Establishing Sanitation Programs for Low-Moisture Ready-to-Eat Human Foods and Taking Corrective Actions Following a Pathogen Contamination Event: Guidance for Industry

Draft Guidance

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Establishing Sanitation Programs for Low-Moisture Ready-to-Eat Human Foods and Taking Corrective Actions Following a Pathogen Contamination Event: Guidance for Industry[1]

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I. Introduction

This guidance is intended to help manufacturers/processors[2] of low-moisture, ready-to-eat (LMRTE) human foods ("you") comply with 21 CFR part 117[3] (part 117). Examples of manufactured/processed LMRTE foods that must be produced in accordance with the requirements of part 117 include powdered infant formula (PIF), peanut butter, nut butters, powdered drink mixes, chocolate, medical foods in powdered and paste forms, processed tree nuts, milk powders, powdered spices, snack foods such as chips and crackers, granola bars, and dry cereal. This guidance also is intended to help manufacturers/processors of PIF comply with 21 CFR part 106[4] (part 106).[5] The recommendations in this guidance can help manufacturers/processors of LMRTE foods comply with the requirements for current good manufacturing practices (CGMPs), hazard analysis, and risk-based preventive controls to ensure a safe and sanitary food supply for these foods.

This guidance provides our current thinking on establishing a routine sanitation program for LMRTE foods that can help prevent pathogen contamination events[6] and also sets forth recommendations for corrective actions, including corrective actions for remediation of

[1] This guidance has been prepared by the Office of Microbiological Food Safety, Office of Critical Foods, and the Office of Compliance and Enforcement in the Human Foods Program at the U.S. Food and Drug Administration.
[2] For purposes of this guidance, we use the term "manufacturers/processors" to discuss entities that conduct manufacturing/processing as defined at 21 CFR 1.227.
[3] Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food.
[4] Infant Formula Requirements Pertaining to Current Good Manufacturing Practice, Quality Control Procedures, Quality Factors, Notification Requirements, and Records and Reports.
[5] More information about the regulatory framework and applicability of FDA's regulations can be found in Appendix 1. Appendix 1 briefly describes the requirements of part 117 for CGMPs, hazard analysis, and risk-based preventive controls for human food and exemptions from those requirements. Appendix 1 also briefly describes the requirements of part 106 for CGMPs for infant formula and provides information about the provisions of § 107.50, in 21 CFR part 107, Subpart C, for exempt infant formulas.
[6] For the purpose of this guidance, we use the term "pathogen contamination event" to mean contamination of food or a food-contact surface (FCS) with a pathogen.

contamination of food-contact surfaces (FCSs) if prevention fails. Specifically, this guidance discusses:

- establishing and implementing a sanitation program and routine environmental monitoring program;
- conducting adequate root cause investigations (RCIs) following a pathogen contamination event;
- applying a sanitizing[7] treatment when remediating a pathogen contamination event;
- taking steps to identify affected food; and
- the limitations of relying solely on a product testing program as verification that pathogen contamination has been eliminated.

Although several recommendations in this guidance are specifically directed to contamination events due to environmental pathogens, the recommendations in this guidance can also be applied to contamination events with other pathogens.

In general, FDA guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe FDA's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in FDA guidances means that something is suggested or recommended, but not required.

II. Background[8]

A. LMRTE Food

Low-moisture foods are naturally low in moisture or are produced from higher-moisture foods through drying or dehydration processes. For purposes of this guidance, we consider a low-moisture food to exhibit a water activity of 0.85 or below (Ref. 1). Our regulations define a "ready-to-eat" food (RTE food) as "any food that is normally eaten in its raw state or any other food, including a processed food, for which it is reasonably foreseeable that the food will be eaten without further processing that would significantly minimize biological hazards" (21 CFR 117.3).

B. Pathogen Contamination Events in LMRTE Food

Pathogen contamination events can result from a variety of circumstances, such as the introduction of a pathogen:

- through a contaminated ingredient (e.g., at the beginning of the line or at an intermediate step when an ingredient is added);

[7] "Sanitize" means to adequately treat cleaned surfaces by a process that is effective in destroying vegetative cells of pathogens, and in substantially reducing numbers of other undesirable microorganisms, but without adversely affecting the product or its safety for the consumer (§ 117.3).
[8] Section VII contains a glossary of terms used in this guidance. Section VIII contains a table of abbreviations used in this guidance.

- elsewhere along the processing line where the product or its ingredients are exposed to the environment (e.g., during holding steps or packaging, or during routine/non-routine interventions into equipment during production);
- onto FCSs from the environment (e.g., introduction of an environmental pathogen by personnel); and
- onto dry processing equipment through introduction of water (e.g., through condensation or a leaking roof).

Once a pathogen is introduced into production equipment within a food processing system, the pathogen can be transferred through the system, contaminating other pieces of equipment and the product moving through the system. For example, transfer can occur by:

- food (e.g., as contaminated product moves through the food processing system);
- people (e.g., if a person touches the contaminated site and then touches other objects, or tracks the pathogen from the contamination site to other sites on shoes);
- equipment (e.g., if the pathogen is picked up by the wheels of a cart or forklift and is transferred to other locations);
- water (e.g., water (which can create an environment in which pathogens can grow) can transfer a pathogen to other areas by splashing); and
- air or aerosols (e.g., dissemination of contaminated dust particles or mist containing pathogens by air handling systems).

An environmental pathogen is a pathogen capable of surviving and persisting within the manufacturing, processing, packing, or holding environment such that food may be contaminated and may result in foodborne illness if that food is consumed without treatment to significantly minimize the environmental pathogen (§ 117.3). These pathogens can be introduced into a food processing plant and can increase in number when water is present. While LMRTE foods generally do not support the growth of environmental pathogens, environmental pathogens can survive in many LMRTE foods and cause foodborne illness. *Salmonella* spp. and *Cronobacter* spp. are examples of environmental pathogens that have a history of contaminating the production environment of LMRTE foods (Ref. 2 through Ref. 5).

Contartailmination of food with *Salmonella* is a leading cause of foodborne illness and associated hospitalization and death (Ref. 6). *Salmonella* spp. is a known or reasonably foreseeable hazard that can become established in dry food production environments (Ref. 2 and Ref. 3). The contamination of foods with *Salmonella* during manufacturing has occurred through transfer of *Salmonella* that has become established in the production environment of the plant and through the addition of contaminated raw materials or ingredients (Ref. 7 and Ref. 8; see also 78 FR 3646 at 3737, January 16, 2013).

It is well established that *Cronobacter* spp. can cause severe foodborne illness in infants (79 FR 7934 at 7977 to 7988, February 10, 2014). *Cronobacter* spp. is a known or reasonably foreseeable hazard that can become established in dry food production environments, such as plants that produce PIF and plants that produce milk powder (Ref. 4 and Ref. 5). There is no current or planned national surveillance for *Cronobacter* spp. infections in populations other than

infants,[9] and while other sources have been reported, there is limited information about potential reservoirs or routes of transmission other than ingestion of contaminated powdered infant formula by infants (Ref. 9 and Ref. 10). In adult populations, emerging information demonstrates that *Cronobacter* spp. most commonly causes urinary tract infections, but also can cause septicemia, pneumonia, osteomyelitis, wound infections, and splenic abscesses (Ref. 9 and Ref. 12).

Environmental pathogens that are readily removed from a food processing plant through routine cleaning and sanitizing are referred to as "transient strains." Environmental pathogens that are not removed through routine cleaning and sanitizing and become established in a food processing plant (either in processing equipment and/or parts of the facility infrastructure) are referred to as "resident strains."[10] The presence of moisture in an LMRTE food production environment can allow the growth of transient or resident environmental pathogens, thereby increasing the risk of contaminating FCSs and/or the LMRTE food. Minimizing the amount of water/moisture in the LMRTE production environment is important for reducing the risk associated with environmental pathogens.

C. Techniques for Cleaning and Sanitizing Food-Contact Surfaces

LMRTE foods are produced, at least in part, in dry processing environments. The manufacturing processes and equipment used to make LMRTE foods vary considerably, even among manufacturing/processing facilities that make similar products. As such, there is likely no single cleaning technique or sanitizing treatment that is appropriate for all circumstances. Similarly, there is likely no single cleaning technique or sanitizing treatment that is appropriate for all circumstances for remediating a pathogen contamination event.

Cleaning techniques are distinct from sanitizing treatments.

- **Cleaning techniques** remove soil, including food residue, dirt, grease, or other objectionable matter, from the FCS;
- **Sanitizing[11] treatments** destroy (i.e., kill) microorganisms, such as pathogens, that contaminate that surface.

Routine sanitary operations include cleaning and, when necessary, sanitizing. A sanitary operation that includes both cleaning and sanitizing generally takes place as a two-step, sequential process in which cleaning precedes sanitizing so that cleaning removes substances that could interfere with the action of some sanitizing treatments. However, some sanitary operations (e.g., hot water or steam systems) are capable of cleaning and sanitizing at the same time. Chemical sanitizing agents for LMRTE foods are often applied after dry cleaning procedures have been used to remove residual product from equipment surfaces; such chemical sanitizing

[9] In 2023, the Council of State and Territorial Epidemiologists recommended that all States and Territories enact laws (statute or rule/regulation as appropriate) to make invasive *Cronobacter* infection in infants reportable in their jurisdiction and that jurisdictions conducting surveillance submit case notifications to the Centers for Disease Control and Prevention (Ref. 11).
[10] We generally consider the finding of the same environmental pathogen strain through environmental monitoring on occasions separated by at least 60 days to indicate the potential presence of a resident pathogen (Ref. 13).
[11] See footnote 7.

agents usually are low-moisture products (such as an alcohol-based product) for which the limited amount of moisture present can evaporate quickly.

Some manufacturers/processors of LMRTE food use "material flush techniques" (also called "product push" or "product purge") for routine cleaning of food processing equipment. Examples of such techniques include moving hot oil (e.g., for products such as nut butters) (Ref. 14) and moving product or other solids through a production system to remove the product that was previously being produced (Ref. 14, Ref. 15, and Ref. 16). At this time, we are not aware of scientific or technical evidence that demonstrates that cleaning techniques alone, including material flush techniques, are effective in mitigating pathogen contamination on FCSs.[12]

D. The Role of Testing in a Modern Food Safety System

It has long been FDA's position that finished product testing alone is not adequate as verification that an environmental pathogen hazard has been controlled during the production of manufactured/processed food. (See the discussion of the role of testing as a verification measure in a modern food safety system at 78 FR 17142 at 17143 to 17151, March 20, 2013.) It is well established that there are limitations of microbiological finished product testing for verifying the safety of food, especially when pathogens, when present, are likely present at very low levels and not uniformly distributed (Ref. 17 and Ref. 18).[13] Finished product testing is most useful when conducted in conjunction with other activities to verify that control measures are functioning as intended. For example, manufacturers/processors frequently make decisions about releasing product produced during a specified time period by considering the results of:

- a review of production records to ensure control measures (e.g., a process preventive control) were implemented according to the food safety plan;
- microbiological testing of samples collected from the food production environment (to identify environmental pathogens that are present in the food production environment and eliminate them before they contaminate FCSs used to produce food); and
- microbiological testing of product samples collected at defined times throughout production, including at the final product stage.

E. Investigations of Pathogen Contamination Events in LMRTE Food Production Plants

Our investigations of LMRTE contamination events (Ref. 19 through Ref. 22) have revealed examples of:

- significant inadequacies in the steps that some LMRTE food facilities took to identify and correct food safety problems and reduce the likelihood that the problem will recur;
- significant inadequacies in the cleaning and sanitizing of some LMRTE food processing plants; and
- an inappropriate reliance on product testing to identify food that is affected by a contamination event.

[12] For more information on current research regarding material flush techniques, see Appendix 2.
[13] See also 78 FR 17142 at 17143 to 17151.

Examples of these circumstances follow.

- In 2021 through 2023, our inspections of multiple U.S. PIF facilities identified significant violations of part 106 and the presence of *Cronobacter* spp. within the production environment (Ref. 19 through Ref. 21, Ref. 23, and Ref. 24). In 2022, our inspection of the peanut butter facility implicated in a 2022 multistate salmonellosis outbreak (Ref. 25) identified violations of part 117 (Ref. 22). In each of these circumstances, we advised these facilities of our concerns that the corrective actions they had taken were not sufficient to address the root cause of pathogen contamination events.
- In some of these inspections and follow-up investigations, we observed that facilities that used "material flush techniques" for routine cleaning of food processing equipment also relied on these techniques to remove contaminated food from FCSs without an accompanying sanitizing treatment (Ref. 20 through Ref. 22). We advised these facilities of our concerns that such techniques have not proven effective against eliminating pathogens from equipment surfaces.[14]
- In some inspections and investigations in which we observed that a facility used material flush techniques to remove contaminated food from FCSs without an accompanying sanitizing treatment, the facility then inappropriately relied on product testing to determine which product was affected by a pathogen contamination event. Based on the assumption that uncontaminated product would push out the contaminated product, these facilities would generally destroy product that tested positive, along with some product produced immediately before and after that tested negative. For example, a peanut butter facility implicated in a 2022 multistate salmonellosis outbreak (Ref. 25) detected *Salmonella* in several lots of finished product using their routine lot sampling program (which involved the sampling and testing of a high number of samples collected from short periods of production). The facility followed its standard practice of conducting intensified sampling and testing (involving a higher number of samples) of lots produced immediately prior to and after the product that tested positive. After this additional intensified testing of lots initially found to be negative, the facility detected additional positive lots and, thus, demonstrated that the routine sampling plan was not effective at identifying all affected product. An intensified sampling and testing plan would also be unlikely to detect all contamination, especially when contamination is present at low levels and not homogeneously distributed. We advised the facility that the positive test results from its intensified sampling and testing show the limitations of relying on its microbiological finished product testing program to identify contamination as a way to prevent contaminated products from reaching consumers.
- Our inspection and follow-up investigation of a peanut butter facility implicated in a 2022 multistate salmonellosis outbreak also revealed that the peanut butter facility did not adequately consider its identified root cause when determining which food was affected by the contamination event (Ref. 22). In that specific situation, *Salmonella* contamination likely resulted from a defect in the air intake vent of the cooling chamber that allowed rainwater and unfiltered outside air to enter the peanut roaster. The peanut butter facility released potentially contaminated products that were produced from peanuts impacted by

[14] See also the discussion of our recommendations for remediation of a pathogen contamination event (in section V.G) and the discussion in Appendix 2 of research regarding adequacy of material flush techniques.

the contamination event (i.e., peanuts exposed to the insanitary conditions created by the roaster defect) but which tested negative for *Salmonella*. In this instance, any product produced from peanuts exposed to this roaster defect could potentially have been contaminated at a low level that might not be detected by sampling and testing (including by intensified sampling and testing); in fact, all of the peanut butter released by this processor that caused illness had tested negative by the processor's finished product testing efforts. We advised the peanut butter facility that the outbreak showed that neither its corrective actions nor its finished product testing was adequate to prevent contaminated product from reaching consumers and causing illnesses.

III. Recommendations for a Sanitation Program

Our investigations of sanitation programs at LMRTE food manufacturing/processing plants demonstrate the importance of an effective sanitation program to help prevent pathogen contamination of LMRTE foods. As such, we recommend that you establish and implement a sanitation program adequate to prevent contamination of your LMRTE food. Such programs help ensure production plants, and production equipment within the plant's food processing system, are operating under sanitary conditions that will prevent contamination of food.

Sanitation programs include CGMP measures and, for facilities subject to the requirements of part 117 for hazard analysis and risk-based preventive controls (PCHF requirements), sanitation controls. Sanitation controls are subject to requirements for verification of implementation and effectiveness (through an environmental monitoring program and product testing) and corrective action procedures. As discussed in more detail below, specific corrective actions you should take when following a contamination event will depend on the nature of that contamination event, e.g., whether you have identified a pathogen in the food you have produced or whether you have identified a pathogen on an FCS through your environmental monitoring program.

Several readily available resources address the production of LMRTE foods, including sanitation programs that are applicable to these foods. These resources include a 2009 publication of the Grocery Manufacturers Association (GMA; now the Consumer Brands Association), "Control of *Salmonella* in Low-Moisture Foods" (Ref. 26), and the Codes of Practice developed by the Codex Alimentarius Commission in 2018 for Low-Moisture Foods (Ref. 1) and in 2009 for Powdered Formulae for Infants and Young Children (Ref. 27).[15] These resources provide additional information on a number of topics, including sanitation practices, equipment design and maintenance, and post-contamination remediation, and could be useful as you develop and implement your own programs.

[15] Reference to these documents is provided for informational purposes only. These documents are not incorporated by reference into this guidance and are not FDA guidance.

IV. Recommendations for CGMP Measures Applicable to Sanitation Programs

A. CGMP Requirements Applicable to a Sanitation Program

CGMPs describe the methods, equipment, facilities, and controls for producing processed food and following CGMPs helps ensure the safety of food. FDA regulations in part 117 and part 106 include requirements for CGMPs intended to help ensure a safe and sanitary food supply. See Appendix 1 for information about the part 117 CGMP requirements applicable to all LMRTE food, including PIF, and the part 106 CGMP requirements specific to the manufacturing and processing of non-exempt PIF.[16]

B. Recommendations for Controlling Water in Dry Production Environments[17]

Water, even if present in very small amounts for short, sporadic time periods, can enable environmental pathogen growth and facilitate transfer of environmental pathogens from one area to another. The presence of water in the dry processing environment can result from improper use of water during cleaning, which has been linked to the occurrence and spread of *Salmonella* (Ref. 26 and Ref. 27). Other events resulting in the presence of water in a dry area include condensate formation, leaking water or steam valves, backed-up floor drains, infiltration of water following heavy rains (e.g., leaky roofs), and the activation of fire suppression systems in the case of fire emergencies (Ref. 26 and Ref. 27). Consistent with 21 CFR parts 117 and 106:

- Whenever practical, you should design and install equipment used in dry production environments in a manner that will facilitate dry cleaning.
- You should remove portable equipment or parts of equipment easily disassembled to a "clean out of place" area that is separated from the dry production environment, and then clean and, when appropriate, sanitize it. The equipment should be thoroughly dry before moving it back to the dry production environment.
- You should use dry-cleaning techniques to the extent practical, and limit the use of controlled wet-cleaning techniques (e.g., for clean-in-place procedures following a pathogen contamination event).
- Any time water is introduced for cleaning, including for clean-in-place procedures, you should minimize the amount of water used and completely remove that water by drying as soon as possible (sometimes referred to as "dry-out") to prevent growth of pathogens that could be present.
- You should promptly address any unanticipated water in the dry production environment so it does not provide an environment in which environmental pathogens can grow.

[16] See section 412(h)(1) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and § 107.50(a).
[17] Sections of part 117 that are relevant to these recommendations regarding the control of water in dry production environments include §§ 117.35(a), 117.35(d)(1), 117.40(a)(1) and (3), and 117.80(c)(1) and (c)(2). Sections of part 106 that are relevant to the recommendations in this guidance regarding the control of water in dry production environments include §§ 106.6, 106.20(a), 106.30(a), 106.30(b), and 106.30(f).

GMA's publication "Control of *Salmonella* in Low-Moisture Foods" includes a detailed discussion of the steps you could take to limit water in a dry processing environment (Ref. 26).[18] This discussion emphasizes the importance of limiting controlled wet cleaning, particularly on equipment not designed for wet cleaning. Ref. 26 includes several tables that provide examples of common industry procedures for controlled wet cleaning (Table 4-2), tools for dry cleaning and their uses (Table 4-3), and desirable design features for vacuum cleaners based on the location of use (Table 4-4).

C. Recommendations for Routine Cleaning and Sanitation Breaks[19]

Both dry-cleaning procedures and wet-cleaning procedures can be appropriate for routine sanitation of an LMRTE food plant. Dry-cleaning procedures include the use of vacuum cleaners, brooms, scrapers, brushes, and wipes (Ref. 26). Wet-cleaning procedures include the use of water and detergents and could be appropriate for routine sanitation as long as they are conducted using controlled wet-cleaning techniques (for cleaning and sanitizing). Because water can enable environmental pathogen growth and can facilitate transfer of environmental pathogens from one area to another, wet-cleaning techniques should be controlled to limit the use of water and/or water-based chemicals (Ref. 26). When using wet-cleaning procedures, we recommend designating a separate area of the plant to conduct wet cleaning of utensils and some parts of equipment, followed by drying.

We recommend that you establish and implement routine "sanitation breaks" in which you stop production to clean and sanitize all FCSs in the production system. Routine sanitation breaks can eliminate pathogens from FCSs and prevent contamination of food. They also can limit the amount of potentially affected food if you experience a pathogen contamination event. We recommend establishing and implementing sanitation breaks as follows based on your specific production system:

- **Non-continuous production systems** – establish and implement a sanitation break at the end of your daily production.
- **Continuous production systems** – establish and implement a sanitation break at intervals that are frequent enough to help limit the amount of food that could be affected by a contamination event.

Regardless of whether your production system is non-continuous or continuous, we recommend that you periodically[20] disassemble equipment to expose, clean, and sanitize surface areas that are not readily accessible during routine sanitary operations.

[18] Reference to this GMA publication is provided for informational purposes only. This GMA publication is not incorporated by reference into this guidance and is not FDA guidance.
[19] Sections of part 117 that are relevant to these recommendations include §§ 117.35(d) and (d)(1)) and 117.35(e). Sections of part 106 that are relevant to these recommendations include § 106.30(b).
[20] The frequency of such periodic disassembly would depend on considerations such as the food and the risk to the consumer if the production line was contaminated.

D. Recommendations for Equipment Design and Maintenance[21]

Equipment design, as well as regular inspection of equipment for any flaws or defects, can help prevent environmental pathogens from becoming established in harborage sites. We recommend that:

- whenever practical, you use surface designs that will not limit the flow of material through the production system and avoid surfaces (such as dead ends, hollow spaces, flat ledges, or sharp bends/angles in product conveyance lines) where food particles, dirt, and organic matter could accumulate;
- you regularly review the condition of FCSs for evidence of cracks, pitting, or other wear-related conditions (which could inhibit the normal flow of food or provide a niche for contaminated food to accumulate) and promptly repair them; and
- redesign or replace equipment that you are unable to effectively clean and sanitize.

V. Recommendations for Hazard Analysis, Preventive Controls, and Associated Preventive Management Components Applicable to a Sanitation Program

A. Requirements of Part 117

The PCHF requirements are primarily in subparts C and G, with associated requirements in subparts A, D, E, and F. The PCHF requirements largely reflect a sequence of activities intended to significantly minimize or prevent food safety hazards. For example, the requirement for hazard analysis leads a facility to determine which hazards require a preventive control. The facility then identifies and implements appropriate preventive controls, together with appropriate "preventive control management components" (i.e., monitoring, corrective actions and corrections, and verification) for each of those preventive controls.[22] The facility establishes and maintains records documenting its hazard analysis, preventive controls, recall plan, and written procedures for monitoring, corrective actions, and verification in its food safety plan (§ 117.126). The facility establishes and maintains records documenting its implementation of preventive control management components (summarized in §§ 117.190 and 117.475). Subpart F specifies general requirements applying to all required records.

See Appendix 1 for additional information about the PCHF requirements.

[21] Sections of part 117 that are relevant to these recommendations include § 117.40(a)(1), (a)(3), (a)(6), and (b). Sections of part 106 that are relevant to these recommendations include § 106.30(a) and (b).

[22] See § 117.3 for definitions of terms associated with the PCHF requirements, including "hazard," "known or reasonably foreseeable hazard," "hazard requiring a preventive control," "preventive control," "monitor," and "verification."

B. Recommendations for Hazard Analysis[23]

1. Hazard analysis for *Salmonella* spp.

Due to the severity of the *Salmonella* illness or injury if the hazard were to occur (Ref. 6) and the probability that the hazard will occur in the absence of preventive controls (Ref. 2 and Ref. 3), we recommend that you identify *Salmonella* spp. as a hazard requiring a preventive control during your hazard analysis if your LMRTE food is exposed to the environment prior to packaging and the packaged food does not receive a treatment or otherwise include a control measure (such as a formulation lethal to the pathogen) that would significantly minimize *Salmonella* spp.[24]

2. Hazard analysis for *Cronobacter* spp.

If your food is PIF or an ingredient that will be incorporated into PIF through dry blending, the food is exposed to the environment prior to packaging, and the packaged food does not receive a treatment or otherwise include a control measure (such as a formulation lethal to the pathogen) that would significantly minimize *Cronobacter* spp., we recommend that:

- For PIF, you identify *Cronobacter* spp. in your hazard analysis as a hazard requiring a preventive control due to the severity of illness or injury if the hazard were to occur (79 FR 7934 at 7977 to 7988) and the probability that the hazard will occur in the absence of preventive controls (Ref. 4 and Ref. 9).
- For ingredients incorporated into PIF through dry blending, you consider in your hazard analysis whether *Cronobacter* spp. is a hazard requiring a preventive control.

3. Hazard analysis for other pertinent pathogens

This guidance focuses on those biological hazards that currently are known or reasonably foreseeable (potential) environmental pathogens in LMRTE foods. For information on other known or reasonably foreseeable (potential) biological hazards in LMRTE foods, see our multi-chapter draft guidance for industry titled "Hazard Analysis and Risk-Based Preventive Controls for Human Food: Guidance for Industry" (Ref. 28; the PCHF guidance). This multi-chapter draft guidance is intended to explain our current thinking on how to comply with the PCHF requirements.[25] In particular, Chapters 2 and 3 of the PCHF guidance provide information about hazards most relevant to food safety and the process of conducting a hazard analysis, and Appendix 1 of the PCHF guidance lists the most relevant food-related hazards for multiple food groups.

[23] See § 117.130.
[24] For example, the manufacturing process for some packaged ground spices includes treatment (such as irradiation) to significantly minimize pathogens after the ground spice is in the package.
[25] See Appendix 1 for additional information about the PCHF guidance. When finalized, the PCHF guidance will reflect FDA's current thinking on this topic.

C. Recommendations for Preventive Controls[26] and Associated Monitoring[27] and Verification[28]

We recommend that the written preventive controls that you establish and implement in your food safety plan to significantly minimize or prevent environmental pathogens include sanitation controls[29] that include procedures, practices, and processes for the cleanliness of FCSs, including FCSs of utensils and equipment, with monitoring or verification through visual observation. Examples of sanitation controls include cleaning and sanitizing procedures (including appropriate frequencies for these procedures, concentrations of cleaning and sanitizing compounds, method of application, and contact time) (78 FR 3646 at 3741).

In developing your sanitation controls, we recommend that you consider adapting one or more CGMP measures to function as a sanitation control by combining a CGMP measure with written procedures that include monitoring or verification. For example, you could adapt a CGMP cleaning procedure for dry cleaning your equipment to be a sanitation control by:

- establishing written procedures, including the frequency they are to be performed, for that cleaning;
- monitoring that the cleaning takes place (e.g., by observing the cleaning or inspecting the equipment after the cleaning); and
- documenting that the procedures were followed (e.g., on a checklist).

D. Recommendations for Verification of Implementation and Effectiveness Through Environmental Monitoring and Associated Trend Analysis

If contamination of an LMRTE food with an environmental pathogen is a hazard requiring a preventive control, you must verify that the preventive controls are significantly minimizing or preventing environmental pathogen hazards from contaminating your food by environmental monitoring (§ 117.165(a)(3)).[30, 31] Environmental monitoring programs involve systematic

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[26] See § 117.135.
[27] The monitoring discussed in this section is monitoring as specified in § 117.145. See section V.D for recommendations for environmental monitoring as specified in § 117.165(a)(3).
[28] The verification discussed in this section is verification as specified in § 117.155. See section V.D for recommendations for environmental monitoring as verification of implementation and effectiveness as specified in § 117.165(a)(3).
[29] This guidance focuses on sanitation controls for environmental pathogens as part of a sanitation program for plants that produce LMRTE foods. It does not address other preventive controls that could apply to the production of LMRTE foods, such as treatments to significantly minimize environmental pathogens (or other pathogens) that could be present in the food or to control hazards that are not biological hazards (such as food allergen hazards). See the PCHF guidance for information on other preventive controls applicable to environmental pathogens (or other pathogens) and to hazards that are not biological hazards.
[30] See § 117.165(b)(3) for the requirements for written procedures for environmental monitoring.
[31] For a manufacturer of infant formula, such environmental monitoring would also be an appropriate mechanism to comply with § 106.55(a) for a system of process controls covering all stages of processing that is designed to ensure that infant formula does not become adulterated due to the presence of microorganisms in the formula or in the processing environment.

sampling and testing of the production environment to identify potential sources of contamination, including pathogens. A well-designed environmental monitoring program promotes a "seek and destroy" (also referred to as "find and fix") approach to identifying and eliminating environmental pathogens. A "seek and destroy" approach means that a facility is able to apply its existing knowledge about the potential for contamination and use that information to "seek" the pathogens by collecting samples from the environment. Part 117 requires that you include written procedures for your environmental monitoring program in your food safety plan (§§ 117.165(b)(3) and 117.126(b)(7)).

Once samples are collected, they are tested to determine the presence of pathogens (or an appropriate indicator organism, where applicable).[32, 33] Part 117 requires that you include your test results in your implementation records (§§ 117.155(b) and 117.190(a)(4)(vi)). When test results are positive for the pathogen or appropriate indicator organism, you can then take steps to eliminate ("destroy") the microorganism on those surfaces from the environment (e.g., by sanitizing the surface on which it was found).

We recommend that you analyze the verification data that you collect through your environmental monitoring program over time for trends (e.g., an increase in the percentage of overall positive environmental samples in the plant). Conducting such trend analyses can help to:

- continuously improve sanitary conditions in a plant;
- identify early when a problem could be developing in a particular area;
- determine whether there is an environmental pathogen in your plant that is not being controlled (e.g., if a resident strain has become established in a harborage site); and
- inform the type of corrective action and verification activities that can adequately remediate identified contamination.

Examples of trends that could indicate that an environmental pathogen in your plant is not being controlled are:

- increases in positive environmental samples in particular sites or areas;
- finding positive environmental samples in the same area on multiple but non-consecutive sampling occasions (e.g., positive one week and again at later sampling with intervening negative samples, so that these positive samples appear to be isolated positives rather than an indication of a potential resident strain);
- an increase in the percentage of overall positive environmental samples in the plant; and
- multiple cycles of cleaning and sanitizing that have failed to eliminate the environmental pathogen.

[32] While testing environmental surfaces for Enterobacteriaceae provides some information on the conditions within the facility, the presence or absence of Enterobacteriaceae on environmental surfaces is not a reliable indicator for the presence of *Cronobacter* spp. (See, e.g., 79 FR 7934 at 7983-7984, February 10, 2014).

[33] There continues to be insufficient data to establish a correlation between the presence of Enterobacteriaceae and *Salmonella* spp. during the production of powdered infant formula. In addition, we are not aware of any information supporting the use of an indicator organism for the purpose of environmental monitoring for *Salmonella* spp. during the production of other foods, particularly dried foods (78 FR 17142 at 17147; 79 FR 7934 at 7983-7984).

If your verification data continue to return positive results for contamination after one or more cycles of cleaning and sanitizing, this could mean that your cleaning and sanitizing is not effective and that the environmental pathogen is not being controlled.

In many cases, it could be helpful to visualize trends in your verification data using a map or diagram of your production environment. A map or diagram that you make (whether manually or electronically) showing positive findings could help you to better understand how repeated positive findings could relate to each other or how traffic patterns in the plant could be contributing to the spread of environmental pathogens in the environment.

See section V.G for recommendations for characterizing positive isolates so that you can determine whether isolates coming from different sampling sites are the same or closely related to each other. If an isolate obtained through your environmental monitoring program is positive for a pathogen on an FCS, we recommend that you treat that positive isolate as an investigative isolate (i.e., a sample for which you would conduct an RCI) and characterize it as described in section V.G.

E. Recommendations for Verification of Implementation and Effectiveness Through Product Testing[34] and Associated Trend Analysis

We recommend that the activities you conduct for verification of implementation and effectiveness include periodic sampling and testing of LMRTE foods.[35] While not an adequate verification on its own that your food safety system is controlling environmental pathogens, periodic sampling and testing can provide a historical reference of performance for the overall food safety system in your plant and verify the adequacy of your control of environmental pathogens over time. The frequency of such periodic sampling and testing would depend on considerations such as the food and the risk to the consumer if the production line was contaminated. Part 117 requires that you include written procedures for your product testing in your food safety plan (§§ 117.165(b)(2) and 117.126(b)(7)) and that you include your test results in your implementation records (§§ 117.155(b) and 117.190(a)(4)(v)).

We also recommend that you analyze the product testing verification data over time for trends that can help you to continuously improve the performance of your food safety system. As with trend analyses for environmental monitoring programs, trend analysis of product testing verification data could provide evidence whether your food safety system is adequately controlling an environmental pathogen.

If your sampling and testing identifies a pathogen in food,[36] we recommend that you treat that positive isolate as an investigative isolate and characterize it as described in section V.G.

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[34] See § 117.165(a)(2) and (a)(3).

[35] Part 106 prescribes specific requirements for testing representative samples of each production aggregate of powdered infant formula at the final product stage, before distribution (§ 106.55(c) and (e)). This guidance does not further address those specific testing requirements.

[36] In a letter dated March 8, 2023, to the infant formula industry, FDA asked that infant formula firms voluntarily notify the Agency any time a product sample is found to be positive for *Cronobacter* spp. or *Salmonella*, even if the affected lot(s) have not been distributed (Ref. 29).

F. Recommendations to Establish and Implement Corrective Action Procedures[37]

1. Recommendations to establish corrective action procedures[38]

Due to the nature of environmental pathogen hazards and the role of sanitation controls in your food safety system, we recommend that you establish corrective action procedures that would apply to the detection of a pathogen or appropriate indicator microorganism in food or in an environmental sample. Part 117 requires that you include written corrective action procedures in your food safety plan (§§ 117. 150(a)(1) and 117.126(b)(6)) and document your corrective actions (§§ 117.150(d) and 117.190(a)(3)). We recommend that these corrective action procedures include, as appropriate:

- convening a multidisciplinary team that has the appropriate expertise to plan and oversee controlled wet cleaning that may be necessary to adequately clean and sanitize affected FCSs;
- disassembly of equipment, with sampling and testing FCSs and other areas that could potentially be sources of contamination prior to cleaning the equipment;
- restoration of potentially affected FCSs to a clean, dry, sanitary condition before use[39] through remediation sanitation procedures that include a sanitizing treatment;
- verification, through collecting and testing environmental samples and product samples, that remediation sanitation procedures have effectively eliminated contamination;
- removal and replacement of contaminated equipment that cannot be adequately cleaned and sanitized; and
- follow-up with the supplier of a contaminated ingredient to determine the actions the supplier will take to prevent such future contamination.

2. Recommendations to implement corrective action procedures by conducting a root cause investigation to identify and correct problems and prevent recurrence[40]

One important aspect of corrective actions to remediate a contamination event is identifying the root cause. In some cases, the root cause of a pathogen contamination event could be obvious – e.g., if water leaks onto food processing equipment. In such cases, it could be possible to focus your actions to:

- correct the contamination event on the areas immediately surrounding, and downstream of, the observed contamination site; and
- prevent the problem from recurring by identifying the source of the water leakage and fixing it.

[37] See § 117.150.
[38] See § 117.150(a).
[39] See § 117.35(d)(1) (specifically requiring FCSs "be in a clean, dry, sanitary condition before use").
[40] See § 117.150(a)(2)(i) and (ii).

In other cases, the root cause of the pathogen contamination event could be more challenging to determine – e.g., if you detect a pathogen on an FCS during routine environmental monitoring, or in food during verification testing, and there is no obvious source of the contamination. In such cases, we recommend that you conduct an RCI to identify the source of the contamination. RCIs can extend over a period of time, depending on the nature of the investigation and the time to receive the results of analytical tests. Thus, some information from your RCI could be obtained early in the investigation whereas other information could take weeks to be received. Regardless, you should not delay taking initial corrective actions (such as collecting and testing environmental samples before cleaning and sanitizing a potentially affected FCS) even if you are not able to identify all appropriate corrective actions until the RCI is complete.

There are a number of steps you can include in your corrective action procedures as activities to conduct through an RCI, including:

- Examining the equipment that yielded the positive finding and the area surrounding the positive site in all directions for potential sources of the environmental pathogen, giving special attention to possible niches that could allow harborage of an environmental pathogen, or to any objects/materials that may have had direct contact with the equipment.
- Conducting intensified sampling and testing of environmental surfaces (both FCSs and non-FCSs):
    - with disassembly of equipment as necessary and appropriate to obtain environmental samples from surfaces that could have been affected by the contamination event, including testing upstream from the positive FCS in the production area to help identify a source of contamination and downstream to identify the extent of equipment contamination; and
    - by collecting environmental samples:
        - before cleaning and sanitizing the surfaces, so that you can determine whether those surfaces could have contributed to the contamination event; and
        - after cleaning and sanitizing the surfaces, so that you can determine whether the cleaning and sanitizing was effective.
- Reviewing the history of results from your environmental monitoring and product testing programs, including in-process or intermediate product testing, because this review could provide information on areas that could be potential sources of the environmental pathogen.
- Testing samples of ingredients to determine if an ingredient could be the source of the contamination.
- Checking maintenance records for modifications or repairs to equipment on which the food was processed, because maintenance activities can contribute to contamination events.
- Interviewing and observing sanitation, maintenance, and production personnel to determine whether appropriate procedures are being followed.
- Reviewing production, maintenance, and sanitation procedures and applicable records documenting implementation of those procedures to determine whether to modify the

procedures to prevent contamination and then make those modifications identified by the review.

- Reviewing traffic patterns, equipment layout, and adherence to personnel hygiene procedures to determine if these could have contributed to the pathogen contamination event.
- When necessary and appropriate, implementing "hold and test" procedures[41] when restarting production as a verification that the pathogen contamination event has been resolved.
- After restarting production, conducting intensified sampling and testing of sites that represent a potential source of the environmental pathogen, including collecting samples several times during production to confirm that environmental pathogens are not detected.

See section V.G for recommendations for characterizing positive isolates during an RCI.

3. Recommendations for identifying affected food[42]

To identify affected food, we recommend that the steps you include in your corrective action procedures:

- consider that all food produced since the last sanitation break is affected; and
- when appropriate, consider expanding the scope of affected food to beyond food produced since the last sanitation break based on the findings of your RCI. For example:
  - If the RCI implicates a contaminated ingredient as the source of the contamination, then all food produced using that contaminated ingredient could be affected; or
  - If the RCI identifies a resident strain in or on an FCS that was not cleaned and sanitized during the sanitation break, then all food produced since the last time that FCS was cleaned and sanitized could be affected.

There are limited circumstances in which it might be possible to limit the scope of affected food based on the outcome of an RCI or root cause analysis. Examples of such limited circumstances could include:

- If you conclusively identify when the production system became contaminated, and you determine that all food produced before that contamination event was not subjected to the insanitary conditions created by the contamination event, then you could have a basis to conclude that food produced before the contamination event is not affected.
- If you conclusively determine that the root cause of the contamination event is a contaminated ingredient, and you have documentation of the date when you began using the contaminated ingredient, then you could have a basis to conclude that only food produced after you began using the contaminated ingredient is affected.

[41] By "hold and test," we mean hold the food under your control pending the results of microbial testing. This guidance does not provide detailed recommendations regarding "hold and test" procedures. When implementing "hold and test" procedures, we recommend that you consult ICMSF's scientifically based sampling plans that can be used to provide statistical confidence for results of product testing (Ref. 30).
[42] See § 117.150(a)(2)(iii).

See section II.E regarding an investigation of an LMRTE pathogen contamination event that revealed an inappropriate reliance on product testing to identify food affected by that event. The findings of this investigation are consistent with our long-standing view[43] that microbiological finished product testing, even when using a robust sampling plan, has a role in identifying affected food, but nonetheless has limitations that prevent its use, in many circumstances, as the only means of verifying implementation and effectiveness of preventive controls as required by § 117.165 and identifying affected food as required by § 117.150. When a hazard is present at very low levels and is not uniformly distributed, microbiological finished product testing alone cannot ensure the absence of a hazard in the food and generally is insufficient to determine and limit the scope of affected food.

The records you establish and maintain as documentation of your corrective actions[44] should include your justification for the scope of food affected by the contamination event.

G. Recommendations for Characterizing Isolates Obtained During Verification Testing and Root Cause Investigations

We recommend that you further characterize any pathogen isolate obtained during routine verification activities (e.g., environmental monitoring, ingredient testing, or product testing) or during corrective actions (e.g., investigative sampling) so that you can determine whether isolates obtained from different sampling sites or on different sampling occasions are the same or closely related to each other. Knowing whether a pathogen isolate is the same or closely related to those previously found on environmental surfaces or in product at your facility can better enable you to identify and implement appropriate and effective corrective actions, including steps to prevent the contamination from recurring.

Pathogen isolates can be characterized by serological methods (e.g., serotyping) and/or molecular methods (e.g., pulsed field gel electrophoresis (PFGE) and whole genome sequencing (WGS)). Of these methods, WGS provides the most definitive information as to whether a particular pathogen isolate is the same as, or closely related to, pathogen isolates previously found in your plant and, thus, is considered the most discriminating method (Ref. 31).[45]

- Serotyping of O (somatic, or outer membrane) antigens and H (flagellar) antigens has historically been used to characterize *Salmonella* isolates and is often a first step in characterizing the potential relationship between isolates (Ref. 31 and Ref. 32). However, there are over 2500 serotypes of *Salmonella* and over 150 different antisera for typing (Ref. 31). Serotyping is not always sufficient to discriminate between different *Salmonella* strains of the same serotype (Ref. 31). For example, most *Salmonella* Enteritidis isolates have been shown to be genetically homogeneous, and it has been difficult to discriminate between strains even using molecular methods such as PFGE (Ref. 33).
- PFGE uses molecular subtyping to generate one type of genetic "fingerprint" of a pathogen such as *Salmonella* and *Cronobacter*. The method involves cutting the DNA of

[43] See the discussion of the role of testing as a verification measure in a modern food safety system at 78 FR 17142 at 17143 to 17151.
[44] See § 117.150(d).
[45] Over time, we expect that additional technologies for characterizing isolates will become available.

a bacterium with an enzyme ("enzyme restriction"), separation of the restriction fragments by size using PFGE, and comparison of banding patterns to those of other bacterial isolates for relatedness (Ref. 34). However, it is difficult for PFGE to discriminate between strains of genetically homogeneous isolates, such as *Salmonella* Enteritidis (Ref. 33 and Ref. 35).

- WGS uses DNA sequencing to provide a detailed fingerprint of a pathogen (Ref. 31). The DNA is cut into shorter pieces and the nucleotide sequence of bases is determined. WGS is more discriminating than PFGE (Ref. 31) and can distinguish strains that have the same PFGE pattern (Ref. 35).[46] Although the use of WGS for characterizing environmental pathogens detected through an environmental monitoring program previously has not been widespread (Ref. 31 and Ref. 37), the increasing availability of laboratories that can sequence microbial isolates and process data obtained from those isolates is now making WGS an efficient and effective tool for characterizing positive isolates.

Because characterization methods such as serotyping and PFGE are less discriminating than WGS, they are less useful in determining whether isolates are the same and, thus, are an indication of a resident strain. If you characterize pathogen isolates found in your facility over time using serotyping or PFGE, you should consider isolates with the same serology or PFGE pattern to represent the same strain for the purposes of taking corrective actions.[47] You also should save your pathogen isolates so that you can characterize them by WGS later, if needed (e.g., as part of an RCI following a contamination event).

During an RCI, we recommend that you use WGS to characterize any pathogen isolates. WGS has the strongest discriminating power of the methods currently available for characterizing isolates and is particularly useful during an RCI when several isolates are obtained and a goal of the investigation is to determine whether they are the same strain with a common source (Ref. 31). For example, in the case of product contamination that repeats in a food plant over time, WGS can help to distinguish between repeated contamination of the food by an environmental pathogen that persists in the food plant and repeated reintroduction of the environmental pathogen from an outside source (Ref. 38). If it appears that contamination is being introduced through a contaminated ingredient, then testing ingredients, characterizing any positives, and comparing the isolates from positive ingredients to isolates from positive finished product can be helpful to determine if an ingredient is the source of the isolate obtained from finished product. You should use information gained from WGS to evaluate if further corrective actions are necessary.

Conducting WGS routinely on pathogen isolates (including those isolates obtained from your routine testing of environmental surfaces (in particular isolates from FCSs and from non-FCSs near FCSs), ingredients, and product) can facilitate the rapid comparison to isolates obtained during RCIs following a pathogen contamination event.

[46] A network of public health and university laboratories collect and share genomic and geographic data from foodborne pathogens for real-time comparison and analysis that can speed foodborne illness outbreak investigations. The data are housed in public databases at the National Center for Biotechnology Information and can be accessed by researchers and public health officials (Ref. 36).

[47] The same would be true of other non-WGS characterization methods not discussed in this guidance.

H. Recommendations for Reanalysis[48]

We recommend that your reanalysis regarding environmental pathogens consider whether environmental pathogens other than *Salmonella* spp. and *Cronobacter* spp. have emerged as known or reasonably foreseeable hazards for LMRTE foods in general or your particular LMRTE food.

VI. Recommendations for Remediation of a Pathogen Contamination Event

The specific actions you take following a pathogen contamination event depend on the nature of that contamination event, e.g., whether you have identified a pathogen in the food you have produced or whether you have identified a pathogen on an FCS through your environmental monitoring program. They also depend, in part, on the regulatory framework that applies to you – e.g., whether you are subject to the PCHF requirements and whether your product is a PIF that is also subject to part 106.

In general, when you become aware of a pathogen contamination event:

- you must:
  - use microbial testing procedures where necessary to identify sanitation failures or possible food contamination (see § 117.80(a)(5));
  - reject or, if appropriate, treat or process all food that has become contaminated to the extent that it is adulterated[49] to eliminate the contamination (see § 117.80(a)(6));
  - take the corrective actions required by § 117.150 (if you are subject to the PCHF requirements); and
  - not approve and release for distribution PIF (see § 106.70(d)); and
- you should:
  - stop production on the line on which a contaminated product has been produced or on which an FCS has tested positive for a pathogen; and
  - clean and sanitize all potentially affected FCSs to return them to a clean, dry, sanitary condition before use (see § 117.35(d)(1)), limiting the use of water in dry production areas to the greatest extent possible.

Cleaning techniques are distinct from sanitizing treatments in that cleaning techniques remove soil from the FCS, whereas sanitizing treatments destroy (i.e., kill) microorganisms that contaminate that surface. We are not aware of any scientific or technical information that would support a conclusion that dry-cleaning techniques (such as material flush techniques) are adequate to remediate a pathogen contamination event unless accompanied by a sanitizing

[48] See § 117.170.

[49] Part 106 specifies criteria whereby PIF that is contaminated with *Cronobacter* spp. or *Salmonella* spp. shall be deemed adulterated under sections 402(a)(1), 402(a)(4), and 412(a)(3) of the FD&C Act (see § 106.55(e)). We have provided our current thinking on when food that is contaminated with *Salmonella* spp. is adulterated under section 402(a)(1) of the FD&C Act in Compliance Policy Guide Sec. 527.300 Dairy Products - Microbial Contaminants and Alkaline Phosphatase Activity (Ref. 39) and Compliance Policy Guide Sec. 555.300 Foods, Except Dairy Products - Adulteration with *Salmonella* (Ref. 40).

treatment. Research studies conducted to evaluate the effectiveness of dry-cleaning techniques (i.e., material flush techniques) to remediate a pathogen contamination event consistently demonstrate that such techniques do not eliminate microbiological contamination from FCSs when they do not include a sanitizing treatment.[50] In the absence of any scientific or technical information to support a conclusion that dry-cleaning techniques, by themselves, are adequate to return FCSs to a clean, dry, sanitary condition before use as required by § 117.35(d)(1), it is our current view that:

- there are significant limitations to dry-cleaning procedures that do not include a sanitizing treatment to effectively eliminate pathogens; and
- adequate remediation for FCSs after a pathogen contamination event includes both cleaning and sanitizing.

During some investigations that followed pathogen contamination events associated with LMRTE foods, we have observed the use of material flush techniques to clean contaminated FCSs without an accompanying sanitizing treatment (Ref. 20, Ref. 21, and Ref. 22). We have been asked to provide information on considerations associated with potentially demonstrating the adequacy of such procedures. Such considerations include:

- the design and construction of equipment to facilitate the flow of material through the system; the design and normal operating conditions of manufacturing equipment that recirculates part of the product stream at certain sections of the process during normal operations (e.g., a partial recirculation of the product stream at the filling step);
- how the chemical and physical attributes of material could cause it to adhere in production equipment rather than flow freely (e.g., some formulated dry powders are less hygroscopic and flow relatively easily over and through equipment surfaces, whereas other formulated dry powders are more hygroscopic and tend to stick to equipment surfaces); and
- how to determine that all FCSs have been adequately cleaned when some FCSs (e.g., narrow pipes) are not accessible (e.g., when necessary for sampling and verification testing for the presence of pathogens), and when it generally is not practical to collect and test samples that cover the entire production system.

[50] See Appendix 2 for a summary of these research studies.

VII. Glossary of Terms That FDA Uses in This Guidance

The following glossary of terms is intended for use in this guidance regarding establishing sanitation programs for LMRTE human foods and corrective actions following a pathogen contamination event.

Clean in place: A system used to clean process piping, bins, tanks, mixing equipment, or larger pieces of equipment without disassembly, where interior product zones are fully exposed and soil can be readily washed away by the flow of the cleaning solution.

Clean out of place: A method (e.g., using cleaning tanks) used to clean equipment parts and ancillary items including piping and valves after disassembly by taking them from the production area to a designated cleaning area.

Cleaning: The removal of soil, including food residue, dirt, grease, or other objectionable matter, from a surface.

Controlled wet cleaning: The removal of soil, including food residues, dirt, grease, or other objectionable matter, from a surface, using a limited amount of water and detergents and controlling the spread of the water used.

Corrective action: An action to identify and correct a problem that occurred during the production of food, reduce the likelihood that the problem will recur, evaluate all affected food for safety, and prevent affected food from entering commerce.

Dry cleaning: The physical removal of soil, including food residues, dirt, grease, or other objectionable matter, from a surface by actions such as wiping, sweeping, brushing, scraping, or vacuuming the residues without water.

Environmental sample: A sample that is collected from a surface, such as equipment or an area of the plant, for the purpose of testing the surface for the presence of microorganisms.

Hold and test procedures: Procedures establishing the criteria for retaining and releasing food until receiving the results of tests conducted to determine the presence of a pathogen on an FCS or in a food.

Intensified sampling and testing: Collecting and testing follow-up samples, including follow-up product samples when product has tested positive and follow-up environmental samples to a positive test site (which could include samples collected from both FCSs and non-FCSs in close proximity to a positive environmental site).

Intensified cleaning and sanitizing: Sanitation measures that are performed in addition to normal sanitation procedures and are escalated in response to continuing findings of positive product samples or positive environmental samples. Intensified cleaning and sanitizing can include increasing the frequency of cleaning and sanitizing for certain pieces of equipment, breaking down the equipment into its parts for further cleaning, and steam treating equipment.

Low-moisture food: A food that has a water activity of 0.85 or below.

Material flush: The movement of uncontaminated product or other material through a production system to push out product in the system.

Pathogen contamination event: Contamination of food or an FCS with a pathogen.

Root cause: The basic or fundamental reason behind a problem.

Root cause analysis: A retrospective evaluation of information from a root cause investigation of a food safety problem to determine what actions can be taken to eliminate the root cause(s) and prevent a recurrence of the problem.

Root cause investigation: An investigation used to attempt to determine the root cause(s) of a food safety problem by systematically examining and evaluating all aspects of the manufacturing process, including the environment, and provide information for use in determining factors that could have contributed to the problem, actions that can be taken to fix the problem, and actions to prevent the problem from recurring.

Sanitation: The process of removing soil and reducing microbiological contaminants on a surface.

Sanitation break: Stopping production to clean and sanitize all FCSs in the production system.

Wet-cleaning procedures: The removal of soil, including food residues, dirt, grease or other objectionable matter, from a surface using water and detergents.

VIII. Abbreviations Used in This Guidance

Abbreviation	What It Means
CGMP	Current good manufacturing practice
FCS	Food-contact surface
FDA	U.S. Food and Drug Administration
FD&C Act	Federal Food, Drug, and Cosmetic Act
GMA	Grocery Manufacturers Association
LMRTE	Low-moisture ready-to-eat food
PCHF	Hazard Analysis and Risk-Based Preventive Controls for Human Food
PIF	Powdered infant formula
RCI	Root cause investigation
RTE food	Ready-to-eat food

IX. References

The following references marked with an asterisk (*) are on display at the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. You may see them in person at this location between 9 a.m. and 4 p.m., Monday through Friday; they are also available electronically at https://www.regulations.gov. References without asterisks are not on public display at https://www.regulations.gov because they have copyright restriction. Some may be available at the website address, if listed. References without asterisks are available for viewing only at the Dockets Management Staff. FDA has verified the website addresses, as of the date this document publishes in the Federal Register, but websites are subject to change over time.

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Appendix 1. Regulatory Framework for the Manufacturing/Processing of Low-Moisture RTE Food

A. Part 117

1. Requirements of part 117

Part 117 covers the manufacturing, processing, packing, and holding of human food. Part 117 contains 7 subparts (subparts A through G) that each have a specific focus. Some of the requirements of part 117 address CGMPs for human food ("part 117 CGMP requirements"). The part 117 CGMP requirements are primarily in subpart B, with associated requirements in subparts A and F. This guidance provides recommendations for a sanitation program for LMRTE food that includes measures to comply with the following part 117 CGMP requirements:

- requirements for sanitary operations regarding general maintenance of the physical plant (§ 117.35(a)), sanitation of FCSs (§ 117.35(d)), and sanitation of non-FCSs (§ 117.35(e));
- requirements for equipment and utensils (§ 117.40(a)(1), (a)(3), and (b));
- requirements for general processes and controls, including requirements for:
  - testing where necessary to identify sanitation failures (§ 117.80(a)(5)); and
  - rejecting or treating all food that has become contaminated to the extent that it is adulterated (§ 117.80(a)(6)); and
- requirements for manufacturing operations, including:
  - maintaining equipment and utensils and food containers in an adequate condition through appropriate cleaning and sanitizing, as necessary, and taking equipment apart for thorough cleaning insofar as necessary (§ 117.80(c)(1)); and
  - requiring all food manufacturing, processing, packing, and holding to be conducted under such conditions and controls as are necessary to minimize the potential for the growth of microorganisms and contamination of food (§ 117.80(c)(2)).

Other requirements of part 117 address "hazard analysis and risk-based preventive controls for human food" ("PCHF requirements"). The PCHF requirements are primarily in subparts C and G, with associated requirements in subparts A, D, E, and F. The PCHF requirements largely reflect a sequence of activities. For example, the requirement for hazard analysis leads a facility to determine which hazards require a preventive control. The facility then identifies and implements appropriate preventive controls, together with appropriate "preventive control management components" (i.e., monitoring, verification, corrective actions, and reanalysis) for each preventive control. This guidance provides recommendations for a sanitation program that addresses the following PCHF requirements:

- requirements for conducting a hazard analysis to determine whether there are any hazards (including environmental pathogens) requiring a preventive control (§ 117.130), which include:
  - requirements for hazard analysis (§ 117.130(a));
  - requirements for hazard identification (§ 117.130(b)); and

  - requirements for hazard evaluation (§ 117.130(c)). The requirements for hazard evaluation include:
    - a requirement to assess the severity of the illness or injury if the hazard were to occur and the probability that the hazard will occur in the absence of preventive controls (§ 117.130(c)(1)(i)); and
    - a requirement that is specific to RTE foods – i.e., the hazard evaluation must include an evaluation of environmental pathogens whenever an RTE food is exposed to the environment prior to packaging and the packaged food does not receive a treatment or otherwise include a control measure (such as a formulation lethal to the pathogen) that would significantly minimize the pathogen (§ 117.130(c)(2)(ii)).

- requirements to identify and implement preventive controls to provide assurances that any hazards requiring a preventive control will be significantly minimized or prevented and the food manufactured, processed, packed, or held by your facility will not be adulterated under section 402 of the FD&C Act (§ 117.135(a)(1)), including sanitation controls (§ 117.135(c)(3)); and
- requirements for preventive control management components (§ 117.140) for:
  - monitoring sanitation controls (§ 117.145);
  - verifying implementation and effectiveness of sanitation controls (§ 117.165), specifically through:
    - environmental monitoring (§ 117.165(a)(3) and (b)(3)); and
    - product testing (§ 117.165(a)(2) and (b)(2)); and
  - establishing and implementing corrective actions if sanitation controls are not properly implemented (§ 117.150).

Subpart F specifies general requirements applying to all required records. Required records include the food safety plan (§ 117.126) and implementation records (§ 117.190). The food safety plan includes requirements for a written hazard analysis, written preventive controls, a recall plan, and written procedures for preventive control management components. This guidance provides recommendations for implementation records for corrective actions (§ 117.150(d)).

2. Persons subject to part 117

With some exceptions (such as for farms)[52], the part 117 CGMP requirements apply to all persons who manufacture, process, pack, or hold human food,[53] including manufacturers of PIF.

[52] See § 117.5(k) for a complete list of exemptions from the CGMP requirements,

[53] Restaurants and retail food establishments (as defined in § 1.227) are not required to register as a food facility (see § 1.226) and generally are inspected by State or local regulatory agencies, often under State or local laws and regulations based on FDA's Food Code (Ref. 41). FDA's Food Code is a model that assists food control jurisdictions at all levels of government by providing a scientifically sound technical and legal basis for regulating the retail and foodservice segment of the industry (e.g., restaurants, grocery stores, and institutions such as nursing homes). Food control jurisdictions (e.g., at the local, State, and tribal level) use the FDA Food Code as a model to develop or update their own food safety rules and to be consistent with national food regulatory policy.

With some exceptions [54], the PCHF requirements generally apply to the owner, operator, or agent in charge of those domestic and foreign facilities that manufacture, process, pack, or hold human food and are required to register as a food "facility."[55] The exception that is most relevant to the manufacturing/processing of LMRTE foods is the exemption for "qualified facilities" (e.g., facilities that are a very small business as defined in § 117.3; see the exemption in § 117.5(a)). A "qualified facility" is subject to the part 117 CGMP requirements but is exempt from the PCHF requirements in subpart C (Hazard Analysis and Risk-Based Preventive Controls) and subpart G (Supply-Chain Program) and is instead subject to modified PCHF requirements in subpart D (see § 117.201).

3. Compliance criteria specified in part 117

- The criteria and definitions in part 117 apply in determining whether a food is:
  - adulterated within the meaning of: (1) section 402(a)(3) of the FD&C Act in that the food has been manufactured under such conditions that it is unfit for food; or (2) section 402(a)(4) of the FD&C Act in that the food 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 (§ 117.1(a)(1)); and
  - in violation of section 361 of the Public Health Service Act (42 U.S.C. 264) (§ 117.1(a)(2)).
- Part 117 specifies that failure of the owner, operator, or agent in charge of a facility to comply with the PCHF requirements of part 117 is prohibited by section 301(uu) of the FD&C Act (21 U.S.C. § 331(uu)) (see § 117.1(b)).
- Subpart E of part 117 provides that FDA may withdraw a qualified facility exemption in circumstances such as active investigation of a foodborne illness outbreak that is directly linked to the qualified facility (§ 117.251(a)(1)) or based on conditions or conduct associated with the qualified facility (§ 117.251(a)(2)).

4. Comprehensive guidance that FDA has announced for the PCHF requirements

Beginning in 2016, we have announced the availability for public comment of several chapters of a multi-chapter draft guidance for industry titled "Hazard Analysis and Risk-Based Preventive Controls for Human Food: Guidance for Industry" (81 FR 57816, August 24, 2016; 82 FR 41364, August 31, 2017; 83 FR 3449, January 25, 2018; 84 FR 53347, October 7, 2019; and 88 FR 66457, September 27, 2023). This multi-chapter draft guidance (Ref. 28) is intended to explain our current thinking on how to comply with the PCHF requirements. We intend to announce the availability for public comment of additional chapters of the draft guidance,

[54] See § 117.5 for a complete list of exemptions from the PCHF requirements.
[55] Under section 415 of the FD&C Act (21 U.S.C. 350d), the requirement to register as a food facility applies to facilities engaged in the manufacturing/processing, packing, or holding of food for consumption in the United States. (See 21 CFR part 1, subpart H). Under section 415 of the FD&C Act, FDA may suspend registration of a facility if FDA determines that the food poses a reasonable probability of serious adverse health consequences or death. A facility that is under suspension is prohibited from distributing food.

including guidance on sanitation controls, as we complete them. When finalized, this multi-chapter guidance will reflect FDA's current thinking on this topic.

B. Infant Formula CGMP Requirements in Part 106

1. Infant formula CGMP requirements

In addition to the part 117 requirements for LMRTE foods, this guidance addresses the CGMP requirements specific to the manufacture and processing of infant formula found in part 106, subpart B ("part 106 CGMP requirements"). With few exceptions,[56] if you manufacture/process PIF, you are subject to the part 106 CGMP requirements.

The part 106 CGMP requirements define the minimum CGMPs that are to be used in, and the facilities or controls that are to be used for, the manufacture, processing, packing, or holding of an infant formula. This guidance provides recommendations for a sanitation program that includes measures to comply with the following part 106 CGMP requirements:

- implementation and documentation of a production and in-process control system (§ 106.6 and § 106.100(e)(3));
- controls to prevent adulteration caused by physical facilities (§ 106.20(a)), with associated records (§ 106.100(f)(1));
- controls to prevent adulteration caused by equipment or utensils (§ 106.30(a), (b), and (f)), with associated records (§ 106.100(f)(2), 106.100(f)(3), and 106.100(f)(4));
- controls to prevent adulteration from microorganisms (§ 106.55(a)) and to test representative samples of each production aggregate of powdered infant formula at the final product stage, before distribution, to ensure that each production aggregate meets specified microbiological quality standards for *Cronobacter* spp. and *Salmonella* spp. (§ 106.55 (c) and (e), with associated records in § 106.55(d) and § 106.100(e)(5)(ii) and 106.100(f)(7)); and
- controls on the release of finished infant formula (§ 106.70(d)).

2. Compliance criteria specified in the infant formula CGMP requirements

If the processing of an infant formula does not comply with any regulation in part 106, subpart B, the formula will be deemed to be adulterated under section 412(a)(3) of the FD&C Act (§ 106.1(a)).

PIF that contains any microorganism that exceeds the value listed for that microorganism in § 106.55(e)[57] shall be deemed adulterated under sections 402(a)(1), 402(a)(4), and 412(a)(3) of the FD&C Act (21 U.S.C. 350a(a)(3)).

[56] See, e.g., the provisions of § 107.50, in 21 CFR part 107, Subpart C—Exempt Infant Formulas. See also FDA's Guidance for Industry: Exempt Infant Formula Production (Ref. 42).
[57] The microbiological quality standards in § 106.55(e) include standards for *Cronobacter* spp. and *Salmonella* spp.

C. How to Determine Which Recommendations Apply to You

If you manufacture/process an LMRTE food and satisfy one of the criteria in § 117.5 for an exemption from subparts C and G of the PCHF requirements (e.g., if you satisfy the definition of "qualified facility" in § 117.3), all the part 117 CGMP recommendations in this guidance apply to you.

If you manufacture/process an LMRTE food and do not satisfy one of the criteria in § 117.5 for an exemption from subparts C and G of the PCHF requirements, all the part 117 recommendations in this guidance (both part 117 CGMP recommendations and PCHF recommendations) apply to you.

If the LMRTE food that you manufacture/process is a non-exempt PIF, all the part 106 CGMP recommendations also apply to you.[58]

[58] Consistent with FDA's Guidance for Industry: Exempt Infant Formula Production (Ref. 42), we recommend that manufacturers of exempt PIF also follow these recommendations.

Appendix 2. Research Regarding Adequacy of Material Flush Techniques

Research studies carried out to evaluate the effectiveness of material flush techniques to remediate a pathogen contamination event in a dry food production environment have consistently demonstrated that such techniques do not eliminate microbiological contamination from FCSs when they do not include a sanitizing treatment.

One study evaluated survival of *Salmonella* on inert contact surfaces such as beads of stainless steel and polypropylene and transfer of *Salmonella* from these surfaces to low-moisture foods (Ref. 15). Three dry food ingredients (wheat flour, corn meal, and sodium chloride) were used to remove *Salmonella* from contaminated beads. Sequential "rinses" of contaminated beads with uncontaminated dry ingredients showed significant differences based on both surface contact material type and food material. *Salmonella* levels on stainless steel were reduced by "rinsing" with dry food ingredients, but *Salmonella* removal from polypropylene by rinsing with dry ingredients was negligible. The authors noted that "the nearly ubiquitous presence of plastics designed into equipment in a dry processing facility could make a purge-flush method of cleaning untenable."

Another study looked at the effectiveness of dry purging for removing *Salmonella* from a contaminated lab scale auger conveyor system (Ref. 16). Contaminated flour was conveyed through the system, followed by uncontaminated flour or corn meal (ten times the volume of the contaminated flour). The "push-through" material was sampled and tested for *Salmonella* and the FCSs were swabbed after the process. The study indicated that *Salmonella* might not be completely removed from a contaminated powder conveyor system using dry purging alone.

Another study, which was conducted in a pilot-scale peanut butter processing system, evaluated the effectiveness of hot oil as a material flush, alone and in combination with a sanitizing agent (Ref. 14). A single step remediation procedure that focused on hot oil cleaning, without application of a sanitizing treatment, was not effective in removing *Salmonella* on contaminated equipment.