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

| DISTRICT ADDRESS AND PHONE NUMBER | DATE(S) OF INSPECTION |
|---|---|
| 12420 Parklawn Drive, Room 2032<br>Rockville, MD 20857 | 9/8/2025-9/16/2025* |
| | FEI NUMBER<br>3000234005 |

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
David L. Rapy, General Manager

| FIRM NAME | STREET ADDRESS |
|---|---|
| Fareva Amboise | Zone Industrielle, 29 route des Industries |
| CITY, STATE, ZIP CODE, COUNTRY | TYPE ESTABLISHMENT INSPECTED |
| Poce Sur Cisse, Indre Et Loire, 37530 France | Sterile and Non-Sterile Drug 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

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

Specifically,

A. The quality unit approved airflow smoke tests to qualify the Grade A aseptic filling line "(b) (4)" that do not show the airflow is functioning properly in the Grade A as required in protocol PQG 24-1209. For example:

1. When the barrier (b) (4) is (b) (4) in front of the (b) (4) airflow does not appear to reach the (b) (4) During simulation of the installation of the (b) (4) there appeared to be stagnant air between the (b) (4) and the (b) (4) The smoke is introduced in a downward direction too close to the operation to thoroughly evaluate air flow in the area. Other interventions that show poor airflow in this area included changing the (b) (4) replacing a (b) (4) and adjustment of the (b) (4)

2. The airflow in the area below the stopper bowl, including the stopper chute down to the conveyor and stoppering machine, appeared to be turbulent and flowing upward during interventions. Interventions included adjustment of detection in critical areas (b) (4) cleaning up after breakage (b) (4) installation of the stopper chute (b) (4) adjustment of the chute (b) (4) changing of the chute (b) (4) adjusting the (b) (4)

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EMPLOYEE(S) SIGNATURE
Vivin George, Investigator
Justin A Boyd, Investigator
Karen A Briggs, Investigator

X Karen A Briggs Investigator Signed By: Karen A. Briggs -S Date Signed: 09-16-2025 15:00:25

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(b) (4) unblocking stoppers in the chute (b) (4) and adjusting the (b) (4)

3. During installation of the stopper bowl (b) (4) the operator reached over the sterile surfaces that contact the (b) (4) closure stoppers to perform the installation.

4. During the intervention for removal of stoppers from the bowl (b) (4) the operator reaches their hand over the bowl with the sterile stoppers.

5. During contact plate surface monitoring (b) (4) at the (b) (4) which occurs during filling operations, it appears the smoke goes over the operators' hands towards the conveyor line that has open vials.

6. During installation of (b) (4) the smoke flows from the operator standing in the Grade B area along their arms towards the (b) (4) installation.

7. The aseptic (b) (4) connection (b) (4) is not performed with aseptic behavior that included slow and controlled movements. The camera was kept outside of the (b) (4) and does not allow for thorough evaluation of the airflow.

8. There has been no evaluation of the filling machine in normal operation including filling and stoppering vials.

B. Media fills have not been designed to ensure they provide a challenge to the aseptic process consistent with a commercial batch. There are no requirements for the minimum number of times an intervention must occur during media fills and there is no trending of the number of interventions that occur during commercial batches.

For example, the (b) (4) intervention at the stopper bowl (b) (4) was documented to occur (b) (4) times during media fill (b) (4) in December 2024, though additional notes by a QA observer identified (b) (4) total instances of interventions at the stopper bowl (b) (4) During commercial batch (b) (4) of (b) (4) Injection for the US market, (b) (4) interventions at the stopper bowl (b) (4) appear to have occurred approximately (b) (4) times. No vials present in the area below the stoppering bowl are cleared during these (b) (4) interventions.

C. During media fills, filled vials are rejected without assurance the same vials would have been rejected during a commercial batch.

1. During commercial batches there is no procedure describing a requirement to reject vials after stoppages, but during media fills filled vials get rejected after stoppages.

2. During non-systematic interventions the media fill records document the rejection of filled vials. There are no procedures for commercial batches describing how to perform interventions or whether vials need to be rejected. There is no documentation required for rejected vials during each intervention that occurs in commercial batches.

D. (b) (4) closure stoppers directly contact parts of the stopper bowl that are left in place between batches and are disinfected, not sterilized.

E. Your firm lacks written procedures for transferring (b) (4) from Grade C to Grade A areas in the sterile manufacturing facility. (b) (4) are transferred from Grade C to Grade A without further disinfection. You verified (b) (4) for batch (b) (4) which were documented as being cleaned and disinfected in the Grade C area on July 2, 2025, were moved to Grade B, then into Grade A on July 3, 2025, without further disinfection. (b) (4) are installed near the Grade A filling machine.

F. Your facility's (b) (4) process lacks scientific justification for the placement of biological indicators used to validate and monitor the (b) (4) cycle effectiveness. During our inspection, your firm could not provide documented rationale, studies, or data supporting the current biological indicator placement strategy within the (b) (4) cycle for the Grade A filling area.

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**OBSERVATION 2**

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

Specifically,

A. Examples of poor aseptic behavior and design were observed during set-up and aseptic filling of (b) (4) Injection batches (b) (4) and (b) (4) which have been distributed to the US market. For example:

1. Operators reached under the barrier at the (b) (4) and removed empty bottles by hand. These were brought into the Grade B area, weighed, and marked. The operator then reached back under the barrier near the filling zone, used their hand to push other bottles down the conveyor line to make space, then introduced the marked bottles from the Grade B area back onto the Grade A conveyor. Immediately after filling, and before stoppering, the filling barrier was (b) (4) and the operator reached their hand in to remove the marked vials. This process is repeated (b) (4) No surrounding vials are removed during this (b) (4) intervention.

2. The operator transferred the (b) (4) bag containing the (b) (4) from a (b) (4) in the Grade B area and placed it inside the Grade A filling barrier with no disinfection. After securing the (b) (4)

assembly, the operator repeatedly reached over the unprotected (b) (4) with their hands and forearms while making tubing connections.

3. The operator removed protective covers from the sterilized stopper bowl in the Grade B area before transferring it into the Grade A area and installing it on the filling line.

4. Operators did not always work using slow and controlled movements.

B. On September 8, 2025, an operator was observed during the connection of the (b) (4) removing a gasket with their fingers, placing it on a (b) (4) used for environmental monitoring plates, then later picking it up and putting it back on the pipe (b) (4) of the (b) (4) Additionally, the operator stored scissors on a (b) (4) exposed to Grade B air before picking it up to use it to open packaging material in the Grade A area without disinfecting it. While performing the operations, the operator placed a phone, an extra gasket, a used wipe, and used (b) (4) bags from the Grade B area onto the base of the filling machine inside the Grade A barrier. This occurred prior to (b) (4) batch, (b) (4) a terminally sterilized product. The procedure to perform this (b) (4) connection is the same for aseptic products.

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**OBSERVATION 3**

Equipment and utensils are not cleaned, maintained and sanitized at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product.

Specifically,

A. The cleaning of non-dedicated (b) (4) equipment used to manufacture US market products was not effective. There are (b) (4) non-dedicated (b) (4) used for US market products. On September 10, 2025,

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| FIRM NAME<br>Fareva Amboise | STREET ADDRESS<br>Zone Industrielle, 29 route des Industries |
| CITY, STATE, ZIP CODE, COUNTRY<br>Poce Sur Cisse, Indre Et Loire, 37530 France | TYPE ESTABLISHMENT INSPECTED<br>Sterile and Non-Sterile Drug Manufacturer |

the following was observed on the cleaned (b) (4) equipment, equipment Id: (b) (4) 005, located in production suite (b) (4)

1. There appeared to be (b) (4) residues on the gasket of the (b) (4) equipment.

2. There were (b) (4) residues on the equipment surfaces inside the (b) (4) equipment that surrounds the product drum on (b) (4) 005.

Analytical testing of the (b) (4) residue was identified to show the presence of the API-(b) (4) This API was last used in the manufacture of (b) (4) mg, Batch no: (b) (4) which was last (b) (4) on January 04, 2024, using the (b) (4) equipment. (b) (4) other batches of other drug products were (b) (4) after and out of which (b) (4) batches of (b) (4) for the US market were (b) (4) using the (b) (4) equipment.

B. Cleaning validation studies did not identify the hardest to clean areas of the (b) (4) equipment, equipment Id: (b) (4) 005. For example:

The cleaning validation studies, 20-193, dated: September 28, 2020, showed the following sampling locations which did not include any sampling points around the drum or (b) (4)

| Testing for Residue | Sampling Points | Number of samples |
|---|---|---|
| (b) (4) | | |

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Additionally, the operator's performing the cleaning verification checks of the cleaned equipment, does not have access to room (b) (4) which is maintained under a lock and key mechanism, to gain access to the back of the (b) (4) drum to inspect and evaluate the effectiveness of the (b) (4)

C. We observed (b) (4) for the aseptic filling and capping lines were damaged in ways that may generate particulate or make them difficult to clean.

1. Apparent (b) (4) was noted on the "(b) (4) " piece and other areas of the (b) (4) for the filling, stoppering, (b) (4) equipment.

Additionally, your firm investigated a critical defect of (b) (4) particles in two batches of (b) (4) in AMB-DEV-2025-71, dated: April 2025, and the investigation did not thoroughly evaluate all (b) (4) (b) (4) including the (b) (4) as a possible source of contamination, even though this piece of equipment is used in both batches where (b) (4) particles were discovered.

2. We observed several areas of fraying (b) (4) on various areas of the equipment, as well as several gouges and scratches were observed on multiple (b) (4) which were in a "clean" and ready to use status.

3. Your firm performed the (b) (4) preventative maintenance on these equipment pieces only (b) (4) (b) (4) before the inspection and noted no deficiencies. No scientific justification exists for the (b) (4) (b) (4) preventative maintenance frequency of these (b) (4)

## OBSERVATION 4

Your firm failed to establish adequate written procedures for production and process controls designed to assure that the drug products have the identity, strength, purity, and quality that they are purported or represented to possess.

Specifically,

A. For the visual inspection of (b) (4) products:

1. The challenge tests sets used to qualify visual inspectors have not been designed to thoroughly challenge the visual inspectors.

a) The challenge test kits used to qualify (b) (4) visual inspectors on (b) (4) visual inspection were created using good and rejected vials from previous batches, with unknown sizes of particles present in the vials and without ensuring all defect types are represented.

b) There is no challenge kit to represent the largest vial size of (b) (4) ml (b) (4) vials used to fill the US product (b) (4)

c) (b) (4) visual inspection is used for (b) (4) products. Visual inspectors were qualified using a (b) (4) ml or (b) (4) ml vial test kit. During commercial batches, (b) (4) ml and (b) (4) ml vials are inspected on the (b) (4) visual inspection equipment.

d) The (b) (4) visual inspection kits do not contain sufficient vials to ensure the test represents the (b) (4) during routine production. The (b) (4) ml kit contains (b) (4) vials and the equipment runs at (b) (4) The (b) (4) ml kit contains (b) (4) vials and the equipment runs at (b) (4) (b) (4)

2. Acceptance criteria used during qualification does not ensure visual inspectors can reliably detect

foreign particles. For example, the (b) (4) ml challenge kit for (b) (4) visual inspection included (b) (4) vials, with (b) (4) defects, including (b) (4) major defects with visible particulate. Operator (b) (6) missed (b) (4) of the (b) (4) major defect vials containing visible particles. This was considered a passing result based on the scoring system in AMB-INST-00965.

3. No limits for individual or total rejects during visual inspection have been established for (b) (4) products.

4. No defect library has been established for training purposes or reference by the visual inspectors.

5. There is no process to routinely identify particles to determine their potential source or determine if they are a new particle type.

B. Process validation data has not been collected to establish acceptable ranges for compression machine setting. For example:

1. The (b) (4) Tablets (b) (4) mg manufactured on the (b) (4) tablet press have a (b) (4) (b) (4) in the batch record. On September 8, 2025, the value was set at (b) (4) There is no established range with process validation data for (b) (4) or other parameters, like filling depth and the displacement value used to accept or reject tablets.

2. The (b) (4) Tablets (b) (4) mg are manufactured on the (b) (4) tablet press. The operator can change (b) (4) (b) (4) filling depth, and percent variation for rejects. There are no validated acceptable ranges for these parameters.

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**OBSERVATION 5**

Appropriate controls are not exercised over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.

Specifically,

Data integrity assessments required by QRM-0070 have not been completed for any of the following pieces of equipment.

A. The user can change the time and date and clear stored data on the (b) (4) Non-Viable Particle Counter. The instrument stores limited electronic data, but it is not reviewed. Only paper printouts are reviewed.

The electronic data showed failing results that were not printed and attached to the reported records. Your action limits are defined in SOP AMB-INST-00379 as > (b) (4) for (b) (4) µm particle size. For example:

1. (b) (4) with a result of (b) (4) in a Grade A area

2. (b) (4) with a result of (b) (4) in a Grade A area

3. (b) (4) while performing media fill for batch (b) (4) a non-conforming result of (b) (4) taken in the (b) (4) area of the Grade A area.

4. (b) (4) while performing media fill for batch (b) (4) a non-conforming result of (b) (4)

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taken in the (b) (4) area of the Grade A area. This non-conforming result was not recorded in the batch record. A "retest" was performed over 30 minutes later, after moving the NVPC into a Class B Area, and returning the counter back to the Class A area, and another test was performed with conforming results, which was included in the media fill batch record.

B. The (b) (4) tablet press used to manufacture (b) (4) mg (b) (4) tablets allows the user to change parameters like (b) (4) filling depth, and the displacement value used to accept or reject tablets. There is no audit trail to track these changes.

C. The (b) (4) press used to manufacture (b) (4) mg (b) (4) tablets, allows users to make changes to parameters. These audit trail and alarms are not reviewed.

D. The Hardness tester (b) (4) allows the user to change the date and time that will appear on the printout. It does not store electronic data and only generates printouts. There is no process to reconcile printouts. On September 8, 2025, a printout associated with the (b) (4) batch, (b) (4) was found in the trash can.

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**OBSERVATION 6**

Aseptic processing areas are deficient regarding the system for monitoring environmental conditions.

Specifically,

A. Personnel performing (b) (4) systematic interventions including weight checks and clearing jammed stoppers, reach their hands and forearms into the Grade A barrier when there are open vials,

sterile equipment surfaces, and sterile surfaces present. These personnel are held to Grade B requirements when their hands are monitored upon exit. For example, on April 17, 2025, during aseptic filling of (b) (4) mL, batch (b) (4) (US batch), Personnel ID: (b) (6) (b) (4) CFU's of Corynebacterium tuberculostearicum, was recovered on the right forearm who participated in the filling activities. No investigation was initiated.

B. The environmental monitoring personnel reach into the Grade A filling area to perform surface monitoring with contact plates inside of the Grade A filling barrier, (b) (4) while aseptic filling operations are ongoing.

C. The assessment QRM-00165 used to establish environmental monitoring procedures did not thoroughly consider the activities performed in the aseptic area.

1. The settle plate in the barrier section (b) (4) with the filling machine is placed (b) (4) (b) (4) where interventions occur near the (b) (4) during set-up and filling.

2. The (b) (4) non-viable particle count and active air samples are taken in the (b) (4) area only after the aseptic connection has been completed.

D. Contact plates are used for surfaces that are not flat, like the (b) (4) scissors, and forceps.

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**OBSERVATION 7**

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

Specifically,

A. There is no routine use of a sporicidal agent on equipment surfaces inside your Grade A filling barrier.

B. Your firm has not conducted or provided scientifically validated disinfection efficacy studies demonstrating the effectiveness of your disinfection procedures for all surfaces within the Grade A filling area, including filling machine (b) (4) made of (b) (4)

C. During cleaning and disinfection of the filling line after aseptic filling of batches (b) (4) and (b) (4) the operators did not use a unidirectional wiping technique or sequentially clean and disinfect the area in the direction of product flow as required by procedure AMB-INST-00487.

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**OBSERVATION 8**

Batch production and control records do not include complete information relating to the production and control of each batch.

Specifically,

A. The type, frequency, and time of interventions are not routinely documented in production batch records.

B. The identity of the person performing visual inspection is not recorded in the (b) (4) visual inspection record.

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**OBSERVATION 9**

Procedures for the preparation of master production and control records are not described in a written procedure.

Specifically,

There is no process to reconcile the GMP forms printed from Master Control to determine whether all issued original GMP forms are used or returned to QA. Employees are permitted to print excess copies of GMP forms and destroy unused form. There is no assurance forms with original GMP data are not similarly destroyed.

Employees have uncontrolled access to paper shredders located in the production and laboratory areas, including:

| Equipment Name and No: | Location |
|---|---|
| (b) (4) | |

***DATES OF INSPECTION**

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9/08/2025(Mon), 9/09/2025(Tue), 9/10/2025(Wed), 9/11/2025(Thu), 9/12/2025(Fri), 9/15/2025(Mon), 9/16/2025(Tue)

X Justin A Boyd
Investigator
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EMPLOYEE(S) SIGNATURE

Vivin George, Investigator
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X Karen A Briggs
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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."