Hazard Analysis and Risk-Based Preventive Controls for Human Food: Draft Guidance for Industry[1]

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Chapter 4: Preventive Controls

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[1] This guidance has been prepared by the Office of Food Safety in the Center for Food Safety and Applied Nutrition at the U.S. Food and Drug Administration. Underlined text in yellow highlights represents a correction from the draft Chapter 4 that we issued for public comment in August 2016.

4.1 Purpose of this Chapter

The guidance provided in this chapter is intended to help you identify and implement preventive controls. The PCHF requirements specify that you must 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 Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C 342) or misbranded under section 403(w) of the FD&C Act (21 U.S.C. 343(w)). (See 21 CFR 117.135(a)(1)). This chapter provides an overview of common preventive controls that you could use to significantly minimize or prevent the occurrence of biological, chemical, and physical hazards in food products and the food production environment when the outcome of your hazard analysis is that one or more of these hazards requires a preventive control.

The guidance in this chapter also is intended to help you monitor the preventive controls that you identify and implement. As appropriate to the nature of the preventive control and its role in the facility's food safety system, the PCHF requirements specify that you must establish and implement written procedures, including the frequency with which they are to be performed, for monitoring the preventive control, and to monitor the preventive controls with adequate frequency to provide assurance that they are consistently performed. (See 21 CFR 117.145.)

This chapter does not provide all the details needed for identifying and implementing preventive controls. You have the flexibility to identify and implement preventive controls from among all procedures, practices, and processes that are available to you and that would provide assurances that the hazard is controlled (i.e., significantly minimized or prevented).

4.2 Overview of Preventive Controls

Part 117 defines "preventive controls" as those risk-based, reasonably appropriate procedures, practices, and processes that a person knowledgeable about the safe manufacturing, processing, packing, or holding of food would employ to significantly minimize or prevent the hazards identified by the hazard analysis that are consistent with the current scientific understanding of safe food manufacturing, processing, packing, or holding at the time of the analysis. (See 21 CFR 117.3.) Preventive controls include: (1) Controls at critical control points (CCPs), if there are any CCPs; and (2) controls, other than those at CCPs, that are also appropriate for food safety (See 21 CFR 117.135(a)(2)). The PCHF requirements specify that preventive controls must be written. (See 21 CFR 117.135(b)).The PCHF requirements also specify that preventive controls must include, as appropriate to the facility and the food: (1) Process controls; (2) Food allergen controls; (3) Sanitation controls; (4) Supply-chain controls; (5) Recall plan; and (6) Other controls. (See 21 CFR 117.135(c)).

Table 4-1 lists the sections in this chapter in which we address process controls, sanitation controls, food allergen controls, supply-chain controls, and recall plans. Although Table 4-1 includes supply-chain controls, we intend to provide more information in our forthcoming "Chapter 15 - Supply-Chain Program for Human Food Products." See Chapters 6 through 14 of this guidance for more detailed discussion of applicable preventive controls.

Table 4-1. Preventive Controls Addressed in this Chapter

Preventive Control	Chapter Section
Process Controls	4.3
Sanitation Controls	4.4
Food Allergen Controls	4.5
Supply-chain Controls	4.6
Recall Plans	4.7

Table 4-2 lists the chapters in this guidance in which we provide additional details regarding certain preventive controls.

Table 4-2. Other Chapters in the Guidance With Additional Information About Specific Preventive Controls

Preventive Control	Chapter

Preventive Control	Chapter
Heat Treatment Process Control	6
Time/Temperature Control Process Control	7
Formulation Process Control (e.g., water activity, pH, and chemical preservatives)	8
Dehydration/Drying Process Control	9
Sanitation Controls	10
Food Allergen Controls	11
Preventive Controls for Chemical Hazards	12
Preventive Controls for Physical Hazards	13
Recall Plan	14

The PCHF requirements specify that you must validate that the preventive controls that you identify and implement are adequate to control the hazard as appropriate to the nature of the preventive control and its role in the facility's food safety system. (See 21 CFR 117.160(a)). The PCHF requirements also specify that validation of the preventive controls must be performed (or overseen) by a preventive controls qualified individual. (See 21 CFR 117.160(b) and the definition of a preventive controls qualified individual in 21 CFR 117.3.) You do not need to validate: (1) Food allergen controls; (2) sanitation controls; (3) the recall plan; and (4) the supply-chain program. You also do not need to validate other preventive controls, if the preventive controls qualified individual prepares (or oversees the preparation of) a written justification that validation of the other control is not applicable based on factors such as the nature of the hazard, and the nature of the preventive control and its role in the facility's food safety system. (See 21 CFR 117.160(c).) We intend to discuss validation in "Chapter 16: Validation of a Process Control."

4.3 Process Controls

Process controls include procedures, practices, and processes to ensure the control of parameters during operations such as heat processing, acidifying, irradiating, and refrigerating foods. Process controls must include, as appropriate to the nature of the applicable control and its role in the facility's food safety system: (1) Parameters associated with the control of the hazard; and (2) the maximum or minimum value, or combination of values, to which any biological, chemical, or physical parameter must be controlled to significantly minimize or prevent a hazard requiring a process control. (See 21 CFR 117.135(c)(1).) Process controls do not include those procedures, practices, and processes that are not applied to the food itself, e.g., controls of personnel or the environment that may be used to significantly minimize or prevent hazards.

Examples of processing parameters that can have a minimum or maximum value (or combination of values) include time, temperature, flow rate, line speed, product bed depth, weight, product thickness or size, viscosity, moisture level, water activity, salt concentration, pH and others, depending upon the process. If a process parameter does not meet a minimum or maximum value (or critical limit), the process is not in control (i.e., a deviation has occurred) and the potential for producing a product that presents a consumer-health risk exists.

Many process controls, such as the application of heat to a food to adequately reduce pathogens, are applied in the same manner and for the same purpose as control measures established within HACCP plans and applied at CCPs as recommended by the National Advisory Committee on Microbiological Criteria for Foods (NACMCF, 1998) and the Codex Alimentarius Commission (CAC, 2003). When a process control is applied to a CCP in a HACCP plan, the maximum or minimum values (or combination of values) for the parameters associated with the control of the hazard are called "critical limits." Critical limits have been defined by the NACMCF as a maximum and/or minimum value to which a biological, chemical or physical parameter must be controlled at a CCP to prevent, eliminate or reduce to an acceptable level the occurrence of a food safety hazard (NACMCF, 1998).

In addition to this guidance, a number of sources of scientific and technical information can be useful in establishing process parameters or critical limits. Our guidance documents entitled "*Fish and Fishery Products Hazards and Controls Guidance*" and "*Juice HACCP Hazards and Controls Guidance*" each have information that can be broadly applied to food products. Other government agencies may also provide information through technical staff, regulations, guidelines, directives, performance standards, tolerances, and action levels. For example, the guidance documents entitled "Meat and Poultry Hazards and Controls Guide" (FSIS, 2005) and FSIS Compliance Guideline HACCP Systems Validation (FSIS, 2015), provided by the Food Safety and Inspection Service (FSIS) of the U.S. Department of Agriculture, has information that can broadly be applied to food products, not just meat and poultry products subject to FSIS' jurisdiction. As another example, EPA lists maximum pesticide residues limits (MRLs) and tolerances in 40 CFR Part 180. (EPA, 2015) and provides Indexes to Part 180 Tolerance Information for Pesticide Chemicals in Food and Feed Commodities on its website (EPA, 2016). Trade associations, process authorities, industry scientists, university and extension scientists, and consultants can provide expertise and guidance. For example, the Grocery Manufacturer's Association (GMA) has provided guidance on Control of *Salmonella* in Low-Moisture Foods (GMA, 2009). Information can also be obtained from peer reviewed scientific literature. For a more comprehensive list of resources, see the training materials provided by the Food Safety Preventive Controls Alliance (FSPCA, 2016) In addition to (or in place of) information from such resources, you also can conduct scientific studies for specific products in-house, at a contract laboratory, or at a university to establish appropriate process parameters and associated values.

You should use care when applying information from any of these sources to processing parameters for a specific product and process. Among other reasons, there may be important differences between the application of processing parameters as discussed in these sources how you would apply the processing parameters to your specific product and process. The processing parameters and/or minimum or maximum values may need to be adjusted to account for those differences. For example, the temperature (and time at that temperature) necessary to kill microorganisms in a food product can depend on the fat level in that food product.

Table 4-3 lists examples of the application of process controls to significantly minimize or prevent ingredient-related and process-related biological, chemical, and physical hazards and the section in this chapter that addresses each listed example.

Table 4-3 Common Process Controls

Process Control Subcategory	Hazard Category	Examples	Chapter Section
Lethal Treatments	Biological	• Heat treatments (also called thermal treatments) (e.g., cooking, roasting, baking) • High Pressure Processing (HPP) • Irradiation • Antimicrobial fumigation (e.g., with polypropylene oxide (PPO))	4.3.1
Time/Temperature of Holding	Biological	• Refrigeration • Freezing	4.3.2
Formulation	Biological	• Reducing the water activity • Reducing the pH • Adding preservatives	4.3.3
Dehydration/Drying	Biological	• Air-drying (forced air and heating) • Freeze drying • Spray drying	4.3.4
Recipe Management	Chemical	• Controlling the maximum level of food ingredients	4.3.5
Storage Conditions	Chemical	• Controlling moisture during storage of raw agricultural commodities	4.3.6
Physical Sorting	Chemical	• Reducing mycotoxin content through sorting by color and physical damage in raw agricultural commodities	4.3.7
Exclusion of Metal and Glass	Physical	• Using magnets • Using metal detectors • Using sieves, screens • Using X-ray systems	4.3.8

4.3.1 Treatments lethal to biological hazards

We use the term “lethality treatment” when referring to a treatment that is used to kill/destroy or inactivate microorganisms. In general, when discussing bacterial pathogens in this document we use the terms “kill” or “destroy” when discussing treatments lethal to vegetative cells and we use the term “inactivate” when discussing treatments lethal to spores. Common lethality treatments include: (1) Heat treatments (e.g., cooking, boiling, pasteurizing, baking, frying); (2)

HPP; (3) irradiation; and (4) antimicrobial fumigation. We discuss each of these in the following sections of this chapter.

4.3.1.1 Use of Heat Treatment (Thermal Processing) as a Lethality Process Control

Heat treatment is a common lethality process control. Heat treatments generally fall into into the following two categories:

- Heat treatment that leads to commercial sterility: heat processing at high temperatures (> 212^{o}F (100°C)) under presssure with the objective of killing all forms of microorganisms, including the spores of bacteria. The treated products are shelf-stable without refrigeration. (Lower temperatures can lead to products that are shelf-stable in some cases, e.g., when the pH is low enough to prevent growth of surviving sporeformers.)
- Heat treatment that reduces microbial pathogens but does not lead to commercial sterility: heat processing at lower temperatures (e.g., 158°F (70°C) to 212°F (100°C)), with the processes designed to kill the vegetative forms of microorganisms with little to no effect on the spores of bacteria. The treated products are not shelf-stable and require controls such as refrigeration to control spores of bacterial pathogens.

This chapter does not address heat treatments that lead to commercial sterility of "low-acid canned foods." Such treatments are subject to the requirements of 21 CFR part 113 (Thermally Processed Low-Acid Foods Packaged in Hermetically Sealed Containers; commonly called "Low-Acid Canned Foods (LACF)) because the microbial hazards in LACF are not subject to the requirements for hazard analysis and risk-based preventive controls. Note that although some hermetically sealed containers (e.g., pouches and glass bottles) used to package thermally processed low-acid foods generally would not be viewed as "cans," the term "low-acid canned foods" has been used for decades as a shorthand description for "thermally processed low-acid foods packaged in hermetically sealed containers," and we continue to use that term (and its abbreviation, LACF) for the purposes of this guidance.

Pasteurization is an example of a lethal heat treatment that reduces microbial pathogens but does not lead to a shelf stable product. Pasteurization typically is applied to foods to kill non-sporeforming pathogens such as *Salmonella*, *Listeria monocytogenes*, and pathogenic strains of *E. coli.* One example is the pasteurization of grade "A" milk and milk products that is covered by the 2015 Pasteurized Milk Ordinance (PMO) (FDA, 2015a). This chapter does not address pasteurization of milk; if you pasteurize milk, you should refer to 21 CFR 1240.61 and the specific requirements in your jurisdiction.

<u>Thermal Destruction of Microorganisms</u>

To design a lethal heat treatment for use as a preventive control, you should have a basic understanding of thermobacteriology (i.e., the relationship between bacteria and heat), including two key types of data and information:

- The kinetics of thermal inactivation or destruction of microorganisms, known as thermal death time data and;
- The rate at which heating occurs within the food material, also known as heat transfer or heat penetration.

Immediately below, we describe basic concepts associated with thermal death time data and heat transfer/heat penetration. For a more extensive review of thermobacteriology, including

graphical representations of the relationship of D values and z values to Thermal Death Time, refer to Stumbo, Chapter 7 (1973).

Some terms and concepts used to describe the thermal destruction of microorganisms include:

- **TDT (Thermal Death Time)** is the time necessary to kill a given number of microorganisms at a specified temperature. The TDT is obtained by keeping temperature constant and measuring the time necessary to kill the amount of cells specified.
- **D Value** (the decimal reduction time) is the time required to kill 90% of the microorganisms. Another way of expressing this is the time required at a specific temperature and under specified conditions to reduce a microbial population by one decimal (see discussion below).
- **z Value** refers to the degrees in Farhenheit required for the thermal destruction curve to cross one log cycle (i.e., for reducing the D value by a factor of 10).

Food processing experts evaluate treatments intended to kill or inactivate pathogens in food in terms of "logs" of kill, where the term "log" is a shorthand expression of the mathematical term logarithm. A logarithm is the exponent of the power to which a base number must be raised to equal a given number. In thermobacteriology, the base number is usually 10. As an example, the number 100 = 10^2 where the base number is 10 and the exponent is 2. Because the exponent is 2, the number 100 = log 2. Likewise, the number 1000 = 10^3 = log 3. The important thing to understand is that each "log" of kill is capable of causing a tenfold reduction in the number of microorganisms that the treatment is designed to kill, i.e., the most resistant microorganism of public health significance.

The decimal reduction time (D) is used synonymously with "log" in the context of thermobacteriology. A 1-log or 1D process would be one that is capable of reducing the level of the most resistant pathogen of concern in the food by 10 fold, e.g., from 10,000 cells of the microorganism per gram of food to 1,000 cells of the microorganism per gram of food. Importantly, it is not possible to technically achieve a level of reduction to zero, or "no microorganisms"; instead, as a technical matter the probability of finding the organism becomes less likely as the magnitude of reduction increases. Thus, a 5-log reduction process would be one that is capable of reducing the level of the most resistant pathogen of concern in the food by 100,000 fold, e.g., from 10,000 cells of the microorganism per gram of food to a probability of 1 cell in 10 g of food.

Table 4-4 provides examples of how food processing experts would describe the effect of lethal heat treatments on microorganisms in foods using terms commonly associated with thermobacteriology.

Table 4-4. The concept of log reductions of microorganisms in foods

Initial number of the most resistant microorganism of public health significance per gram of food	Log reduction (also known as D)	Decrease in most resistant microorganism of public health significance per gram of food	Percent of change	Final number of bacteria per gram of food
10,000 or log 4[1]	1	10-fold	90%	1,000 or log 3
10,000 or log 4	2	10 X 10 = 100 fold	99%	100 or log 2
10,000 or log 4	3	10 X 10 X 10 = 1000-fold	99.9%	10 or log 1
10,000 or log 4	4	10 X 10 X 10 X 10 = 10,000-fold	99.99%	1 or log 0

Initial number of the most resistant microorganism of public health significance per gram of food	Log reduction (also known as D)	Decrease in most resistant microorganism of public health significance per gram of food	Percent of change	Final number of bacteria per gram of food
10,000 or log 4	5	10 X 10 X 10 X 10 X 10 = 100,000-fold	99.999%	0.1 or log -1[2]
10,000 or log 4	6	10 X 10 X 10 X 10 X 10 = 1,000,000-fold	99.9999%	0.01 or log -2

[1] Additional equivalent ways to express 10,000 include 10^4, 10^4, and 10E4
[2] Additional equivalent ways to express 0.1 include 10^{-1} or 1 in 10.

Relative Heat Resistance of Microorganisms

Some microorganisms are more resistant to heat than other microorganisms and, thus, the require more stringent heating conditions to kill or inactivate them. Table 4-5 shows the relative heat resistance of common types of microorganisms.

Table 4-5. Relative Heat Resistance of Microbial Forms

Resistance to Heat	Microbial Form
Highest	Bacterial Spores
Moderate	• Some Vegetative bacterial cells • Cysts of Parasites • Fungi, including fungal spores
Least	• Some vegetative bacterial cells • Viruses

As already noted, this chapter addresses relatively mild heat treatments that reduce microbial pathogens but do not lead to commercial sterility. These relatively mild heat treatments are used to reduce the number of vegetative cells of bacterial pathogens such as *Listeria monocytogenes* (*L. monocytogenes*), *Salmonella,* and enteropathogenic *E. coli*, and the spores of non-proteolytic strains of *Clostridium botulinum* (*C. botulinum*) and *Bacillus cereus* (*B. cereus*). These processes are designed to ensure product safety by achieving a 6-log reduction (6D). For a more detailed review of the relative heat resistance of food pathogens in mildly heat processed foods, see Jay (1996), FDA (2000), and Farkas (2007).

Factors Affecting the Heat Resistance of Microorganisms

In addition to the inherent heat resistance of specific microorganisms (or life stages of microorganisms, such as the spore stage), other factors associated with foods (such as water activity, pH, salt content, fat, and protein) can affect the heat resistance of microorganisms. Table 4-6 lists the most common factors that you should consider when designing a heat treatment as a process preventive control.

Table 4-6. Factors That Influence the Heat Resistance of Microorganisms in Foods

Factor	Effect on Microbial Heat Resistance

Factor	Effect on Microbial Heat Resistance
Water	As the humidity or moisture goes down, in general the heat resistance increases
Fat	As the fat content increases, there is a general increase in heat resistance of some microorganisms
Salts	The effect of salt varies and depends on the kind of salt and concentration. Some salts that decease water activity appear to increase heat resistance of microorganisms while other salts that may increase water activity (e.g., Ca^{2+} and Mg^{2+}) appear to decrease heat resistance.
Carbohydrates	The presence of sugars can increase the heat resistance of microorganisms due in part to the decrease in water activity. However, the impact can be variable, particularly among sugars and sugar alcohols.
pH	Most microorganisms are more heat resistant near their optimum pH for growth. Generally, as the pH increases or decreases relative to this optimum pH, the microorganisms become more sensitive to heat.
Proteins	Proteins have a protective effect and, thus, increase the heat resistance of microorganisms.

Other factors that can influence the heat resistance of microorganisms include the numbers of organisms, the age of the microorganisms, the temperatures at which microbial growth occurs, the presence of inhibitory compounds, and the time-temperature combination utilized. For a comprehensive compilation of data and research on the effect of food factors on the heat resistance of food pathogens of public health concern, see ICMSF (1996).

Lethal Heat Treatments

Cooking:

Baking, boiling, roasting, steaming, and frying are conventional heating methods used for cooking a wide variety of foods (e.g., cereal-grain products, vegetables, soups, sauces, legumes, and assembled multi-component meals). Cooking is performed for two primary reasons: to make food palatable and to make it safe by eliminating vegetative pathogens such as *Salmonella*, *L. monocytogenes*, and enteropathogenic *E. coli*. This discussion focuses on the food safety aspects of the cooking methods.

You should design a cooking process to target heat resistant vegetative pathogens, such as *L. monocytogenes*. Typically, we recommend a thermal process that achieves a 5D to 7D reduction for most cooking treatments. However, if the expected initial microbial load is low, a less severe thermal process may be adequate. For cooking processes that target pathogenic sporeformers such as *C. botulinum* type E and non-proteolytic types B and F (i.e., 194°F (90°C)) for 10 min), generally a 6D reduction in the level of contamination is suitable.

Table 3-D in Appendix 3 of this document provides 6D process times for a range of cooking temperatures, with *L. monocytogenes* as the target pathogen. It is possible that higher levels of destruction may be necessary in some foods, e.g., if you expect especially high initial levels of the target pathogen.

Table 3-E in Appendix 3 of this document provides 6D process times for a range of heating temperatures, with non-proteolytic *C. botulinum* type B (the most heat-resistant form of non-proteolytic *C. botulinum*) as the target pathogen.

There are a variety of ways to control the application of these cooking processes depending upon the type of food and the method of delivery (e.g., boiling, steaming). For example, for liquid and semi-liquid food products that are batch-cooked in a cooking vessel such as a kettle agitated during the thermal process, the simplest way to control the process is to check the internal temperature of the product at the end of the designated cooking time (i.e., check the time-temperature parameters of the treatment). A dial thermometer with a long probe works quite well. If the temperature is taken at or near the center of the cooking vessel, it is reasonable to assume that all product in the cooking vessel is at or above that temperature, because foods processed in this manner generally heat by convection or forced convection. You can monitor a simple boiling heat process by visually observing and timing the boil. Usually, a temperature distribution study is performed to ensure that no point in the cooking vessel is at a lower temperature than the minimum value (or critical limit) for temperature required during the process.

Heating food with large particles, like vegetables in stews and some soups, occurs primarily by conduction, rather than by convection. Particle size and consistency can greatly affect the rate of heating at the center of the particle. You cannot control cooking processes for products with large particles by periodically checking the internal temperature of some of the product particles as they leave the cooker because you cannot verify that each particle reached the appropriate temperature for adequate time. Therefore, you should establish the process scientifically and validate it through a scientific study demonstrating that if the minimum/maximum values are met for all the critical factors (e.g., cooking temperature, time, particle size) all particles will receive an adequate heat treatment.

Normally, a study to validate a cooking process is performed by a person or group knowledgeable in the design of thermal processes to determine the critical parameters required for the heat process being applied to ensure that it delivers the desired reduction level (logs of kill, as described in section 4.3.1.1 of this chapter). A preventive controls qualified individual must conduct (or oversee) such a study. See 21 CFR 117.180(a). (Because it is common practice for these studies to be conducted by entities with special expertise in the area, the preventive controls qualified individual likely will oversee, rather than conduct, the study.) Once that study has been completed, the person conducting the study will provide a time and temperature for the processor to monitor during processing, as well as any other parameters that are critical to delivery of an adequate heat treatment, such as maximum particle size). You can then monitor the time and temperature of the heat process to effectively ensure that all product particles have achieved the desired internal temperature. It may also be necessary to monitor other factors of the product or the process, such as the internal temperature of the product before the start of the process--called the initial temperature (IT), particle size, or relative humidity, where they affect the rate of heating. These factors, and their limits, will be determined by the process design study.

For some products, such as soups or sauces, you may be able to monitor End-Point Internal Product Temperature (EPIPT), a measurement of the internal temperature of the product at the end of the heat process, instead of performing continuous time and temperature monitoring. This approach is suitable if you have conducted a scientific study to validate that the EPIPT that you have selected will provide an appropriate reduction (e.g., 6D) in the numbers of the target pathogen in the slowest heating unit or portion of product under the worst set of heating conditions covered by the scientific study. If you want to monitor EPIPT, you should:

- Conduct a temperature distribution study within the heating system to identify any cold spots;

- Conduct a heat penetration study that accounts for the slowest heating product under the worst case heating conditions covered by the scientific study; and
- Identify other critical factors of processing and/or packaging that affect the rate of product heating when scientifically establishing a heat process.

You should use the EPIPT as a monitoring technique only under those conditions that were evaluated by the scientific study, with those conditions identified as process parameters with minimum/maximum values (or critical limits) that are monitored as part of your process controls. See "Chapter 6 – Use of Heat Treatments as a Process Control" in this guidance for additional information about the EPIPT monitoring technique.

Other common forms of cooking that are used to produce commercially manufactured foods are baking and roasting. These are essentially the same unit operation because they both use heated air to alter the eating quality of foods. However, the term "baking" is usually used when heated air is applied to flour-based foods or fruits, and the term "roasting" is usually used when heated air is applied to meats, nuts, or vegetables. Baking and roasting operations use dry heat in gas-fired or electric ovens. For some products such as bakery products, the effectiveness of the dry heat in ovens is increased by the addition of steam for various cooking purposes. Cooking equipment may be batch-type or continuous. In a continuous system the food is moved through the cooking equipment by conveyor or auger systems. The methods of controlling and monitoring the time-temperature parameters of these types of cooking processes will vary depending upon whether it is batch-type or continuous process. See "Chapter 6 – Use of Heat Treatments as a Process Control" for an example using baking as a preventive control.

Emerging Technologies Based on Thermal Effects

Microwave, radio frequency, ohmic heating, and inductive heating are heat-based processes that can kill microorganisms by thermal effects. Microwave and radio frequency heating are based on the use of electromagnetic waves of certain frequencies to generate heat in a material through two mechanisms - dielectric and ionic. Ohmic heating is the process of passing electric currents (primarily alternating) through foods or other materials to heat them. The heating occurs in the form of internal energy generation within the material. Ohmic heating is distinguished from other electrical heating methods either by the presence of electrodes contacting the food (as opposed to microwave heating, where electrodes are absent), and depends on frequency of the current and waveform (typically sinusoidal). Inductive heating is a process of inducing electric currents within the food due to oscillating electromagnetic fields generated by electric coils.

For any of these heat-based processes, the magnitude of time/temperature history and the location of the cold points will determine the effect on microorganisms. The effectiveness of these processes also depends on water activity and pH of the product. Although the shape of the destruction or inactivation curves is expected to be similar to those in conventional heating, the intricacies of each of the technologies need special attention if you plan to use them for microbial destruction or inactivation. For instance, in microwave heating a number of factors influence the location of the cold points, such as the composition, shape, and size of the food, the microwave frequency, and the applicator design. The location of the coldest-point and time/temperature history can be predicted through simulation software, and we expect that food processors may be able to use these emerging technologies in the future.

For a detailed overview of these processing technologies, as well as alternative thermal processing techniques, see Sun (2005).

4.3.1.2 Use of High Pressure Processing (HPP) as a Lethality Process Control

The pressure processing of foods for preservation was studied as early as the end of the 19th century and the beginning of the 20th century in the United States by people like Hite (1899) and Bridgman (1912). However the potential microbiological effects of HPP were not recognized by the food industry until around 1985. HPP has recently received a great deal of attention in the food, pharmaceutical, and biotechnology industries. Japan has been a leader in this technology, producing products such as jams, jellies, fruit juices, and yogurt.

Microorganisms vary in their sensitivity to high pressure. If you plan to use HPP, you should consider the organism of concern, product characteristics and, whether the process is to result in product that is to be refrigerated or that will be shelf stable. Destruction of the microorganism is primarily caused by changes in the structure and permeability of the cell wall which causes fluids to be forced into the cell.

Bacterial spores are well established as the most pressure-resistant biological forms known. Spores resist inactivation by high pressure alone and most require the addition of heat or some other mechanism to achieve appropriate levels of destruction. *C. botulinum* is one of the most pressure-resistant and hazardous microorganisms, which is a challenge in the design of high-pressure processes. Because of this, the best candidates for HPP continue to be acid foods and foods that will be refrigerated following processing (which provide control of sporeformers).

High pressure processing of foods requires pressures of 400 to 700 MPa, or 4000 - 7000 bars (58,000 - 101,000 psig). The unit of measure frequently used for HPP in the food industry is the pascal (Pa) or megapascal (MPa, 1,000,000 Pa). Most commercial food industry applications use pressures in the range of 600 to 700 MPa.

High pressure processing requires very specialized and costly equipment. Currently foods using HPP are being processed by batch systems. For batch processing, the food is packaged in a flexible or semi-flexible package, prior to placing the product in the HPP system, where the product is placed into a chamber and immersed in water or some other pressurizing fluid, then subjected to the high pressure for a time of 1 - 20 minutes, depending on the temperature and pressure. The chamber would then be depressurized and the product removed. Applications and the feasibility for commercialization for other HPP systems such as semi-continuous, continuous, and pulsed HPP have been described elsewhere (FDA, 2000; Indrawati et al. 2003; Z. Berk, 2009).

For a detailed review of the application and use of HPP as a process control, see FDA (2000 and 2001) and Hogan et al. (2005).

4.3.1.3 Use of Irradiation as a Lethality Process Control

The application of radiation treatments to food for the purpose of improving safety (e.g. by reducing or eliminating pathogenic bacteria) or extending shelf life by (e.g. by reducing or eliminating spoilage microorganisms and insects) can use sources that have high enough energy levels to cause ionization (the creation of ions by expulsion of orbital electrons from atoms) or have lower energy levels that will not cause ionization. These are known as ionizing and non-ionizing radiation, respectively. The most commonly used form of radiation to treat foods as a lethality process control is ionizing radiation and the discussion in this section of this chapter focuses on ionizing radiation. Non-ionizing radiation in the form of lower energy

electromagnetic waves such as UV light and infrared heating can be used to treat foods similar to that described for microwaves, radio frequency, and ohmic heating in the section of this chapter entitled "Emerging Technologies Based on Thermal Effects" and will not be addressed here. For more information on the application of infrared (IR) radiation in food processing operations, see the review by Krishnamurthy et al. (2008). For more information on the application and use of UV light in food processing, see the discussion by FDA (2000, 2001).

FDA is responsible for regulating the sources of radiation that are used to irradiate food (21 CFR Part 179 Subpart B). Irradiation is considered a food additive in the United States and, as such, its use in foods requires premarket approval by FDA (21 CFR Part 179). There are three sources of ionizing radiation approved for use on foods (21 CFR 179.26):

- Gamma rays – emitted from radioactive forms of the element cobalt (Cobalt 60) or the element cesium (Cesium 137). Gamma radiation is also used routinely in medicine to sterilize medical and dental products and for the radiation treatment of cancer.
- X-rays – produced by reflecting a high-energy stream of electrons into food off a target substance (usually one of the heavy metals) using electron accelerators. X-rays are also widely used in medicine and industry to produce images of internal structures.
- Electron beam – (or e-beam) is similar to X-rays and is a stream of high-energy electrons propelled from an electron accelerator into food.

Some common terms that are used when describing the application of ionizing radiation in the treatment of foods are:

- Dose (absorbed) – The amount of energy absorbed per unit mass of irradiated material.
- D_{10} value – Amount of radiation required to reduce the population of a specific microorganism by 90% (one $\log_{10}$ cycle) under the stated conditions.
- Gray (Gy) - A unit of absorbed dose of ionizing radiation, equal to 1 joule/kg of absorbed energy.
- Electron volt (eV) – A unit of energy. One electron volt is the kinetic energy acquired by an electron in passing through a potential difference of one volt in a vacuum.

The primary reason food irradiation is used as a lethal process control is to inactivate pathogens and microorganisms that cause food spoilage (Farkas et al., 2014). The application of ionizing radiation damages DNA and very effectively inhibits DNA synthesis and further cell division in microorganisms that are exposed to these forms and levels of energy. The amount of radiation energy used to bring about the control of microorganisms varies according to the radiation resistance of the particular organism, which is often specific to the species level and the number or load of the microorganisms present.

Radiation treatment at doses of 2–7 kiloGray (kGy), depending on the source of radiation and the food, have been reported to effectively eliminate potentially pathogenic non-sporeforming bacteria, including both long-time recognized pathogens such as *Salmonella* and *S. aureus,* as well as more recently emerged pathogens such as *Campylobacter*, *L. monocytogenes* or *E. coli* O157:H7, from suspected food products (Farkas, 1998). As an example, Table 4-7 provides a summary of compiled data on the ranges of decimal reduction doses (D_{10} values) for the most important non-sporeforming pathogenic bacteria determined in various foods under various conditions.

Table 4-7. D_{10} Values (kGy) for Some Foodborne Non-sporeforming Pathogenic Bacteria

Bacteria	Non-frozen food	Frozen food
Vibrio spp.	0.02-0.14	0.04-0.44
Yersinia enterocolitica	0.04-0.21	0.20-0.39
Campylobacter jejuni	0.08-0.20	0.18-0.32
Aeromonas hydrophila	0.11-0.19	0.21-0.34
Shigella spp.	0.22-0.40	0.22-0.41
Escherichia coli O157:H7	0.24-0.43	0.30-0.98
Staphylococcus aureus	0.26-0.57	0.29-0.45
Salmonella spp.	0.18-0.92	0.37-1.28
Listeria monocytogenes	0.20-1.0	0.52-1.4

Adapted from Farkas et al., 2014

Bacterial spores are more resistant to irradiation than non-sporeforming bacteria. The spores of *C. botulinum* types A and B are particularly resistant.

For illustrative purposes, Table 4-8 lists the approved uses of ionizing radiation for application as a process control in food processing as of April, 2016. We adapted Table 4-8 from 21 CFR 179.26(b), which specifies the limitations on the approved uses of ionizing radiation for the treatment of food and includes uses for purposes other than as a process control. For example, 21 CFR 179.26(b) also specifies limitations on the use of ionizing radiation for use in disinfestation of arthropod pests in food. You should refer to 21 CFR 179.26 for the most current limitations on the approved uses for the treatment of food using ionizing radiation.

Table 4-8. Approved Uses for the Treatment of Food Using Ionizing Radiation

Use	Limitations
For control of *Trichinella spiralis* in pork carcasses or fresh, non-heat-processed cuts of pork carcasses	Minimum dose 0.3 kiloGray (kGy) (30 kilorad (krad)); maximum dose not to exceed 1 kGy (100 krad).
For microbial disinfection of dry or dehydrated enzyme preparations (including immobilized enzymes)	Not to exceed 10 kGy (1 megarad (Mrad)).
For microbial disinfection of the following dry or dehydrated aromatic vegetable substances when used as ingredients in small amounts solely for flavoring or aroma: culinary herbs, seeds, spices, vegetable seasonings that are used to impart flavor but that are not either represented as, or appear to be, a vegetable that is eaten for its own sake, and blends of these aromatic vegetable substances. Turmeric and paprika may also be irradiated when they are to be used as color additives. The blends may contain sodium chloride and minor amounts of dry food ingredients ordinarily used in such blends	Not to exceed 30 kGy (3 Mrad).

Use	Limitations
For control of food-borne pathogens in fresh (refrigerated or unrefrigerated) or frozen, uncooked poultry products that are: (1) Whole carcasses or disjointed portions (or other parts) of such carcasses that are "ready-to-cook poultry" within the meaning of 9 CFR 381.l(b) (with or without non-fluid seasoning; includes, e.g., ground poultry), or (2) mechanically separated poultry product (a finely comminuted ingredient produced by the mechanical deboning of poultry carcasses or parts of carcasses)	Not to exceed 4.5 kGy for non-frozen products; not to exceed 7.0 kGy for frozen products.
For the sterilization of frozen, packaged meats used solely in the National Aeronautics and Space Administration space flight programs	Minimum dose 44 kGy (4.4 Mrad). Packaging materials used need not comply with §179.25(c) provided that their use is otherwise permitted by applicable regulations in 21 CFR parts 174 through 186.
For control of foodborne pathogens in, and extension of the shelf-life of, refrigerated or frozen, uncooked products that are meat within the meaning of 9 CFR 301.2(rr), meat byproducts within the meaning of 9 CFR 301.2(tt), or meat food products within the meaning of 9 CFR 301.2(uu), with or without non-fluid seasoning, that are otherwise composed solely of intact or ground meat, meat byproducts, or both meat and meat byproducts	Not to exceed 4.5 kGy maximum for refrigerated products; not to exceed 7.0 kGy maximum for frozen products.
For control of *Salmonella* in fresh shell eggs.	Not to exceed 3.0 kGy.
For control of microbial pathogens on seeds for sprouting.	Not to exceed 8.0 kGy.
For the control of *Vibrio* bacteria and other foodborne microorganisms in or on fresh or frozen molluscan shellfish.	Not to exceed 5.5 kGy.
For control of food-borne pathogens and extension of shelf-life in fresh iceberg lettuce and fresh spinach.	Not to exceed 4.0 kGy.
For control of foodborne pathogens, and extension of shelf-life, in unrefrigerated (as well as refrigerated) uncooked meat, meat byproducts, and certain meat food products	Not to exceed 4.5 kGy.
For control of food-borne pathogens in, and extension of the shelf-life of, chilled or frozen raw, cooked, or partially cooked crustaceans or dried crustaceans (water activity less than 0.85), with or without spices, minerals, inorganic salts, citrates, citric acid, and/or calcium disodium EDTA	Not to exceed 6.0 kGy.

Adapted from 21 CFR Part 179.26(b)

For additional information on processes, application, and equipment used in the ionizing radiation treatment of foods see FDA (2004), Lacroix (2005), Fellows (2009a), Farkas and Mohacsi-Farkas (2011) and FDA (2015b).

4.3.1.4 Use of Antimicrobial Fumigation as a Lethality Process Control

In California, treatment processes for almonds must use technologies that have been determined to achieve a minimum 4-log reduction of *Salmonella* in almonds (see 7 CFR part 981, Almonds Grown in California). The Almond Board of California (ABC) has processes in place to review treatment processes for scientific adequacy. ABC has funded research projects demonstrating that fumigation with propylene oxide (PPO) (a registered fumigant in the United States for the reduction of bacteria, yeasts, and mold on raw nut meats) is an effective treatment for achieving a minimum 4-log reduction of *Salmonella* in almonds (ABC, 2008).

4.3.2 Use of Time-Temperature as a Process Control

Temperature is an essential factor that affects the growth of bacteria. Bacterial growth can occur over a wide range of temperatures from about 23°F (-5°C) to 194°F (90° C). Table 4-9 lists four types of bacteria based on their temperature growth ranges.

Table 4-9. Temperature Ranges for the Growth of Microorganisms

Group	Minimum Temperature °C (°F)	Optimum Temperature °C (°F)	Maximum Temperature °C (°F)
Thermophiles	40 - 45 (104 - 113)	55 - 75 (131 - 167)	60 - 90 (140 - 194)
Mesophiles	5 - 15 (41 - 59)	30 - 45 (86 - 113)	35 - 47 (95 - 117)
Psychrophiles	-5 - +5 (23 - 41)	12 - 15 (54 - 59)	15 - 20 (59 - 68)
Psychrotrophs	-5 - +5 (23 – 41)	25 - 30 (77 - 86)	30 - 35 (86 - 95)

Thermophiles grow at hot temperatures above 131°F (55°C). Mesophiles grow at or near room temperatures. Psychrophiles grow at or near refrigeration temperatures. Psychrotrophs are capable of growth at refrigeration temperatures, but their optimal growth temperature is in the mesophilic range.

Most pathogenic bacteria are mesophiles and their optimum growth temperature corresponds to human body temperature (see Table 3-A of Appendix 3 of this guidance). Typically, the higher the temperature (within the normal growth range), the more rapid the growth of the microorganism.

It is not only the temperature that is of concern; it is the total time of exposure at temperatures that allow growth that needs to be controlled. The most general recommendation is to hold cold foods below 41°F (5°C) and to keep hot foods above 135°F (57°C). However, in some situations it may not be possible to completely avoid product exposure to mesophilic temperatures.

4.3.2.1 Use of Refrigeration as a Time-Temperature Process Control

Refrigeration works well for controlling the growth of most pathogenic bacteria. However, some pathogens, like *L. monocytogenes* and *Yersinia enterocolitica*, can grow at temperatures close to freezing. Refrigeration has the added advantage of slowing down biological and chemical processes that result in spoilage, oxidative rancidity, and other quality defects.

Control of temperature during storage can be accomplished in several ways, such as ice, chemical coolant gel packs, and mechanical dry refrigeration (e.g., in a cooler).

Controlling temperature with ice or gel packs can be effective if there is an adequate amount of ice or gel packs. Therefore, you should monitor the control by checking whether an adequate amount of coolant is present on the product at all times, including when it is shipped and when it is received and checking the temperature of the food with a thermometer or temperature recording device.

For mechanical dry refrigerated storage in a cooler, if the ambient temperature can be related to the product temperature, monitoring the temperature of the storage area will ensure that the product temperature is under control. Ordinarily monitoring of the cooler requires use of continuous monitoring instruments such as recorder thermometer charts, maximum-indicating thermometers, and high temperature alarms.

Time/Temperature

When food is removed from refrigeration, the temperature of the food gradually increases and can reach the temperature associated with the growth range specific to particular pathogens. Bacterial pathogens go through a lag phase, where little or no growth occurs as the microorganisms adjust to their new environment. Depending upon the ambient temperature, it is possible that food can stay out of refrigeration for at least a couple of hours with no risk of significant pathogen growth. As the product temperature approaches the growth range, pathogens enter what is called the "log phase" (because they grow logarithmically). The object is to prevent that from happening, ideally keeping pathogens in their lag phase. We call the temperature range of concern (41°F (5°C) to 135°F (57°C)) the "danger zone."

Traditionally, the rule of thumb for foods that will support microbial growth has been no more than 4 hours in the danger zone (41°F (5°C) to 135°F (57°C)). Different pathogens have different rates of growth at different temperatures, and the rate of growth will be affected by the type of food and its inherent properties. Therefore, the actual maximum time that a product may be safely held in the danger zone depends on a number of factors, including the type of pathogens that are present and the ability of the food to support their growth. Guidance on this issue is available in the US Food Code[2] (FDA, 2013) and in Table 3-B in Appendix 3 of this document. You may set limits based on these factors or based on studies done on your own specific food products, rather than relying on the 4-hour rule of thumb. Food inspectors should also use these factors when they evaluate the significance of time - temperature abuse.

Control of time and temperature during processing may be more complicated than during storage, because it involves information about the time and temperature exposure of the product during production. You can obtain this information in a variety of ways, such as marking units of product and tracking how long they remain at unrefrigerated temperatures; monitoring the ambient temperature in a chill room operation; or monitoring product temperatures during different phases of production. See "Chapter 7 – Use of Time/Temperature Control as a Process Control" of this guidance for additional information about the application of time-temperature holding conditions.

Cooling after Cooking

Cooling after cooking can be a critical function influencing the safety of a food (FDA, 2013). Depending upon the food and ingredients, cooked foods can still have viable pathogenic bacteria present. For example, the spores of sporeforming pathogens such as *C. botulinum* can survive cooking processes. For non-sporeforming pathogens that are particularly heat tolerant (such as *L. monocytogenes*), vegetative cells can sometimes survive the cooking process; however, this should not be the case if you selected the appropriate target pathogen for control by the applied process and you validated the control. More often, it is the spores of

[2] The U.S. Food Code (FDA, 2013) is a model that assists food control jurisdictions at all levels of government by providing them with a scientifically sound technical and legal basis for regulating the retail and food service segment of the industry (restaurants and grocery stores and institutions such as nursing homes). Local, state, tribal, and federal regulators 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. Although the target audience for the U.S. Food Code does not include most food processing facilities, the U.S. Food Code nonetheless contains scientifically-based information that you can use as a resource where appropriate in establishing some preventive controls particularly regarding use of refrigeration to control the growth of microbial pathogens.

sporeforming pathogens (such as *C. botulinum*) that survive the cooking process if they are present because temperatures that can only be achieved under pressure are usually needed to inactivate spores. These spores will begin to germinate when the product temperature drops to a temperature at which they can grow (usually below 135°F (57°C)) and will be present in the food during storage. Some spores, such as those from non-proteolytic *C. botulinum* and some strains of *B. cereus*, have the ability to germinate and grow at refrigeration temperatures, although long times are required. Other spores that may be present in the food remain dormant until the product is temperature-abused (i.e., held in the temperature range at which these pathogens can grow). In such an event, pathogenic spores are able to germinate, grow, and the resulting cells can possibly produce toxin due to the fact that most spoilage bacteria (which may otherwise compete for growth) have been eliminated by the cooking process. For further discussion on the importance of cooling food after cooking see Factors that Influence Microbial Growth (Chapter 3 in the Evaluation and Definition of Potentially Hazardous Foods) (FDA, 2001).

If the cooking process is adequate to inactivate spores and the product is protected from recontamination during cooling, the cooling step will not be critical. Situations where these conditions exist are probably limited to certain pressurized steam processes.

Simply putting food in a refrigerator is not adequate to prevent microbiological growth. When large volumes of hot food are cooled, it can take a long time, sometimes as long as 36 hours, to chill the food to a point where pathogen growth is inhibited. The U.S. Food Code specifies the application of a two part cooling protocol In order to cool foods safely and keep bacteria in the lag phase. First, drop the temperature from 135°F (57°C) to 70°F (21°C) within two hours. The temperature must be lowered through this range quickly because foodborne pathogens multiply most rapidly between these temperatures. Second, after dropping the initial temperature to 70°F (21°C), you can take up to additional 4 hours to get the product down to 41°F (5°C). FSIS also recommends a two part cooling for meat and poultry, but uses slightly different temperatures: “temperature should not remain between 130°F (54°C) and 80°F (27°C) for more than 1.5 hours nor between 80°F (27°C) and 40°F (4°C) for more than 5 hours” (FSIS, 1999). Both these protocols are adequate to minimize the potential for growth of foodborne pathogens.

A blast freezer is one of the best cooling methods. High velocity cold air can drop the temperature of large volumes of hot food in less than an hour. The containers of food that have been chilled can then be shifted to a holding cooler.

Cooling tunnels and spiral freezers are similar to blast freezers but are more compatible with moving production lines. They use high velocity cold air, or liquid carbon dioxide or nitrogen for rapid cooling. Products may be frozen before or after packaging depending upon the product and package size.

Heat exchangers are used for cooling liquids like milk and juice after pasteurization. Lines containing a coolant such as water or cold, raw product run adjacent to lines of hot, pasteurized product. No actual exchange or co-mingling of coolant or raw product with heat-treated product occurs. However, the cold raw liquid, for example, picks up heat from the hot, pasteurized juice. This helps preheat the raw product and also helps precool the heat-treated liquid. See “Chapter 6 – Use of Heat Treatments as a Process Control” in this guidance for additional information about heat exchangers.

Cook-chill operations are typically used in large institutional settings such as prisons, hospitals, and schools as well as in food processing plants. Food is cooked in nylon reinforced plastic

bags or is cooked and then pumped into these bags. The bags are chilled in a tumble chiller that tumbles the bags in ice water. This drops the temperature of large volumes of hot food quickly. Typically, an ice tank where coils of refrigerant are run through the tank of water provides the large volume of cold water needed.

Be advised that food can be recontaminated during the cooling process as a result of hand contact, condensate drip, or contact with other foods. See "Chapter 10 – Sanitation Controls" in this guidance for additional information about controlling the risk of recontamination.

4.3.2.2 Use of Freezing as a Time-Temperature Process Control

Foods are microbiologically stable when held at temperatures below 17.6^{o}F (-8^{o}C). During frozen storage, populations of viable microorganisms in most foods will decrease; however, some microorganisms remain viable for long periods of time during frozen storage. Most viruses, bacterial spores, and some bacterial vegetative cells survive freezing unchanged. Some of the other microorganisms are sensitive to the freezing and thawing process (i.e., freezing, frozen storage, or thawing). Since multi-celled organisms (such as such as parasitic protozoa, nematodes, and trematodes) are generally more sensitive to low temperatures than are bacteria; freezing and frozen storage are good methods for killing these organisms in various foods. This is especially important if consumers are likely to eat the foods raw or undercooked. See Kennedy (2003) and Fellows (2009b) for a detailed review on the use of freezing technologies in the preservation of foods.

4.3.3 Use of Product Formulation as a Process Control

Most food preservation techniques used by processors employ knowledge of factors (such as water activity, pH, temperature, nutrients, chemical inhibitors, competitive microflora, and atmosphere) that affect the growth of bacteria. For more information on how these factors affect microbial growth, see International Commission on Microbiological Specifications for Foods (ICMSF) (1996, 2002), Jay (1996), and Zeuthen and Bogh-Sorensen (2003).

In this section of this chapter, we discuss two key factors that are frequently used as a formulation process control – i.e., water activity and pH. We also discuss the use of preservatives as a formulation process control.

4.3.3.1 Use of Water activity (a_w) as a Formulation Process Control

Microorganisms need water to survive as well as to grow. Water activity (a_w) refers to the availability of water to the organism. In general, microorganisms survive and grow better when the water activity is high than when the water activity is low.

If you have a closed container of water, the air over the water becomes saturated with water. The relative humidity is 100%, which equals a water activity of 1.0. Thus, water has a water activity of 1.0. Foods are more complex systems than water, and the water can bind to components of the food so not all the water in the food is available to microorganisms; thus, the water activity of most food products is less than 1.0.

Water activity is directly related to the vapor pressure of the water in a solution. You can determine water activity by measuring the equilibrium relative humidity of the air over the solution in a closed container. Relative humidity divided by 100 equals the water activity:

$$(a_w) = RH/100$$
or
$$a_w = p/p_o$$

Foods vary in their water activity as shown in Table 4-10. Although you can measure the water activity of your specific food if you have the appropriate equipment, for many purposes you can rely on the water activity values shown in Table 4-10.

Table 4-10. Principal Groups of Foods Based on Water Activity (a_w) (ICMSF, 1980)

Water Activity	Food Groups
0.98 and above	• Fresh meats and fish • Fresh fruits and vegetables • Milk and other beverages • Canned vegetables in brine • Canned fruit in light syrup
Below 0.98 to 0.93	• Evaporated milk • Tomato paste • Lightly salted pork and beef products • Canned cured meats • Fermented sausages (not dried) • Cooked sausages • Processed cheese • Gouda cheese • Canned fruits in heavy syrup • Bread
Below 0.93 to 0.85	• Dry or fermented sausage • Dried venison • Cheddar cheese • Sweetened condensed milk
Below 0.85 to 0.60	• Intermediate moisture foods • Dried fruits • Flour • Cereals • Jam and jellies • Molasses • Heavily salted fish • Meat extract • Nuts
Below 0.60	• Confectionery • Chocolate • Honey • Dried Noodles • Crackers • Potato Chips • Dried egg, milk and vegetables

Table 4-10 organizes the foods into five categories, based on their water activity. Table 4-11 further classifies these five categories into three categories – i.e., moist foods, intermediate-moisture foods (often included in the low-moisture foods category), and low-moisture foods. Moist foods (i.e., foods with water activity above 0.85) require refrigeration or another barrier to control the growth of pathogens (see Table 4-11). Intermediate-moisture foods (i.e., foods with water activities between 0.60 and 0.85) do not require refrigeration to control pathogens, but they may have a limited shelf life because of spoilage, primarily by yeast and mold. The microbiological stability of intermediate-moisture foods may depend on factors other than water activity, such as reduced pH, chemical preservatives, heat treatments, or combinations of these, even though the reduced water activity is of major importance. Low-moisture foods (i.e., foods with a water activity below 0.60) have an extended shelf life, even without refrigeration.

Table 4-11. Classification of Foods and Control Requirements Based on Water Activity

Water Activity	Classification	Requirements for Control
Above 0.85	Moist Foods	Require refrigeration or another barrier to control the growth of pathogens
0.60 and 0.85	Intermediate-Moisture Foods	• Do not require refrigeration to control pathogens • Limited shelf life because of spoilage, primarily by yeast & mold
Below 0.60	Low-Moisture Foods	Extended shelf life, even without refrigeration

See Table 4-12 for some examples of moist foods (water activities above 0.85). Most fresh meats, fruits, and vegetables, and many dairy products, fall into this category. The big surprise here is probably the bread. Most of us tend to think it is a dry, shelf-stable product. Actually, the "crumb" (interior) has a relatively high water activity. It is safe because of the multiple barriers of pH, water activity (the crust has a low water activity), and preferential growth by mold rather than pathogens. In other words, the bread spoils before it becomes hazardous.

Table 4-12. Examples of High Moisture (High Water Activity (a_w)) Foods

Moist Foods	Water Activity (a_w)
Lettuce	0.99
Apples	0.99
Milk	0.98
Bread	0.95

See Table 4-13 for some examples of intermediate-moisture foods (water activity between 0.60 and 0.85). Some unique products like soy sauce appear to be a high moisture product, but actually are in the intermediate-moisture category because salt, sugars or other ingredients bind the moisture. Because jams and jellies have a water activity that will support the growth of yeast and mold, they are mildly heat-treated immediately before packaging to prevent spoilage.

Table 4-13. Examples of Intermediate Moisture Foods

Intermediate Moisture Foods	Water Activity (a_w)
Soy sauce	0.80
Jams	0.80
Molasses	0.76
Honey	0.75
Flour	0.70
Dried fruit	0.70
Candies	0.65

See Table 4-14 for some examples of low-moisture foods (water activity below 0.60).

Table 4-14. Examples of Low-Moisture Foods

Low-Moisture Foods	Water Activity (a_w)
Dried noodles	0.50
Cookies	0.30
RTE Cereals	0.20
Crackers	0.10

Some of the intermediate and low water activity foods have naturally low water activity (e.g., molasses and flour). We do not discuss those foods because water activity does not have to be controlled during processing.

Other intermediate and low water activity foods, like dried fruit, strawberry jam, crackers, soy sauce, and dried noodles, start with a high water activity and, through processing, end up with a reduced water activity. This section of this chapter focuses on these types of foods.

Control of Water Activity

Some products require careful control of water activity for food safety, while others do not. For example, the production of jam does not need careful control of water activity for food safety because the food would not thicken (and, thus, become jam) unless the water activity was reduced through the addition of the necessary amount of sugar. On the other hand, dried fruit products need careful control of water activity for food safety, because fruit products with a variety of moisture levels could still appear to be "dried fruit."

There are two primary ways of reducing water activity in foods: (1) product formulation (such as by adding salt or sugar); and (2) dehydration (drying). In this section of this chapter, we discuss reducing water activity by product formulation. In section 4.3.4 of this document, we discuss reducing water activity by dehydration.

Every organism has a minimum, optimum, and maximum water activity for growth (see Table 3-A in Appendix 3 of this document). Yeasts and molds can grow at low water activity; however 0.85 is considered the safe cutoff level for pathogen growth. Water activity of 0.85 is based on the minimum water activity for *S. aureus* growth. For a detailed discussion and listing of the minimal water activities for microorganisms of public health concern, see ICMSF (1996).

There are two basic ways for how you can approach product formulation that uses control of water activity for food safety. One approach is to closely follow a scientifically established process for formulation that ensures a water activity of 0.85 or below. The other approach is to develop your own process for formulation and to validate it by taking finished product samples and testing them for water activity.

4.3.3.2 Use of Acidity (pH) as a Formulation Process Control

The term "pH" refers to a numeric scale used to describe acidity and alkalinity. The pH reflects the concentration of hydrogen ions and is expressed mathematically as the negative logarithm of the hydrogen ion concentration. The pH scale ranges from 0 to 14, with 7 being neutral.

pH = (-log of the [H+])

Microorganisms can only grow at certain pH levels (Table 4-15). Table 4-15 shows that mold and yeast can grow over a broad range of pH, including very low pH. Table 4-15 also shows that the pH range where bacteria can grow is more restricted in that bacteria don't grow at very low pH.

Table 4-15. Growth Limiting pH Ranges for Microorganisms

Type of Microorganism	pH Range for Growth
Bacteria (Gram+)	4.0 to 8.5
Bacteria (Gram -)	4.5 to 9.0
Molds	1.5 to 9.0
Yeast	2.0 to 8.5

Table 4-15 classifies bacteria as "Gram positive" and "Gram negative." In general, "Gram positive" and "Gram negative" are designations associated with the cell walls of bacteria, and how the bacterial cell walls appear under a microscope when a stain is used to see them. Gram positive bacteria appear blue, and gram negative bacteria appear red.

Lowering the pH is considered primarily a method of inhibiting the growth of bacteria rather than a method for killing bacteria. Although many microorganisms held at low pH for an extended time will be killed, keep in mind that some pathogenic bacteria, and in particular *E. coli* O157:H7, can survive acidic conditions for extended periods of time, even if their growth is inhibited. For details on the minimum and maximum pH limits for bacterial pathogens, see Table 3-A of Appendix 3 of this document.

Foods with a natural pH of 4.6 and below are considered acid foods. Some foods are naturally acidic, including most fruits (e.g., many peaches, pH 4.0; apples, pH 3.5). However, some tropical fruits, including some pineapple, may fall in the pH range above 4.6, depending in part on variety and growing conditions. Foods with a pH above 4.6 are said to be low-acid foods. Examples of low-acid foods include protein foods (such as milk and eggs), most vegetables, and starch based foods (such as bread and crackers).

Acidification

Because an acid pH can inhibit the growth of many bacteria, acidification of foods is a common formulation process control. Acidification is the direct addition of acid to a low-acid food. Examples of foods that are acidified as a process control include pickled beets and peppers. There are a variety of acids (such as acetic acid, lactic acid, and citric acid) that can be used to acidify foods, depending on the desired attributes of the finished product.

We have established specific CGMP requirements for thermally processed low-acid foods packaged in hermetically sealed containers (commonly called "low-acid canned foods" or LACF (21 CFR part 113). We also have established requirements for acidified foods (21 CFR part 114). At the time when we established these regulations, the focus of these CGMP requirements was the control of *C. botulinum*; when the pH of a food is 4.6 or below, spores of *C. botulinum* will not germinate and grow. As a result, the pH of 4.6 is a dividing line for the purpose of determining whether a food other than an acid food is subject to part 113 as an LACF or part 114 as an acidified food. See 21 CFR 114.3.

An acid food, such as tomatoes with a pH of 4.2, is not subject to either the LACF regulations or the acidified foods regulations. Under the acidified foods regulations, "acidified foods" are low-acid foods to which acid(s) or acid food(s) are added; they have a water activity greater than 0.85 and have a finished equilibrium pH of 4.6 or below (21 CFR 114.3(b)). The definition of acidified foods provides that carbonated beverages, foods that are stored, distributed, and retailed under refrigeration, and certain other foods are excluded from the coverage of 21 CFR part 114 (21 CFR 114.3(b)).

Processors of acidified foods must register with FDA to obtain a Food Canning Establishment number (21 CFR 108.25(c)(1)). Processors of acidified foods also must file a scheduled process with FDA (21 CFR 108.25(c)(2)); the scheduled process is the process selected by a processor as adequate for use under the conditions of manufacture for a food in achieving and maintaining a food that will not permit the growth of pathogens. The scheduled process includes control of pH and other critical factors equivalent to the process established by a competent processing authority (21 CFR 114.3). Acidified foods must be so manufactured, processed, and packaged that a finished equilibrium pH value of 4.6 or lower is achieved within the time designated in the scheduled process and maintained in all finished foods; manufacturing must be in accordance with the scheduled process (21 CFR 114.80(a)(1)). Sufficient control, including frequent testing and recording of results, must be exercised so that the finished equilibrium pH values for acidified foods are not higher than 4.6 (21 CFR 114.80(a)(2)). An equilibrium pH is achieved when a natural pH balance has been reached by all ingredients - which can take several days in foods with very large particulates (National Canners Association, 1968). You should refrigerate products that require several days to reach equilibrium pH to prevent the growth of *C. botulinum* or other pathogens.

There are several different methods of adding the acid to the product. One method is called direct acidification, where predetermined amounts of acid and the low-acid foods are added to individual finished product containers during production. With this method, it is important that the processor control the acid-to-food ratio. This is probably the most common method used for acidified vegetables. Another method of acidification is batch acidification. As the name implies, acid and food are combined in large batches and allowed to equilibrate. The acidified food is then packaged.

Acidified foods must be treated sufficiently to control spoilage microorganisms in addition to vegetative pathogens. Although one reason is to prevent spoilage triggering economic loss, the food safety reason is that the action of the spoilage organisms can raise the pH, compromising the safety of the product because any spores of *C. botulinum* that are in the food can germinate, grow, and produce botulinum toxin. The acidified foods regulation requires that you thermally process the food to an extent that is sufficient to destroy the vegetative cells of pathogenic and non-pathogenic microorganisms capable of reproducing in the food under the conditions in which the food is stored, distributed, retailed and held by the user. However, you may use permitted preservatives to inhibit reproduction of non-pathogenic microorganisms in lieu of thermal processing. (21 CFR 114.80(a)(1))

For further information on the use of acidification of foods as a process control, see 21 CFR part 114. The regulation provides detailed information on appropriate procedures to measure pH for foods.

Fermentation

During bacterial fermentation, acid-producing bacteria produce lactic acid, which reduces the pH. Because the reduced pH can inhibit the growth of many bacteria, bacterial fermentation of foods is a common formulation process control. Examples of low-acid foods fermented by bacterial fermentation to a pH below 4.6 include fermented olives, fermented cucumber pickles, cheeses, and sauerkraut. Molds are used to ferment some foods such as soy sauce, tamari sauce, and other oriental foods, mainly for taste and other characteristics.

In practice, fermentation is an art. You need to encourage growth of favorable organisms and discourage the growth of organisms that can cause spoilage. This is usually accomplished by adding salt or a starter culture to the food, or in some cases slightly acidifying it. A starter culture can be either yeast or bacteria.

In many fermented products, there is no process to eliminate the acid-producing bacteria. These fermented products are kept refrigerated so that the culture bacteria and bacteria not killed during the fermentation process do not spoil the product.

4.3.3.3 Use of Preservatives as a Formulation Process Control

Preservatives can be used to prevent the growth of microorganisms – e.g., if a food product is not thermally processed (or not thermally processed to an extent that is sufficient to kill the vegetative cells of non-pathogenic microorganisms (such as spoilage microorganisms) that are capable of reproducing in the food under the conditions in which the food is stored, distributed, retailed and held by the user). Preservatives work by denaturing protein, inhibiting enzymes, or altering or destroying the cell walls or cell membranes of microorganisms. Examples of products that use preservatives as a formulation process control include acidified foods that are either not thermally processed or only minimally thermally processed, hummus (which uses sodium benzoate to inhibit yeast and mold), and many breads (which use calcium propionate to inhibit mold).

Some of the more commonly used preservatives are:

- **Acetic aci**d and its salts (e.g., sodium acetate, sodium diacetate), which is added to reduce bacterial growth.
- **Benzoates**, which include benzoic acid, sodium benzoate and potassium benzoate. Benzoates are used primarily to inhibit yeast or mold. Also can inhibit bacterial pathogens (e.g., *S. aureus*, *L. monocytogenes*).
- **Natamycin** is applied on cheese to inhibit the growth of fungi.
- **Nisin** is used as an antimicrobial agent to inhibit the outgrowth of *C. botulinum* spores and toxin formation in a variety of pasteurized process cheese spreads.
- **Propionates,** which include propionic acid, and sodium, potassium and calcium propionates, are used in breads, cakes, and cheeses to inhibit mold. Also can inhibit bacterial pathogens (e.g., *S. aureus*, *Salmonella*).
- **Sorbates**, which include sorbic acid, and sodium and potassium sorbates. Sorbates are primarily used to inhibit yeast and mold. Also can inhibit bacterial pathogens (e.g., *E. coli* O157:H7, *L. monocytogenes*).

- **Sulfites,** such as sulfur dioxide, are used in a variety of products including lemon juice, seafood, vegetables, molasses, wines, dried fruit, and fruit juices. Sulfites are used primarily as an antioxidant but also have antimicrobial properties.

Table 4-16 provides examples of how some of these commonly used preservatives are used.

Table 4-16. Preservatives Commonly Used in Conjunction with Main Groups of Foods in the United States

Foodstuff	Acetic Acid	Benzoates	Natamycin	Nisin	Propionates	Sorbates	Sulfites
Fat Emulsions	+	+	-	-	-	++	-
Cheese	-	(+)	+	+	+	++	-
Vegetable Products	++	++	-	-	-	++	+
Fruit products	+	++	-	-	-	++	++
Beverages	-	++	-	-	-	++	(+)
Baked goods	+	-	-	-	++	++	-
Confectionery	-	(+)	-	-	-	++	-

Source: Adapted from Davidson and Branen 1993; Table 11 in Lück and Jager 1997, p 61
++ used frequently
+ used occasionally
(+) used in exceptional cases only
- not used

A food category that may benefit from the use of preservatives as a formulation process control is fresh, refrigerated, RTE deli salads. This category of food, which is typically formulated with multiple components, including spices and fresh vegetables, may experience a high bio-load at the time of preparation if treated ingredients are not used. Maintaining quality (e.g., by preventing spoilage by yeasts and molds) and ensuring product safety cannot always be achieved by reducing pH (e.g., by using an acidified food as a salad dressing (such as mayonnaise) or an acid food as a salad dressing (such as vinegar)). Antimicrobial substances such as potassium sorbate and propionic acid are commonly used for a variety of RTE deli salads to inhibit bacteria, yeast, and mold, extending the product shelf-life.

For further regulatory guidance on the use of antimicrobial substances, see FDA (1999). For a comprehensive review on the application of antimicrobials, see Davidson, et al. (2005).

4.3.4 Use of Dehydration/Drying as a Process Control

Dehydration (which reduces water activity) is one of the oldest methods of food preservation. In the United States, there are three primary methods of dehydration as a process control.

- Freeze-drying - used for a variety of products
- Forced air drying - used for solid foods like vegetables and fruit
- Spray drying - used for liquids and semi-liquids like milk

Dehydrated/dried products are usually considered shelf stable due to their low water activity (a_w) and, therefore, are often stored and distributed unrefrigerated. Examples of shelf-stable dehydrated/dried food products include milk powders, powdered beverages, pasta, and dried peas and beans.

If you use dehydration/drying as a process control, you should select a packaging material that will prevent rehydration of the product under the expected conditions of storage and distribution. Additionally, finished product package closures should be free of gross defects that could expose the product to moisture during storage and distribution.

See "Chapter 9 – Use of Dehydration/Drying as a Process Control" of this guidance for additional information on the use of dehydration/drying as a process control. For a detailed overview of dehydration/drying technologies commonly used in the United States (including freeze drying, forced air drying, and spray drying), as well as other dehydration technologies such as drum drying and fluid bed drying, see Greensmith (1998) and Heldman and Lund (2007). For a discussion on the effects of drying on microorganisms, see Jay (1996).

4.3.5 Use of Recipe Management as a Process Control for Food Ingredients

A food ingredient (such as a food additive, color additive, or GRAS substance) can be a chemical hazard if it is added in excess of a maximum use level, regardless of whether the maximum use level is established due to food intolerance (such as for sulfites) or is otherwise a condition of safe use of a food additive, color additive, or GRAS substance. Control strategies to prevent misformulation of food ingredients generally include recipe management to ensure that excessive amounts are not added.

4.3.6 Use of Storage Conditions as a Process Control for Mycotoxins

Mycotoxins are toxic metabolites produced by certain fungi (i.e., molds) that can infect and proliferate on raw agricultural commodities (e.g., grains such as wheat and corn, peanuts, fruits, and tree nuts) in the field and during storage. Contamination by toxigenic fungi during storage and transportation is caused by improper drying or re-wetting of the crop from rain or condensation. Thus, effective process controls involve correct drying and storage.

By far the most critical environmental factors determining whether a raw agricultural commodity will support mold growth are temperature, moisture content, and time, and each of these parameters can be manipulated and controlled to manage the prevention of mold growth in a raw agricultural commodity. The principal process control for prevention of mold growth in storage conditions is the control of moisture. Although low-temperature storage can help control mold growth in some conditions, large-scale storage of raw agricultural commodities generally takes place in structures that do not provide for low-temperature and, thus, low-temperature storage generally is not a control measure for mold during the storage of raw agricultural commodities.

4.3.7 Use of Physical Sorting as a Process Control for Mycotoxins

In most cases, mycotoxins in raw agricultural commodities are present in a very small proportion of individual seeds or kernels. As a result, removing the contaminated seeds or kernels mechanically is a practical and effective process control to reduce the mycotoxin content of the bulk raw agricultural commodity (West and Bullerman, 1991). Various techniques have been devised, based on color and visual appearance of decay or damage, to separate out

contaminated seeds during inspection processes. This may be manual or by more advanced electronic instrumental selection.

4.3.8 Use of Exclusion Strategies as a Process Control for Physical Hazards

4.3.8.1 Exclusion Strategies as a Process Control for Metal Hazards

Metal-to-metal contact during processing can introduce metal fragments into products. For example, metal fragments can break off during mechanical cutting and blending operations, and some metal equipment has parts that can break or fall off, such as wire-mesh belts. You can control metal hazards by using physical separation techniques (such as magnets, sieves, screens, or flotation tanks), by using electronic or X-ray metal detection devices, and by regularly inspecting at-risk equipment for signs of damage.

The effectiveness of physical separation techniques depends on the nature of the product. These measures are more likely to be effective in liquids, powders, and similar products in which the metal fragment will not become imbedded.

The use of electronic metal detectors is complex, especially with regard to stainless steel, which is difficult to detect. The orientation of the metal object in the food affects the ability of the equipment to detect it. For example, if a detector is not properly calibrated and is set to detect a sphere 0.08 inch (2 mm) in diameter, it may fail to detect a stainless steel wire that is smaller in diameter but up to 0.9 inch (24 mm) long, depending on the orientation of the wire as it travels through the detector. Processing factors, such as ambient humidity or product acidity, may affect the conductivity of the product and create an interference signal that may mask metal inclusion unless the detector is properly calibrated. You should consider these factors when calibrating and using this equipment.

X-ray devices can also be used for metal detection. One advantage in using such a device is that X-rays can detect non-metal foreign objects that may also be hazardous, such as glass fragments.

Preventive maintenance of equipment and periodically examining your processing equipment for damage that can contribute metal fragments can be a useful control measure, particularly when you have a piece of equipment that is prone to break, such as saw blades, or equipment that has metal-to-metal contact. The success of this strategy depends in large part on the nature of the equipment inspected and the frequency of the inspection. However, this approach will not necessarily prevent metal fragments from being incorporated into the product in all cases, but may enable you to separate products that may have been exposed to metal fragments. Visually inspecting equipment for damaged or missing parts may only be feasible with relatively simple equipment, such as band saws, small orbital blenders, and wire mesh belts. More complex equipment that contains many parts, some of which may not be readily visible, may not be suitable for visual inspection and may require controls such as metal detection or physical separation techniques.

See “Chapter 13-- Preventive Controls for Physical Hazards” of this guidance for additional information on the control of metal hazards.

4.3.8.2 Exclusion Strategies as a Process Control for Glass Hazards

Glass fragments can be introduced into food whenever processing involves the use of glass containers. Normal handling and packaging methods, especially mechanized methods, can result in breakage. Ingesting glass fragments can cause injury to the consumer. Most products packed in glass containers are intended to be a ready-to-eat (RTE) commodity that requires minimal handling on the part of the consumer before eating, so that consumers have little opportunity to detect glass inclusion.

This chapter addresses the hazard of glass fragments that may occur from the use of glass containers. You should address the hazard of glass fragments originating from sources such as overhead light fixtures through CGMPs.

You can help prevent glass from getting into your food products by periodically checking the processing areas and equipment for glass breakage. In addition, the line operator can listen for breakage and can look for broken glass on the floor. (You can enhance the utility of these controls by painting the floor under the processing line in a color that highlights the container glass.) These types of controls will not necessarily prevent glass fragments from being incorporated into your product, but they can enable you to separate products that may have been exposed to glass fragments from those that have not.

You also can help prevent glass fragments from getting into your food products by cleaning empty containers before filling into the product package. You can do so by using water or compressed air and inverting the container during or after cleaning. You should be mindful that container cleaning may not fully control glass hazards in some processes that use automated filling systems because this equipment can result in glass breakage during the filling and capping process.

See “Chapter 13--Preventive Controls for Physical Hazards” of this guidance for additional information on the control of glass hazards.

4.4 Sanitation Controls

CGMPs require sanitary operations (21 CFR 117.35) and sanitary facilities and controls (21 CFR 117.37). There are requirements applicable to the cleanliness of equipment and utensils, including food-contact surfaces (21 CFR 117.40), and plant construction and design (21 CFR 117.20(b)). To comply with these CGMP requirements, sanitation procedures, practices, and processes should take place every day in your facility.

Sanitation controls include procedures, practices, and processes to ensure that the facility is maintained in a sanitary condition adequate to significantly minimize or prevent hazards such as environmental pathogens, biological hazards due to employee handling, and food allergen hazards. Sanitation controls must include, as appropriate to the facility and the food, procedures, practices, and processes for the: (1) Cleanliness of food-contact surfaces, including food-contact surfaces of utensils and equipment; and (2) prevention of allergen cross-contact and cross-contamination from insanitary objects and from personnel to food, food packaging material, and other food-contact surfaces and from raw product to processed product. (See 21 CFR 117.135(c)(3).)

You determine which hazards require a sanitation control, rather than CGMPs, through your hazard analysis. Thus, some – but not all - of your sanitation procedures, practices, and

processes will be “sanitation controls”; other sanitation procedures, practices, and processes will be CGMPs. For your sanitation controls to be effective, you should first assess the sanitation procedures, practices, and processes that you will have in place to comply with the CGMP requirements. For example, equipment design that ensures that all surfaces can be accessed and cleaned is essential for the effective application of sanitation controls. Effective sanitary design should consider factors such as whether equipment includes hollow bodies or poorly developed welds and seams, as well as whether ease of disassembly allows adequate access to all food-contact surfaces to ensure thorough cleaning and sanitation. Sanitary design also applies to food facility structures (e.g., floors, walls, piping, and ceilings) to ensure effective cleaning and sanitation practices. The required elements for cleaning – time, temperature, mechanical force and chemical concentration – simply cannot be reliably applied if the equipment and facility structural design does not allow adequate access (Marriott and Gravani, 2010). Due to this link between your CGMP procedures, practices, and processes and your sanitation controls, your CGMP procedures, practices, and processes are sometimes called “prerequisite programs.”

The nature of the processing conditions (i.e., wet or dry) required for the manufacture of a particular product (such as a dry processing environment for spray dried milk powder, and a wet processing environment for soft cheese) impacts the selection of the appropriate CGMP sanitation procedures, practices, and processes or the appropriate sanitation control. For example, moisture control is critically important in preventing contamination by an environmental pathogen, such as *Salmonella*, in low-moisture products. Water in a dry processing environment is one of the most significant risk factors for *Salmonella* contamination, because the presence of water allows for pathogen growth leading to product contamination from the environment or from insanitary food contact surfaces. Therefore, dry cleaning or controlled wet cleaning practices should be considered for use as sanitation control measures in a dry processing environment. Any time water is used for cleaning, the equipment should be thoroughly dried before use. Wet processing operations are subject to wet cleaning. However, water, in particular standing water, should be minimized even if facilities are wet cleaned. This is particularly true for facilities that need to control *L. monocytogenes* because they are producing RTE products exposed to the environment.

The nature of a bacterial pathogen (e.g., whether it is a transient or a resident strain of an environmental pathogen) also impacts the selection of the appropriate CGMP sanitation procedures, practices, and processes, or the appropriate sanitation control. (See section 3.2.5.2 (Transient vs. resident facility-related environmental pathogens) in “Chapter 3-- Potential Hazards Associated with the Manufacturing, Processing, Packing, and Holding of Human Food” in this guidance for additional information about transient and resident strains of environmental pathogens.

Table 4-17 lists examples of the application of sanitation controls to significantly minimize or prevent biological and chemical hazards and the section in this chapter that addresses each listed example.

Table 4-17. Examples of Sanitation Controls

Sanitation Control Subcategory	Examples	Chapter Section
Cleaning food-contact surfaces	• Applying a full wet clean with detergents and sanitizers for Clean in Place and Clean out of Place (CIP/COP) • Applying controlled wet clean with minimum water usage and wipe down (COP) • Dry cleaning with vacuums, brushes, wipes	4.4.1
Control cross-contact / cross-contamination	• Using hygienic zoning for separation of process operations such as raw vs. Work-in-Process (WIP) vs. finished product; wet vs. dry; personnel and materials flow; air balance • Using dedicated cleaning / sanitation practices in designated hygiene zones *(see cleaning food-contact surfaces)* • Cleaning between different products containing different allergens	4.4.2

See "Chapter 10 – Sanitation Controls" of this guidance for additional information about sanitation controls. In addition to this guidance, a number of sources of scientific and technical information can be useful in establishing sanitation controls. See Holah, 2014 and Marriott and Gravani, 2010.

4.4.1 Use of Sanitation Controls for the Cleanliness of Food-Contact Surfaces

The CGMP requirements for sanitary operations include specific requirements for cleaning food-contact surfaces. See 21 CFR 117.35(d). All food-contact surfaces, including utensils and food-contact surfaces of equipment, must be cleaned as frequently as necessary to protect against allergen cross-contact and against contamination of food (21 CFR 117.35(d)). Food-contact surfaces used for manufacturing/processing, packing, or holding low-moisture food must be in a clean, dry, sanitary condition before use (21 CFR 117.35(d)(1)). When the surfaces are wet-cleaned, they must, when necessary, be sanitized and thoroughly dried before subsequent use (21 CFR 117.35(d)(1)). In wet processing, when cleaning is necessary to protect against allergen cross-contact or the introduction of microorganisms into food, all food-contact surfaces must be cleaned and sanitized before use and after any interruption during which the food-contact surfaces may have become contaminated (21 CFR 117.35(d)(2)). Where equipment and utensils are used in a continuous production operation, the utensils and food-contact surfaces of the equipment must be cleaned and sanitized as necessary (21 CFR 117.35(d)(2).

Part 117 does not define the term "cleaning." In this guidance, we use the term "cleaning" to mean removing the "soil"– i.e., bacteriological nutrients, such as fats, carbohydrates, proteins,

and minerals"– that can build up on food-contact surfaces in the plant and processing equipment. Part 117 defines "sanitize" to mean 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. (21 CFR 117.3) Although cleaning operations and sanitizing operations often are conducted separately – and sequentially – some systems (such as steam systems) both clean and sanitize the surfaces; we consider that such systems satisfy the definition of ''sanitize.'' (See 80 FR 55908 at 55956.)

Table 4-16 describes three types of cleaning strategies that you can use to remove soil, depending upon the processing conditions (wet or dry). Table 4-16 includes our recommendations for using these cleaning strategies. See Appendix 4 of this guidance for more details about these cleaning strategies.

Table 4-18. Types of Cleaning Strategies

Cleaning Strategy	Description and Recommendations
Wet Cleaning	Uses water-based and/or wet chemical cleaning solutions. When using wet cleaning, you should avoid certain practices, e.g., excessive use of water (e.g., floor is flooded with water), high pressure hoses. Instead, you should use water on an as-needed basis. You also should minimize and isolate your use of water to specific areas where possible. Drying after wet cleaning helps to minimize growth of remaining microorganisms.
Dry Cleaning	Does not use any water. Dry cleaning is the physical removal of residues (e.g., food particles and dust) without water. You should remove food residues by actions such as sweeping, brushing, scraping, or vacuuming the residues from equipment surfaces and the facility environment. Be careful to not distribute food particles to other equipment or areas during removal.
Controlled Wet Cleaning	Uses a limited amount of water, generally for dry operations. Complete drying should follow immediately after the controlled wet cleaning. You can move specific pieces of equipment out of the area to be wet cleaned, sanitized, and dried and then return the equipment after the area is cleaned.

After the surfaces are cleaned and rinsed you should sanitize food contact surfaces and other areas as appropriate. You should use all sanitizers in accordance with the EPA-registered (or similar registration in other countries) label use instructions, including approval for use in food establishments.

As noted in section 4.4, sanitation controls must include, as appropriate to the facility and the food, procedures, practices, and processes for the cleanliness of food-contact surfaces, including food-contact surfaces of utensils and equipment. (See 21 CFR 117.135(c)(3).) Examples of sanitation controls related to the cleanliness of food-contact surfaces include cleaning and sanitizing procedures, practices, and processes (including appropriate frequencies for these procedures, concentrations of cleaning and sanitizing compounds, method of application, and contact time) (Holah, 2014). See "Chapter 10 – Sanitation Controls" of this guidance for a practical example of the application of cleaning and sanitizing of food-contact surfaces as a preventive control for bacterial contamination.

4.4.2 Use of Sanitation Controls to Prevent Allergen Cross-contact and Cross-contamination

As noted in section 4.4, sanitation controls must include, as appropriate to the facility and the food, procedures, practices, and processes for the prevention of allergen cross-contact and cross-contamination from insanitary objects and from personnel to food, food packaging material, and other food-contact surfaces and from raw product to processed product. (See 21 CFR 117.135(c)(3).)

Table 4-19 describes three common practices that you can use to prevent allergen cross-contact and to prevent cross-contamination of foods from insanitary objects, poor hygienic practices, different processing operations, and environmental pathogens.

Table 4-19. Common Practices to Prevent Allergen Cross-contact and Cross-contamination

Practice	Description
Hygienic Zoning	Hygienic zoning for separation and segregation of process operations such as raw vs. work-in-process vs. finished product; wet vs. dry; personnel and materials traffic flow; air balance
Hygienic Zone Specific Cleaning	Dedicated cleaning / sanitation practices within hygiene zones
Allergen Specific Cleaning	Cleaning between different products containing different allergens

The objective of hygienic zoning is to reduce the potential for transient pathogens to enter sensitive areas in the facility, such as packing areas where an RTE product is exposed to the processing environment. Typically, this type of sanitation control is applied in facilities that make RTE products.

You should determine the need for, and scope of, a hygienic zoning program based on your facility, the products you make, and the outcome of your hazard analysis. For example, the need for, and scope of, a hygienic zoning program are likely to be very different for a flour mill, a facility that makes RTE refrigerated food, and a facility that makes canned acidified foods. In determining the need for, and scope of, a hygienic zoning program, you should take into account the structure of your plant, packaging, personnel and ingredient traffic flows, and any cross over areas. You also should consider potential contaminants from raw materials, air flow, support areas, and other activities taking place in the facility.

Some facilities implement hygienic zoning for quality reasons (e.g., to control mold contamination); however, the sanitation controls that are the subject of this guidance need only address food safety. See “Chapter 10 – Sanitation Controls” of this guidance for a practical example for the application of hygienic zoning to prevent recontamination by environmental pathogens.

4.5 Food Allergen Controls

Food allergen controls include procedures, practices, and processes to control food allergens. Food allergen controls must include those procedures, practices, and processes employed for: (1) Ensuring protection of food from allergen cross-contact, including during storage, handling,

and use; and (2) labeling the finished food, including ensuring that the finished food is not misbranded under section 403(w) of the FD&C Act (21 U.S.C. 343(w)). See 21 CFR 117.135(c)(2).

Examples of procedures, practices, and processes to ensure protection of food from allergen cross-contact are:

- Identifying and marking allergen-containing ingredients at receiving;
- Segregating and storing allergen-containing materials at receiving and warehousing;
- Scheduling production of products based on allergen-containing recipes;
- Physical separation of processes for non-allergen-containing and allergen-containing products;
- Sanitation and cleaning practices;
- Using full wet cleaning to remove allergenic materials prior to producing a non-allergen-containing product on the same line;
- Using dedicated cleaning utensils and equipment for removing allergenic materials from food processing equipment.

Examples of procedures, practices, and processes to label the finished food are:

- Performing label review for each new batch of labels received at the facility;
- Implementing procedures for application of correct label to product.

See "Chapter 11 - Food Allergen Controls" of this guidance for in-depth guidance on preventive control strategies for food allergen hazards.

4.6 Supply-chain Controls

Supply-chain controls include the supply-chain program required by 21 CFR part 117, subpart G (21 CFR 117.135(c)(4)). Subpart G specifies:

- The requirement to establish and implement a supply-chain program (21 CFR 117.405);
- General requirements applicable to a supply-chain program (21 CFR 117.410);
- Responsibilities of the receiving facility (21 CFR 117.415);
- Requirements for using approved suppliers (21 CFR 117.420);
- Requirements for determining appropriate supplier verification activities (including determining the frequency of conducting the activity) (21 CFR 117.425);
- Requirements for conducting supplier verification activities for raw materials and other ingredients (21 CFR 117.430);
- Requirements for an onsite audit (21 CFR 117.435); and
- Requirements for records documenting the supply-chain program (21 CFR 117.475).

In this section of this guidance, we discuss the use of ingredient specifications as a supply-chain control for several chemical hazards – i.e., pesticides, drug residues, heavy metals, and mycotoxins. See our forthcoming "Chapter 15: Supply-Chain Program for Human Food Products" for in-depth guidance on supply-chain controls.

4.6.1 Supply-chain Controls for Pesticides

Pesticides used in the growing of vegetables fruits, and grain crops include fungicides, insecticides, and rodenticides that control pests found in growing environments. These may also be used in manufacturing environments. If you determine through your hazard analysis that a pesticide hazard requires a preventive control (e.g., due to residual pesticide level violations in a particular raw agricultural commodity), and that control is applied by your supplier, you would have a supply-chain program in which you would verify that your supplier controls pesticides. You could have specifications for your supplier that pesticide levels in raw materials and other ingredients must be within permitted levels and you could ask to review your supplier's pesticide control program. Your program could have verification activities such as periodic testing by you or your supplier for pesticide residues.

4.6.2 Supply-chain Controls for Drug Residues

Drug residues due to the use of antibiotics or related drugs in livestock are principally a potential concern for milk-based products. If you determine through your hazard analysis that a drug residue hazard requires a preventive control, and that control is applied by your supplier, you would have a supply-chain program in which you would verify that your supplier controls drug residues to ensure that drug residues in raw materials and other ingredients are within permitted levels.

4.6.3 Heavy Metals

Heavy metals are principally a concern in raw agricultural commodities grown in soils that are contaminated either naturally or through industrial activity. If you determine through your hazard analysis that a heavy metal hazard requires a preventive control, and that control is applied by your supplier, you would have a supply-chain program in which you would verify that suppliers source raw agricultural commodities from regions that do not have high levels of heavy metal contamination in soil, and specifications that heavy metals in raw materials and other ingredients will be within permitted levels.

4.6.4 Supply-chain Controls for Mycotoxins

Mycotoxins are toxic metabolites produced by certain fungi (i.e., molds) that can infect and proliferate on raw agricultural commodities (e.g., grains such as wheat and corn, peanuts, fruits, and tree nuts) in the field and during storage. Critical environmental factors determining whether a raw agricultural commodity will support mold growth are temperature, moisture content, and time, and each of these parameters can be manipulated and controlled to manage the prevention of mold growth in a raw agricultural commodity. As noted in section 4.3.7 of this chapter, effective process controls for mycotoxins involve correct drying and storage as well as physical sorting techniques to remove damaged or moldy raw agricultural commodities.

If you determine through your hazard analysis that a mycotoxin hazard requires a preventive control, and that control is applied by your supplier, you would have a supply-chain program in which you would verify that your supplier controls mycotoxins. You could have specifications that mycotoxins in raw materials and other ingredients will be within permitted levels.

4.7 Recall Plan

For food with a hazard requiring a preventive control, you must establish a written recall plan for the food. The written recall plan must include procedures that describe the steps to be taken, and assign responsibility for taking those steps, to perform the following actions as appropriate to the facility: (1) Directly notify the direct consignees of the food being recalled, including how to return or dispose of the affected food; (2) Notify the public about any hazard presented by the food when appropriate to protect public health; (3) Conduct effectiveness checks to verify that the recall is carried out; and (4) Appropriately dispose of recalled food—e.g., through reprocessing, reworking, diverting to a use that does not present a safety concern, or destroying the food. See 21 CFR 117.139.

We recommend that you consult our general guidance on policy, procedures, and industry responsibilities regarding recalls in 21 CFR part 7, subpart C (§§ 7.40 through 7.59) and FDA's Guidance for Industry: Product Recalls, Including Removals and Corrections (FDA, 2015c).

A recall can be disruptive to your operation and business, but there are several steps you can take in advance to minimize this disruptive effect:

- Adequately code products to make possible positive lot identification and to facilitate effective recall of all violative lots.
- Maintain such product distribution records as are necessary to facilitate location of products that are being recalled. You should maintain such records for a period of time that exceeds the shelf life and expected use of the product.

4.8 References

Almond Board of California (ABC). 2008. "Guidelines for validation of propylene oxide pasteurization." http://www.almonds.com/sites/default/files/content/attachments/ppo-validation-guidelines.pdf.

Alzamora, S. M., M. S. Tapia, and J. Welti-Chanes. 2003. "Chapter 8: The control of water activity." In *Food Preservation Techniques*, edited by Zeuthen, P. and L. Bøgh-Sørensen. Woodhead Publishing.

Berk, Z. 2009. "Ionizing irradiation and other non-thermal preservation processes." In *Food Process Engineering and Technology*, edited by Elsevier, 533-544.

Bridgman, P. W. 1912. "Water in the liquid and five solid forms under pressure." *Proceedings of the American Academy of Arts and Sciences* 47:441-558.

Codex Alimentarius Commission (CAC). 2003. "Hazard analysis and critical control point (HACCP) system and guidelines for its application, Annex to CAC/RCP 1-1969." (Rev. 4/2003). Accessed December 12, 2011. http://www.mhlw.go.jp/english/topics/importedfoods/guideline/dl/04.pdf.

Davidson, P. M., and A. L. Branen. 1993. *Antimicrobials in Foods*, 2nd edition.

Davidson, P. M., J. N. Sofos, and A. L. Branen. 2005. *Antimicrobials in Foods*. 3rd Edition: CRC Press.

Environmental Protection Agency (EPA). 2015. "Regulation of pesticide residues on food." Accessed June 23, 2016. https://www.epa.gov/pesticide-tolerances.

Environmental Protection Agency (EPA). 2016. "Indexes to Part 180 tolerance information for pesticide chemicals in food and feed commodities." Accessed May 31, 2016. https://www.epa.gov/pesticide-tolerances/indexes-part-180-tolerance-information-pesticide-chemicals-food-and-feed.

Farkas, J. 2007. "Chapter 32: Physical methods of food preservation." In *Food Microbiology: Fundamentals and Frontiers*, third edition, edited by Doyle, M. P., Beauchat, L. R., 685-712. Washington, DC: American Society of Microbiology.

Farkas, J., D. A. E. Ehlermann, and C. Mohacsi-Farkas. 1998. "Irradiation as a method for decontaminating food - a review." *Int J Food Micro* 44:189-204.

Farkas, J., D. A. E. Ehlermann, and C. Mohacsi-Farkas. 2014. "Chapter 27: Food Technologies: Food irradiation." In *Encyclopedia of Food Safety*, edited by Motarjemi, Y., Moy, G., Todd, E., Elsevier Publishing.

Farkas, J., and C. Mohacsi-Farkas. 2011. "History and future of food irradiation." *Trends in Food Science and Technology* 22:121-126.

Fellows, P. J. 2009a. "Chapter 7: Irradiation." In *Food Processing and Technology - Principles and Practices*, 271-289. Woodhead Publishing.

Fellows, P. J. 2009b. "Chapter 22: Freezing." In *Food Processing and Technology - Principles and Practices*, 650-686. Woodhead Publishing.

Food and Drug Administration (FDA). 1999. "Guidance for industry: Antimicrobial food additives." Accessed June 14, 2016. http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/IngredientsAdditivesGRASPackaging/ucm077256.htm.

Food and Drug Administration (FDA). 2000. "Kinetics of microbial inactivation for alternative food processing technologies - overarching principles: Kinetics and pathogens of concern for all technologies." Accessed May 31, 2016. http://www.fda.gov/Food/FoodScienceResearch/SafePracticesforFoodProcesses/ucm100198.htm.

Food and Drug Administration (FDA). 2001. "Evaluation and definition of potentially hazardous foods: Chapter 3 Factors that influence microbial growth." Accessed 05/31/2016. http://www.fda.gov/Food/FoodScienceResearch/SafePracticesforFoodProcesses/ucm094145.htm.

Food and Drug Administration (FDA). 2003. "Guidance for industry: Product recalls, including removals and corrections." Accessed February 19, 2015. http://www.fda.gov/Safety/Recalls/IndustryGuidance/ucm129259.htm.

Food and Drug Administration (FDA). 2004. "Irradiation of food and packaging: An overview." http://www.fda.gov/Food/IngredientsPackagingLabeling/IrradiatedFoodPackaging/ucm081050.htm.

Food and Drug Administration (FDA). 2013. "Food Code." Accessed July 26, 2016. http://www.fda.gov/downloads/Food/GuidanceRegulation/RetailFoodProtection/FoodCode/UCM374510.pdf.

Food and Drug Administration (FDA). 2015a. "Grade "A" Pasteurized Milk Ordinance, 2015 revision." http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/Milk/ucm2007966.htm.

Food and Drug Administration (FDA). 2015b. "Understanding food irradiation: What industry needs to know." Accessed May 31, 2016. http://www.fda.gov/food/ingredientspackaginglabeling/irradiatedfoodpackaging/ucm242021.htm.

Food Safety and Inspection Service (FSIS). 1999. "Compliance guidelines for cooling heat-treated meat and poultry products (stabilization)." http://www.fsis.usda.gov/wps/wcm/connect/a3165415-09ef-4b7f-8123-93bea41a7688/95-033F-Appendix-B.pdf?MOD=AJPERES.

Food Safety and Inspection Service (FSIS). 2005. "Meat and poultry hazards and controls guide." http://www.fsis.usda.gov/wps/wcm/connect/3cd0a6a5-fcff-4809-a298-030f3cd711a9/Meat_and_Poultry_Hazards_Controls_Guide_10042005.pdf?MOD=AJPERES.

Food Safety and Inspection Service (FSIS). 2013. "FSIS compliance guideline HACCP systems validation." Accessed March 13, 2015. http://www.fsis.usda.gov/shared/PDF/HACCP_Systems_Validation.pdf.

Food Safety Preventive Controls Alliance (FSPCA). 2016. "Chapter 7: Resources for preparing food safety plans." In *Preventive Controls for Human Food* Participant Manual, First Edition v. 1.2.

Goullieux, A., and J. P. Pain. 2005. "Chapter 18: Ohmic heating." In *Emerging Technologies in Food Processing*, edited by Sun, D., 469-505. London: Elsevier Academic Press.

Greensmith, M. 1998. “Chapter 4: Dryers”. In *Practical Dehydration*. 2nd ed. Cambridge, England: Woodhead Publishing.

Grocery Manufacturers Association (GMA). 2009. "Control of *Salmonella* in low-moisture foods." http://www.gmaonline.org/downloads/technical-guidance-and-tools/SalmonellaControlGuidance.pdf.

Hite, B. H. 1899. The effect of pressure in the preservation of milk. In *West Virginia Agricultural Experiment Station*. Morgantown, WV.

Hogan, E., A. L. Kelly, and D. Sun. 2005. "Chapter 1: High pressure processing of foods: An overview." In *Emerging Technologies in Food Processing*, edited by Sun, D., 3-33. London: Elsevier Academic Press.

Holah, J. T. 2014. "Cleaning and disinfection practices in food processing." In *Hygiene in Food Processing - Principles and Practices*, edited by Lelieveld, H. L. M., Holah, J. T., Napper, D., Elsevier Publishing.

Indrawati, A. Van Loey, C. Smout, and M. H. Katholieke. 2003. "Chapter 19: Hydrostatic pressure technology in food preservation." In *Food Preservation Techniques*, edited by Zeuthen, P., Bøgh-Sørensen, L., 428-448. Cambridge, England: Woodhead Publishing.

International Commission on Microbiological Specification for Foods (ICMSF). 1980. *Microbial Ecology of Foods 1: Factors affecting life and death of microorganisms*, 88-89. Orlando: Academic Press.

International Commission on Microbiological Specification for Foods (ICMSF). 1996. *Microorganisms in Foods 5: Characteristics of microbial pathogens*: Blackie Academic & Professional.

Jay, J. M. 1996. "Intrinsic and extrinsic parameters of foods that affect microbial growth." In *Modern Food Microbiology*, 38-66. Chapman & Hall.

Kennedy, C. 2003. "Developments in freezing." In *Food Preservation Techniques*, edited by Zeuthen, P., Bøgh-Sørensen, L., 228-240. Cambridge, England: Woodhead Publishing.

Krishnamurthy, K., H. K. Khurana, S. Jun, J. Irudayaraj, and A. Demirci. 2008. "Infrared heating in food processing: An overview." *Comprehensive Reviews in Food Science and Food Safety* 7:2-13.

LaCroix, M. 2005. "Irradiation of foods." In *Emerging Technologies for Food Processing*, edited by Sun, D., 353-386. Elsevier.

Luck, E., and M. Jager. 1997. *Antimicrobial Food Additives: Characteristics, Uses, Effects, 61*. Berlin: Springer.

Lucke, F. K. 2003. "Chapter 7: The control of pH." In *Food Preservation Techniques*, edited by Zeuthen, P., 61. Bøgh-Sørensen, L., Woodhead Publishing.

Marriott, N. G., and R. B. Gravani. 2010a. "Chapter 8: Quality assurance for sanitation." In *Principles of Food Sanitation*, 116-140. Aspen Publications.

Marriott, N. G., and R. B. Gravani. 2010b. "Chapter 9: Cleaning compounds." In *Principles of Food Sanitation*, 141-164. Aspen Publications.

National Advisory Committee on Microbiological Criteria for Foods (NACMCF). 1998. "Hazard analysis and critical control point principles and application guidelines." *Journal of Food Protection* 61 (9):1246-1259.

National Canners Association. 1968. *Laboratory Manual for Food Canners and Processors: Chapter 9 Process Calculations* Vol. 1., p 220. Westport, CT: The AVI Publishing Company, Inc.

Okos, M. R., O. Campanella, G. Narsimhan, R. K. Singh, and A. C. Weitnauer. 2007. "Chapter 10: Food dehydration." In *Handbook of Food Engineering* (2nd edition), edited by Heldman, D. R. and D. B. Lund. Taylor & Francis.

Orsat, V., and G. Vijaya Raghavan. 2005. "Chapter 17: Radio-frequency processing." In *Emerging Technologies in Food Processing*, edited by Sun, D., 445-468. London: Elsevier Academic Press.

Stumbo, C. R. 1973. "Death of bacteria subjected to moist heat." In *Thermobacteriology in Food Processing*. New York, NY: Academic Press.

Sumnu, G., and S. Sahin. 2005. "Chapter 16: Recent developments in microwave heating." In *Emerging Technologies in Food Processing*, edited by Sun, D., 419-444. London: Elsevier Academic Press.

West, D. I., and L. B. Bullerman. 1991. "Physical and chemical separation of mycotoxins from agricultural products." In *Mycotoxins and Animal Foods*, edited by Smith, J. E., Henderson, R. S., 777-784. Boca Raton: CRC Press.