Date of This Update: July 27, 2023

FDA Citations/Recalls/Warning Letters Relevant to Microbiological Issues

Reason for Recall/Warning Letter may be redacted to remove information identifying specific companies.
https://www.accessdata.fda.gov/scripts/ires/index.cfm

The purpose of this service is to provide helpful information related to recalls/citations/warning letters related to microbiological issues. It in not intended to replace the information provided by the FDA, nor is it guaranteed to be complete.

Product Type	Citation [C], Recall [R], Warning Letter [WL]	Reason for Citation/Recall/Warning Letter
Biologics	**R**	Blood Products, collected in a manner that compromises the sterility of the collection system, were distributed.
Biologics	**R**	Apheresis Platelets, collected in a manner that compromises the sterility of the collection system, were distributed.
Biologics	**C**	Failure of the transfusion service that identified platelets as bacterially contaminated to notify the blood collection establishment that provided the platelets and take appropriate steps to identify the organism.
Biologics	**C**	The standard operating procedures fail to include a written description of the procedures to control the risks of bacterial contamination of platelets.
Biologics	**WL**	"1. Failure to establish and follow appropriate written procedures designed to prevent microbiological contamination of drug products purporting to be sterile, including procedures for validation of all aseptic and sterilization processes [21 CFR 211.113(b)]. For example: a. The aseptic processes used to manufacture your products have not been validated (i.e., by performing media fill simulations). By the nature of their routes of administration, your products purport to be sterile and are expected to be sterile. b. You have not established appropriate written procedures for environmental monitoring in the aseptic processing areas where your products are manufactured. For example, you do not have written procedures that require surface sampling, personnel monitoring, viable air monitoring, and non-viable particulate monitoring to be performed in association with each production run. Such procedures are important to detect problems and demonstrate control of the aseptic processing areas. c. Your written gowning procedure for personnel who perform aseptic processing is inadequate to protect your products from contamination. For example, in accordance with your written procedure: i. Personnel wear non-sterile gowning components, such as surgical masks and hairnets, while processing your products without any barrier between open products and personnel. Additionally, during the inspection, FDA investigators observed a technician with exposed skin processing your products." "d. You have not established and followed written procedures for the (b)(4) sterilization of the (b)(4) filter that comes into direct contact with your AmnioAllograft and AmnioAMP-WJ products during processing." "2. Failure to have an adequate system for cleaning and disinfecting the room and equipment to produce aseptic conditions [21 CFR 211.42(c)(10)(v)]. For example: a. You have not validated your process for cleaning and disinfecting the cleanrooms, the critical processing areas where your products are manufactured. b. According to your Standard Operating Procedure (SOP) SB-024 titled "Clean Environment Cleaning and Maintenance", your cleanrooms require cleaning with a (b)(4) only (b)(4). (b)(4)-forming microorganisms are routinely detected in your environmental samples. c. Standard Operating Procedure (SOP) SB-024 titled "Clean Environment Cleaning and Maintenance" lacks adequate instructions for cleaning and disinfection of your cleanrooms, including the disinfectant contact time and cleaning agents used. Additionally, this procedure does not require cleaning (b)(4) manufacture of batches nor is there data or rationale for the cleaning agents used. d. Your SOP SB-027 titled "Equipment Management and Cleaning" lacks adequate cleaning procedures for the equipment (e.g., incubators) used during aseptic processing operations, including but not limited to, use of a (b)(4) agent, frequency of disinfectants used, and disinfectant contact times. Additionally, this procedure does not address cleaning between batches."

FDA Citations/Recalls/Warning Letters Relevant to Microbiological Issues

Reason for Recall/Warning Letter may be redacted to remove information identifying specific companies.
https://www.accessdata.fda.gov/scripts/ires/index.cfm

The purpose of this service is to provide helpful information related to recalls/citations/warning letters related to microbiological issues. It in not intended to replace the information provided by the FDA, nor is it guaranteed to be complete.

Product Type	Citation [C], Recall [R], Warning Letter [WL]	Reason for Citation/Recall/Warning Letter
Biological Products	**WL**	"a. The aseptic processes used to manufacture your products have not been validated (e.g., by performing (b)(4)) since your firm's manufacturing operations began in February 2020. Your products purport to be sterile and are expected to be sterile. b. You have not established appropriate written procedures for environmental monitoring in your firm's aseptic processing area where your products are manufactured. For example: i. Your action limits for microbiological monitoring (i.e., active viable air, surface samples, and personnel gloved fingertips) within the critical area (i.e., inside the biological safety cabinet (BSC)) were observed to be (b)(4) colony forming units (CFUs) per m3, greater than (b)(4) CFUs per "plate and floor", and (b)(4) CFUs per plate, respectively. Such high numbers of microorganisms could contribute to product contamination and pose a potentially significant safety concern. ii. Your action limit for active viable air samples within the cleanroom was observed to be greater than or equal to (b)(4) CFUs per m3. Such high numbers of microorganisms could contribute to product contamination and also pose a potentially significant safety concern. iii. You do not perform non-viable particulate monitoring, active or passive viable air sampling, or sampling of critical surfaces in the BSC for microorganisms in association with each production batch. c. During the inspection, FDA investigators observed personnel practices that do not adequately protect against microbiological contamination of your products. For example: i. Operators were observed processing ProTextTM (ID: (b)(6), (b)(7)(C)) without changing or disinfecting the outer pair of sterile gloves donned in the ISO 8 hallway. Processing steps include (b)(4) of birth tissue, including removing debris and aseptic transfer of in-process material. ii. Operators performing aseptic processing of ProTextTM (ID: (b)(6), (b)(7)(C)) were also observed repeatedly passing gloved hands and sleeves over containers of open, in-process umbilical cord tissue within the BSC as well as using gloved hands as a seal to cover open containers of in-process umbilical cord tissue during processing." "As another example, your revised gowning procedure indicates exam gloves should be removed in the ISO-7 cleanroom prior to performing a (b)(4) hand scrub and donning sterile gloves. We have concerns that this may result in exposure of skin in the aseptic processing area, which may increase the risk of contamination during the manufacturing process."
Devices	**R**	Metal sterilization trays used to encase and protect medical devices during sterilization have a new 510(k) with instructions for use that is for the first time specific to the tray models, that also includes information regarding the sterilization modality.
Devices	**R**	Plastic sterilization trays used to encase and protect medical devices during sterilization have a new 510(k) with instructions for use that is for the first time specific to the tray models, that also includes information regarding the sterilization modality.
Devices	**R**	The outer package seal could be open, or compromised which affects the sterility of the procedure pack inside.
Devices	**R**	Affected product lots were mislabeled as "STERILE PVP SLN" when they should have been titled "NON-STERILE PVP SOLUTION, STERILE PACKAGING".
Devices	**R**	The scissors were manufactured without a tip protector resulting in the scissors breaking through the semi-rigid plastic tray compromising sterility.

FDA Citations/Recalls/Warning Letters Relevant to Microbiological Issues

Reason for Recall/Warning Letter may be redacted to remove information identifying specific companies.
https://www.accessdata.fda.gov/scripts/ires/index.cfm

The purpose of this service is to provide helpful information related to recalls/citations/warning letters related to microbiological issues. It in not intended to replace the information provided by the FDA, nor is it guaranteed to be complete.

Product Type	Citation [C], Recall [R], Warning Letter [WL]	Reason for Citation/Recall/Warning Letter
Devices	**WL**	"A). You failed to validate the cleaning process for controlled environmental areas used for the aseptic processing of Mueller Hinton Agar antimicrobial susceptibility test culture media and other culture media devices." "B). You failed to validate the (b)(4) sterilization of tubing sets used in aseptic fill operations for culture media devices." "Furthermore, your firm does not conduct analysis of environmental monitoring data for aseptic processing operations." "B). Your firm failed to adequately investigate and identify actions needed to correct and prevent the recurrence of product sterility failures of (b)(4), Lot (b)(4), identified on 04/29/2021 and Lot (b)(4), identified on 05/07/2021, as required by your procedure QA-008/L, Product/Process Quality Incidents (PQI's)." "4. Failure to maintain a device master record, as required by 21 CFR 820.181. For example, your firm failed to demonstrate that the Mueller Hinton Agar was manufactured according to the Device Master Record (DMR). Your quality manager could not locate the DMR to ensure the device production record (DHR) for each batch or lot of the Mueller Hinton Agar met specifications, including specifications for manufacturing, label requirements, and testing." "5. Failure to adequately establish procedures to control environmental conditions, as required by 21 CFR 820.70(c). For example, your firm failed to implement the procedure 003-007, Environmental Monitoring, revised on 02/26/2021. Updates made to Attachment's A, B, and H located within the procedure 003-007 were not implemented within the facility. (b)(4), Mueller Hinton Agar, and other culture media is manufactured each day in controlled area which are not monitored as specified in your Environmental Monitoring procedure."
Devices	**WL**	
Drugs	**R**	cGMP deviations: potential for Microbial Contamination of Non-Sterile Products
Drugs	**R**	Lack of assurance of sterility: bags have the potential to leak.
Drugs	**R**	Non-Sterility: FDA analysis found unopened products to have bacterial contamination.
Drugs	**R**	Lack of Assurance of Sterility
Drugs	**R**	Lack of Assurance of Sterility
Drugs	**WL**	"A retrospective, independent review of water system failures, batch failures, rejected batches, returned drug products, complaints, and deviations that may have been related to microbiological contamination over the last three years."
Food & Beverages	**WL**	"In your response you stated that you revised your Environmental Monitoring Program on February 15, 2023 "to implement the appropriate procedure for *[L]isteria* and *[S]almonella* swabbing zone sample sites and assurance of compliance of positive result corrective actions practices, with assurance of sanitation and re-testing to be completed and analyzed until a negative result is obtained three consecutive times." However, you did not provide any corrective actions in response to the previous positive *Listeria* findings described in this letter. You should address your repeated *Listeria* positives in the **(b)(4)** and **(b)(4)** to determine if your sanitation program is working effectively."
Food & Beverages	**WL**	"Your significant deviation is as follows: 1. The HACCP plan does not list the food safety hazards that are reasonably likely to occur. Specifically, the HACCP plan for histamine forming species including frozen, raw, individually vacuum-packaged, wild caught, mahi-mahi portions and fillets does not list the food safety hazard of Clostridium botulinum growth and toxin formation, and undeclared allergens as required by 21 CFR 123.6(c)(1)."
Food & Beverages	**WL**	"1. You did not take reasonable precautions and measures to ensure that all persons working in direct contact with food wash hands thoroughly (and sanitize if necessary to protect against contamination with undesirable microorganisms) after each absence from the workstation and at any other time when hands may have become soiled or contaminated, as required by 21 CFR 117.10(b)(3). Specifically, on November 8 and November 9, 2022, (b)(4) employees were observed not washing and sanitizing hands prior to donning gloves before separating by hand the RTE gummy candy products from excess sugar and hand-packing the products into finished product packaging."
Food/Cosmetics	**R**	Potential for the product to develop mold and spoil.
Food/Cosmetics	**R**	Product may be contaminated with Salmonella
Food/Cosmetics	**R**	Products were not properly pasteurized.

FDA Citations/Recalls/Warning Letters Relevant to Microbiological Issues		
Reason for Recall/Warning Letter may be redacted to remove information identifying specific companies. https://www.accessdata.fda.gov/scripts/ires/index.cfm		
The purpose of this service is to provide helpful information related to recalls/citations/warning letters related to microbiological issues. It in not intended to replace the information provided by the FDA, nor is it guaranteed to be complete.		
Product Type	**Citation [C], Recall [R], Warning Letter [WL]**	**Reason for Citation/Recall/Warning Letter**
Food/Cosmetics	**R**	Products may be contaminated with Listeria monocytogenes.
Food/Cosmetics	**R**	Products may be contaminated with Listeria monocytogenes.
Food/Cosmetics	**R**	Products may contain Salmonella
Food/Cosmetics	**R**	Potential contamination with Hepatitis A.
Food/Cosmetics	**R**	Product may contain Staphylococcus aureus.
Food/Cosmetics	**R**	Potential for contamination with Listeria monocytogenes. Pineapples are recalled by supplier Sunrise Growers Inc.
Food/Cosmetics	**R**	Fruit products have the potential to be contaminated with Listeria monocytogenes.
Food/Cosmetics	**R**	Potential to be contaminated with Listeria monocytogenes.
Foods	**C**	You did not implement a written environmental monitoring plan designed to identify L. monocytogenes if it is present in the growing, harvesting, packing or holding environment.
Foods	**C**	You did not take and analyze samples of bottled drinking water for bacteriological testing at least once a week for each type of bottled drinking water produced during a day's production run.
Foods	**C**	You did not take a bacteriological swab or rinse count at least every three months from at least four containers and closures selected just prior to filling and sealing.
		Current Sponsors of the PMF
ASSOCIATES OF CAPE COD INCORPORATED		http://www.acciusa.com/
Microbiologics		http://www.microbiologics.com
NOVATEK INTERNATIONAL		https://ntint.com/
Rapidmicro biosystems®		https://www.rapidmicrobio.com

FDA Citations/Recalls/Warning Letters Relevant to Microbiological Issues		
Reason for Recall/Warning Letter may be redacted to remove information identifying specific companies. https://www.accessdata.fda.gov/scripts/ires/index.cfm		
The purpose of this service is to provide helpful information related to recalls/citations/warning letters related to microbiological issues. It in not intended to replace the information provided by the FDA, nor is it guaranteed to be complete.		
Product Type	**Citation [C], Recall [R], Warning Letter [WL]**	**Reason for Citation/Recall/Warning Letter**
STERIS®		http://www.sterislifesciences.com/
vai VELTEK ASSOCIATES, INC.		http://www.sterile.com
Giles Scientific, Inc.		https://www.biomic.com/trinity-v3.html
Special Process Services, LC		https://www.linkedin.com/in/joseph-connaghan-b663929