U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR VETERINARY MEDICINE

Inspection Experiences in
GOOD MANUFACTURING PRACTICES for ANIMAL DRUGS

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FDA INSPECTIONS & METRICS

TOP INSPECTION CITATIONS

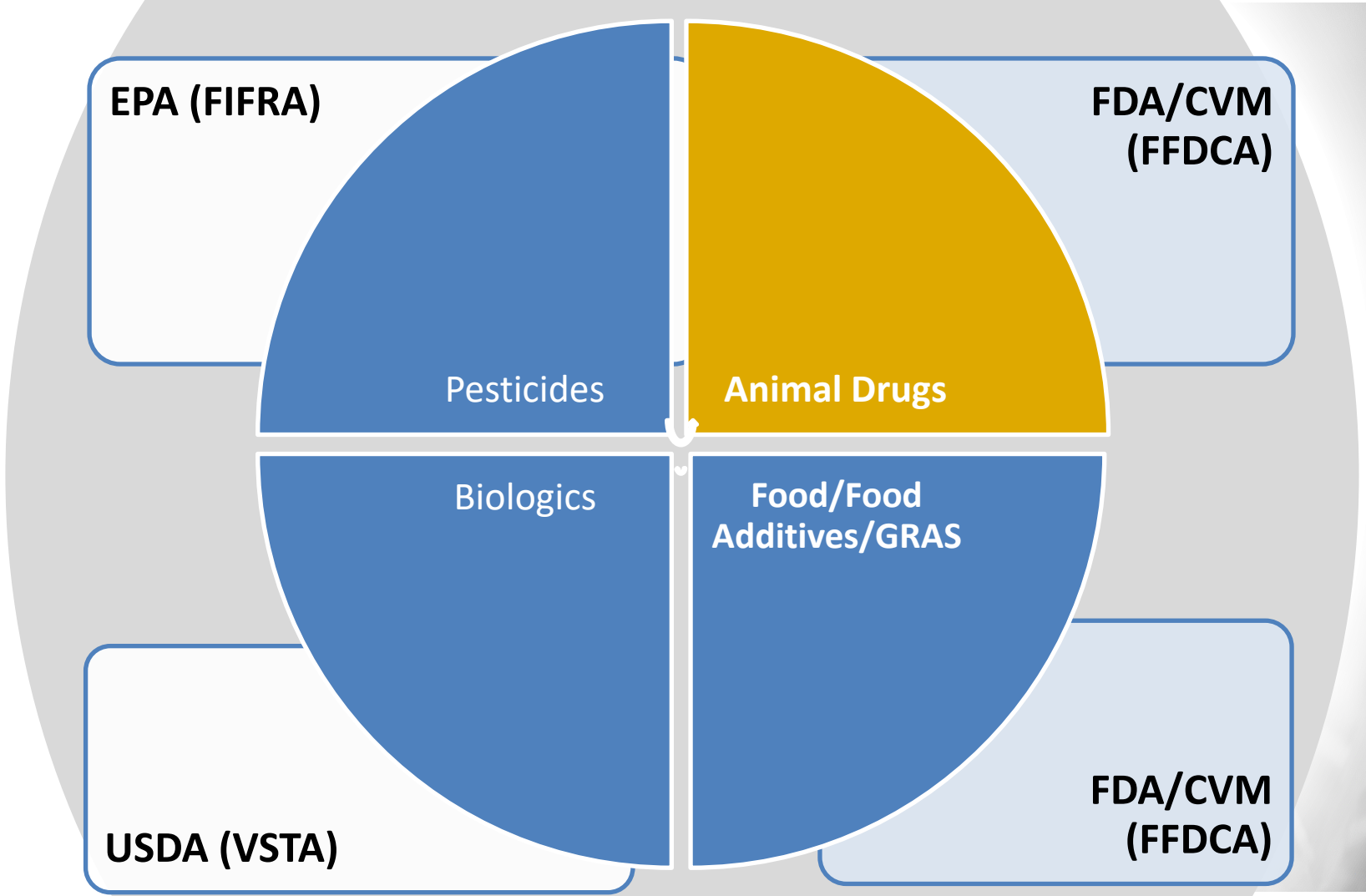
REGULATORY ACTIONS

INTERNATIONAL

ANIMAL PRODUCT JURISDICTION IN THE USA

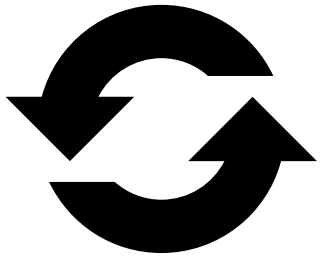
Environmental Protection Agency

U.S. Department of Agriculture



PRE-APPROVAL *versus* ROUTINE SURVEILLANCE

Pre-approval inspections are conducted for a subset of new products when the product information is still being reviewed by FDA (before approval and marketing). They are part of the review process to market a new animal drug to determine whether the new product is manufactured in compliance with FDA regulations and to ensure the facility is capable of manufacturing the product consistently and that submitted data are accurate and complete.



Routine Surveillance inspections are conducted to monitor the manufacturing process and the quality of FDA regulated products on the market. The agency uses the inspection to evaluate whether a manufacturer is complying with quality manufacturing practices.

Not going to cover in today's presentation:

For-cause inspections are triggered when the agency has reason to believe that a facility has quality problems, to follow up on complaints or to evaluate corrections that have been made to address previous violations.

GMP INSPECTION APPROACH

FDA Compliance Program for Animal Drugs, https://www.fda.gov/media/74730/download?attachment

Risk-based approach:

- concentration of active pharmaceutical ingredient in dosage form, emergency use, etc.
- whether the facility has been inspected by a foreign regulatory partner

EVALUACIONES REGULATORIAS REMOTAS (RRA)

RECORDS REQUESTS under §704(a)(4) – instead of **pre-approval inspections**

REMOTE INTERACTIVE EVLUATIONS (RIE)

NEW Draft Guidance,
https://www.fda.gov/media/173286/download

FDA's Remote Regulatory Assessment Tools,
https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-references/fdas-remote-oversight-tools

GMP INSPECTION CLASSIFICATIONS

No action indicated (NAI)

which means no objectionable conditions or practices were found during the inspection.

Voluntary action indicated (VAI)

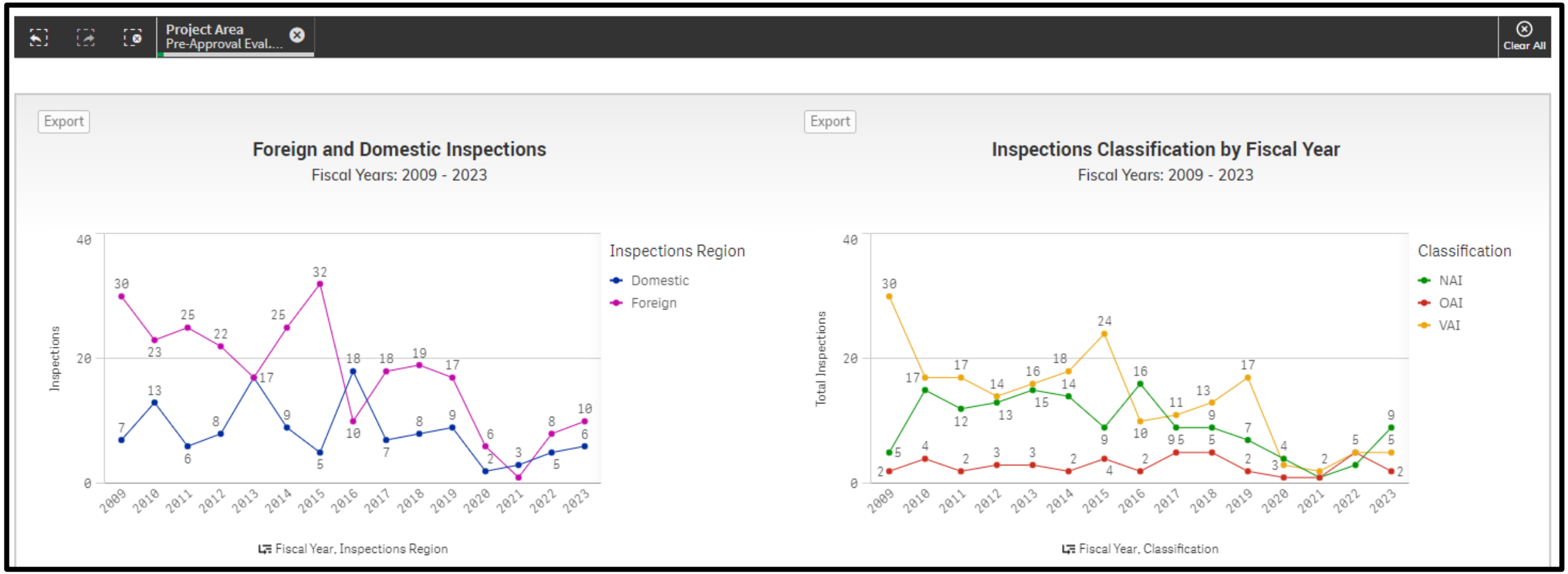
which means objectionable conditions or practices were found, but the agency is not prepared to take or recommend any administrative or regulatory action.

Official action indicated (OAI)

which means regulatory and/or administrative actions are recommended.

FDA DASHBOARD

Access: https://datadashboard.fda.gov/ora/cd/inspections.htm



FY 2022 – Inspection Data

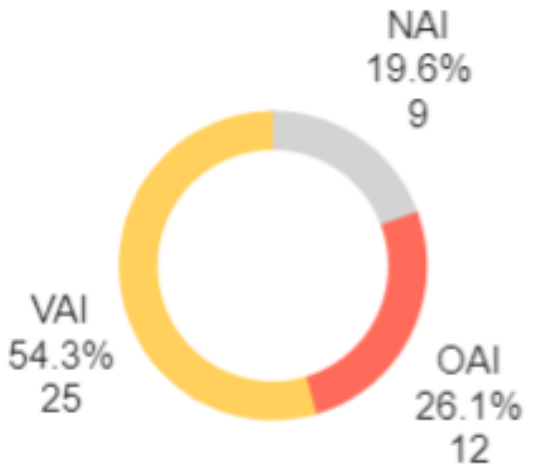
46
Domestic Inspections

11
Foreign Inspections

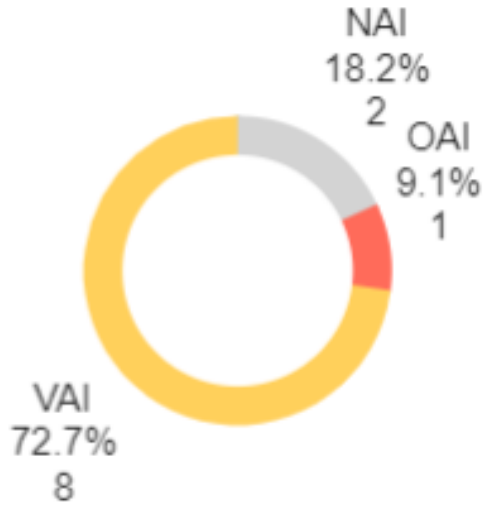
57
Animal Drug Inspections

Inspection Classifications

Domestic Inspection



Foreign Inspection



FY 2023 – Inspection Data

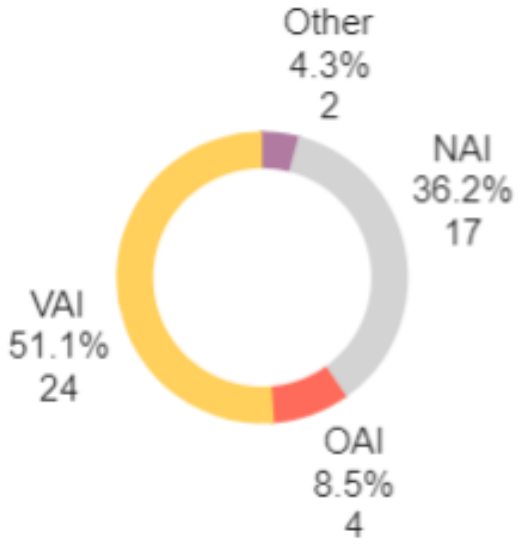
46 Domestic Inspections — **47**

11 Foreign Inspections — **32**

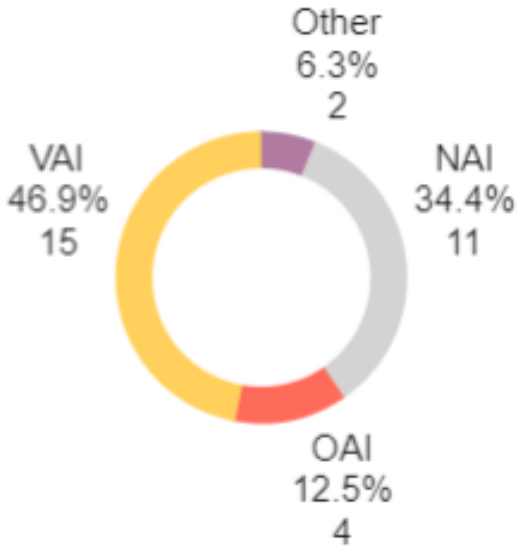
57 Animal Drug Inspections — **79**

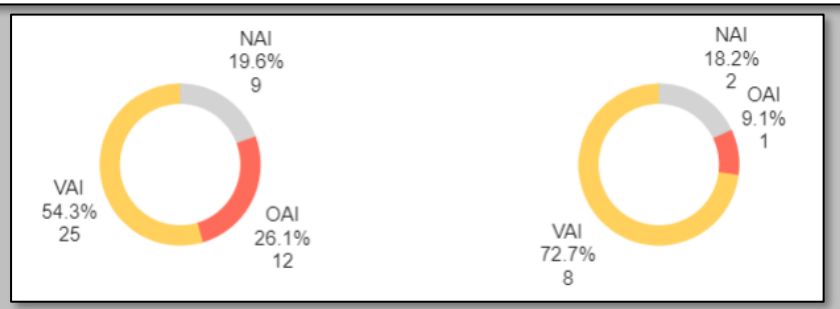
Inspection Classifications

Domestic Inspection



Foreign Inspection





Top 5 FDA 483 Citations

What is an FDA 483 Citation?

- An FDA Form 483 is issued to firm management at the conclusion of an inspection when an investigator(s) has observed any conditions that in their judgment may constitute violations of the Food Drug and Cosmetic (FD&C) Act and related Acts.

- The FDA Form 483 notifies the company's management of objectionable conditions. At the conclusion of an inspection, the FDA Form 483 is presented and discussed with the company's senior management. Companies are encouraged to respond to the FDA Form 483 in writing with their corrective action plan and then implement that corrective action plan expeditiously.

Tied for # 1

CFR/FDCA Number	SHORT DESCRIPTION	FULL LONG DESCRIPTION	COUNT
21 CFR 211.22(d)	**Procedures not in writing, fully followed**	The responsibilities and procedures applicable to the quality control unit are not [in writing] [fully followed]. Specifically, ***	9
21 CFR 211.192	**Investigations of discrepancies, failures**	There is a failure to thoroughly review [any unexplained discrepancy] [the failure of a batch or any of its components to meet any of its specifications] whether or not the batch has been already distributed. Specifically, ***	9

Tied for # 3

CFR/FDCA Number	SHORT DESCRIPTION	FULL LONG DESCRIPTION	COUNT
21 CFR 211.113(b)	**Procedures for sterile drug products**	Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not [established] [written] [followed]. Specifically, ***	6
21 CFR 211.160(b)	**Scientifically sound laboratory controls**	Laboratory controls do not include the establishment of scientifically sound and appropriate [specifications] [standards] [sampling plans] [test procedures] designed to assure that [components] [drug product containers] [closures] [in-process materials] [labeling] [drug products] conform to appropriate standards of identity, strength, quality and purity. Specifically, ***	6

5

CFR/FDCA Number		SHORT DESCRIPTION	FULL LONG DESCRIPTION	COUNT
21 CFR 211.100(a)		**Absence of Written Procedures**	Your firm failed to establish [adequate] written procedures for production and process controls designed to assure that the drug products have the identity, strength, purity, and quality that they are purported or represented to possess. Specifically, ***	4

Regulatory Actions

REGULATORY OPTIONS

Advisory Actions

- Untitled Letter
- Warning Letter
- Regulatory Meeting

Judicial Actions

- Seizure
- Injunction

Recall Procedures

- Call I
- Class II
- Class III

Import Operations and Actions

- Import Alert

International Harmonization & Collaboration

Mutual Recognition Agreement

European Union	• **<u>On May 31, 2023</u>**, U.S. FDA & the European Union announced the decision to expand the scope of the U.S.-EU MRA to include inspections of animal drugs. • With this announcement, FDA found 17 member states capable and have already relied on 5 EU inspection reports in lieu of conducting its own inspection. • FDA is currently working on the remaining 10 EU member states capability assessments.
United Kingdom	• Since entering into a MRA with the UK on **<u>September 24, 2021</u>**, FDA has requested and received numerous inspection reports from the Veterinary Medicines Directorate (VMD) in the UK. • This has increased collaboration and decreased resource burden, additionally allowing resources to be redirected to other inspection activities.
Switzerland	• The FDA, the U.S. Office of the Trade Representative, and the Swiss Confederation signed an MRA on **<u>January 12, 2023</u>**, and it entered into force July 27, 2023. • The U.S. and Switzerland can now begin to rely on each other's factual findings from a GMP inspection of a pharmaceutical manufacturing facility.

Pharmaceutical Inspection Co-operation Scheme (PIC/S)

CVM continues to collaborate on veterinary-specific GMP Guidelines through PIC/S.

Goal: **Better international implementation of GMP** standards and quality systems for the manufacturing of **Active Pharmaceutical Ingredients (APIs)** and **Veterinary Medicinal Products (VMPs).**

PIC/S

PHARMACEUTICAL INSPECTION CO-OPERATION SCHEME

VICH Guidelines

VICH GL 39: *Test Procedures And Acceptance Criteria For New Veterinary Drug Substances And New Medicinal Products: Chemical Substances*

- https://www.fda.gov/media/69909/download

VICH GL 60: *Good Manufacturing Practice for Active Pharmaceutical Ingredients Used in Veterinary Medicinal Products*

- ICH Q7 → VICH GL 60
- https://vichsec.org/en/component/attachments/attachments/2643.html?task=download
- Public consultation: can submit comments to the VICH Secretariat until March 2024.

SPECIAL MANUFACTURING CONSIDERATIONS

- Manufacturing Considerations for Penicillin or Cephalosporin Animal Drugs | FDA
- *Draft* Guidance for Industry: Non-Penicillin Beta-Lactam Drugs: A CGMP Framework for Preventing Cross-Contamination

Manufacturing Considerations for Penicillin or Cephalosporin Animal Drugs

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Thanks!