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U.S. FOOD & DRUG ADMINISTRATION

FDA Oversight of Compounding

NABP Regional Conference - Districts 6, 7 and 8
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Statutory Framework

Section 503A	Section 503B
Conditions under which drug products compounded by a **licensed pharmacist in a State-licensed pharmacy or Federal facility**, or by a **licensed physician**, can qualify for exemptions from three requirements of the FD&C Act: (1) New drug approval requirements (section 505), (2) Labeling with adequate directions for use (section 502(f)(1), and (3) Current good manufacturing practice (CGMP) requirements (section 501(a)(2)(B)).	Conditions under which drug products compounded by or under the direct supervision of a licensed pharmacist in an **outsourcing facility** can qualify for exemptions from three requirements of the FD&C Act: (1) New drug approval requirements (section 505), (2) Labeling with adequate directions for use (section 502(f)(1)), and (3) Drug supply chain security requirements (section 582). **Outsourcing facilities remain subject to CGMP requirements.**

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Compounders under Section 503A

- State-licensed pharmacies, Federal facilities, physicians
- Number in the many thousands
- Generally do not register with FDA
- Pharmacies primarily overseen by the states
  - Frequency and depth of state oversight of pharmacies varies from state to state
  - Compounding physicians are generally not routinely overseen by any regulatory body
  - Quality standards vary from state to state

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Outsourcing Facilities under Section 503B

- Section 503B defines "outsourcing facility" as a facility that:
  - Is engaged in the compounding of sterile drugs
  - Has elected to register as an outsourcing facility
  - Complies with all of the requirements in section 503B
- In addition, an outsourcing facility:
  - Is NOT required to be a licensed pharmacy, but compounding must be by or under the direct supervision of a licensed pharmacist
  - May or may not obtain prescriptions for identified individual patients

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Policy, Oversight and Enforcement, and State Collaboration

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Policy Goals

1. Address significant public health concerns
2. Provide clarification on provisions of the law and answer questions presented by industry
3. Decrease regulatory burden to the extent possible without sacrificing critical public health protections
4. Clarify responsibilities of FDA and the states

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Final Guidances and Regulations Issued

- Final Guidances
  - Prescription requirement under section 503A
  - Repackaging drugs
  - Interim policies on compounding from bulk drug substances
  - 503B Product reporting
  - 503B Adverse event reporting
  - 503B Registration
  - Compounding under section 503A
  - Entities considering whether to register under section 503B
- Final Rules
  - Modifications to the withdrawn or removed list under sections 503A and 503B

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Final Guidance: Prescription Requirement Under Section 503A

PURPOSE	POLICY
Section 503A(a) of the FD&C Act requires that compounding be based on the receipt of a valid prescription for an identified individual patient. Compounding can occur: • In limited quantities before the receipt of such a prescription, or • After the receipt of the prescription. Outsourcing facilities need not receive patient-specific prescriptions for their compounded drugs. The guidance provides FDA's thinking on these requirements and some regulatory policies	Supports the prescription requirement: • Ensures that compounding under section 503A is based on individual patient need; • Supports the integrity of the DQSA by supporting the viability of outsourcing facilities. Preserves access to non-patient specific compounded drugs for healthcare facilities to administer to patients who have a medical need for them, while seeking to prevent compounders from engaging in large-scale manufacturing, like conventional manufacturers.

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Prescription Requirement Under Section 503A: Case Study

- Main Street Family Pharmacy
- Compounded methlyprednisolone acetate and other drugs
- 26 cases of fungal infections in patients in 17 states in 2013
- Drugs distributed without patient-specific prescriptions

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Final Guidance: Repackaging

PURPOSE	POLICY
Unlike compounded drugs, repackaged drugs are not eligible for exemptions under sections 503A or 503B. Policy addresses concerns about access and patient safety raised with FDA.	Guidance describes conditions under which FDA does not intend to enforce new drug approval, labeling with adequate directions for use, and, except with respect to outsourcing facilities, current good manufacturing practice requirements, when pharmacies, Federal facilities, and outsourcing facilities repackage drugs.

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Repackaged Drugs: Case Study

- Specialty Compounding
- Nationwide distributor
- Repackaged calcium gluconate under insanitary conditions and assigned long beyond-use-dates
- 15 patients infected
- 2 patients died

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Guidances and Regulations Under Development

- Current good manufacturing practice requirements for outsourcing facilities
- Insanitary conditions
- 503B facility definition
- Radiopharmaceutical compounding
- Compounded drugs that are essentially a copy
- Mixing, diluting, or repackaging biological products
- Bulk drug substances lists
- Withdrawn or removed list

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CGMP Requirements for Outsourcing Facilities

PURPOSE	POLICY – DRAFT GUIDANCE
This guidance reflects FDA's intent to recognize the differences between compounding outsourcing facilities and conventional drug manufacturers, and to tailor CGMP requirements to the nature of the specific compounding operations conducted by outsourcing facilities while maintaining the minimum standards necessary to protect patients from the risks of contaminated or otherwise substandard compounded drug products.	The draft guidance proposes a policy to focus FDA's inspectional and enforcement efforts, particularly on aspects of outsourcing facility compounding operations that pose the highest risk to patient safety, and discusses applicable CGMP requirements in detail to help outsourcing facilities to comply with the law. FDA intends to promulgate more specific CGMP regulations for outsourcing facilities

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Insanitary Conditions

PURPOSE	POLICY
This guidance is intended to provide examples of conditions that FDA considers to be insanitary within the meaning of section 501(a)(2)(A) of the FD&C Act to assist compounding facilities in identifying such conditions at their facilities and to assist state inspectors.	The law provides that a drug is adulterated if it was prepared, packed, or held under insanitary conditions whereby it may become contaminated with filth or rendered injurious to health. This guidance provides examples of insanitary conditions.

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Compounded Drugs that are Essentially Copies

PURPOSE	POLICY – DRAFT GUIDANCE
The restrictions on making drugs that are essentially copies ensure that pharmacists, physicians, and outsourcing facilities do not compound drugs for patients who could use an approved or otherwise commercially available drug product. Copies undermine the FDA approval process and put patients at unnecessary risk for receiving a substandard drug product.	Draft guidances describe FDA's proposed policies regarding the "essentially a copy" provisions of sections 503A and 503B, including clarifying certain statutory terms such as "regularly or in inordinate amounts" and "commercially available."

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Why is the copies provision important?

- Compounded drugs pose a higher risk to patients than FDA-approved drugs. Compounded drugs have not undergone FDA premarket review for safety, effectiveness, and quality, and drugs compounded in accordance with section 503A are exempt from CGMP requirements.
- Numerous serious adverse events and poor compounding conditions and practices.
- The restrictions on making drugs that are essentially copies ensure that pharmacists and physicians do not compound drugs for patients who could use an approved or, under section 503A, otherwise commercially available drug product.
- Unrestricted compounding of drugs that are essentially copies would also undermine the drug approval process.

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Copies: Case Study

- Franck's Compounding Lab
- In 2012, more than 40 patients experienced infections, many resulting in permanent vision loss, from contaminated triamcinolone acetate and brilliant blue G ophthalmic injections distributed nationwide.
- FDA-approved triamcinolone acetate may have been medically appropriate for the patients.

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Mixing, Diluting, or Repackaging Biological Products

PURPOSE	POLICY – DRAFT GUIDANCE
Biological products subject to licensure are not eligible for exemptions under section 503A or 503B from requirements of the FD&C Act or PHS Act. Policy is to address concerns about access and patient safety raised with FDA.	Draft guidance proposes conditions under which FDA does not intend to enforce licensure, labeling with adequate directions for use, and, except with respect to outsourcing facilities, current good manufacturing practice requirements, when pharmacies, federal facilities, and outsourcing facilities mix, dilute, or repackage drugs.

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Mixing, Diluting, or Repackaging Biological Products – Case Study

- Eastern Pharmacy
  - At least 37 patients experienced eye infections after receiving intravitreal injections of repackaged Avastin and Lucentis, that was contaminated.
  - Long beyond-use-dates
  - Repackaged under non-sterile conditions
- Since 2007, more than 100 adverse events associated with repackaged Avastin that may have been contaminated

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Bulk Drug Substances

- 503A bulks list (rulemaking)
- 503B bulks list (*Federal Register* notice)
- Final guidances

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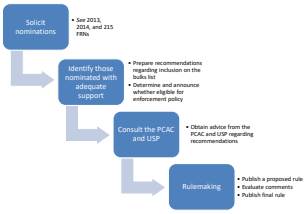
503A Bulks List: Process



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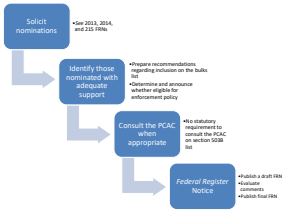
503B Bulks List: Process



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Final Guidances: 503A and 503B Bulks

PURPOSE	POLICY
Prevent unnecessary disruptions in patient access to drugs compounded from bulk drug substances while FDA develops the lists of substances that can be used in compounding.	While the bulks lists are in development, FDA does not object to the compounding of drugs from bulk drug substances provided that certain conditions are met, including that they were nominated with adequate supporting information for FDA to evaluate them.

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Policy, Oversight and Enforcement, and State Collaboration

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When FDA Conducts 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)

- Limited surveillance of pharmacies of which FDA is aware
- Going forward, we are focusing on outsourcing facilities, and we are looking to identify other compounders that engage in large-scale interstate distribution

Follow-Up (over 95 inspections conducted)

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

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FDA Surveillance Inspections

- FDA intends to focus its surveillance inspections on outsourcing facilities and other compounders that ship large volumes of compounded drugs to multiple states, which could
  - Help FDA identify firms that are distributing non-patient specific compounded drugs and should consider registering as outsourcing facilities;
  - Focus FDA oversight on facilities that, should quality issues occur, have the potential to affect the largest number of patients;
  - Target FDA oversight in a manner that is useful to states, especially for those who are not able to conduct frequent oversight of nonresident pharmacies.
- FDA does not intend to conduct surveillance inspections of the vast majority of compounders that do not elect to register as outsourcing facilities and are primarily regulated by the states.

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503A INSPECTION ASSIGNMENT

Phase I	• VISUAL INSPECTION/INTERVIEW AND EVALUATION OF COMPLIANCE WITH CERTAIN CONDITIONS OF SECTION 503A
Phase II	• DETERMINING THE NATURE OF THE FIRM'S OPERATIONS AND DRUG PRODUCTS
Phase III	• STERILE DRUG PRODUCT-SPECIFIC INSPECTION AND RECORDS REVIEW
Phase IV	• NON-STERILE DRUG PRODUCTION

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503A Compliance Assessment

Does the firm appear to receive patient-specific prescriptions for the compounded drug products that it distributes?

YES — Drugs may be eligible for 503A exemptions

NO — Drugs are not eligible for 503A exemptions

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Preliminary Assessment

Preliminary Assessment Regarding Form FDA 483 Citations

- Process since August 1, 2016 - FDA investigators make a preliminary assessment regarding the firm's compliance with certain conditions of section 503A before closing an inspection, and if a Form FDA-483 is issued to the firm, it will not include observations that represent deviations only from CGMP requirements unless the investigator's preliminary assessment is that the firm compounds drugs that do not qualify for the exemptions under section 503A

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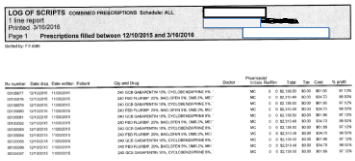
Prescription Log


LOG OF SCRIPTS COMBINED PRESCRIPTIONS Scheduler ALL
1 line report
Printed 3/16/2016
Page 1 Prescriptions filled between 12/10/2015 and 3/16/2016

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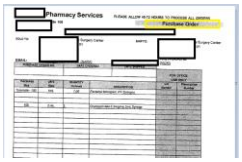
Individual Prescriptions



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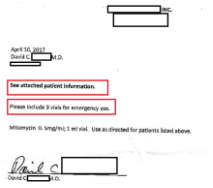
Individual Prescriptions



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503B INSPECTION ASSIGNMENT

- Step 1: • VISUAL INSPECTION
- Step 2: • FACILITY RECORD REVIEW AND PRODUCT SPECIFIC REVIEW
- Step 3: • EVALUATION OF CONFORMANCE WITH SECTION 503B

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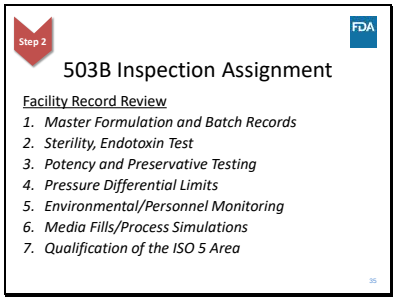

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Frequent Inspectional Findings

- Insanitary conditions
- CGMP violations (only applicable to outsourcing facilities and pharmacies not in compliance with section 503A)
- Non-compliance with the conditions of section 503A
  - Lack of patient-specific prescriptions
  - Bulks that cannot be used in compounding (e.g., domperidone)
  - Drugs on the withdrawn or removed list
- Non-compliance with the conditions of section 503B
  - Labeling deficiencies
  - Failure to submit a product report
  - Bulks that cannot be used in compounding (e.g., domperidone)

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Insanitary Condition Example

Visible microbial contamination on a ceiling tile in a clean room

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Insanitary Condition Example

Filth under the hood including multiple pieces of medical supply waste and dust build up in the pre-filter for the ISO 5 hood

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Insanitary Condition Example

The glove box that provides ISO 5 conditions where aseptic processing operations occur, was located in an unclassified carpeted room where the room air was not HEPA filtered. Note the wooden stool.

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Insanitary Condition Example

Gowned employee working in the cleanroom, exposing legs

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Insanitary Condition Example

The HEPA filter located immediately above the ISO 5 workbench was observed to have been stained on the filter surface.

The HEPA filter stain was due to drug product which had exploded due to excessive pressure applied when forcing non-sterile product through a sterilizing filter. The device used to force the product sterilizing filter was a stainless steel caulking gun that was not sterilized.

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Insanitary Condition Example

Sleeve used in the aseptic glove box for aseptic manipulations is damaged

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Insanitary Condition Example

Toaster oven used to dry heat sterilize and depyrogenate glassware; oven was not capable of reaching high enough temperature to be effective

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Insanitary Condition Example

Ceiling above the doorway to cleanroom with exposed insulation

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Insanitary Condition Example

Kitchen dishwasher (supplied with tap water) and home detergent used to clean equipment and utensils that comes in contact with product intended to be sterile – no subsequent cleaning step

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Insanitary Condition Example

Insects (vermin) dead or alive

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Lack of Routine Surface, Personnel, and Viable and Nonviable Air Count Air Monitoring

- Sterility tests are <u>not</u> statistically reliable to ensure sterility of products.
- Firms need to be able to control and maintain their environment to minimize risk of contamination.

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Lack of Routine Surface, Personnel, and Viable and Nonviable Air Count Air Monitoring

- Corrective actions, what's needed:
  - Environmental/personnel monitoring SOPs that address equipment and supplies needed, methods used and frequency of performance
    - CGMP: Daily monitoring required
    - 503A: *USP* <797> recommends regular monitoring; minimal every 6 months
  - Invoice of equipment and supplies needed
  - Training records
  - EM logs

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Non-representative or Biased Environmental Monitoring

- For example:
  - Not performing EM under dynamic/operational conditions – no compounding has occurred that day
  - Locations of samples not significant
  - Cleaning and disinfecting occurs before sampling
  - Growth media do not contain "neutralizers" to prevent interference from any cleaning agent and/or disinfectant residue
  - Growth media not demonstrated to be growth promoting
  - Incubation not performed under temperatures that promote growth.

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Non-representative or Biased Environmental Monitoring

- Corrective actions, what's needed:
  - Revised environmental/personnel monitoring SOPs that address the conditions and location in which EM is be performed
  - Invoice of equipment and supplies needed
  - Training records
  - EM logs
  - May also want to observe revised procedure in action (repeat inspection)

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Cleaning and Disinfecting Issues

- Microbial contamination is brought into the cleanrooms through personnel and supplies. The amount of microbes present needs to be controlled and minimized.
- Examples:
  - Use of non-sterile cleaning agents, including wipes, and/or disinfectants in an ISO-5 area
  - No routine use of sporicidal disinfectant
  - Inadequate contact time for disinfectant
  - Failure to clean and disinfect from clean to dirty
  - Failure of aseptic operators to frequently disinfect gloves during aseptic manipulations
  - Failure to adequately disinfect supplies and equipment entering from non-classified areas to ISO-5 area

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Cleaning and Disinfecting Issues

- Corrective actions, what's needed:
  - Revised SOP that addresses deficiencies.
  - Invoices of needed supplies.
  - Training material and training records.
  - May also want to observe revised procedure in action (repeat inspection).

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Gowning Issues

- Personnel are the primary source of microbial contamination in a pharmacy cleanroom and represent the principal risk to product.
- Examples:
  - Non-sterile gowning items:
    - Insanitary condition guidance and *USP* <797>: sterile gloves required
    - CGMP: all outer gowning items sterile on donning
  - Exposed skin
    - Insanitary condition guidance and USP <797>: no exposed wrist or arm skin
    - CGMP: no exposed skin anywhere
  - Contaminating sterile gowning items during donning

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Gowning Issues

- Corrective actions, what's needed:
  - Revised gowning SOPs that address the observed conditions
  - Invoice of supplies needed
  - Training material and records
  - Recertification records
  - May also want to observed revised procedure and activity in action (repeat inspection)

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Qualification of the ISO-5

- ISO-5 unit (e.g. hood, BSC, glovebox) has not been demonstrated to produce unidirectional airflow under dynamic/operational conditions
  - Smoke study not performed
  - Smoke study performed, but not under dynamic conditions
  - Requirement of CGMP, *USP* <797>; discussed in draft guidance on insanitary conditions
  - The "so what?" – sterile drug products, open to the environment, are protected from microbial contamination by the supply of "clean" unidirectional airflow sweeping across the opening (no turbulence, no areas of stagnation)

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Qualification of the ISO-5

- What does "dynamic conditions" mean?
  - ISO-5 unit contains all equipment and supplies that are used in aseptic processing during the study
  - The maximum number of personnel allowed in cleanroom are present during the study
  - All aseptic operations and manipulations are simulated
  - All of the above are capable of disrupting unidirectional airflow within ISO-5 unit

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Qualification of the ISO-5

- Corrective actions, what's needed:
  - Revised SOP that addresses the observed deficiency (e.g., lack of smoke studies, inadequate smoke study)
  - Certification/recertification of IS0-5 performed under dynamic conditions and supporting documentation
    - Documentation includes certificate and, preferably, video

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Aseptic Technique Issues

- Examples:
  - Disruption of unidirectional airflow by aseptic operator
  - Touching with gloved hands the container closure surfaces that come into direct contact with the drugs
  - Inadequate media fills/qualification of aseptic operator – not performed under the most stressful or challenging conditions
- Aseptic operators' poor practices are frequently a major contributor to sterility failures.

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Aseptic Technique Issues

- Corrective actions, what's needed:
  - Revised SOP that addresses the deficiencies
  - Invoice of supplies needed
  - Training material and recertification records
  - May also want to re-inspect to observe aseptic operators
    - Appropriate cleanroom behavior of personnel is both a conscious awareness and a habit

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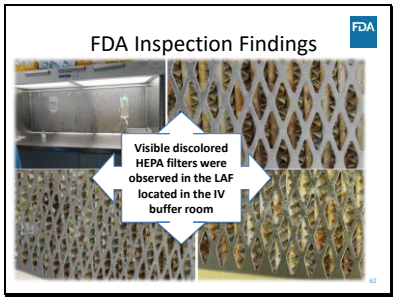

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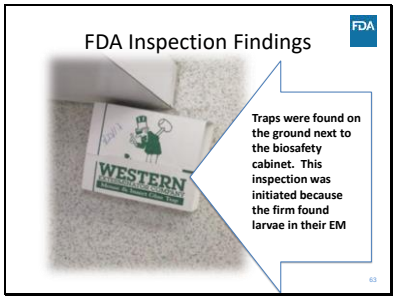

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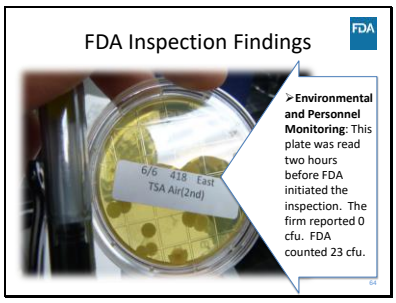

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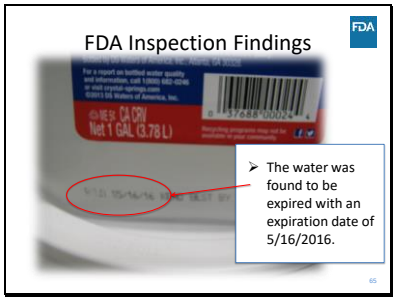

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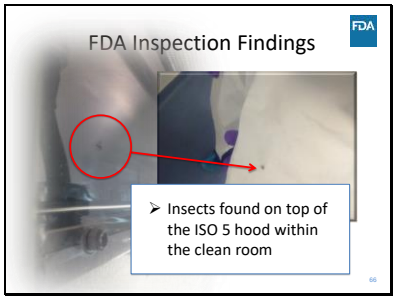

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FDA Inspection Findings

- ISO 5 glove boxes located in an unclassified space.

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This Fall: State Compliance Officer Educational Session on FDA Compounding Inspections

- FDA will provide an educational session on **November 28-29** at NABP's Interactive Compliance Officer & Legal Counsel Forum.
- In addition to a review of FDA's assessment of 503A compliance and common observations identified at facilities, the session will cover FDA assessment of certain current good manufacturing practice requirements during outsourcing facility inspections, including review of:
  - Aseptic operations
  - Process and facility design
  - Environmental and personnel monitoring
  - Records

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When does FDA take regulatory action?

Examples of factors that may inform whether to take regulatory action / what action to take:

- 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 FDA actions taken with respect to compounders

VOLUNTARY ACTIONS Informal recommendations for voluntary recalls Formal FDA requests for voluntary recalls	**ADVISORY ACTIONS** Warning letters Untitled letters
ENFORCEMENT ACTIONS Civil injunctions Criminal actions Seizures	**STATE REFERRALS** For 503A facilities Inspectional findings

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State Referral Letters

- **State referral letter: FDA referral of inspectional findings for a 503A facility to a state for further action.** Shared when a:
  - Pharmacy apparently obtains prescriptions for identified individual patients; and
  - Pharmacy has promised to correct deviations, and pharmacy's corrective actions can be appropriately overseen by the state
  - FDA has issued over 60 state referral letters since October 2012

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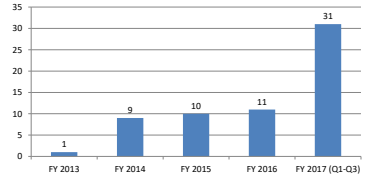
Compounding State Referral Letters



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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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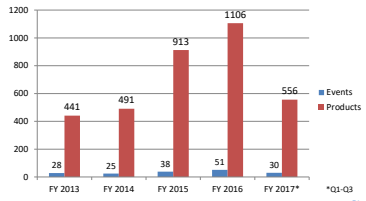
Compounding Recalls



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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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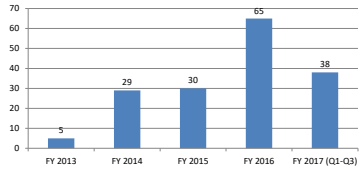
Compounding Warning Letters



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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 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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Compounding Incidents and Risk Alerts

- FDA inspections and subsequent actions are often triggered by reports of incidents from healthcare practitioners, patients, and others.
- FDA frequently conducts extensive follow-up of such reports, and endeavors to share the results publicly when in the interest of public health.
- Going forward we will be posting "compounding risk alerts" to inform healthcare practitioners, compounders, and patients of the risks associated with compounded drugs.

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2017: compounded curcumin product linked to one illness and one death

- Two patients given infusions of curcumin (a component of turmeric) with polyethylene glycol (PEG) 40 castor oil to treat eczema and low blood platelets experienced severe hypersensitivity reactions. One patient subsequently died.
- Risks illustrated by this case include:
  - use of an ungraded inactive ingredient
  - subpotency
  - presence of impurities
  - lack of evidence that IV curcumin is safe or effective for these uses

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2017: compounded eye injections linked to vision problems in 43 patients

- At least 43 patients received eye injections of a drug containing triamcinolone (steroid) and moxifloxacin (anti-infective) compounded by a Texas pharmacy.

- Patients developed vision impairment (blurred or decreased vision), loss of color perception, glare, halos, pain, and loss of balance among other symptoms.

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2016: compounded morphine sulfate linked to adverse events in three infants

- Three infants received a compounded morphine sulfate preparation at a strength 20-fold greater than that indicated on the prepared label.

- After receiving this adverse event report, FDA inspected the compounding facility where this product was made and observed insanitary conditions, including poor sterile production practices. The facility subsequently recalled all products intended to be sterile and ceased sterile compounding.

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State Transfer Letters

- When appropriate, FDA intends to transfer a complaint (e.g., product quality) or incident (e.g., adverse event) report about a compounded a drug to the state regulator for appropriate follow-up.
- FDA does not intend to investigate the complaint or incident report because the state regulator appears to have the primary responsibility to address the matter.
  - Possible criterion: Drug is compounded in a facility that only ships compounded drugs intrastate.
  - FDA is currently developing procedures for this process.

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Policy, Oversight and Enforcement, and State Collaboration

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State Collaboration

- Objectives:
  - Seek to ensure clear lines of accountability
    - Define "who is on the flagpole," i.e., primarily responsible for oversight of compounders, depending on the nature of their operations
  - Discuss emerging issues of mutual concern
  - Share updates on FDA/State policy and enforcement matters
  - Identify opportunities for improved FDA/State collaboration
- Opportunities for collaboration:
  - Annual Intergovernmental Working Meetings
    - Action items to improve collaboration
  - Frequent teleconferences with state officials regarding specific compounders
  - States invited to join FDA on all inspections of compounders
  - Monthly meetings with the National Association of Boards of Pharmacy

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Thank You - Questions?

FDA contact for state regulators: iga@fda.hhs.gov