



# Update on Inspections of Drug Compounding Facilities

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# Summary of Presentation

- FDA inspections update
- FDA inspectional procedures
- Insanitary conditions observed during inspections



# Overview: Types of Compounding Inspections

## Surveillance inspections

- Risk based model
  - Based on a history of serious adverse events and product quality problems
  - Historical inspection data

## For-cause inspections

- Reports of
  - Serious adverse events
  - Serious product quality issues
  - Complaints about sterile practices at the facilities
- State information / request for FDA assistance

## Compliance follow up

- To regulatory action, prior inspection, recall, or to gather additional information.
- Verify corrective actions to a warning letter, injunction, or other regulatory action.

## 503B Reinspection

- Follow-up to a prior 503B inspection which revealed noncompliance that was materially related to applicable requirements of the FD&C Act.
- Purpose is to determine whether the earlier noncompliance has been corrected
- FDA charges a fee for reinspections (currently \$15,610.00)

# FDA Inspections Update

- **503A Inspection Objective:** The purpose of the inspection is to determine the **current operational status of the firm concerning:**
  1. Qualification of the firm's drug products for the exemptions under 503A.
  2. **Sterile and non-sterile** drug production and to obtain information about its current production practices and facility conditions.



# FDA Inspections Update

## 503B Inspection Objective:

- Assess the outsourcing facility's conformance with applicable standards for producing compounded products
  1. Prevent the production and distribution of drugs produced under conditions that may represent a significant risk to patient safety, and
  2. Evaluate compliance with certain conditions of section 503B, including labeling and adverse event reporting (see sections 503B (a)(10) and 503B(b)(5)).



# FY16 FDA Inspections Update

	Surveillance	For Cause	Follow Up	503B Reinspection	Total
<b>503A</b>	<b>33</b>	<b>44</b>	<b>20</b>	<b>-</b>	<b>97</b>
<b>503B</b>	<b>8</b>	<b>3</b>	<b>5</b>	<b>6</b>	<b>22</b>
					<b>119</b>

*\*Data gathered as of 8/23/2016*

# FDA Inspections Update

Investigators Continue to Encounter Refusals such as:

- Observation of production
- Review of Prescriptions
- Photography
- Photocopying of documents

# FDA Inspections Update

- **503B Inspection Obstacles**

- Outsourcing facility is not currently operational, therefore the 503B assignment can not be completed.
- Outsourcing Facility licensure requirements may differ per state. Some states require an FDA inspection as part of the licensure to produce and distribute. However, FDA's complete evaluation of the firm's operation requires that production be observed during the inspection.



# FDA Inspectional Procedures

- Section 503A does not provide an exemption from the prohibition on insanitary conditions. Therefore, even if a compounder qualifies for exemptions under section 503A, FDA investigators will continue to include observations on Forms FDA-483 that appear to constitute insanitary conditions.

# FDA Inspectional Procedures

- **Insanitary Conditions**
  - Definition
  - Examples
  - Potential for Environmental Sampling

# FDA Inspectional Procedures

- Insanitary Conditions Definition
  - Under section 501(a)(2)(A) of the Federal Food, Drug, and Cosmetic Act (FDCA) [21 U.S.C. § 351(a)(2)(A)], a drug is adulterated if it has been prepared, packed, or held under insanitary conditions whereby it may have been contaminated with filth or rendered injurious to health.

## FDA 483 Observations that appear to constitute insanitary conditions



- Culligan drinking water, obtained from an office-style top loaded 5-gallon bottled water dispenser in the kitchen area, was not tested by the firm after dispensing to confirm chemical purity or microbial/endotoxin content was suitable for the intended use in formulating sterile or injectable product.

## FDA 483 Observations that appear to constitute insanitary conditions

- Top of the Right photo showing the ISO 7 & ISO 8 classified.
- Bottom photo showing the portable fence and pet bed



## FDA 483 Observations that appear to constitute insanitary conditions

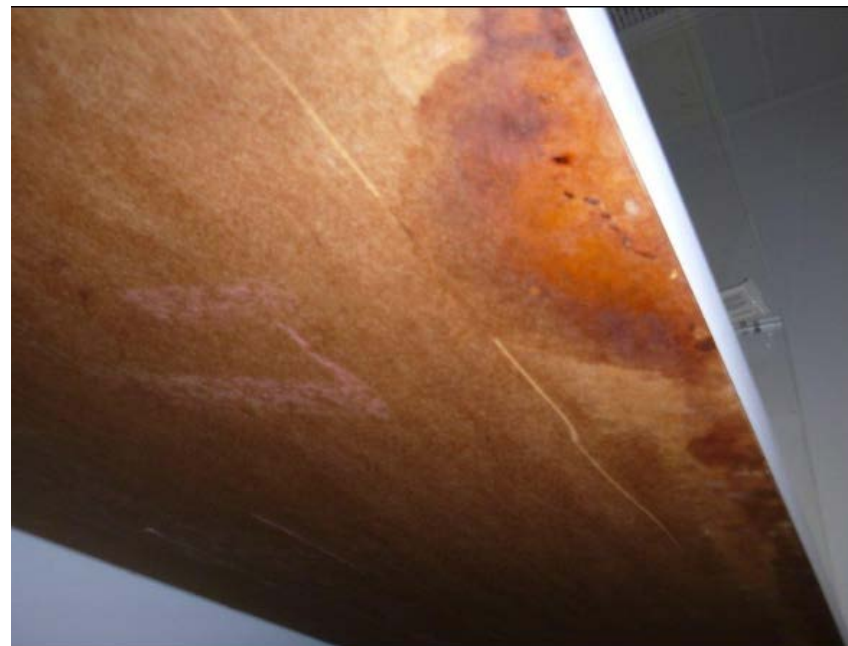


View of the bottom surface of the ISO 5 LAFW showing wood like surface that appears to be stained.



## FDA 483 Observations that appear to constitute insanitary conditions

- Photo of the Top of the ISO 5 bench
- Photo of the stained Wooden Bottom of the ISO 5 bench



The ISO 5 should not have work surfaces made of wood.

## FDA 483 Observations that appear to constitute insanitary conditions



- The firm's ISO 7 ante room design is not adequate. The ISO 7 ante room is 20 inches in width. Personnel could not gown without touching the walls and the sliding door of the ISO 6 clean room.



## FDA 483 Observations that appear to constitute insanitary conditions



- Dirty Home Depot container is used to store Master Suspensions which are prepared and kept as a stock solution for up to 6 months.

## FDA 483 Observations that appear to constitute insanitary conditions



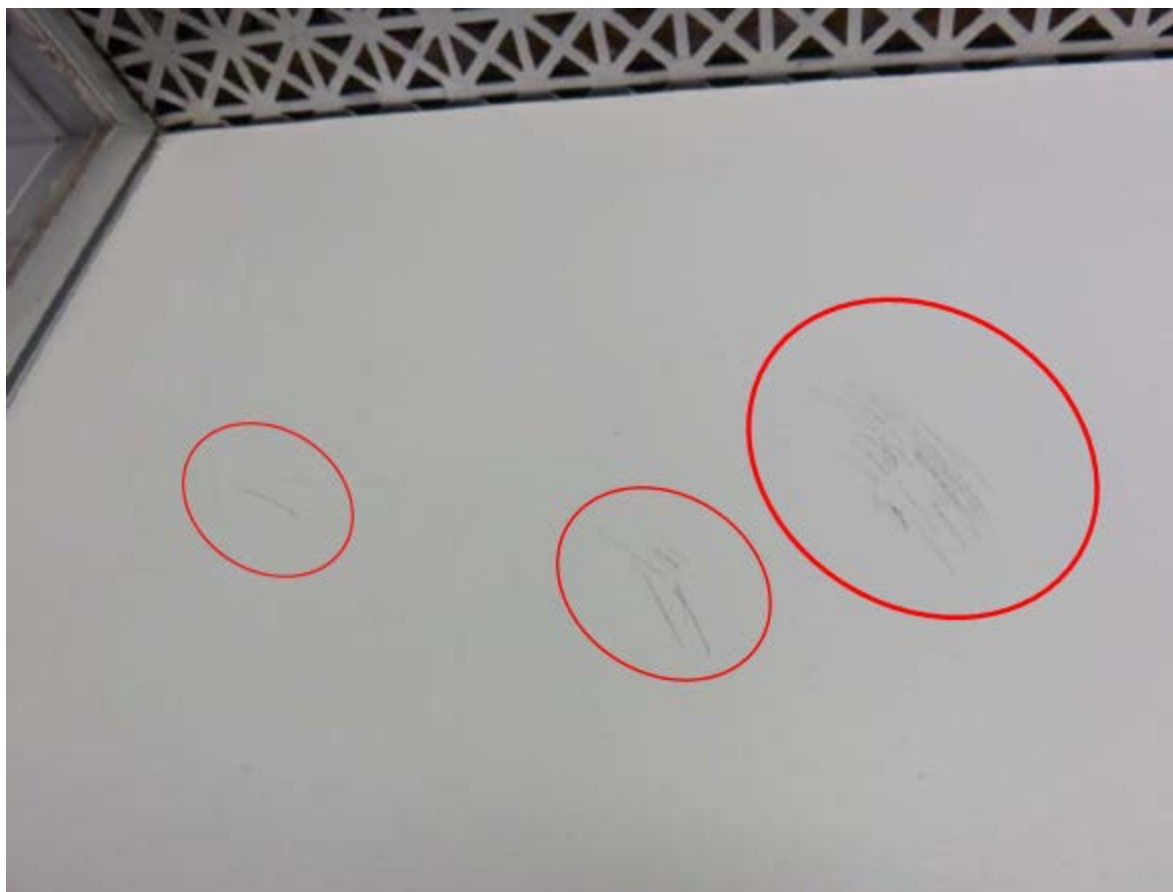
Soiled material was observed on the metal grate covering the pre-filter of the ISO 5 LFH.

## FDA 483 Observations that appear to constitute insanitary conditions



The clean room's positive pressure air handling system was observed to be turned off.

## FDA 483 Observations that appear to constitute insanitary conditions



The ISO 5 LAFW is stained on the work surface.

## **FDA 483 Observations that appear to constitute insanitary conditions**

- It is important to determine whether the deficiencies observed during the inspection are insanitary conditions as
  - **Drugs compounded by 503A facilities are not exempt from insanitary conditions section 501(a)(2)(A)**
  - Regulatory action may be pursued to prevent production and distribution of adulterated drug products

# FDA 483 Observations and Environmental Sampling

- **FDA Environmental Sampling**
  - EM sampling would likely be limited to samples of the ISO 5 area and on surfaces that pose potential routes of contamination such as equipment, supplies, and components that enter the ISO 5 area.
  - The EM samples are collected and analyzed by ORA microbiologists.

# FDA 483 Observations and Environmental Sampling

- **FDA Environmental Sampling**

- During FY16, EM samples were collected by FDA during 9 inspections.
  - 8 Inspections of 503A
  - 1 Inspection of 503B
- Microbial growth was present in all 9 sample collections performed by ORA.
- EM samples were collected during the FDA inspections photographed in this presentation.





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