Date of This Update: October 10, 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

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Product Type	Citation [C], Recall [R], Warning Letter [WL]	Reason for Citation/Recall/Warning Letter
Biologics	**WL**	a. During the annual product review periods ranging from January 01, 2021 to February 28, 2022, approximately 28 batches/lots of your terminally sterilized products exceeded your firm's action limit for bioburden samples taken from bulk solutions (i.e., "mixing tanks") or "finished unsterilized units." Results for approximately 21 lots were considered too numerous to count (TNTC). Additionally, approximately 31 lots of finished unsterilized units exceeded the spore count action limit. At the time of the inspection, your investigations into these excursions were not thorough because the investigations did not include an evaluation to determine the root cause, although batches had been released. b. Your firm does not investigate "swarming organisms" as a TNTC result, as required by your established, written Procedure for Plate Counting of Microbiological Samples applicable to bioburden testing, water testing, and environmental monitoring among other tests. 2. Failure to test in-process materials for identity, strength, quality, and purity, as appropriate, and approve or reject by the quality control unit, during the production process [21 CFR 211.110(c)]. For example, your firm failed to reject lots of your bulk solutions (i.e., "mixing tanks") and finished unsterilized units with in-process bioburden results of TNTC. 3. 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. Your firm has failed to establish that your sterilization process can achieve your established minimum sterility assurance level (SAL) of (b)(4) when TNTC bioburden levels are present in your finished unsterilized units. b. Your firm has failed to establish and follow appropriate written procedures to prevent microbiological contamination of finished units of your products prior to terminal sterilization. Bioburden control is critical for preventing a challenge to your validated sterilization process and to minimize bioburden-associated byproducts.
Biologics	**WL**	1. Failure to establish and follow appropriate written procedures designed to prevent microbiological contamination of drug products purporting to be sterile [21 CFR 211.113(b)]. Your firm failed to adequately validate the aseptic processes used to manufacture your Signature Cord™ product in that the media fill batches used for your validation studies did not represent the maximum commercial batch size. For example, your validation studies entitled "Aseptic Processing Validation Report—Signature Cord" utilized a maximum of (b)(4) vials per batch. However, from November 2018 through February 2020, your firm manufactured (b)(4) commercial batches of Signature Cord™ with (b)(4) vials. 2. Failure to have an adequate system for monitoring environmental conditions in an aseptic processing area [21 CFR 211.42(c)(10)(iv)]. Your firm has not established an adequate system for environmental monitoring in the aseptic processing areas where your products are manufactured. For example: a. You have not performed microbiological monitoring of viable air in the ISO 7 supporting cleanrooms in association with each production run. b. Your environmental monitoring procedure describes the following as acceptable results for microbiological monitoring: (b)(4) colony forming units (CFUs) for surfaces within the ISO 7 supporting cleanrooms, (b)(4) CFUs for settling plate samples within the ISO 7 supporting cleanrooms, (b)(4) CFUs for personnel glove samples within the ISO 7 supporting cleanrooms, and (b)(4) CFUs for personnel garment samples within the ISO 7 supporting cleanrooms. Your allowance for such high numbers of microorganisms could contribute to product contamination and pose a potentially significant safety concern. 4. Each of batch of drug product purporting to be pyrogen-free is not laboratory tested to determine conformance to such requirements [21 CFR 211.167(a)]. For example, your firm failed to perform endotoxin testing as a release criterion on (b)(4) units of Signature Cord™ product manufactured and distributed by your firm since November 2018. By the nature of the route of administration, your product is purported to be pyrogen-free and is expected to be pyrogen-free.
Devices	**R**	Sterility of device may be compromised due to breach of the chevron seal of the packaging.

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Devices	**R**	Product dispositioned for scrap for sterility failure investigation that was inadvertently shipped to customers.
Devices	**R**	Specific lots of 3M Attest Super Rapid Readout Biological Indicators (1492V), 3M Attest Super Rapid 5 Steam-Plus Challenge (41482V, 41482VF), and 3M Attest Super Rapid Readout Steam Challenge (1496V) may contain biological indicators with a cap that melts, deforms and/or cracks following a steam sterilization cycle of 132¿C and 135¿C.
Devices	**R**	Sterile barrier might be damaged compromising the sterility of the device.
Devices	**R**	The sterile blister packaging may be damaged, and sterility may be compromised.
Drugs	**R**	Lack of Assurance of Sterility
Drugs	**R**	Lack of Assurance of Sterility:Lack of validation data for sanitization cycles
Drugs	**R**	Lack of Assurance of Sterility: Potential presence of leaks originating from the Luer component.
Drugs	**R**	Lack of Assurance of Sterility: Powder discoloration due to small crack in some vials.
Drugs	**R**	Lack of Assurance of Sterility
Drugs	**R**	Lack of Assurance of Sterility: out-of-specification test results observed for Filter Integrity Test (FIT).
Drugs	**R**	Non-Sterility
Drugs	**C**	Buildings used in the manufacture, processing, packing or holding of drug products are not maintained in a clean and sanitary condition.
Drugs	**C**	Procedures designed to prevent objectionable microorganisms in drug products not required to be sterile are not followed.
Drugs	**WL**	1. Your firm failed to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that includes validation of all aseptic and sterilization processes (21 CFR 211.113(b)).
Drugs	**WL**	2. 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. (21 CFR 211.160(b))
Drugs	**WL**	3. Your firm failed to conduct, for each batch of drug product, appropriate laboratory testing, as necessary, required to be free of objectionable microorganisms (21 CFR 211.165(b)).
Food & Beverages	**WL**	1. Your firm failed to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that includes validation of all aseptic and sterilization processes (21 CFR 211.113(b)).
Food & Beverages	**WL**	1. You did not establish a system of process controls covering all stages of processing that was designed to ensure that infant formula does not become adulterated due to the presence of microorganisms in the formula or in the processing environment, as required by 21 C.F.R. § 106.55(a).

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Product Type	Citation [C], Recall [R], Warning Letter [WL]	Reason for Citation/Recall/Warning Letter
Food & Beverages	**WL**	a. You did not identify and evaluate bacterial growth and/or toxin formation due to reduced oxygen packaging (i.e., Clostridium botulinum (C. botulinum)) during storage of refrigerated RTE ROP baby food products. Your hazard analysis identifies pathogens including L. monocytogenes as a biological hazard requiring a preventive control at the Cold Storage step, but it does not specifically identify sporeforming C. botulinum growth and/or toxin formation due to reduced oxygen packaging. RTE baby food products (including (b)(4), and (b)(4)) are packaged and stored in ROP. Various ingredients in these products grow in the ground or are associated with soil, where spores of C. botulinum may be present. Therefore, bacterial growth and/or toxin formation due to reduced oxygen packaging (i.e., anaerobic C. botulinum) is a known or reasonably foreseeable hazard at the cold storage step. These products do not receive a treatment lethal to nonproteolytic or proteolytic C. botulinum before or after packaging, and their formulation does not control for the growth and/or toxin formation of C. botulinum. A knowledgeable person manufacturing/ processing food in your circumstances would identify bacterial growth and/or toxin formation due to reduced oxygen packaging as a hazard requiring a preventive control. Process controls include procedures, practices, and processes to ensure the control of parameters during operations. Such controls could include formulation (e.g., decreasing pH or water activity), heat processing (e.g., a cook that targets nonproteolytic C. botulinum), or refrigeration (e.g., temperature control below (b)(4) with the use of time temperature indicators on each package). Process controls must include the parameters associated with the control of the hazard and the minimum and maximum values needed to significantly minimize or prevent the hazards (see 21 CFR § 117.135(c)(1)).
Food/Cosmetics	**R**	We note that you do not have adequate controls in place for bacterial growth and/or toxin formation due to reduced oxygen packaging, as evidenced by the following:
Food/Cosmetics	**R**	i. Your written Process Control (HACCP Plan) states, “Product temperature will not rise above (b)(4), In the event of a natural disaster, loss of power for an extended period of time, or air temperature above (b)(4) for any other reason, product temperatures will be monitored to ensure product temperature does not exceed (b)(4).” This maximum value for temperature is insufficient to control for the hazard of C. botulinum toxin formation in RTE sealed baby food in ROP. Nonproteolytic C. botulinum can grow at a minimum temperature of (b)(4); it can grow and produce a deadly toxin after two days when temperatures are between (b)(4)°F. During the inspection you indicated that sealed baby food products can remain in Cooler (b)(4) for up to (b)(4) until being transported off-site.
Food/Cosmetics	**R**	Listeria monocytogenes
Food/Cosmetics	**R**	Listeria monocytogenes
Food/Cosmetics	**R**	Potential contamination of Listeria monocytogenes.
Food/Cosmetics	**R**	Product tested positive for Salmonella.
Food/Cosmetics	**R**	South Carolina Department of Health discovered the product contained Listeria monocytogenes.
Food/Cosmetics	**R**	Products contain high water activity in the formula that provides a potential for microbial growth.
Food/Cosmetics	**R**	Products may be contaminated with Listeria monocytogenes.
Food/Cosmetics	**R**	Surface mold visible on product.
Foods	**C**	You did not clean and sanitize your utensils or equipment as frequently as necessary to protect against contamination of food.
Foods	**C**	You did not establish a system of process controls covering all stages of processing that was designed to ensure that infant formula does not become adulterated due to the presence of microorganisms in the formula or in the processing environment.
Foods	**C**	You did not conduct operations under conditions and controls necessary to minimize the potential for growth or survival of microorganisms, allergen cross-contact and contamination of food.
Foods	**C**	You did not ensure that your cleaning compounds and sanitizing agents are safe and adequate under the conditions of use.
Foods	**C**	You did not conduct operations under conditions and controls necessary to minimize the potential for growth or survival of microorganisms.
Foods	**C**	You did not treat your seeds for sprouting with a scientifically valid method to reduce microorganisms of public health significance.

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Product Type	**Citation [C], Recall [R], Warning Letter [WL]**	**Reason for Citation/Recall/Warning Letter**
Foods	**C**	You did not conduct operations under conditions and controls necessary to minimize the potential for growth or survival of microorganisms and contamination of food.
Foods	**C**	You did not conduct operations under conditions and controls necessary to minimize the potential for growth or survival of microorganisms and contamination of food.
Foods	**C**	You did not ensure that raw materials and other ingredients were not adulterated by pathogenic microorganisms at levels that may render the food injurious to health.
Foods	**C**	You did not ensure that raw materials and other ingredients were not adulterated by pathogenic microorganisms at levels that may render the food injurious to health.
Parts 1240 and 1250	**C**	Hot water is used as the bactericidal agent for multiuse eating and drinking utensils and equipment used in the preparation of food and beverages, but no indicating thermometer is provided to determine the hot water temperature.
Parts 1240 and 1250	**C**	Adequate facilities are not provided for the bactericidal treatment of multiuse eating and drinking utensils.
Veterinary	**R**	Positive Salmonella Sample
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rapid microbiology FOCUSED ON MICROBIOLOGY		https://www.rapidmicrobiology.com/subscribe
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