Key Elements of Outsourcing Facilities Inspections

Susan Laska, Senior Advisor Medical Products

FDA /ORA /OMPTO

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503B INSPECTION ASSIGNMENT

Part III – Assignment: Inspectional Coverage

Inspections are to be conducted as described below:

Step 1
- VISUAL INSPECTION

Step 2
- FACILITY RECORD REVIEW AND PRODUCT SPECIFIC REVIEW

Step 3
- EVALUATION OF CONFORMANCE WITH SECTION 503B

503B Inspection Assignment

Visual Inspection

1. *General Work Environment and Equipment*
2. *Aseptic Operations*
3. *Process and Facility Design*
4. *Environmental and Personnel Monitoring*
5. *Product Inspection*
6. *Equipment, Containers, and Closures*
7. *Lyophilization Process Sterility Control*
8. *Packaging and Labeling Control*

Step 1

FDA 483

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503B Inspection Assignment

1) General Work Environment and Equipment

OBSERVATION:

Aseptic processing areas are deficient regarding systems for maintaining any equipment used to control the aseptic conditions.

A piece of apparent exposed particle board measuring approximately ¾ inches thick, 44 inches wide, and 6 inches deep was observed through the front edge guard vent of the ISO 5 LFH.

Step 1

FDA 483

503B Inspection Assignment

2) Aseptic Operations

a) <u>Gowning for aseptic operations</u>:

OBSERVATION:

Clothing of personnel engaged in the manufacturing and processing of drug products is not appropriate for the duties they perform.

The following attire worn by the operator on 2/8/17 during sterile production was inadequate as follows:

- Non-sterile boot covers, non-sterile coveralls, non-sterile hair cover, non-sterile surgical mask, and non-sterile protective eyewear were worn during sterile production.
- The hood of the non-sterile coverall and non-sterile surgical mask worn did not provide adequate coverage of the forehead, cheeks, and chin of the operator during sterile drug production.

Step 1

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503B Inspection Assignment

3) Process and Facility Design

d) Disinfection of the aseptic area:

OBSERVATION:

Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room and equipment to produce aseptic conditions.

Firm uses non-sterile, low shedding wipes sprayed with 70% IPA to clean and wipe the metal HEPA filter grate and metal workbench of the ISO 5 LFH prior to sterile drug production.

Step 1

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503B Inspection Assignment

4) Environmental and Personnel Monitoring

OBSERVATION:

Aseptic Processing Areas are deficient regarding the system for monitoring environmental conditions.

Personnel monitoring of production operators is not conducted at least daily when sterile drug products are produced.

Non-viable air sampling is not performed in the ISO 5 LFH and adjacent ISO classified areas when sterile drug products are produced.

Step 2

503B Inspection Assignment

Facility Record Review

1. *Master Formulation and Batch Records*
2. *Sterility, Endotoxin Test*
3. *Potency and Preservative Testing*
4. *Pressure Differential Limits*
5. *Environmental/Personnel Monitoring*
6. *Media Fills/Process Simulations*
7. *Qualification of the ISO 5 Area*

Step 2

FDA 483

503B Inspection Assignment

Facility Record Review

2) Sterility, Endotoxin Test

OBSERVATION:

Each batch of drug product purporting to be sterile and pyrogen-free is not laboratory tested to determine conformance to such requirements.

Sterility testing was not performed on each finished batch for 20 of 23 drug products produced since 7/26/16 that are purported to be sterile.

Endotoxin testing was not performed on each finished batch for the 23 drug products produced since 7/26/16.

Step 2

FDA 483

503B Inspection Assignment

Facility Record Review

3) Potency and Preservative Testing

OBSERVATION:

Testing and release of drug product for distribution does not include appropriate laboratory determination of satisfactory conformance to the final specifications and identify and strength of each active ingredient prior to release.

Potency testing is not performed for each batch of finished sterile and non-sterile drug products produced prior to release.

Step 2

503B Inspection Assignment

Product Specific Review

1. *Product Stability*
2. *Sterilization Control Strategy*
3. *Hold Times*
4. *Equipment, Containers, and Closures*

Step 2

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503B Inspection Assignment

Product Specific Review

1) Product Stability

OBSERVATION:

There is no written testing program designed to assess the stability characteristics of drug products. For example, stability testing has not been performed for the following sterile drugs:

-Sterile drugs repackaged in the LFH

-Phenylephrine Hydrochloride Ophthalmic Solution

Step 2

FDA 483

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503B Inspection Assignment

Product Specific Review

2) Sterilization Control Strategy

Observation:

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile do not include adequate validation of the sterilization process.

The autoclave has not been validated to confirm effective sterilization through the designated sterilization time and temperature cycle of 7 minutes at 273°F for the syringe capper/de-caper device used in sterile drug production. Also Biological indicators are not used during the sterilization process.

Step 3

503B Inspection Assignment

503B Conformance Evaluation

1. *Licensed Pharmacist Supervision*
2. *State Pharmacy Licensure*
3. *Drug Reporting Information*
4. *Bulk Drug Substances*
5. *Drug Products Withdrawn or Removed from the Market*
6. *Compounded Drug Product Labels and Containers*
7. *Wholesaling Prohibition*
8. *Adverse Event Reporting*
9. *Prescriptions*

Step 3

FDA 483

503B Inspection Assignment

503B Conformance Evaluation

Observation:

The labels of your outsourcing facility's drug products do not include information required by section 503B(a)(10)(A) and (B).

(A) Product labels consisting of the statement "Compounded Drug" are deficient in that it does not include the statements "This is a compounded drug", quantity or volume, and inactive ingredients.

(B) A list of active and inactive ingredients ~~,~~identified by established name and the quantity or proportion of each ingredient.

Step 3

FDA 483

503B Inspection Assignment

503B Conformance Evaluation

Observation:

The drug product report your outsourcing facility submitted to the FDA as required by section 503B(b)(2)(A) is not accurate. Specifically, you underreported 6 units of Vancomycin syringe and 6 units of Ceftazidime syringe in the drug product report your OF submitted to FDA on 12/28/16 for drugs produced during the previous six months.

QUESTIONS?


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