# Overview of FDA Oversight and Enforcement on Drug Compounding

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# Today's Agenda

- When does FDA conduct a compounding inspection
- Examples of inspectional findings
- When does FDA take regulatory actions and the type of actions

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# When does FDA Conduct a Compounding Inspection

**For-cause (over 175 inspections conducted)**

- Serious adverse events
- Product quality or facility concerns (e.g., contamination, insanitary conditions)
- Complaints (e.g., compounding without patient-specific prescriptions)

**Surveillance (over 200 inspections conducted)**

- Routine risk-based surveillance of all outsourcing facilities
- Limited risk-based surveillance of pharmacies of which FDA is aware

**Follow-Up (over 95 inspections conducted)**

- Follow-up on corrective actions implemented after prior FDA inspections or regulatory actions

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# Frequent Inspectional Findings

- Insanitary conditions
- CGMP violations (only applicable to outsourcing facilities and firms that do not meet the conditions of section 503A)
- Failure to meet the conditions of section 503A
  - E.g., Lack of patient-specific prescriptions
- Failure to meet the conditions of section 503B
  - E.g., Failure to submit a product report

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# Insanitary Condition Example

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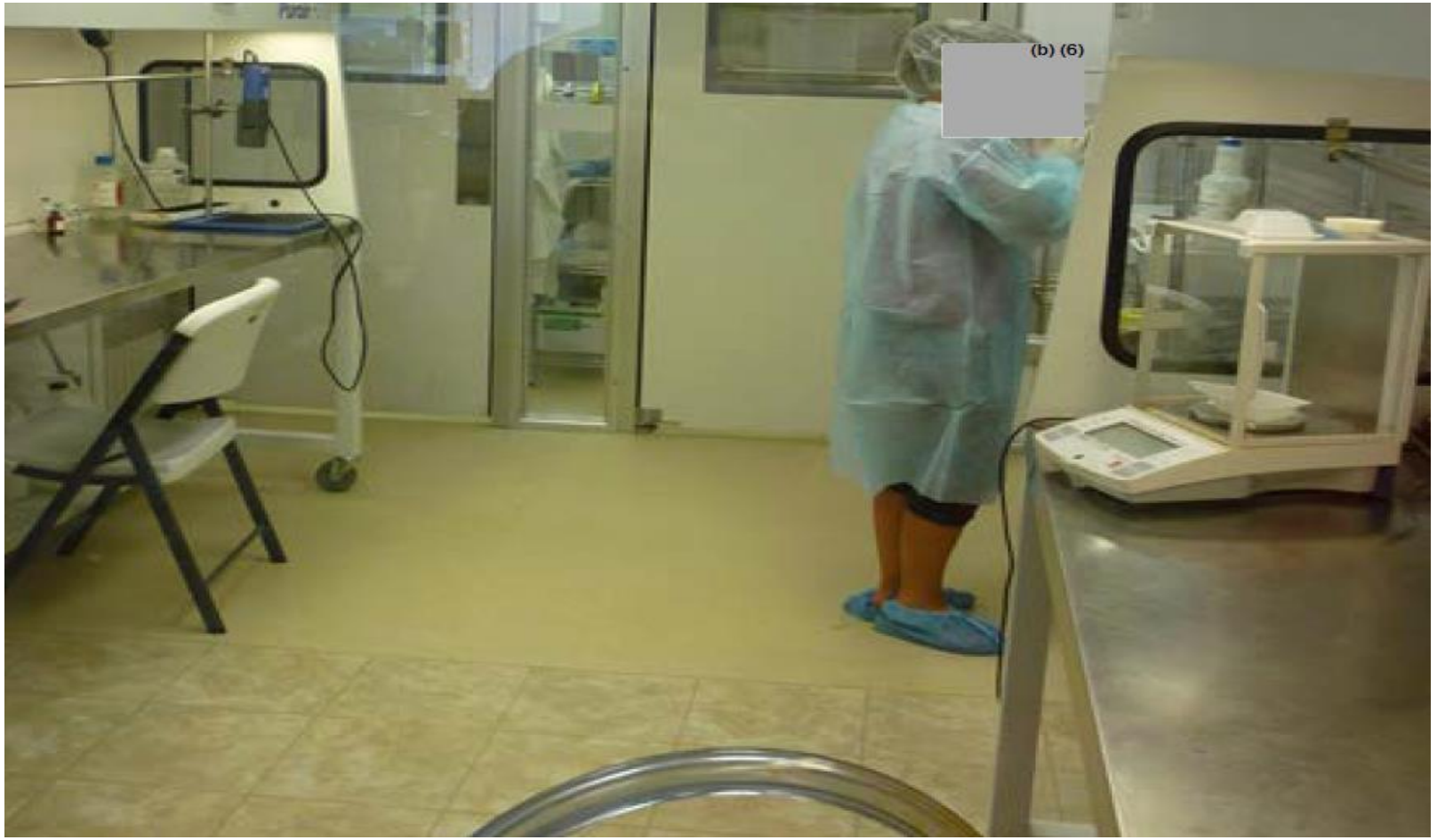
# Insanitary Condition Example



# Insanitary Condition Example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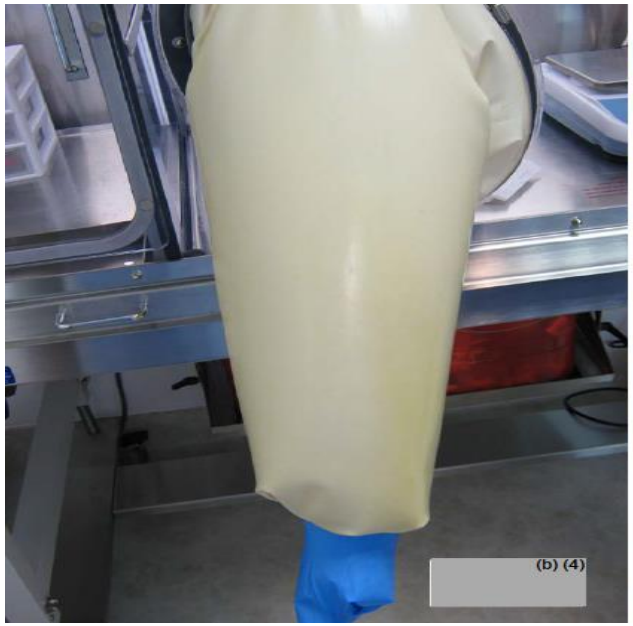


# Insanitary Condition Example

# Insanitary Condition Example

Ceiling above the doorway to cleanroom with exposed insulation

# Insanitary Condition Example


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# Insanitary Condition Example

# When Does FDA Take Regulatory Action

**Factors may include:**

- The nature of the violation
- Risk to public health
  - Lack of sterility assurance
  - Actual contamination
- Prior violations
- The overall adequacy of the firm's corrective action
- Whether documentation of the corrective action was provided

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# Frequent Actions in Response to Compounding Inspections

| | |
|---|---|
| **RECALLS**<br>Informal recommendations for voluntary recalls<br>Formal FDA requests for voluntary recalls | **ADVISORY ACTIONS**<br>Warning letters<br>Untitled letters |
| **ENFORCEMENT ACTIONS**<br>Civil injunctions<br>Criminal actions | **STATE REFERRALS**<br>For 503A facilities |

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# Voluntary Actions: Compounding Recalls

- Since October 2012 there have been over 170 recall events involving compounded drugs, many due to conditions and practices resulting in a lack of drug sterility assurance
    - FY 2013 – 28 recall events
    - FY 2014 – 25 recall events
    - FY 2015 – 38 recall events
    - FY 2016 – 51 recall events
    - FY 2017 – 30 recall events (Q1-Q3)
- Since October 2012 FDA has issued four letters formally requesting firms to recall compounded drugs after they refused informal recommendations

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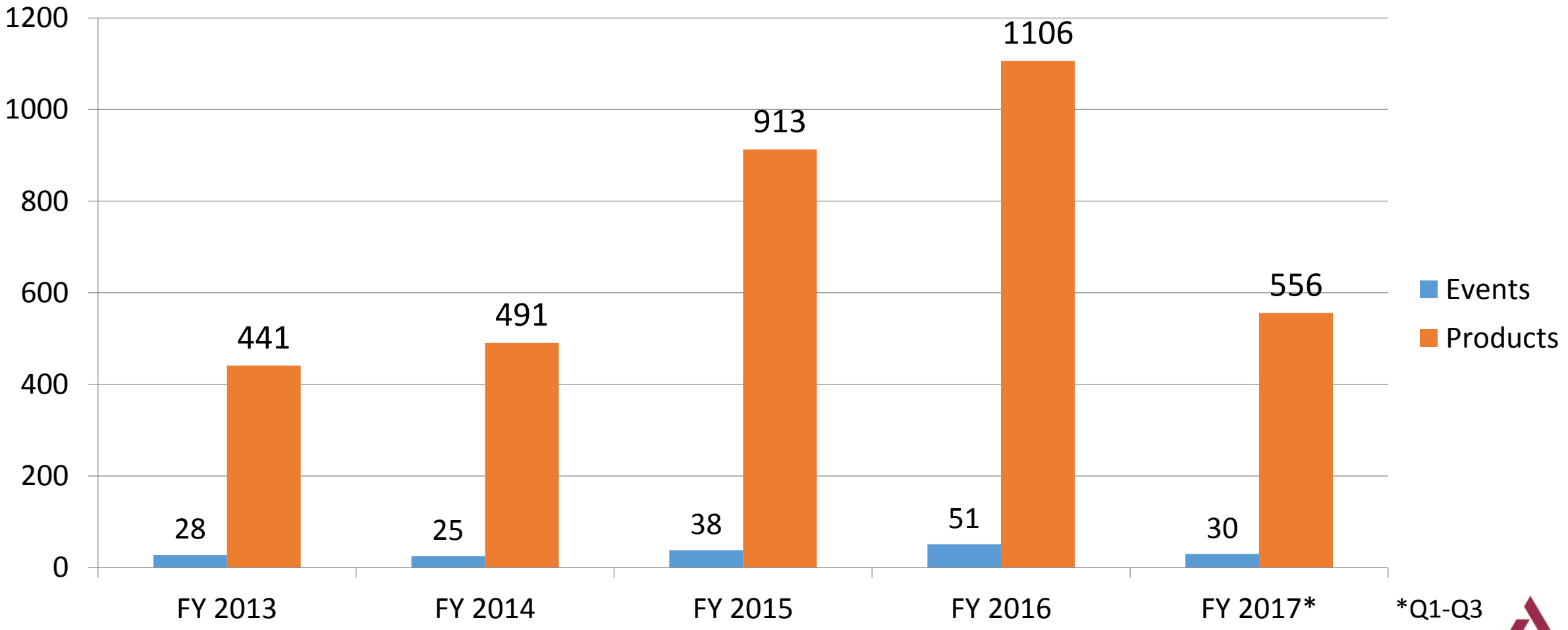
# Compounding Recalls

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# Voluntary Recalls: Examples

- Potency
  - Voluntary recall of compounded multivitamin capsules containing high amounts of Vitamin D3 (Cholecalciferol). FDA received reports of several adverse events potentially associated with these compounded capsules made by this firm. (November 2015)
- Labeling
  - Voluntary recall of compounded drug products due to concerns over mislabeling. FDA received two adverse event reports from patients taking drug products labeled as biotin but actually contained a different drug. Products were shipped to multiple states. (March 2016)
- Sterility Assurance
  - Voluntary nationwide recall of all drug products intended to be sterile due to lack of sterility assurance. Among other deficiencies, the firm's environmental monitoring showed persistent microbial contamination in sterile processing areas. (March 2017)

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# Warning Letters

- Warning letters:
  - Communicate the Agency's position
  - Issued to achieve voluntary and prompt corrective action
  - Generally used when there is no history of repeat violations
- FDA has issued over 160 warning letters to compounders since October 2012
  - Insanitary conditions
  - Failure to comply with conditions of sections 503A or 503B
  - Violations of new drug approval, labeling with adequate directions for use, and CGMP provisions of the Act

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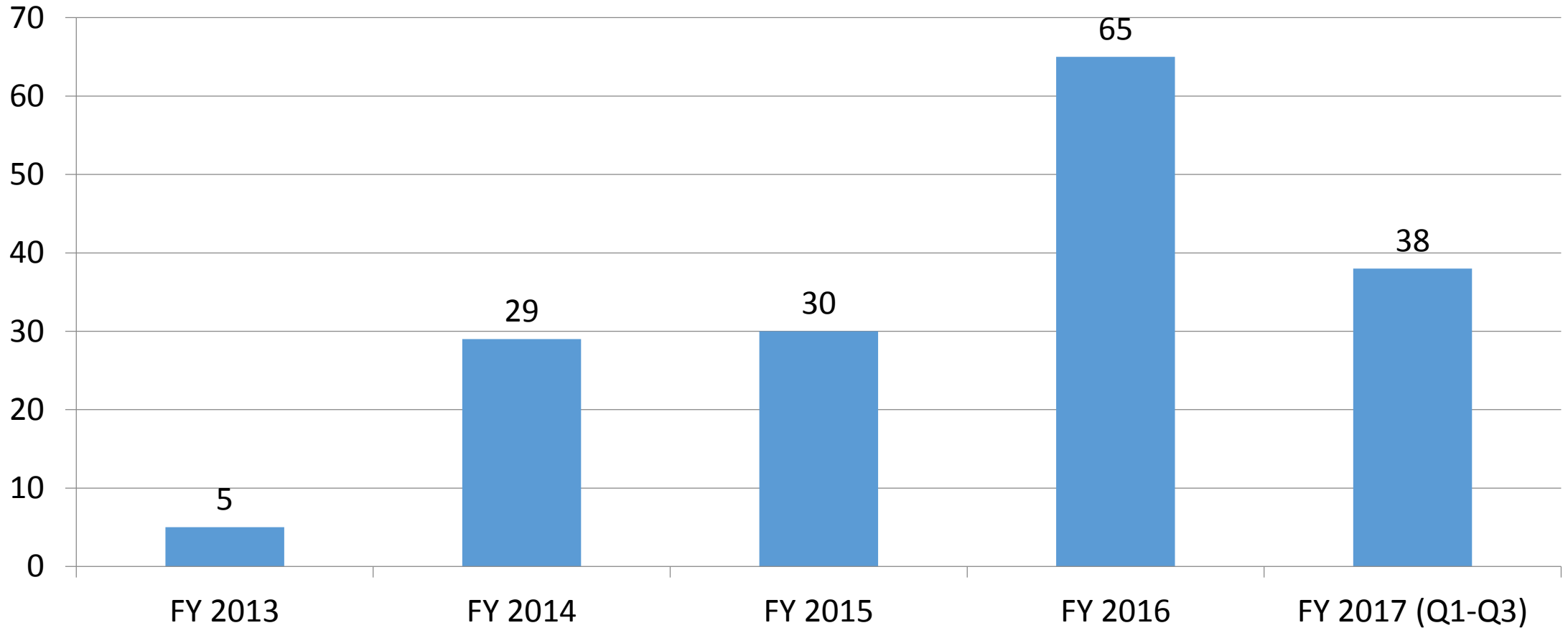
# Compounding Warning Letters

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# Enforcement Actions: Injunctions

- To prevent further production and/or distribution of adulterated, misbranded, and/or unapproved new drug products and to correct the root cause of the violations
- If a firm has a history of repeated violations and has promised to make corrections in the past but has not made the corrections, an injunction may be necessary to stop or prevent the violation.

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# Injunction: Medistat, 2017

- On July 6, 2017, an order of permanent injunction was entered against Medistat (Foley, Alabama).
- The order prohibits Medistat, its owners, and pharmacist-in-charge from manufacturing, holding, and distributing drugs until they comply with the FD&C Act and its regulations.
- Medistat manufactured and distributed purportedly sterile drug products that were adulterated because the drugs were made under insanitary conditions and in violation of current good manufacturing practice requirements under the FD&C Act.

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# Criminal Charges: Pharmakon, 2017

- On June 22, 2017, the owner and director of compliance of an Indiana compounding facility named Pharmakon Pharmaceuticals Inc. were charged criminally in connection with defrauding the United States and distributing adulterated compounded drugs.
- The indictment alleges that in early February 2016, Pharmakon distributed superpotent morphine sulfate, an opioid typically used for relief of moderate to severe acute and chronic pain, to hospitals.
- Three infants at the Indiana hospital received the morphine sulfate which was nearly 25 times the strength indicated on its label; one infant of the three was taken by emergency helicopter to a nearby children's hospital.

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# Thank You

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