records by employees."*

Limiting Access to Information During Inspection

- *During the inspection, the only computer with electronic CGMP data was unavailable because a QC analyst "took the computer home," and a second laptop was provided with "all recent files and drives apparently deleted," limiting FDA's ability to assess CGMP compliance.*
- *You also allowed COAs to be sent via WhatsApp to a personal cell phone, with the QC analyst admitting he "deleted all the received COAs," showing a lack of controls to ensure integrity and traceability of third-party laboratory data.*



Data Manipulation, Fabrication & Destruction

Response Tip: Revoking access or firing the involved employees is not enough, even with an investigation into the specific incidences.

Serious DI problems must have a comprehensive investigation (w. detailed advance protocol) performed by an independent party that includes:

- Interviews with current and former employees
- Identification of all records that could be impacted throughout the facility/operations
- Retrospective evaluation of what records could be impacted from former batches
- Interim and long-term measures
- To be effective, you should look at Adverse Incentives and Pressures

Big Hint from FDA: "Inform FDA if you will be hiring a Chief Integrity Officer who is fully empowered to receive anonymous complaints from employees reporting data integrity concerns and with the authority to ensure any potential breach is promptly investigated (by independent quality assurance function, along with expertise from outside entities whenever needed)."

Consider DI in Quality Agreements

- Your quality agreements with your partners must ensure you can adequately assess your vendor/contract partners' records to allow robust DI audits.

- You can do a lot with pivot tables and looking for anomalies in the data you can access.

- Quality culture can often be a good indicator that data integrity problems exist beneath the surface.

Tip: The Office of Generic Drugs in March said "Data Integrity issues are the main reason for ANDA Delays"

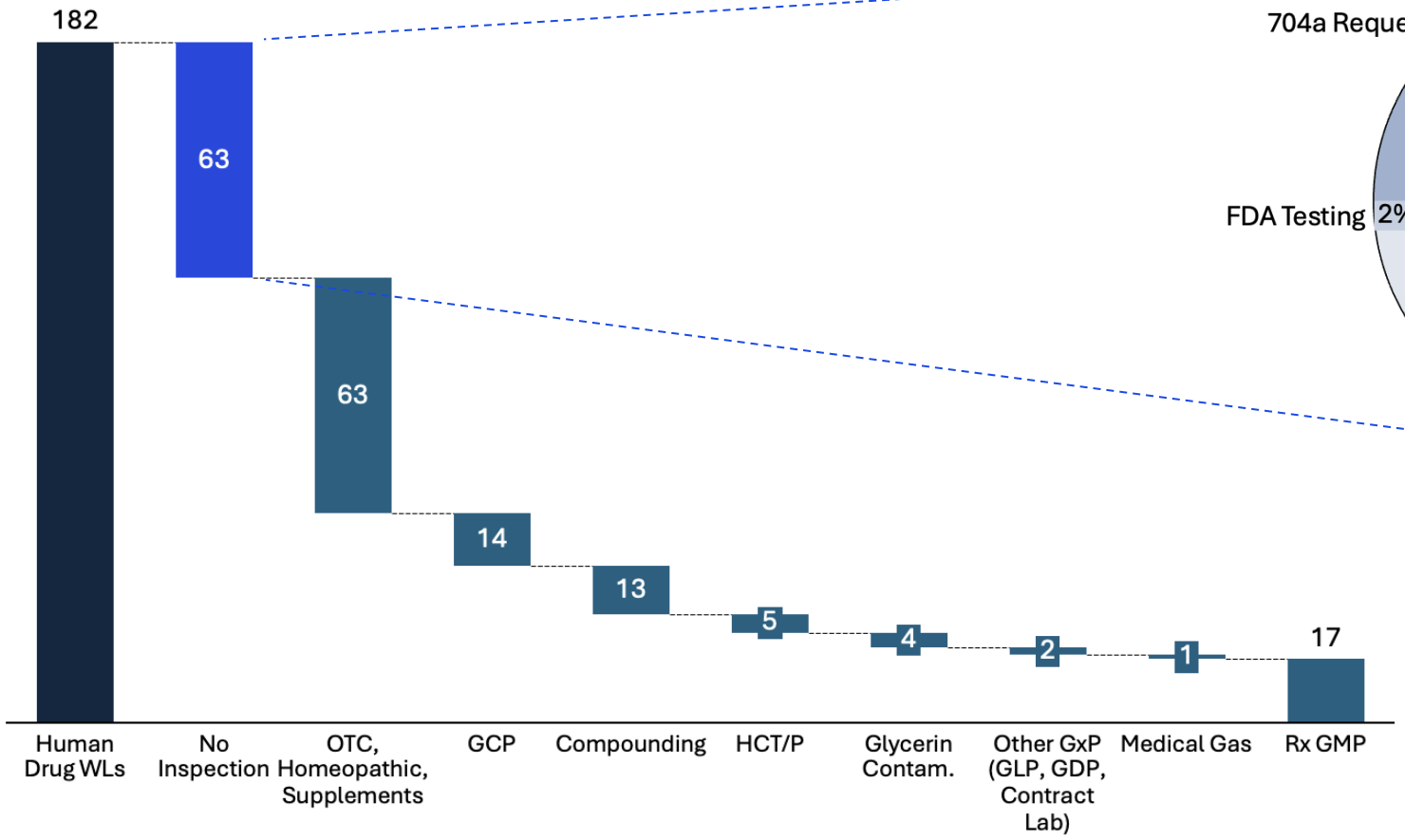
CGT Manufacturer

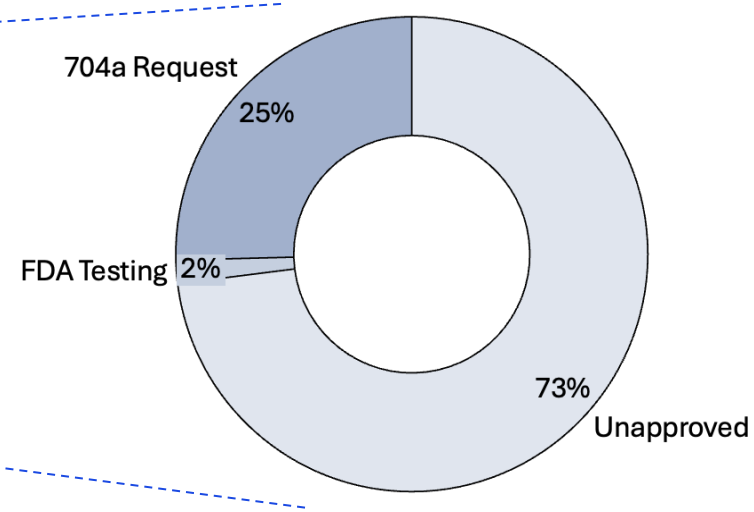
1. Your firm failed to maintain the buildings used in the manufacture, processing, packing, or holding of a drug product in a clean and sanitary condition and to keep them free of infestation by rodents, birds, insects, and other vermin. Trash and organic waste matter shall be held and disposed of in a timely and sanitary manner. [21 CFR 211.56(a)].	• *Severe insect infestation control failure: A box of food "covered in scuttle fly pupae" was observed on July 14, 2023, but "failed to [be] remove[d]...until July 31, 2023," leading to "scuttle fly larvae...found in ten environmental and personnel monitoring samples" and a "living scuttle fly...observed on the tube rack" in a cleanroom.*
2. Your firm failed to establish an adequate system for preventing contamination and monitoring environmental conditions in aseptic processing areas. [21 CFR 211.42(c)(10 (iv)]. Your firm also failed to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile. [21 CFR 211.113(b)].	• *Non-viable particulate monitoring is not conducted during open manufacturing manipulations in the Grade (b)(4) aseptic area for Humanized Anti-claudin 18.2 Autologous CAR T Cells (CT041), despite its critical role since "microorganisms can travel on particulates to contaminate the product."* • *Viable microbial active air monitoring is also not conducted during open manufacturing manipulations, even though it is "important for the detection of microorganisms in the environment surrounding the product."*
3. Your firm failed to establish an adequate system for cleaning and disinfecting the room and equipment to produce aseptic conditions. [21 CFR 211.42(c)(10)(v)].	• *The firm "has not conducted a cleaning validation" for the (b)(4) equipment used in sterile product manufacturing, and there is no evidence the cleaning process "can adequately remove contamination" from equipment and cleanrooms, posing a contamination risk to sterile products.*
4. Your firm failed to establish written procedures for production and process control designed to assure that the drug products you manufacture have the identity, strength, quality, and purity they purport or are represented to possess. [21 CFR 211.100(a)].	• *"There was no procedure for 100% visual inspection of the final drug product" to verify it is "essentially free from visible particulates," a critical step to ensure quality and purity before intravascular administration.*
5. Your firm failed to thoroughly investigate any unexplained discrepancy or failure of a batch or any of its components to meet any of its specifications, whether or not the batch had already been distributed. [21 CFR 211.192].	• *Repeated microbial monitoring excursions without corrective action: "CAPAs were proposed but never implemented" following action limit excursions in Grade (b)(4) personnel monitoring, and "additional excursions...have occurred" with products still being released, showing a failure to "prevent recurrence of excursions."*

Warning Letters without a Preceding Inspection

Warning Letters Issued to Human Drug Manufacturers Without an Inspection

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

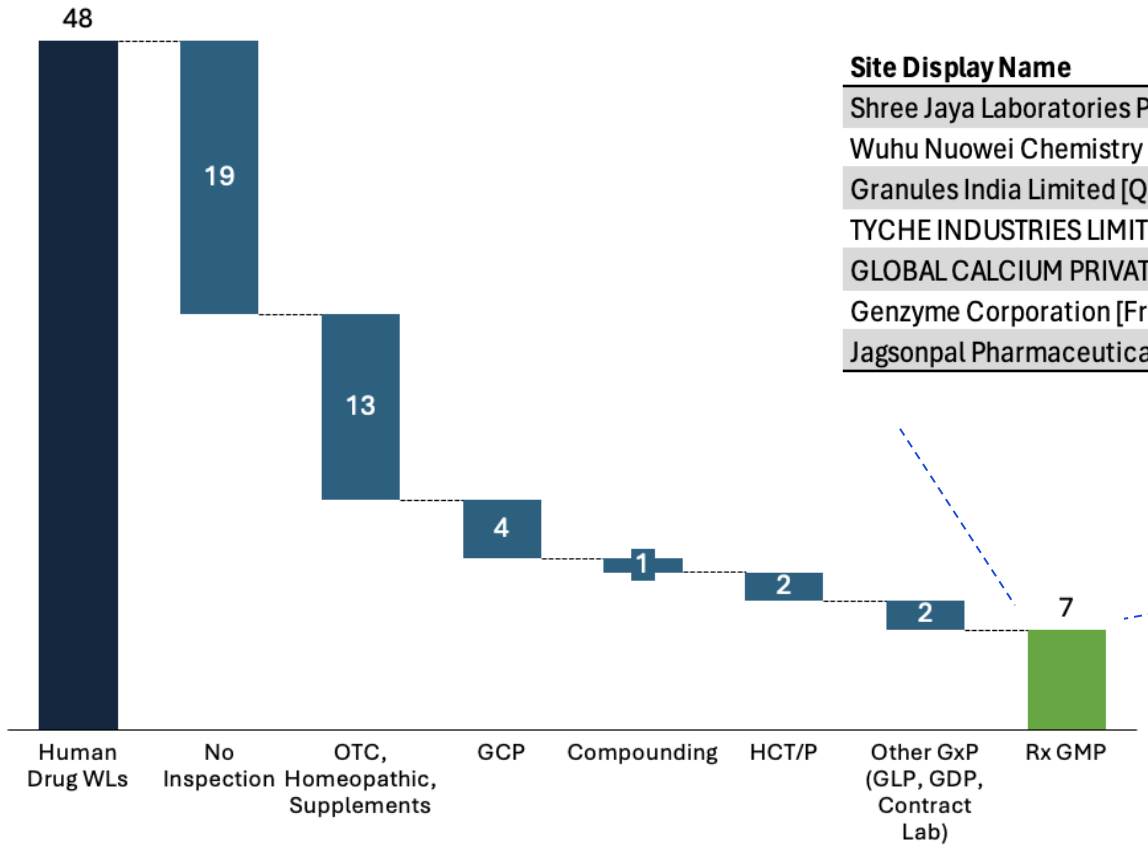




Turning to the Present

Seven Human Drugs GMP Rx Warning Letters Issued Start of 2025

Human Drugs Warning Letters Jan 2025 - Mar 2025,
Warning Letters



Site Display Name	Facility Type	Product Type	Import Alert Issued	Inspection End 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

Six out of Seven Warning Letters Issued to **API Manufacturers**; **Top Citations** Issued to API Manufacturers

1. Data Integrity and Documentation

- Torn, duplicate batch production records found in discarded, with two conflicting “original” versions.
- Batch records filled out after-the-fact by supervisors instead of contemporaneously by operators.
- Operators admitted to falsifying temperature data; managers submitted backdated calculation sheets.
- Deletion of electronic files during inspection.

2. Investigations and Deviation Handling

- Complaint investigation into contaminated intermediates was incomplete and ignored environmental factors.
- Contamination-related batch failures not investigated with scientific rigor.
- Past-due deviation investigations with no approved procedural extensions; 80+ open cases.
- Unaddressed deviations discovered by FDA, including improper aseptic practices and unreported line contact with floor.

3. Equipment Cleaning and Facility maintenance

- “Cleaned” equipment found with rust-like residues and visible contamination.
- Footprints observed inside cleaned production vessels.
- Water leaks from ceiling pipes onto equipment labeled ready for use.
- Equipment design flaws previously linked to contamination events still in active use.

4. Impurity Control and Analytical Testing

- Use of Chinese Pharmacopoeia impurity test methods without showing equivalency to USP methods.
- Impurity limits exceeded USP specifications, with actual lots shipped to the U.S. found out-of-spec.
- No impurity profile development tailored to the manufacturer’s own processes.
- Impurities not monitored during stability studies.

5. Noncompliance and Contract Manufacturing

- Contract manufacturer was unregistered with the FDA; firm failed to verify CGMP compliance.
- Refusal and delay of inspection access, including withholding key records.
- Misbranding violations due to failure to list drugs correctly and identify the true manufacturing site.

FDF Manufacturer

1. Your firm failed to establish and follow adequate written procedures for cleaning and maintenance of equipment (21 CFR 211.67(b)).	• *Significant contamination in multiple (b)(4) ducts* • *Inadequate cleaning and maintenance processes rendered them [filters] ineffective.* • *Detected residues from multiple previously manufactured drug products and too numerous to count (TNTC)microbial contamination.* • *Lacked documented cleaning procedures*
2. Your firm failed to maintain buildings used in the manufacture, processing, packing, or holding of drug products in a good state of repair (21 CFR 211.58)	• *Bird droppings and feathers were observed during the inspection in the AHU area* • *The conditions in your AHU area raise concerns about potential contamination affecting the air supplied to critical manufacturing equipment*
3. Your firm failed to routinely calibrate, inspect, or check according to a written program designed to assure proper performance of automatic, mechanical, electronic equipment, or other types of equipment, including computers, used in the manufacture, processing, packing, and holding of a drug product (21 CFR 211.68(a)).	• *Failed to adequately inspect and maintain your AHUs to ensure air filters would be effective at preventing contamination* • *The procedure for HEPA filter integrity and particle count testing did not clearly define the quality unit's role in verifying the condition of critical AHU components …during preventive maintenance* • *Lack of oversight led to insufficient monitoring of the filter replacement process during routine maintenance, preventing the detection of potential filter failures, air leakage, and contamination*

Thank you.

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