

**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER

Detroit District Office
300 River Place, Suite 5900
Detroit, MI 48207
(313) 393-8100

DATE(S) OF INSPECTION

08/01/2022 – 09/01/2022

FEI NUMBER

3005949964

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Andrew Espejo, General Manager.

FIRM NAME

Catalent Indiana, LLC

STREET ADDRESS

1300 S Patterson Dr

CITY, STATE, ZIP CODE, COUNTRY

Bloomington, IN 47403

TYPE ESTABLISHMENT INSPECTED

Sterile Human Drug and Biologic Product
Manufacturer

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM, WE OBSERVED:

OBSERVATION 1

Your firm failed to thoroughly investigate any unexplained discrepancy or failure of a batch or any of its components to meet any of its specifications, whether or not the batch has already been distributed.

Specifically,

- A. Per various (b) (4) batch records, the Visible Particles USP <790> testing list a specification of (b) (4) ". Between 8/11/21 and 4/7/22, (b) (4) batches were released after exceeding the supplemental visible particles testing.

- B. Deviation 523897 regarded an atypical particle found in the (b) (4) on the (b) (4) in Zone (b) (4) which lies above the filling line where filling takes place and units are (b) (4) during aseptic filling of (b) (4), lot (b) (4), dated 4/28/22. Particle was identified as (b) (4) with proteinaceous material. (b) (4) is not used in the manufacturing of lot (b) (4). (b) (4) is within the formulation of (b) (4), lot (b) (4) which was manufactured directly before this batch. The investigation states, "(b) (4) "

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Muna Algharibeh
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- The investigation is isolated to lot (b) (4) and does not extend to other batches previously manufactured after the aseptic filling of (b) (4) which could have been potentially affected by the inadequate cleaning procedure.
- The investigation did not question how (b) (4) could have potentially contaminated non-product contact equipment which lies above the filling line.
- Action REC 546084 was initiated on 6/15/22 to change cleaning method. A-SOP-21-01-056 Filling Line Disassembly and (b) (4) Cleaning has yet to be updated to implement (b) (4) to be used during (b) (4) cleaning following a client (b) (4) batch on vial line (b) (4). This change control is still open and is not due to be closed until 4/28/23. Deviation 523897 is still open.

C. Batches that exceeded internal control limits were not always adequately investigated. For example:

The following lots exceeded internal control limit for various categories of visual defects such as Major A defect, defined as Fibers or Intrinsic Particulate (Elongated undissolved matter or particulate matter originating from a normal manufacturing process that is floating freely within the product or that is attached to the product contact area of the stopper), or Major B defect, defined as non-conformities that could lead to serious impairments of the container or potential impact to product quality. Investigation into these limit breaches to determine potential root causes did not occur as appropriate.

1. Product (b) (4), lot # (b) (4)
2. Product (b) (4), lot # (b) (4)
3. Product (b) (4), lot # (b) (4)

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D. OOS 520278 regarded out of specification result for (b) (4)-Particulates Matter for (b) (4) product testing for (b) (4), lot (b) (4), dated 4/21/22. One particle was observed, exceeding the specification of (b) (4) foreign particles. Identification determined 2 particles were present, one was polypropylene (potentially from a hair/beard cover) and butyl rubber (potentially from a needle puncture). No obvious errors were determined to have contributed to the OOS result.

- Adequate justification could not be provided for only retesting (b) (4) vials during a retest of the (b) (4)-Particulates Matter for (b) (4) Product instead of the (b) (4) vials required per the OOS procedure. A-SOP-09-01-019, *Investigation of Out of Specification Quality Control Analytical Results*, procedure requires a retesting of (b) (4) times the original independent test samples (b) (4) vials). Deviation 542608, dated 6/8/22, was initiated to address the retesting (b) (4)-particulate matter for (b) (4) product testing for (b) (4), lot (b) (4). Sr. Manager of QC stated they wanted to retest (b) (4) samples, but the client felt that since rubber was identified, the initial results were contamination from the QC laboratory and therefore, only approved (b) (4) vials to be retested. The retest of the (b) (4) vials resulted in (b) (4) individual vials with foreign particles ((b) (4) (b) (4)). There is no evidence to support the particles are isolated to the QC laboratory environment. Deviation 542608 is still open.
- Replacement of the (b) (4) on vial line (b) (4) theorized to be the root cause of the particle, characterized as acrylic resin from the retest, was not being performed in a timely manner. The investigation referenced a previously initiated change control 482695, dated 2/3/22, regarding replacing (b) (4) on vial line (b) (4). Management stated this change control was initiated due to the previous (b) (4) no longer being available and the new (b) (4) are (b) (4) and are planned on being replaced as needed. The due date is listed as 9/30/23.

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E. Deviation 518372 regarded syringe critical rejects exceeding quantity limit for (b) (4), (limit (b) (4)%, actual 1.34%), lot (b) (4), dated 4/16/22. After discussions with the client, the investigation concluded the cause of the deviation was hyper awareness of slight yet acceptable bends in the needle guard. Visual inspectors were retrained in what constitutes a bent needle, i.e., the needle guard is (b) (4).

- This definition does not consider the diameter of the syringe or the length of the needle.
- Justification for the change in the bent needle definition could not be provided.
- The rejected syringes were not reevaluated to determine if hyper awareness of slight yet acceptable bends in the needle guard caused critical rejects to exceed the quantity limit.
- Additional inspection was not performed for a potentially unstable process (bent needles)
- The root cause of the bent needles was not investigated (i.e., supplier was not notified).

F. Deviation 390307, dated 7/19/21, regarded a fiber found in the syringe stopper of a retain, product (b) (4), lot (b) (4). The retains were reviewed as a response to complaints regarding lack of effect. The fiber was identified on 7/28/21 as polyester, organized, white non-magnetic fiber (not product related). The investigation states the fiber has the characteristics of manufactured fiber which implies the fiber is intrinsic to the process (i.e., most likely from the (b) (4)).

- No FAR was initiated when fiber was found in the retains.
- The investigation stated fibers can become trapped in small crevasses inside the syringe (such as the stopper) causing them to not be detected until they become dislodged. This fiber was observed during the retain review prior to being dislodged. The inspection procedure for syringes was not reviewed or retraining did not take place to ensure visual inspection would capture this defect in the future.

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G. In-process checks during manufacturing are performed to justify the removal of fibers discovered during aseptic filling without adequate investigation into the source of the fibers. A-SOP-21-01-074, *In-Process Checks*, procedure requires an (b) (4) inspection of critical processing areas during aseptic filling. If fibers are found/noticed inside the (b) (4) during the (b) (4) inspection or during aseptic filling, a deviation is required, and trays are segregated back to the last passing in-process check. These trays are evaluated separately from the batch. After the particle is removed, aseptic filling resumed. From 10/3/21 to 4/22/22, ten product (b) (4) batches had fibers discovered during production without adequate investigation into the source of the fibers.

H. Your firm does not document the identity of particulates found during visual inspection of aseptically filled product. All particulates identified by the (b) (4) are grouped into a single category regardless of whether it is intrinsic or extrinsic particles. During (b) (4) inspection, all intrinsic particles are grouped together and are not categorized as glass, fiber, colored particle, etc. This is significant as no trending can be performed on the particulates without sub-classification and complaints, or other investigations are hampered due to lack of information documented in the batch records.

OBSERVATION 2

Written records of investigation of a drug complaint do not include the findings of the investigation and the follow-up. Specifically,

A. As provided by your firm, a total of 179 complaints were received for particles (foreign matter, particulate matter, black specks, black particles, foreign particle, black impurities, black dots and other particulates, dark particles, foreign material, foreign object, dark gray particulate, or pieces

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of rubber in vial) between 03 Sep 2020 to 01 Aug 2022. Complaints were not adequately investigated to include an identification of the particle in the complaint sample.

For example:

1. On 23 Mar 2021, a Customer Complaint#333544 reported black specks in four vials of (b) (4), lot#(b) (4). Four vials and four syringes were returned to your firm for evaluation. The black specks were not analyzed in the lab. Retain samples review did not include an inspection for particles.
 2. On 01 Feb 2021, a client reported particles in a vial of (b) (4), lot# (b) (4), Customer Complaint# 308230. The vial was returned to your firm for evaluation. The particles were not analyzed in the lab. Retain samples review did not include an inspection for particles.
- B. As provided by your firm, a total of 52 supplier complaints for stopper related issues were submitted between 01 Jul 2019 to 05 Aug 2022. Out of these, 17 supplier complaints were related to Stopper item# (b) (4). Three of these investigations are still open (SCR 555104, SCR 540975, SCR 534591 opened on 04 Jul 2022, 05 June 2022, and 22 May 2022, respectively). Your firm did not perform an adequate investigation into the repeat stopper defect reported. Your investigation of the 14 supplier complaints related to stopper item # (b) (4) relied in large part on the supplier investigation. For the 14 SCR, the supplier investigations concluded that that stopper item # (b) (4) either “met agreed qualification” or “a root cause cannot be determined”.
- C. Your firm did not adequately extend your complaint investigation to other batches of the same lot or product when warranted. For example, Per the firm’s procedure, A-SOP-03-01-024, titled *Customer Complaints*, Recurring Complaint is defined as “A complaint that has occurred previously and had a corrective or preventative action(s) implemented, then occurred after implementation of the action(s).” Your firm did not conduct a thorough investigation for the

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multiple number of complaints reported for the same lot and the high number of complaints reported for the same defect for the same product manufactured at the firm. For example:

1. Complaint# 413054 on 07 Sep 2021, product (b) (4), lot# (b) (4)
2. Complaint# 339767 on 06 Apr 2021, product (b) (4), lot#(b) (4).

D. Complaints were not always classified according to your SOP-03-01-024, titled *Customer Complaints*, for classification of complaints: Critical, Major, and Minor. For example, On 30 Oct 2020, a Customer Complaint # 272397 reported an empty syringe (autoinjector) of product ((b) (4)). You firm classified this customer complaint as a Major complaint rather than a Critical complaint.

OBSERVATION 3

Control procedures are not established which monitor the output and validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product. Specifically,

Internal defect control limits were not established for the (b) (4) inspection process.

This was noted during the review of the following batches:

- Product ((b) (4)), lot# (b) (4) inspection on 11 Dec 2019
- Product ((b) (4)), lot# (b) (4) inspection on 12 Jul 2019 and 12 Aug 2019.

OBSERVATION 4

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Acceptance criteria for the sampling and testing conducted by the quality control unit is not adequate to assure that batches of drug products meet appropriate statistical quality control criteria as a condition for their approval and release. Specifically,

A-SOP-03-04-001, *Performance of AQL for Parenteral Inspections*, states AQL sampling should be a representation of the entire batch. "During (b) (4) if AQL fails for an equipment related issue that can be corrected, (b) (4) (b) (4) is the proper course. A (b) (4) AQL will be performed on (b) (4) materials. If the issue is not able to be corrected by (b) (4); the AQL will be completed in its entirety to satisfy this requirement, and a (b) (4) AQL on the batch will be completed when appropriate."

Your firm does not take AQL samples that are reflective of the entire batch. Your firm has had approximately 34 drug products which exceeded AQL limits during visual inspection since 9/1/2020. It is in your procedure, A-SOP-03-04-001, to (b) (4) that has exceeded AQL at the time of inspection and (b) (4) (b) (4) under (b) (4) inspection. The remaining, uninspected, portion is then continued to be visually inspected under normal AQL inspection levels with a (b) (4). AQL inspection is performed while visual inspection (b) (4), however, there is no documentation for when AQL samples are inspected. There is also no documentation for which (b) (4) have been sampled. According to the AQL procedure, the samples should represent (b) (4) (b) (4) throughout the batch, however this is not verifiable based on current AQL documentation. (b) (4) of the AQL portion that exceeded limits relies on immediate action from the QA inspector to hold and (b) (4) those AQL portions.

In addition, the uninspected portion is not included in the portion exceeding the AQL limit. The uninspected portion should be considered a part of the total AQL population. For example:

- Lot (b) (4) for product (b) (4) exceeded AQL for critical defects. This lot was run on the (b) (4)

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and (b) (4) at the time of exceeding AQL limits, according to DEV 483844. The defect was determined to be a crack in the neck of the vial. The (b) (4) portion was (b) (4) (b) (4) AQL on (b) (4). The remaining, uninspected, portion was allowed to continue normal AQL inspection levels on the (b) (4) with a (b) (4) determined from the remaining population.

OBSERVATION 5

Equipment used in the manufacturing of a drug product is not of appropriate design to facilitate operations for its intended use.

A.

1. Your firm did not demonstrate that the (b) (4) is better than or equivalent to (b) (4) inspection. Your firm did not consider individual defect vial performance when establishing acceptance criteria during (b) (4) (b) (4) Performance Qualification (PQ) (b) (4) (b) (4) recipe (b) (4) Rev 1.0.
2. Additionally, instances where defects were not caught by the (b) (4) were not evaluated because they were averaged out based on the acceptance criteria in part A. Your firm runs (b) (4) and (b) (4) on the (b) (4) in (b) (4). According to your Senior Manager of Engineering, the particulates could no longer be free floating in the vial for a number of reasons such as being stuck in the stopper or on the vial wall. The (b) (4) qualification documents also did not demonstrate that the (b) (4) inspection method could resuspend the particulates in the product once they became undetectable/stuck on the vial wall.
3. Your firm did not evaluate extrinsic particulate, such as hair, detectability during

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qualification of the (b) (4)) for recipe (b) (4)
Extrinsic Particulate Matter is a Syringe Critical Defect that is checked during visual inspection.

B.

1. The product used for your (b) (4) inspection base line study (b) (4) did not have the same properties as the product used during (b) (4) qualification. Your firm used a surrogate product for particulate analysis performed during the (b) (4) as a baseline to qualify recipe (b) (4) on (b) (4). The surrogate product attributes are not detailed in the summary or executed report for the (b) (4).
2. Your firm does not have a program to re-evaluate performance qualifications based on continued process improvements. For example, your firm has implemented a test case for (b) (4) evaluation for new recipe performance qualifications. Your firm also now performs (b) (4) calculations for acceptance criteria of (b) (4) (b) (4) Baseline. These recently implemented test cases have not been retroactively applied to previously qualified recipes to assure they are still in a qualified state.

C. Your firm has an ongoing issue of (b) (4) issues that are involved in low and high-risk aseptic interventions during the aseptic filling of sterile drugs. Your firm performed a Deviation Trending Investigation for Building B on February 9, 2022 and determined the root cause to be the (b) (4) material was not robust enough to maintain integrity during use. Your firm initiated corrective action to remediate the issue to related (b) (4) integrity by opening a change control to switch to a (b) (4) from the same (b) (4) manufacture. Your firm has since cancelled that change control and as of the current establishment inspection your firm is still using the original (b) (4) that continue to experience many integrity issues.

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OBSERVATION 6

Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established, written, or followed.

A. The airflow studies demonstrate a number of instances that document a lack of successfully meeting the acceptance criteria. For example, A-VPQ-00178-S-VL-070MAR21 Vial Filling (b) (4) Static and Dynamic Airflow Visualization Study Summary Report, v0, dated 5/10/21 establishes the acceptance criteria for the airflow visualization studies as in part, “(b) (4)

_____”.

The March 2021 airflow studies show discrepancies which do not meet the acceptance criteria, for example,

- there is no smoke over many of the manual activities to determine that the manual operations do not create/generate air eddies or air turbulence;
- there are numerous instances where there has been no smoke evaluations performed for the operators gloved hands and forearms;
- the smoke nozzle is not positioned in such a manner to capture the airflow when personnel perform the manual operations;
- the videos do not include an evaluation of the fill equipment & fill needles to determine that the equipment configuration does not negatively impact the unidirectional airflow;
- due to the angle of the camera unable to observe smoke over the manual operations;
- no visible smoke can be observed during various manual operations;

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- there are numerous instances when equipment and/or personnel hands & arms block the view, which precludes the company from performing an evaluation of the unidirectional airflow.
 These discrepancies potentially affect the other vial and filling lines used to aseptically fill drug and biologic products.
- B. Adequate justification could not be provided for not performing contact plating of all (b) (4) (b) (4) used during the aseptic filling of sterile product. Instead, environmental monitoring of (b) (4) is based on the frequency of typical batch usage and what can be performed at that (b) (4). Usage is based on A-SOP-21-01-054, *Drug Product* (b) (4), v16, dated 6/20/22 which specifies typical batch usage as low, medium or high. Only high usage (b) (4) and (b) (4) used to perform high risk interventions are monitored at the end of an aseptic fill. No supporting data could be provided to justify the typical batch usage categories. Only the use of (b) (4) used to perform high risk interventions is documented. The firm has ^{(b) (4)} vial filling lines, (b) (4) filling lines and (b) (4) filling line.
- C. The rationale to only require Quality oversight of high-risk interventions during aseptic filling is inadequate. Documentation only supports Quality oversight during high-risk interventions.

OBSERVATION 7

Routine checking of equipment is not performed -according to a written program designed to assure proper performance. Specifically,

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**DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION**

DISTRICT ADDRESS AND PHONE NUMBER

Detroit District Office
300 River Place, Suite 5900
Detroit, MI 48207
(313) 393-8100

DATE(S) OF INSPECTION

08/01/2022 – 09/01/2022

FEI NUMBER

3005949964

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

Andrew Espejo, General Manager.

FIRM NAME

Catalent Indiana, LLC

STREET ADDRESS

1300 S Patterson Dr

CITY, STATE, ZIP CODE, COUNTRY

Bloomington, IN 47403

TYPE ESTABLISHMENT INSPECTED

Sterile Human Drug and Biologic Product
Manufacturer

- A. Your firm does not assure that the (b) (4) is working within expected parameters during set up for a run. Your firm uses a challenge set with (b) (4) only prior to running in order to check machine operability. The challenge set does not include vials that are at a known visible range of detection. According to A-SOP-22-03-014, (b) (4) *Test Set Composition and Handling*, “(b) (4) ”
- B. Your firm did not qualify the (b) (4)) (b) (4) (b) (4) during any qualification activities. Your procedure, A-SOP-22-05-009, (b) (4) *Process Operational Flow*, states “(b) (4) ” during set up. This verification is not documented, and no data has been generated during qualification to show that all vial sizes will perform (b) ((b) (4) during inspection. (b) (4) (b) (4) are the only parameter verified during set up. The firm uses vial sizes ranging from (b) (4) mL on the (b) (4) system.

OBSERVATION 8

Your firm failed to establish and follow adequate control procedures to monitor the output and to validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product.

The following discrepancies were noted during the review of visual inspector qualification for aseptic filling:

- A. Although included in the emulsion visual inspection kit, visual inspectors for emulsion products are not qualified to detect Major A defects. This category contains fibers or intrinsic particulate matter.

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- B. The emulsion visual inspection kits do not represent extrinsic particulate matter.
- C. A visual inspection kit does not exist for plastic vials. Instead, the inspectors train on the (b) (4) kit. The (b) (4) kit does not contain the following defects specific to plastic vials:
- Critical Burn
 - Short Shot
 - Gated Vistage
 - Streak Flowmark
 - String
 - Parting line mismatch
 - Void
- D. Per A-SOP-22-01-009, titled (b) (4) *Inspection Test Set Composition and Handling*, version 13, dated 25 Jan 2021, "(b) (4) _____". This procedure was not followed during the initial qualification of operator (b) (6) performed on 20 and 21 Jul 2021 and the emulsion qualification of (b) (6) on March 8, 2021.
- E. You cannot confirm through documentation the inspection times during the execution of visual inspection qualification tests is representative of routine visual inspections.

OBSERVATION 9

In-process samples are not representative. Specifically,

There is no scientific justification for not performing particles testing on routinely inspected product. Batches of aseptically filled (b) (4) are inspected by (b) (4). The

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particulate defects are rejected and the “ejects” are run through the (b) (4) machine for additional inspection. Instead of performing destructive particles testing on the good vials remaining after the (b) (4) inspection, (b) (4) vials are sampled from the batch prior to being visually inspected by this process and rather are inspected by ISC (Inspection Sample Control) personnel. The samples undergoing destructive particles testing are not fully representative of routine production.

OBSERVATION 10

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

- A. The (b) (4)) for vial filler (b) (4) has not been qualified for LIMs labels. Deviation 493708 dated 2/25/22 was initiated due to action levels being obtained on an (b) (4) in vial line (b) (4) between the (b) (4) and the (b) (4) . The root cause determined the validation requirements for layout, configuration and/or label orientation for (b) (4) labels in the (b) (4) are not qualified. The risk assessment for batch impact determined the labels achieve a (b) (4) (b) (4)), and not the preferred 6-log reduction. Action 552193 was initiated 6/28/22, to update A-WI-21-06-005-02 to label contact plates in the (b) (4) with (b) (4) instead of (b) (4) labels. The (b) (4) is still used to pass through (b) (4) labels. This fill line is not dedicated and can be used to aseptically fill both biologic and drug products.

- B. There is no assurance that media fills are representative of routine production as media fills are not performed under the most challenging or stressful conditions and do not simulate your production process.

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1. Trending of interventions during sterile manufacturing does not take into consideration packaging configuration (i.e., vial size and run speed). Instead, trending of interventions is performed by (b) (4) all interventions from all batches run on a particular line. Vial sizes could range from (b) (4).
2. Adequate scientific justification was not provided for grouping interventions. TEC-000-300-068 Drug Product Manufacturing Media Fill Interventions Rational and Risk Assessment, v7, dated 2/22/22, states all interventions have been grouped based on the required steps to perform each intervention. The intervention with the (b) (4) was chosen to represent all interventions in that grouping during the media fills. The document equates (b) (4) as the same risk level as (b) (4).
3. Multiple line speeds are addressed within a single media fill batch (i.e., (b) (4) (b) (4)). This is significant as there is no assurance that the media fills performed are representative of routine manufacturing. The Senior Manager of (b) (4) stated the intention during production is to run at 100%.

OBSERVATION 11

Records are not maintained so that data therein can be reviewed at least (b) (4) to evaluate the quality standards of each drug product to determine the need for changes in specifications or manufacturing or control procedures.

Your firm did not establish criteria during supplier qualification and requalification based on recurring supplier complaints in A-SOP-03-03-003, *Supplier Qualification*. In addition, your firm has not been

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tracking and trending supplier complaint reports when a complaint is filed to the supplier. Records are opened for many months before tracking is completed. For example:

- Record# 533727, dated 5/15/2022, regarding (b) (4) needle assembly.
- Record# 565406, dated 5/20/2022, regarding (b) (4) needle assembly.
- Record# 566111, dated 05/12/2022, regarding sterile bag used for sterile filling operations.

OBSERVATION 12

Your firm failed to establish laboratory controls that include scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity.

- The verification of method AM-256-100-018 Supplemental Destructive Visual Inspection for Visible Particulates of Client (b) (4) Drug Product Samples, v1, on 7/12/22, demonstrated the analyst could execute the method. The verification did not show the method or the analyst's ability to detect particles.
- A-SOP-09-01-061, *Manual Inspection of Media Filled Vials*, v9, dated 12/13/21 states to (b) (4) (b) (4) the containers for approximately (b) (4) prior to inspection to suspend any potential microbial growth. (b) (4) the vial prior to initial review could potentially disperse the microbial film on the surface of the media if it existed.
- On 8/1/22 during the walk-through inspection of the Microbial Testing Laboratory, (b) (4) were observed between the (b) (4) and the (b) (4) plate. Four out of (b) (4) sampling plates corresponding to samples collected on 7/19-20/22 were observed having

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(b) (4) . Inadequate contact between the (b) (4) and the (b) (4) might compromise microbial recovery. The impact of the (b) (4) on any microbial film on the surface of the media was not provided.

- D. During the walk-through inspection of the Microbial Testing Laboratory, a discrepancy on CFU counts was noted (11 CFUs on 7/25/22, 14 CFUs on 8/1/22). There was no evidence that the reviewer contacted management when the discrepancy was noted. A-SOP-09-01-039, *Counting and Reporting Counts of Microbial Plates*, v7, effective 12/27/21 states in section 2.1, "When reviewing microbial plates, if the reviewer count differs from that of the original count, then the review must take place within (b) (4) of the original count to change the count or be changed at management discretion". This may impact the original count, and the discrepancy is not documented, and management may not be notified.
- E. Full reconciliation of injections performed in the quality control laboratory is not performed. The analysts are trained to choose between normal, don't process or don't process or report. A-SOP-09-06-180, *Use of (b) (4) Chromatography Data System*, does not address these choices. If 'don't process or report' is chosen, these chromatograms are not processed and are not reviewed.

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."