

GMP COMPARISON

<p style="text-align: center;">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p style="text-align: center;">Food cGMP (21 CFR Part 110)</p>	<p style="text-align: center;">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p style="text-align: center;">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
			<p><i>PART 111--CURRENT GOOD MANUFACTURING PRACTICE IN MANUFACTURING, PACKING, OR HOLDING DIETARY INGREDIENTS AND DIETARY SUPPLEMENTS</i></p> <p>Subpart A--General Provisions</p> <p>§ 111.1 Who is subject to these regulations? You are subject to the regulations in this part if you manufacture, package, or hold a dietary ingredient or dietary supplement.</p>
			<p>§ 111.2 What are these regulations intended to accomplish?</p> <p>The regulations in this part establish the minimum current good manufacturing practices that you must use to the extent that you manufacture, package, or hold a dietary ingredient or dietary supplement.</p>
<p>§ 210.3 Definitions.</p> <p>(a) The definitions and interpretations contained in section 201 of the act shall be applicable to such terms when used in this part and in parts 211 through 226 of this chapter.</p> <p>(b) The following definitions of terms apply to this part and to parts 211 through 226 of this chapter.</p>	<p>¶110.3 Definitions</p> <p>The definitions and interpretations of terms in section 201 of the Federal Food, Drug, and Cosmetic Act (the act) are applicable to such terms when used in this part. The following definitions shall also apply:</p>	<p>Definitions</p> <p>The definitions and interpretations of terms in section 201 of the Federal Food, Drug, and Cosmetic Act (the act) are applicable to such terms when used in this part. The following definitions shall also apply:</p>	<p>§ 111.3 What definitions apply to this Part?</p> <p>The definitions and interpretations of terms in section 201 of the Federal Food, Drug, and Cosmetic Act (the act) apply to such terms when used in these regulations. For the purpose of these regulations, the following definitions also apply:</p>
<p>(20) <i>Acceptance criteria</i> means the product specifications and acceptance/rejection criteria, such as acceptable quality level and unacceptable quality level, with an associated sampling plan, that are necessary for making a decision to accept or reject a lot or batch (or any other convenient subgroups of manufactured units).</p>			
	<p>(a) <i>Acid foods or acidified foods</i> means foods that have an equilibrium pH of 4.6 or below.</p>		
<p>(1) <i>Act</i> means the Federal Food, Drug, and Cosmetic Act, as amended (21 U.S.C. 301 <i>et seq.</i>).</p>			
<p>(7) <i>Active ingredient</i> means any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or other animals. The term includes those components that may undergo chemical change in the manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect.</p>			

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<p>(18) <i>Actual yield</i> means the quantity that is actually produced at any appropriate phase of manufacture, processing, or packing of a particular drug product.</p>			<p><u>Actual yield</u> means the quantity that is actually produced at any appropriate step of manufacture or packaging of a particular dietary ingredient or dietary supplement.</p>
	<p>(b) Adequate means that which is needed to accomplish the intended purpose in keeping with good public health practice.</p>	<p>(a) "Adequate" means that which is needed to accomplish the intended purpose in keeping with good public health practice.</p>	
<p>(2) <i>Batch</i> means a specific quantity of a drug or other material that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture.</p>		<p>(b) "Batch or Lot" means a specific quantity of a finished product or other material that is intended to have uniform character and quality, within specified limits, and is produced according to a single manufacturing order during the same cycle of manufacture.</p>	<p><u>Batch</u> means a specific quantity of a dietary ingredient or dietary supplement that is intended to meet specifications for identity, purity, quality, strength, and composition, and is produced during a specified time period according to a single manufacturing record during the same cycle of manufacture.</p>
<p>(11) <i>Lot number, control number, or batch number</i> means any distinctive combination of letters, numbers, or symbols, or any combination of them, from which the complete history of the manufacture, processing, packing, holding, and distribution of a batch or lot of drug product or other material can be determined.</p>		<p>(j) "Lot number" means any distinctive combination of letters, numbers, or symbols, or any combination of them from which the complete history of the manufacture, processing, packing, holding, and distribution of a batch or lot of a finished dietary ingredient, dietary supplement or other material can be determined.</p>	<p><u>Batch number, lot number, or control number</u> means any distinctive group of letters, numbers, or symbols, or any combination of them, from which the complete history of the manufacturing, packaging, or holding of a batch or lot of dietary ingredients or dietary supplements can be determined.</p>
	<p>(c) Batter means a semifluid substance, usually composed of flour and other ingredients, into which principal components of food are dipped or with which they are coated, or which may be used directly to form bakery foods.</p>		
	<p>(d) Blanching, except for tree nuts and peanuts, means a prepackaging heat treatment of foodstuffs for a sufficient time and at a sufficient temperature to partially or completely inactivate the naturally occurring enzymes and to effect other physical or bio-chemical changes in the food.</p>	<p>(c) "Blanching" means a prepackaging heat treatment of a dietary product for a sufficient time and at a sufficient temperature to partially or completely inactivate the naturally occurring enzymes and to effect other physical or bio-chemical changes in the product.</p>	
<p>(3) <i>Component</i> means any ingredient intended for use in the manufacture of a drug product, including those that may not appear in such drug product.</p>		<p>(q) "Raw material" means any ingredient intended for use in the manufacture of a dietary ingredient or dietary supplement, including those that may not appear in such finished product.</p>	<p><u>Component</u> means any substance intended for use in the manufacture of a dietary ingredient or dietary supplement including those that may not appear in the finished dietary ingredient or dietary supplement. Component includes ingredients and dietary ingredients as, described in section 201(ff) of the act.</p>
		<p>(d) "Composition" means, as appropriate: (1) the identity of a dietary ingredient or dietary supplement, and (2) the concentration of a dietary ingredient (e.g., weight or other unit of use/weight or volume), or the potency or activity of one or more dietary ingredients, as indicated by appropriate procedures.</p>	

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			<p><u>Consumer complaint</u> means communication that contains any allegation, written or oral, expressing dissatisfaction with the quality of a dietary ingredient or a dietary supplement related to good manufacturing practices. Examples of product quality related to good manufacturing practices are: Foul odor, off taste, super-potent, subpotent, wrong ingredient, drug contaminant, other contaminant (e.g., bacteria, pesticide, mycotoxin, glass, lead), disintegration time, color variation, mycotoxin, glass, lead), disintegration time, color variation, tablet size or size variation, under-filled container, foreign material in a dietary supplement container, improper packaging, or mislabeling. For the purposes of the regulations in this part, a consumer complaint about product quality may or may not include concerns about a possible hazard to health. However, a consumer complaint does not include an adverse event, illness, or injury related to the safety of a particular dietary ingredient independent of whether the product is produced under good manufacturing practices.</p>
	<p>(e) Critical control point means a point in a food process where there is a high probability that improper control may cause, allow, or contribute to a hazard or to filth in the final food or decomposition of the final food.</p>		
		<p>(e) "Dietary ingredient" means an ingredient intended for use or used in a dietary supplement that is:</p> <ol style="list-style-type: none"> (1) a vitamin, (2) a mineral, (3) an herb or other botanical, (4) an amino acid, (5) a dietary substance for use by man to supplement the diet by increasing the total dietary intake, or (6) a concentrate, metabolite, constituent, extract, or combination of any of the foregoing ingredients. 	
		<p>(f) "Dietary product" means either a dietary ingredient or dietary supplement as defined in this part.</p>	
		<p>(g) "Dietary supplement" means dietary supplement as defined in section 201 (ff) of the act.</p>	
<p>(4) <i>Drug product</i> means a finished dosage form, for example, tablet, capsule, solution, etc., that contains an active drug ingredient generally, but not necessarily, in association with inactive ingredients. The term also includes a finished dosage form that does not contain an active ingredient but is intended to be used as a placebo.</p>			

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(5) <i>Fiber</i> means any particulate contaminant with a length at least three times greater than its width.			
	(f) Food means food as defined in section 201(f) of the act and includes raw materials and ingredients.		
	(g) Food-contact surfaces are those surfaces that contact human food and those surfaces from which drainage onto the food or onto surfaces that contact the food ordinarily occurs during the normal course of operations. "Food-contact surfaces" includes utensils and food-contact surfaces of equipment.		<u>Contact surface</u> means any surface that contacts a component, dietary ingredient, dietary supplement, and those surfaces from which drainage onto the component, dietary ingredient, dietary supplement, or onto surfaces that contact the component, dietary ingredient, or dietary supplement ordinarily occurs during the normal course of operations. Examples of contact surfaces include, but are not limited to, containers, utensils, tables, contact surfaces of equipment, and packaging.
(22) <i>Gang-printed labeling</i> means labeling derived from a sheet of material on which more than one item of labeling is printed.			
(8) <i>Inactive ingredient</i> means any component other than an active ingredient.			
			<u>Ingredient</u> means any substance that is used in the manufacture of a dietary ingredient or dietary supplement that is intended to be present in the finished dietary ingredient or dietary supplement. An ingredient includes, but is not necessarily limited to, a dietary ingredient as described in section 201(ff) of the act.
(9) <i>In-process material</i> means any material fabricated, compounded, blended, or derived by chemical reaction that is produced for, and used in, the preparation of the drug product.		(h) "In-process material" means any material fabricated, compounded, blended, ground, extracted, sifted, sterilized, derived by chemical reaction or processed in any other way that is produced for, and used in, the preparation of a dietary product.	<u>Inprocess material</u> means any material that is fabricated, compounded, blended, ground, extracted; sifted, sterilized, derived by chemical reaction, or processed in any other way for use in the manufacture of a dietary ingredient or dietary supplement.
(10) <i>Lot</i> means a batch, or a specific identified portion of a batch, having uniform character and quality within specified limits; or, in the case of a drug product produced by continuous process, it is a specific identified amount produced in a unit of time or quantity in a manner that assures its having uniform character and quality within specified limits.	(h) Lot means the food produced during a period of time indicated by a specific code.	(i) "Lot" means "batch" as defined in this part.	<u>Lot</u> means a batch, or a specific identified portion of a batch intended to have uniform identity, purity, quality, strength, and composition; or, in the case of a dietary ingredient or dietary supplement produced by continuous process, a specific identified amount produced in a specified unit of time or quantity in a manner that is intended to have uniform identity, purity, quality, strength, and composition.
(12) <i>Manufacture, processing, packing, or holding of a drug product</i> includes packaging and labeling operations, testing, and quality control of drug products.		(k) "Manufacture" or "manufacturing" includes all operations associated with the production of dietary products, including packaging and labeling operations, testing, and quality control of a dietary ingredient or dietary supplement.	

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<p>(13) The term <i>medicated feed</i> means any Type B or Type C medicated feed as defined in §558.3 of this chapter. The feed contains one or more drugs as defined in section 201(g) of the act. The manufacture of medicated feeds is subject to the requirements of part 225 of this chapter.</p>			
<p>(14) The term <i>medicated premix</i> means a Type A medicated article as defined in §558.3 of this chapter. The article contains one or more drugs as defined in section 201(g) of the act. The manufacture of medicated premixes is subject to the requirements of part 226 of this chapter.</p>			
	<p>(i) Microorganisms means yeasts, molds, bacteria, and viruses and includes, but is not limited to, species having public health significance. The term "undesirable microorganisms" includes those microorganisms that are of public health significance, that subject food to decomposition, that indicate that food is contaminated with filth, or that otherwise may cause food to be adulterated within the meaning of the act. Occasionally in these regulations, FDA used the adjective "microbial" instead of using an adjectival phrase containing the word microorganism.</p>	<p>(l) "Microorganisms" means yeasts, molds, bacteria, and viruses and includes, but is not limited to, species having public health significance. The term "undesirable microorganisms" includes those microorganisms that are of public health significance, that subject a dietary product to decomposition, that indicate that a dietary ingredient or dietary supplement is contaminated with filth, or that otherwise may cause a dietary product to be adulterated within the meaning of the act. Occasionally in these regulations, the adjective "microbial" is used instead of an adjectival phrase containing the word microorganism.</p>	<p><u>Microorganisms</u> means yeasts, molds, bacteria, viruses, and other similar microscopic organisms having public health or sanitary concern. This definition includes, but is not limited to, species that:</p> <ol style="list-style-type: none"> (1) Have public health significance; (2) Could cause a component, dietary ingredient, or dietary supplement to decompose; (3) Indicate that the component, dietary ingredient, or dietary supplement is contaminated with filth; or (4) Otherwise may cause the component, dietary ingredient, or dietary supplement to be adulterated.
	<p>(p) Shall is used to state mandatory requirements.</p>	<p>(u) "Shall" is used to state mandatory requirements.</p>	<p><u>Must</u> is used to state mandatory requirements.</p>
<p>(6) <i>Non-fiber-releasing filter</i> means any filter, which after any appropriate pretreatment such as washing or flushing, will not release fibers into the component or drug product that is being filtered. All filters composed of asbestos are deemed to be fiber-releasing filters.</p>			
<p>(19) <i>Percentage of theoretical yield</i> means the ratio of the actual yield (at any appropriate phase of manufacture, processing, or packing of a particular drug product) to the theoretical yield (at the same phase), stated as a percentage.</p>			
	<p>(j) Pest refers to any objectionable animals or insects including, but not limited to, bird, rodents, flies, and larvae.</p>	<p>(m) "Pest" refers to any objectionable animals or insects including, but not limited to, bird, rodents, flies, and larvae.</p>	<p><u>Pest</u> means any objectionable insects or other animals including, but not limited to, birds, rodents, flies, mites, and larvae.</p>
	<p>(k) Plant means the building or facility or parts thereof, used for or in connection with the manufacturing, packaging, labeling, or holding of human food.</p>	<p>(n) "Plant" means the building or facility or parts thereof, used for or in connection with the manufacturing, packaging, labeling, or holding of a dietary product.</p>	<p><u>Physical plant</u> means all or parts of a building or facility used for or in connection with manufacturing, packaging, or holding a dietary ingredient or dietary supplement.</p>
	<p>(l) Quality control operation means a planned and systematic procedure for taking all actions necessary to prevent food from being adulterated within the meaning of the act.</p>	<p>(o) "Quality control operation" means a planned and systematic procedure for taking all actions necessary to prevent a dietary product from being adulterated within the meaning of the act.</p>	<p><u>Quality control</u> means a planned and systematic operation or procedure for preventing a dietary ingredient or dietary supplement from being adulterated.</p>

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<p>(15) <i>Quality control unit</i> means any person or organizational element designated by the firm to be responsible for the duties relating to quality control.</p>		<p>(p) "Quality control unit" means any person or organizational element designated by the firm to be responsible for the duties relating to quality control operations.</p>	<p><u>Quality control unit</u> means any person or group that you designate to be responsible for quality control operations.</p>
<p>(21) <i>Representative sample</i> means a sample that consists of a number of units that are drawn based on rational criteria such as random sampling and intended to assure that the sample accurately portrays the material being sampled.</p>		<p>(r) "Representative sample" means a sample that consists of a number of units that are drawn based on rational criteria, such as random sampling, and is intended to assure that the sample accurately portrays the material being sampled.</p>	<p><u>Representative sample</u> means a sample that consists of a number of units that are drawn based on rational criteria, such as random sampling, and intended to ensure that the sample accurately portrays the material being sampled.</p>
	<p>(m) Rework means clean, unadulterated food that has been removed from processing for reasons other than insanitary conditions or that has been successfully reconditioned by reprocessing and that is suitable for use as food.</p>	<p>(s) "Rework" means clean, unadulterated material that has been removed from processing for reasons other than insanitary conditions or that has been successfully reconditioned by reprocessing and that is suitable for use in the manufacture of a dietary product.</p>	<p><u>Reprocessing</u> means using, in the manufacture of a dietary ingredient or a dietary supplement, clean, unadulterated components, dietary ingredients, or dietary supplements that have been previously removed from manufacturing for reasons other than insanitary conditions and that have been made suitable for use in the manufacture of a diet any ingredient or dietary supplement.</p>
	<p>(n) Safe moisture level is a level of moisture low enough to prevent the growth of undesirable microorganisms in the finished product under the intended conditions of manufacturing, storage, and distribution. The maximum safe moisture level for a food is based on its water activity (a_w). An a_w will be considered safe for food if adequate data are available that demonstrate that the food at or below the given a_w will not support growth of undesirable microorganisms.</p>		
	<p>(o) Sanitize means to adequately treat food-contact surfaces by a process that is effective in destroying vegetative cells of microorganisms of public health significance, and in substantially reducing numbers of other undesirable microorganisms, but without adversely affecting the product or its safety for the consumer.</p>	<p>(t) "Sanitize" means to adequately treat equipment, containers or utensils by a process that is effective in destroying vegetative cells of microorganisms of public health significance, and in substantially reducing numbers of other undesirable microorganisms, but without adversely affecting the product or its safety for the consumer.</p>	<p><u>Sanitize</u> means to adequately treat equipment, containers, utensils, or any other dietary product contact surface by applying cumulative heat or chemicals on cleaned food contact surfaces that when evaluated for efficacy, yield a reduction of 5 logs, which is equal to 99.999 percent reduction, of representative disease microorganisms of public health significance and substantially reduce the numbers of other undesirable microorganisms, but without adversely affecting the product or its safety for the consumer.</p>
	<p>(q) Should is used to state recommended or advisory procedures or identify recommended equipment.</p>	<p>(v) "Should" is used to state recommended or advisory procedures or identify recommended equipment.</p>	

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<p>(16) <i>Strength</i> means:</p> <p>(i) The concentration of the drug substance (for example, weight/weight, weight/volume, or unit dose/volume basis), and/or</p> <p>(ii) The potency, that is, the therapeutic activity of the drug product as indicated by appropriate laboratory tests or by adequately developed and controlled clinical data (expressed, for example, in terms of units by reference to a standard).</p>			
<p>(17) <i>Theoretical yield</i> means the quantity that would be produced at any appropriate phase of manufacture, processing, or packing of a particular drug product, based upon the quantity of components to be used, in the absence of any loss or error in actual production.</p>			<p><u>Theoretical yield</u> means the quantity that would be produced at any appropriate step of manufacture or packaging of a particular dietary ingredient or dietary supplement, based upon the quantity of components or packaging to be used; in the absence of any loss or error in actual production.</p>
	<p>(r) Water activity (a_w) is a measure of the free moisture in a food and is the quotient of the water vapor pressure of the substance divided by the vapor pressure of pure water at the same temperature.</p>	<p>(w) "Water activity (a_w)" is a measure of the free moisture in a dietary ingredient or dietary supplement and is the quotient of the water vapor pressure of the substance divided by the vapor pressure of pure water at the same temperature.</p>	<p><u>Water activity (a_w)</u> is a measure of the free moisture in a component, dietary ingredient, or dietary supplement and is the quotient of the water vapor pressure of the substance divided by the vapor pressure of pure water at the same temperature.</p>
			<p><u>We</u> means the United States Food and Drug Administration (FDA).</p>
			<p><u>You</u> means a person who manufactures, packages, or holds dietary ingredients or dietary supplements.</p>
			<p><u>§ 111.5 Do other statutory provisions and regulations apply?</u></p> <p>In addition to the regulations in this part, you must comply with other applicable statutory provisions and regulations under the act related to the manufacturing, packaging, or holding of dietary ingredients or dietary supplements.</p>
	<p>¶110.19 Exclusions</p> <p>(a) The following operations are not subject to this part: Establishments engaged solely in the harvesting, storage, or distribution of one or more "raw agricultural commodities," as defined in section 201(r) of the act, which are ordinarily cleaned, prepared, treated, or otherwise processed before being marketed to the consuming public.</p> <p>(b) FDA, however, will issue special regulations if it is necessary to cover these excluded operations.</p>	<p>Exclusions</p> <p>The following operations are not subject to this part: Establishments engaged solely in the harvesting, storage, or distribution of one or more "raw agricultural commodities," as defined in section 201(r) of the act, which are ordinarily cleaned, prepared, treated, or otherwise processed before being marketed to the consuming public.</p>	<p><u>§ 111.6 Exclusions.</u> The regulations in this part do not apply to a person engaged solely in activities related to the harvesting, storage, or distribution of raw agricultural commodities that will be incorporated into a dietary ingredient or dietary supplement by other persons.</p>

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<p>§ 211.28 Personnel responsibilities.</p> <p>(d) Any person shown at any time (either by medical examination or supervisory observation) to have an apparent illness or open lesions that may adversely affect the safety or quality of drug products shall be excluded from direct contact with components, drug product containers, closures, in-process materials, and drug products until the condition is corrected or determined by competent medical personnel not to jeopardize the safety or quality of drug products. All personnel shall be instructed to report to supervisory personnel any health conditions that may have an adverse effect on drug products.</p>	<p>110.10 Personnel</p> <p>The plant management shall take all reasonable measures and precautions to ensure the following:</p> <p>(a) Disease control. Any person who, by medical examination or supervisory observation, is shown to have, or appears to have, an illness, open lesion, including boils, sores, or infected wounds, or any other abnormal source of microbial contamination by which there is a reasonable possibility of food, food-contact surfaces, or food-packaging materials becoming contaminated, shall be excluded from any operations which may be expected to result in such contamination until the condition is corrected. Personnel shall be instructed to report such health conditions to their supervisors.</p>	<p>Personnel</p> <p>The plant management shall take all reasonable measures and precautions to assure the following:</p> <p>(a) Disease control. Any person who, by medical examination or supervisory observation, is shown to have, or appears to have, an illness, open lesion, including boils, sores, or infected wounds, or any other abnormal source of microbial contamination by which there is a reasonable possibility of an in-process or finished dietary product becoming adulterated, or processing equipment, utensils or packaging materials becoming contaminated, shall be excluded from any operations which may be expected to result in such adulteration or contamination until the condition is corrected. Personnel shall be instructed to report such health conditions to their supervisors.</p>	<p>Subpart B--Personnel</p> <p><u>§ 111.10 What microbial contamination and hygiene requirements apply?</u></p> <p>(a) <u>Microbial contamination.</u> You must take measures to exclude from any operations any person who might be a source of microbial contamination of any material including components, dietary ingredients, dietary supplements, and contact surfaces used in the manufacture, packaging, or holding of a dietary ingredient or a dietary supplement. Such measures include, but are not limited to, the following:</p> <p>(1) Excluding any person who, by medical examination or supervisory observation, is shown to have, or appears to have an illness, open lesion, or any other abnormal source of microbial contamination, which may be expected to result in microbial contamination of components, dietary ingredients, dietary supplements, or contact surfaces, from working in any operations until the condition is corrected; and</p> <p>(2) Instructing your employees to notify their supervisor(s) if they have or if there is a reasonable possibility that they have a health condition, described in paragraph (a) (1) of this section that could contaminate any components, dietary ingredients, dietary supplements, or any contact surface.</p>
	<p>(b) Cleanliness. All persons working in direct contact with food, food-contact surfaces, and food-packaging materials shall conform to hygienic practices while on duty to the extent necessary to protect against contamination of food. The methods for maintaining cleanliness include, but are not limited to:</p>	<p>(b) Cleanliness. All persons working in direct contact with raw materials, in-process or finished dietary products, processing equipment, utensils or packaging materials shall conform to hygienic practices while on duty to the extent necessary to protect against adulteration or contamination of such materials. The methods for maintaining cleanliness include, but are not limited to:</p>	<p>(b) <u>Hygienic Practices.</u> If you work in operations during which adulteration of the component, dietary ingredients, dietary supplement, or contact surface may occur, you must use hygienic practices to the extent necessary to protect against contamination of components, dietary ingredients, dietary supplements, or contact surfaces. The hygienic practices include, but are not limited to:</p>
<p>(a) Personnel engaged in the manufacture, processing, packing, or holding of a drug product shall wear clean clothing appropriate for the duties they perform...</p>	<p>(1) Wearing outer garments suitable to the operation in a manner that protects against the contamination of food, food-contact, surfaces or food-packaging materials.</p>	<p>(1) Wearing outer garments suitable to the operation in a manner that protects against the adulteration of in-process or finished dietary products, or contamination of processing equipment, utensils or packaging materials.</p>	<p>(1) Wearing outer garments in a manner that protects against the contamination of components, dietary ingredients, dietary supplements, or any contact surface;</p>
<p>(b) Personnel shall practice good sanitation and health habits.</p>	<p>(2) Maintaining adequate personal cleanliness</p>	<p>(2) Maintaining adequate personal cleanliness.</p>	<p>(2) Maintaining adequate personal cleanliness;</p>

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	<p>(3) Washing hands thoroughly (and sanitizing if necessary to protect against contamination with undesirable microorganisms) in an adequate hand-washing facility before starting work, after each absence from the work station, and at any other time when the hands may have become soiled or contaminated.</p>	<p>(3) Washing hands thoroughly (and sanitizing if necessary to protect against contamination with undesirable microorganisms) in an adequate hand-washing facility before starting work, after each absence from the work station, and at any other time when the hands may have become soiled or contaminated.</p>	<p>(3) Washing hands thoroughly (and, sanitizing if necessary to protect against contamination with microorganisms) in an adequate hand-washing facility:</p> <p>(i) Before starting work; and</p> <p>(ii) At any time when the hands may have become soiled or contaminated;</p>
	<p>(4) Removing all unsecured jewelry and other objects that might fall into food, equipment, or containers, and removing hand jewelry that cannot be adequately sanitized during periods in which food is manipulated by hand. If such hand jewelry cannot be removed, it may be covered by material which can be maintained in an intact, clean, and sanitary condition and which effectively protects against the contamination by these objects of the food, food-contact surfaces, or food-packaging materials.</p>	<p>(4) Removing all unsecured jewelry and other objects that might fall into raw materials, in-process or finished dietary product, equipment, or containers, and removing hand jewelry that cannot be adequately sanitized during periods in which in-process or finished product is manipulated by hand. If such hand jewelry cannot be removed, it may be covered by material which can be maintained in an intact, clean, and sanitary condition and which effectively protects against the adulteration of dietary products or contamination of processing equipment, utensils or packaging materials.</p>	<p>(4) Removing all unsecured jewelry and other objects that might fall into components, dietary ingredients, dietary supplements, equipment, or packaging, and removing hand jewelry that cannot be adequately sanitized during periods in which components, dietary ingredients, or dietary supplements are manipulated by hand. If hand jewelry cannot be removed, it must be covered by material that is maintained in an intact, clean, and sanitary condition and that effectively protects against contamination of components, dietary ingredients, dietary supplements, or contact surfaces;</p>
	<p>(5) Maintaining gloves, if they are used in food handling, in an intact, clean, and sanitary condition. The gloves should be of an impermeable material.</p>	<p>(5) Maintaining gloves, if they are used in in-process or finished product handling, in an intact, clean, and sanitary condition. The gloves should be of a material that adequately protects the product from contamination.</p>	<p>(5) Maintaining gloves used in handling components, dietary ingredients, or dietary supplements in an intact, clean, and sanitary condition. The gloves must be of an impermeable material;</p>
<p>(a)...Protective apparel, such as head, face, hand, and arm coverings, shall be worn as necessary to protect drug products from contamination.</p>	<p>(6) Wearing, where appropriate, in an effective manner, hair nets, headbands, caps, beard covers, or other effective hair restraints.</p>	<p>(6) Wearing, where appropriate, in an effective manner, hair nets, caps, beard covers, or other effective hair restraints.</p>	<p>(6) Wearing, where appropriate, in an effective manner, hairnets, caps, beard covers, or other effective hair restraints;</p>
	<p>(7) Storing clothing or other personal belongings in areas other than where food is exposed or where equipment or utensils are washed.</p>	<p>(7) Storing clothing or other personal belongings in areas other than where in-process or finished product is exposed or where processing equipment or utensils are washed.</p>	<p>(7) Not storing clothing or other personal belongings in areas where components, dietary ingredients, or dietary supplements or any contact surfaces are exposed or where contact surfaces are washed;</p>
	<p>(8) Confining the following to areas other than where food may be exposed or where equipment or utensils are washed: eating food, chewing gum, drinking beverages, or using tobacco.</p>	<p>(8) Confining the following to areas other than where in-process or finished product may be stored or exposed, or where processing equipment or utensils are washed: eating food, chewing gum, drinking beverages, or using tobacco.</p>	<p>(8) Not eating food, chewing gum, drinking beverages and using tobacco products in areas, where components, dietary ingredients, dietary supplements, or any contact surfaces are exposed, or where contact surfaces are washed; and</p>
	<p>(9) Taking any other necessary precautions to protect against contamination of food, food-contact surfaces, or food-packaging materials with micro-organisms or foreign substances including, but not limited to, perspiration, hair, cosmetics, tobacco, chemicals, and medicines applied to the skin.</p>	<p>(9) Taking any other necessary precautions to protect against adulteration of raw materials, in-process or finished product, or contamination of processing equipment, utensils or packaging materials with micro-organisms or foreign substances including, but not limited to, perspiration, hair, cosmetics, tobacco, chemicals, and medicines applied to the skin.</p>	<p>(9) Taking any other precautions necessary to protect against the contamination of components, dietary ingredients, dietary supplements, or contact surfaces with microorganisms, filth, or any other extraneous materials, including, but not limited to, perspiration, hair, cosmetics, tobacco, chemicals, and medicines applied to the skin.</p>

<p align="center">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p align="center">Food cGMP (21 CFR Part 110)</p>	<p align="center">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p align="center">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
<p>(c) Only personnel authorized by supervisory personnel shall enter those areas of the buildings and facilities designated as limited-access areas.</p>			
<p>§ 211.25 Personnel qualifications.</p> <p>(a) Each person engaged in the manufacture, processing, packing, or holding of a drug product shall have education, training, and experience, or any combination thereof, to enable that person to perform the assigned functions. Training shall be in the particular operations that the employee performs and in current good manufacturing practice (including the current good manufacturing practice regulations in this chapter and written procedures required by these regulations) as they relate to the employee's functions. Training in current good manufacturing practice shall be conducted by qualified individuals on a continuing basis and with sufficient frequency to assure that employees remain familiar with CGMP requirements applicable to them.</p>	<p>(c) Education and training. Personnel responsible for identifying sanitation failures or food contamination should have a background of education or experience, or a combination thereof, to provide a level of competency necessary for production of clean and safe food. Food handlers and supervisors should receive appropriate training in proper food handling techniques and food-protection principles and should be informed of the danger of poor personal hygiene and insanitary practices.</p>	<p>(c) Education and training. Each person engaged in the manufacture of a dietary product should have the proper education, training, and experience (or any combination thereof) needed to perform the assigned functions. Training should be in the particular operation(s) that the employee performs as they relate to the employee's functions. Appropriate documentation of training shall be retained by the manufacturer.</p>	<p>§ 111.12 <u>What personnel qualification requirements apply?</u></p> <p>(a) You must have qualified employees to manufacture, package, or hold dietary ingredients or dietary supplements; and</p> <p>(b) Each person engaged in manufacturing, packaging, or holding must have the training and experience to perform the person's duties.</p>
<p>(b) Each person responsible for supervising the manufacture, processing, packing, or holding of a drug product shall have the education, training, and experience, or any combination thereof, to perform assigned functions in such a manner as to provide assurance that the drug product has the safety, identity, strength, quality, and purity that it purports or is represented to possess.</p>	<p>(d) Supervision. Responsibility for assuring compliance by all personnel with all requirements of this part shall be clearly assigned to competent supervisory personnel.</p>	<p>(d) Supervision. Responsibility for assuring compliance by all personnel with all requirements of this part shall be clearly assigned to qualified personnel with proper education, training and experience (or any combination thereof).</p>	<p>§ 111.13 <u>What supervisor requirements apply?</u></p> <p>(a) You must assign qualified personnel to supervise the manufacturing, packaging, or holding of dietary ingredients and dietary supplements.</p> <p>(b) You and the supervisors you use must be qualified by training and experience to supervise.</p>
<p>(c) There shall be an adequate number of qualified personnel to perform and supervise the manufacture, processing, packing, or holding of each drug product.</p>			

<p align="center">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p align="center">Food cGMP (21 CFR Part 110)</p>	<p align="center">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p align="center">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
<p>§ 211.34 Consultants.</p> <p>Consultants advising on the manufacture, processing, packing, or holding of drug products shall have sufficient education, training, and experience, or any combination thereof, to advise on the subject for which they are retained. Records shall be maintained stating the name, address, and qualifications of any consultants and the type of service they provide.</p>			
<p>§ 211.56 Sanitation.</p> <p>(a) Any building used in the manufacture, processing, packing, or holding of a drug product shall be maintained in a clean and sanitary condition. Any such building shall be free of infestation by rodents, birds, insects, and other vermin (other than laboratory animals). Trash and organic waste matter shall be held and disposed of in a timely and sanitary manner.</p> <p>§ 211.58 Maintenance.</p> <p>Any building used in the manufacture, processing, packing, or holding of a drug product shall be maintained in a good state of repair.</p>	<p>¶110.35 Sanitary operations.</p> <p>(a) General maintenance. Buildings, fixtures, and other physical facilities of the plant shall be maintained in a sanitary condition and shall be kept in repair sufficient to prevent food from becoming adulterated within the meaning of the act....</p>	<p>Sanitation of Buildings and Facilities</p> <p>(a) General maintenance. Buildings, fixtures, and other physical facilities of the plant shall be maintained in a sanitary condition and shall be kept in repair sufficient to prevent raw materials, in-process or finished dietary products from becoming adulterated within the meaning of the act.</p>	<p>Subpart C--Physical Plant</p> <p>§ 111.15 <u>What sanitation requirements apply to your physical plant?</u></p> <p>(a) <u>Physical plant facilities.</u></p> <p>(1) You must maintain your physical plant in a clean and sanitary condition; and</p> <p>(2) You must keep your physical plant in repair sufficient to prevent components, dietary ingredients, dietary supplements or contact surfaces from becoming contaminated.</p>
<p>§ 211.56 Sanitation.</p> <p>(b) There shall be written procedures assigning responsibility for sanitation and describing in sufficient detail the cleaning schedules, methods, equipment, and materials to be used in cleaning the buildings and facilities; such written procedures shall be followed.</p>			
	<p>(b) Substances used in cleaning and sanitizing; storage of toxic materials.</p> <p>(1) Cleaning compounds and sanitizing agents used in cleaning and sanitizing procedures shall be free from undesirable microorganisms and shall be safe and adequate under the conditions of use.</p>	<p>(b) Cleaning and sanitizing materials.</p> <p>(1) Cleaning compounds and sanitizing agents used in cleaning and sanitizing procedures shall be free from undesirable microorganisms and shall be safe and adequate under the conditions of use.</p>	<p>(b) <u>Cleaning compounds, sanitizing agents, and pesticides.</u></p> <p>(1) You must use cleaning compounds and sanitizing agents that are free from microorganisms of public health significance and safe and adequate under the conditions of use.</p>
	<p>...Compliance with this requirement may be verified by any effective means including purchase of these substances under a supplier's guarantee or certification, or examination of these substances for contamination.</p>	<p>...Compliance with this requirement may be verified by any effective means including purchase of these substances under a supplier's guarantee or certification, or examination of these substances for contamination.</p>	

PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)	Food cGMP (21 CFR Part 110)	Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)	Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)
	<p>Only the following toxic materials may be used or stored in a plant where food is processed or exposed:</p> <ul style="list-style-type: none"> (i) Those required to maintain clean and sanitary conditions; (ii) Those necessary for use in laboratory testing procedures; (iii) Those necessary for plant and equipment maintenance and operation; and (iv) Those necessary for use in the plant's operations. 	<p>Only the following toxic materials may be used or stored in a plant where product is processed or exposed:</p> <ul style="list-style-type: none"> (i) Those required to maintain clean and sanitary conditions; (ii) Those necessary for use in laboratory testing procedures; (iii) Those necessary for plant and equipment maintenance and operation; and (iv) Those necessary for use in the plant's operations. 	<p>(2) You must not use or hold toxic materials in a physical plant in which contact surfaces, components, dietary ingredients, or dietary supplements are manufactured or exposed, unless those materials are necessary:</p> <ul style="list-style-type: none"> (i) To maintain clean and sanitary conditions; (ii) For use in, laboratory testing procedures; (iii) For maintaining or operating the physical plant or equipment; or (iv) For use in the plant's operations.
<p>§ 211.56 Sanitation.</p> <p>(c) There shall be written procedures for use of suitable rodenticides, insecticides, fungicides, fumigating agents, and cleaning and sanitizing agents. Such written procedures shall be designed to prevent the contamination of equipment, components, drug product containers, closures, packaging, labeling materials, or drug products and shall be followed.</p>	<p>(2) Toxic cleaning compounds, sanitizing agents, and pesticide chemicals shall be identified, held, and stored in a manner that protects against contamination of food, food-contact surfaces, or food-packaging materials.</p>	<p>(2) Toxic cleaning compounds, sanitizing agents, and pesticide chemicals shall be identified, used, held, and stored in a manner that protects against adulteration of raw materials, in-process or finished product, or contamination of processing equipment or packaging materials.</p>	<p>(3) You must identify and hold toxic cleaning compounds, sanitizing agents, pesticides, and pesticide chemicals in a manner that protects against contamination of components, dietary ingredients, dietary supplements, or contact surfaces.</p>
<p>Rodenticides, insecticides, and fungicides shall not be used unless registered and used in accordance with the Federal Insecticide, Fungicide, and Rodenticide Act (7 U.S.C. 135).</p>	<p>All relevant regulations promulgated by other Federal, State, and local government agencies for the application, use or holding of these products should be followed.</p>	<p>All relevant regulations promulgated by other Federal, State, and local government agencies for the application, use or holding of these products should be followed. Rodenticides, insecticides, and fungicides should be registered and used in accordance with the Federal Insecticide, Fungicide, and Rodenticide Act.</p>	
<p>(d) Sanitation procedures shall apply to work performed by contractors or temporary employees as well as work performed by full-time employees during the ordinary course of operations.</p>			

PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)	Food cGMP (21 CFR Part 110)	Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)	Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)
	<p>(c) Pest control. No pests shall be allowed in any area of a food plant. Guard or guide dogs may be allowed in some areas of a plant if the presence of the dogs is unlikely to result in contamination of food, food-contact surfaces, or food-packaging materials. Effective measures shall be taken to exclude pests from the processing areas and to protect against the contamination of food on the premises by pests. The use of insecticides or rodenticides is permitted only under precautions and restrictions that will protect against the contamination of food, food-contact surfaces, and food-packaging materials.</p>	<p>(c) Pest control. No pests shall be allowed in any area of a dietary product manufacturing plant. Effective measures shall be taken to exclude pests from the processing areas and to protect against the adulteration of product on the premises by pests. The use of insecticides or rodenticides is permitted only under precautions and restrictions that will protect against the adulteration of raw materials, in-process or finished product, or contamination of processing equipment, utensils or packaging materials.</p>	<p>(c) <u>Pest control.</u></p> <p>(1) You must not allow animals or pests in any area of your physical plant. Guard or guide dogs are allowed in some areas of your physical plant if the presence of the dogs will not result in contamination of components, dietary ingredients, dietary supplements, or contact surfaces;</p> <p>(2) You must take effective measures to exclude pests from the physical plant and to protect against contamination of components, dietary ingredients, dietary supplements, and contact surfaces on the premises by pests; and</p> <p>(3) You must not use insecticides, fumigants, fungicides or rodenticides, unless you take precautions to protect against the contamination of components, dietary ingredients, dietary supplements, or contact surfaces.</p>

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<p>§ 211.48 Plumbing.</p> <p>(a) Potable water shall be supplied under continuous positive pressure in a plumbing system free of defects that could contribute contamination to any drug product. Potable water shall meet the standards prescribed in the Environmental Protection Agency's Primary Drinking Water Regulations set forth in 40 CFR part 141. Water not meeting such standards shall not be permitted in the potable water system.</p>	<p>¶110.37 Sanitary facilities and controls.</p> <p>Each plant shall be equipped with adequate sanitary facilities and accommodations including, but not limited to:</p> <p>(a) Water supply. The water supply shall be sufficient for the operations intended and shall be derived from an adequate source. Any water that contacts food or food-contact surfaces shall be safe and of adequate sanitary quality. Running water at a suitable temperature, and under pressure as needed, shall be provided in all areas where required for the processing of food, for the cleaning of equipment, utensils, and food-packaging materials, or for employee sanitary facilities.</p>	<p>(d) Water supply. Potable water at a suitable temperature, and under pressure as needed, shall be provided in all areas where required for the processing of dietary products, for the cleaning of processing equipment, utensils, and packaging materials, or for employee sanitary facilities. Any water that contacts in-process or finished dietary products, utensils or processing equipment shall meet the standards prescribed in the Environmental Protection Agency's Primary Drinking Water Regulations (40 CFR Part 141).</p>	<p>(d) <u>Water supply.</u></p> <p>(1) You must provide water that is safe and of adequate sanitary quality, at suitable temperatures, and under pressure as needed, in all areas where water is necessary for:</p> <p>(i) Manufacturing dietary ingredients or dietary supplements;</p> <p>(ii) Making ice that comes in contact with components, dietary ingredients, dietary supplements or contact surfaces;</p> <p>(iii) Cleaning any surface; and</p> <p>(iv) Employee bathrooms and hand-washing facilities.</p> <p>(2) Water that contacts components, dietary ingredients, dietary supplements, or any contact surface must at a minimum comply with the National Primary Drinking Water regulations prescribed by the Environmental Protection Agency under 40 CFR part 141 and any state and local government requirements;</p> <p>(3) You must have documentation or otherwise be able to show that water that contacts components, dietary ingredients, dietary supplements, or any contact surface meets the requirements in paragraph (d) (2) of this section.</p>

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<p>(b) Drains shall be of adequate size and, where connected directly to a sewer, shall be provided with an air break or other mechanical device to prevent back-siphonage.</p>	<p>(b) Plumbing. Plumbing shall be of adequate size and design and adequately installed and maintained to:</p> <p>(1) Carry sufficient quantities of water to required locations throughout the plant.</p> <p>(2) Properly convey sewage and liquid disposable waste from the plant.</p> <p>(3) Avoid constituting a source of contamination to food, water supplies, equipment, or utensils or creating an unsanitary condition.</p> <p>(4) Provide adequate floor drainage in all areas where floors are subject to flooding-type cleaning or where normal operations release or discharge water or other liquid waste on the floor.</p> <p>(5) Provide that there is not backflow from, or cross-connection between, piping systems that discharge waste water or sewage and piping systems that carry water for food or food manufacturing.</p>	<p>(e) Plumbing. Plumbing shall be of adequate size and design and adequately installed and maintained to:</p> <p>(1) Carry sufficient quantities of water to required locations throughout the plant.</p> <p>(2) Properly convey sewage and liquid disposable waste from the plant.</p> <p>(3) Avoid constituting a source of adulteration to product, or contamination of water supplies, processing equipment, or utensils or creating an unsanitary condition.</p> <p>(4) Provide adequate floor drainage or other appropriate means of water removal in all areas where floors are subject to flooding-type cleaning or where normal operations release or discharge water or other liquid waste on the floor.</p> <p>(5) Provide that there is not backflow from, or cross-connection between, piping systems that discharge waste water or sewage and piping systems that carry water used for the manufacture of dietary products.</p>	<p>(e) Plumbing. The plumbing in your physical plant must be of an adequate size and design and be adequately installed and maintained to:</p> <p>(1) Carry sufficient amounts of water to required locations throughout the physical plant;</p> <p>(2) Properly convey sewage and liquid disposable waste from your physical plant;</p> <p>(3) Avoid being a source of contamination to components, dietary ingredients, dietary supplements, water supplies, or any contact surface, or creating an unsanitary condition;</p> <p>(4) Provide adequate floor drainage in all areas where floors are subject to flooding-type cleaning or where normal operations release or discharge water or other liquid waste on the floor; and</p> <p>(5) Not allow backflow from, or cross connection between, piping systems that discharge waste water or sewage and piping systems that carry water used for manufacturing dietary ingredients or dietary supplements, for cleaning contact surfaces, or for use in bathrooms or hand-washing facilities.</p>

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<p>§ 211.50 Sewage and refuse.</p> <p>Sewage, trash, and other refuse in and from the building and immediate premises shall be disposed of in a safe and sanitary manner.</p>	<p>(c) Sewage disposal. Sewage disposal shall be made into an adequate sewerage system or disposed of through other adequate means.</p>	<p>(f) Sewage disposal. Sewage disposal shall be made into an adequate sewerage system or disposed of through other adequate means.</p>	<p>(f) Sewage disposal. You must dispose of sewage into an adequate sewerage system or through other adequate means.</p>
<p>§ 211.52 Washing and toilet facilities.</p> <p>Adequate washing facilities shall be provided, including hot and cold water, soap or detergent, air driers or single-service towels, and clean toilet facilities easily accessible to working areas.</p>	<p>(d) Toilet facilities. Each plant shall provide its employees with adequate, readily accessible toilet facilities. Compliance with this requirement may be accomplished by:</p> <p>(1) Maintaining the facilities in a sanitary condition.</p> <p>(2) Keeping the facilities in good repair at all times.</p> <p>(3) Providing self-closing doors.</p> <p>(4) Providing doors that do not open into areas where food is exposed to airborne contamination, except where alternate means have been taken to protect against such contamination (such as double doors or positive air-flow systems).</p>	<p>(g) Toilet facilities. Each plant shall provide its employees with adequate, readily accessible toilet facilities. Compliance with this requirement may be accomplished by:</p> <p>(1) Maintaining the facilities in a sanitary condition.</p> <p>(2) Keeping the facilities in good repair at all times.</p> <p>(3) Providing self-closing doors.</p> <p>(4) Providing doors that do not open into areas where dietary product is exposed to airborne contamination, except where alternate means have been taken to protect against such contamination (such as double doors or positive air-flow systems).</p>	<p>(g) <u>Bathrooms</u>. You must provide your employees with adequate, readily accessible bathrooms. The bathrooms must be kept clean and must not become a potential source of contamination to components, dietary ingredients, dietary supplements, or contact surfaces. You must:</p> <p>(1) Keep the bathrooms in good repair at all times;</p> <p>(2) Provide self-closing doors; and</p> <p>(3) Provide doors that do not open into areas where components, dietary ingredients, dietary supplements, or contact surfaces are exposed to airborne contamination except where alternate means have been taken to protect against contamination (such as double doors or positive airflow systems).</p>

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	<p>(e) Hand-washing facilities. Hand-washing facilities shall be adequate and convenient and be furnished with running water at a suitable temperature. Compliance with this requirement may be accomplished by providing:</p> <p>(1) Hand-washing and, where appropriate, hand-sanitizing facilities at each location in the plant where good sanitary practices require employees to wash and/or sanitize their hands.</p> <p>(2) Effective hand-cleaning and sanitizing preparations.</p> <p>(3) Sanitary towel service or suitable drying devices.</p> <p>(4) Devices or fixtures, such as water control valves, so designed and constructed to protect against recontamination of clean, sanitized hands.</p> <p>(5) Readily understandable signs directing employees handling unprotected food, unprotected food-packaging materials, food-contact surfaces to wash and, where appropriate, sanitize their hands before they start work, after each absence from post of duty, and when their hands may have become soiled or contaminated. These signs may be posted in the processing room(s) and in all other areas where employees may handle such food, materials, or surfaces.</p> <p>(6) Refuse receptacles that are constructed and maintained in a manner that protects against contamination of food.</p>	<p>(h) Hand-washing facilities. Hand-washing facilities shall be adequate and convenient and be furnished with running water at a suitable temperature. Compliance with this requirement may be accomplished by providing:</p> <p>(1) Hand-washing and, where appropriate, hand-sanitizing facilities at each location in the plant where good sanitary practices require employees to wash and/or sanitize their hands.</p> <p>(2) Effective hand-cleaning and sanitizing preparations.</p> <p>(3) Air driers, sanitary towel service or suitable drying devices.</p> <p>(4) Devices or fixtures, such as water control valves, so designed and constructed to protect against recontamination of clean, sanitized hands.</p> <p>(5) Readily understandable signs directing employees handling unprotected product, packaging materials, utensils or processing equipment to wash and, where appropriate, sanitize their hands before they start work, after each absence from post of duty, and when their hands may have become soiled or contaminated. These signs may be posted in the processing room(s) and in all other areas where employees may handle such products, materials, utensils or equipment.</p> <p>(6) Refuse receptacles that are constructed and maintained in a manner that protects against adulteration of dietary products.</p>	<p>(h) <u>Hand-washing facilities</u>. You must provide hand-washing facilities that are adequate, convenient, and furnish running water at a suitable temperature. You must do this by providing:</p> <p>(1) Hand-washing and, where appropriate, hand-sanitizing facilities at each location in your physical plant where good hygienic practices require employees to wash or to sanitize or both wash and sanitize their hands;</p> <p>(2) Effective hand-cleaning and sanitizing preparations;</p> <p>(3) Air driers, sanitary towel service, such as disposable paper towels, or other suitable drying devices;</p> <p>(4) Devices or fixtures, such as water control valves, designed and constructed to protect against recontamination of clean, sanitized hands;</p> <p>(5) Signs that are easy to understand and are posted throughout the physical plant that direct employees handling components, dietary ingredients, dietary supplements, or contact surfaces to wash and, where appropriate, to sanitize their hands before they start work, after each absence from their duty station, and when their hands may have become soiled or contaminated; and</p> <p>(6) Trash bins that are constructed and maintained in a manner to protect against recontamination of hands and contamination of components, dietary ingredients; dietary supplements, or any contact surface.</p>

<p>PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p>Food cGMP (21 CFR Part 110)</p>	<p>Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p>Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
	<p>(f) Rubbish and offal disposal. Rubbish and any offal shall be so conveyed, stored, and disposed of as to minimize the development of odor, minimize the potential for the waste becoming an attractant and harborage or breeding place for pests, and protect against contamination of food, food-contact surfaces, water supplies, and ground surfaces.</p>	<p>(i) Rubbish disposal. Rubbish shall be so conveyed, stored, and disposed of as to minimize the development of odor, minimize the potential for the waste becoming an attractant and harborage or breeding place for pests, and protect against adulteration of raw materials, in-process or finished dietary products, or contamination of utensils, processing equipment, water supplies, and ground surfaces.</p>	<p>(i) <u>Trash disposal</u>. You must convey, store, and dispose of trash to:</p> <p>(1) Minimize the development of odor;</p> <p>(2) Minimize the potential for the trash to attract, harbor, or become a breeding place for pests;</p> <p>(3) Protect against contamination of components, dietary ingredients, dietary supplements, any contact surface, water supplies, and grounds surrounding your physical plant; and</p> <p>(4) Control hazardous waste to prevent contamination of components, dietary ingredients, dietary supplements, and contact surfaces.</p>
	<p>¶110.80 Processes and controls. ...Overall sanitation of the plant shall be under the supervision of one or more competent individuals assigned responsibility for this function...</p>	<p>(j) <u>Supervision</u>. Overall sanitation of the plant shall be under the supervision of one or more individuals qualified by education, experience and training (or any combination thereof) assigned responsibility for assuring that sanitation procedures are accomplished.</p>	<p>(j) <u>Sanitation supervisors</u>. You must assign one or more employees to supervise overall sanitation. These supervisors must be qualified by training and experience to develop and supervise sanitation procedures.</p>

<p style="text-align: center;">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p style="text-align: center;">Food cGMP (21 CFR Part 110)</p>	<p style="text-align: center;">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p style="text-align: center;">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
	<p>Subpart B--Buildings and Facilities</p> <p>¶110.20 Plant and grounds.</p> <p>(a) Grounds. The grounds about a food plant under the control of the operator shall be kept in a condition that will protect against the contamination of food. The methods for adequate maintenance of grounds include, but are not limited to:</p> <p>(1) Properly storing equipment, removing litter and waste, and cutting weeds or grass within the immediate vicinity of the plant buildings or structures that may constitute an attractant, breeding place, or harborage for pests.</p> <p>(2) Maintaining roads, yards, and parking lots so that they do not constitute a source of contamination in areas where food is exposed.</p> <p>(3) Adequately draining areas that may contribute contamination to food by seepage, foot-borne filth, or providing a breeding place for pests.</p> <p>(4) Operating systems for waste treatment and disposal in an adequate manner so that they do not constitute a source of contamination in areas where food is exposed. If the plant grounds are bordered by grounds not under the operator's control and not maintained in the manner described in paragraph (a)(1) through (3) of this section, care shall be exercised in the plant by inspection, extermination, or other means to exclude pests, dirt, and filth that may be a source of food contamination.</p>	<p>Plant and Grounds</p> <p>(a) Grounds. The grounds about a dietary product manufacturing plant under the control of the operator shall be kept in a condition that will protect against the adulteration of dietary products. The methods for adequate maintenance of grounds include, but are not limited to:</p> <p>(1) Properly storing equipment, removing litter and waste, and cutting weeds or grass within the immediate vicinity of the plant buildings or structures that may constitute an attractant, breeding place, or harborage for pests.</p> <p>(2) Maintaining roads, yards, and parking lots so that they do not constitute a source of adulteration in areas where product is exposed.</p> <p>(3) Adequately draining areas that may contribute to product adulteration by seepage, foot-borne filth, or providing a breeding place for pests.</p> <p>(4) Operating systems for waste treatment and disposal in an adequate manner so that they do not constitute a source of adulteration in areas where product is exposed. If the plant grounds are bordered by grounds not under the operator's control and not maintained in the manner described in paragraph (a)(1) through (3) of this section, care shall be exercised in the plant by inspection, extermination, or other means to exclude pests, dirt, and filth that may be a source of product adulteration.</p>	
<p>§ 211.42 Design and construction features.</p> <p>(a) Any building or buildings used in the manufacture, processing, packing, or holding of a drug product shall be of suitable size, construction and location to facilitate cleaning, maintenance, and proper operations.</p>	<p>(b) Plant construction and design.</p> <p>Plant buildings and structures shall be suitable in size, construction, and design to facilitate maintenance and sanitary operations for food-manufacturing purposes. The plant and facilities shall:</p>	<p>(b) Plant construction and design. Plant buildings and structures shall be suitable in size, construction, and design to facilitate maintenance, cleaning and sanitary operations for dietary product manufacturing purposes and to prevent mixups between different raw materials and products. The plant and facilities shall:</p>	<p>§ 111.20 <u>What design and construction requirements apply to your physical plant?</u></p> <p>Any physical plant you use in the manufacture, packaging, or holding of dietary ingredients or dietary supplements must:</p> <p>(a) Be suitable in size, construction, and design to facilitate maintenance, cleaning, and sanitizing operations;</p>
<p>(b) Any such building shall have adequate space for the orderly placement of equipment and materials to prevent mixups between different components, drug product containers, closures, labeling, in-process materials, or drug products, and to prevent contamination. The flow of components, drug product containers, closures, labeling, in-process materials, and drug products through the building or buildings shall be designed to prevent contamination.</p>	<p>(1) Provide sufficient space for such placement of equipment and storage of materials as is necessary for the maintenance of sanitary operations and the production of safe food.</p>	<p>(1) Provide sufficient space for such placement of equipment and storage of materials as is necessary for the prevention of mixups, maintenance of sanitary operations and the production of safe dietary products.</p>	<p>(b) Have adequate space for the orderly placement of equipment and holding materials as is necessary for maintenance, cleaning, and sanitizing operations and to prevent contamination and mixups of components, dietary ingredients, and dietary supplements during manufacturing, packaging, or holding;</p>

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<p>(c) Operations shall be performed within specifically defined areas of adequate size. There shall be separate or defined areas or such other control systems for the firm's operations as are necessary to prevent contamination or mixups during the course of the following procedures:</p> <p>(1) Receipt, identification, storage, and withholding from use of components, drug product containers, closures, and labeling, pending the appropriate sampling, testing, or examination by the quality control unit before release for manufacturing or packaging;</p> <p>(2) Holding rejected components, drug product containers, closures, and labeling before disposition;</p> <p>(3) Storage of released components, drug product containers, closures, and labeling;</p> <p>(4) Storage of in-process materials;</p> <p>(5) Manufacturing and processing operations;</p> <p>(6) Packaging and labeling operations;</p> <p>(7) Quarantine storage before release of drug products;</p> <p>(8) Storage of drug products after release;</p> <p>(9) Control and laboratory operations;</p> <p>(10) Aseptic processing, which includes as appropriate:</p> <ul style="list-style-type: none"> (i) Floors, walls, and ceilings of smooth, hard surfaces that are easily cleanable; (ii) Temperature and humidity controls; (iii) An air supply filtered through high-efficiency particulate air filters under positive pressure, regardless of whether flow is laminar or nonlaminar; (iv) A system for monitoring environmental conditions; (v) A system for cleaning and disinfecting the room and equipment to produce aseptic conditions; (vi) A system for maintaining any equipment used to control the aseptic conditions. 	<p>(2) Permit the taking of proper precautions to reduce the potential for contamination of food, food-contact surfaces, or food-packaging materials with microorganisms, chemicals, filth, or other extraneous material. ...The potential for contamination may be reduced by adequate food safety controls and operating practices or effective design, including the separation of operations in which contamination is likely to occur, by one or more of the following means: location, time, partition, air flow, enclosed systems, or other effective means.</p>	<p>(2) Permit the taking of proper precautions to reduce the potential for mixups or adulteration of in-process or finished dietary product, or contamination of processing equipment, utensils or packaging materials with microorganisms, chemicals, filth, or other extraneous material. The potential for mixups and product adulteration may be reduced by adequate product safety controls and operating practices or effective design, including the separation of operations in which contamination is likely to occur, by one or more of the following means: location, time, partition, air flow, enclosed systems, or other effective means.</p>	<p>(c) Permit the use of proper precautions to reduce the potential for mixups or contamination of components, dietary ingredients, dietary supplements, or contact surfaces, with microorganisms, chemicals, filth, or other-extraneous material. Your physical plant must have and you must use separate or defined areas of adequate size or other control systems, such as computerized inventory controls or automated systems of separation, to prevent contamination and mixups of components, dietary ingredients, and dietary supplements during the following operations:</p> <p>(1) Receiving, identifying, holding, and withholding from use, components, dietary ingredients, dietary supplements, packaging, and labels that will be used in or during the manufacturing, packaging, or holding of dietary ingredients and dietary supplements;</p> <p>(2) Separating, as necessary, components, dietary ingredients, dietary supplements, packaging, and labels, that are to be used from components, dietary ingredients, dietary supplements, packaging, or labels that are awaiting material review and disposition decision, reprocessing, or are awaiting disposal after rejection;</p> <p>(3) Separating the manufacturing, packaging, and holding of different product types including, but not limited to, different types of dietary ingredients, dietary supplements and other foods, cosmetics, and pharmaceutical products;</p> <p>(4) Performing laboratory analyses and holding laboratory supplies and samples;</p> <p>(5) Cleaning and sanitizing contact surfaces;</p> <p>(6) Packaging and label operations; and</p> <p>(7) Holding dietary ingredients or dietary supplements.</p>

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<p>(c) (10) Aseptic processing, which includes as appropriate:</p> <p>(i) Floors, walls, and ceilings of smooth, hard surfaces that are easily cleanable;</p>	<p>(4) Be constructed in such a manner that floors, walls, and ceilings may be adequately cleaned and kept clean and kept in good repair; that drip or condensate from fixtures, ducts and pipes does not contaminate food, food-contact surfaces, or food-packaging materials; ...</p>	<p>(4) Be constructed in such a manner that floors, walls, and ceilings may be adequately cleaned and kept clean and kept in good repair; that drip or condensate from fixtures, ducts and pipes does not adulterate raw materials, in-process or finished dietary products, or contaminate product containers, utensils or packaging materials; ...</p>	<p>(d) Be designed and constructed in a manner that prevents contamination of components, dietary ingredients, dietary supplements, or contact surfaces. The design and construction must include, but not be limited to:</p> <p>(1) Floors, Walls, and ceilings that are of smooth and hard surfaces that can be adequately cleaned and kept clean and in good repair;</p> <p>(2) Fixtures, ducts, and pipes that do not contaminate components, dietary ingredients, dietary supplements, or contact surfaces by dripping or condensate;</p>
<p>(d) Operations relating to the manufacture, processing, and packing of penicillin shall be performed in facilities separate from those used for other drug products for human use.</p>			
<p>§ 211.46 Ventilation, air filtration, air heating and cooling.</p> <p>(a) Adequate ventilation shall be provided.</p> <p>(b) Equipment for adequate control over air pressure, micro-organisms, dust, humidity, and temperature shall be provided when appropriate for the manufacture, processing, packing, or holding of a drug product.</p> <p>(c) Air filtration systems, including prefilters and particulate matter air filters, shall be used when appropriate on air supplies to production areas. If air is recirculated to production areas, measures shall be taken to control recirculation of dust from production. In areas where air contamination occurs during production, there shall be adequate exhaust systems or other systems adequate to control contaminants.</p> <p>(d) Air-handling systems for the manufacture, processing, and packing of penicillin shall be completely separate from those for other drug products for human use.</p>	<p>(6) Provide adequate ventilation or control equipment to minimize odors and vapors (including steam and noxious fumes) in areas where they may contaminate food; and locate and operate fans and other air-blowing equipment in a manner that minimizes the potential for contaminating food, food-packaging materials, and food-contact surfaces.</p>	<p>(6) Provide adequate ventilation or control equipment to maintain adequate control over microorganisms, dust, humidity, and temperature, when appropriate, for the manufacture of dietary products; to minimize odors and vapors (including steam and noxious fumes) in areas where they may adulterate dietary products; and locate and operate fans and other air-blowing equipment in a manner that minimizes the potential for adulterating raw materials, in-process or finished dietary products, or contaminating processing equipment, utensils or packaging materials.</p>	<p>(3) Adequate ventilation or environmental control equipment such as air flow systems, including filters, fans, and other air-blowing equipment, that minimize odors and vapors (including steam and noxious fumes) in areas where they may contaminate components, dietary ingredients, dietary supplements, or contact surfaces;</p> <p>(4) Fans and other air-blowing equipment located and operated in a manner that minimizes the potential for microorganisms and particulate matter to contaminate components, dietary ingredients, dietary supplements, or contact surfaces;</p> <p>(5) Equipment that controls temperature and humidity; and</p>
	<p>(4)...and that aisles or working spaces are provided between equipment and walls and are adequately unobstructed and of adequate width to permit employees to perform their duties and to protect against contaminating food or food-contact surfaces with clothing or personal contact.</p>	<p>(4)...and that aisles or working spaces are provided between equipment and walls and are adequately unobstructed and of adequate width to permit employees to perform their duties and to protect against adulterating in-process or finished product, or contaminating processing equipment with clothing or personal contact.</p>	<p>(6) Aisles or working spaces between equipment and walls that are adequately unobstructed and of adequate width to permit all persons to perform their duties and to protect against contamination of components, dietary ingredients, dietary supplements, or contact surfaces with clothing or personal contact.</p>

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<p>§ 211.44 Lighting.</p> <p>Adequate lighting shall be provided in all areas.</p>	<p>(5) Provide adequate lighting in hand-washing areas, dressing and locker rooms, and toilet rooms and in all areas where food is examined, processed, or stored and where equipment or utensils are cleaned; and ...</p>	<p>(5) Provide adequate lighting in hand-washing areas, dressing and locker rooms, and toilet rooms and in all areas where product is examined, processed, or stored and where equipment or utensils are cleaned; and ...</p>	<p>(e) Provide adequate light in:</p> <p>(1) All areas where components, dietary ingredients, or dietary supplements are examined, processed, or held;</p> <p>(2) All areas where contact surfaces are cleaned; and</p> <p>(3) Hand-washing areas, dressing and locker rooms, and bathrooms.</p>
	<p>(5)...provide safety-type light bulbs, fixtures, sky-lights, or other glass suspended over exposed food in any step of preparation or otherwise protect against food contamination in case of glass breakage.</p>	<p>(5)...provide safety-type light bulbs, fixtures, sky-lights, or other glass suspended over exposed product in any step of preparation or otherwise protect against product adulteration in case of glass breakage.</p>	<p>(f) Use safety-type light bulbs, fixtures, skylights, or other glass that is suspended over exposed components, dietary ingredients, or dietary supplements in any step of preparation, unless otherwise constructed in a manner that will protect against contamination of components, dietary ingredients, or dietary supplements in case of glass breakage.</p>
	<p>(3) Permit the taking of proper precautions to protect food in outdoor bulk fermentation vessels by any effective means, including:</p> <ul style="list-style-type: none"> (i) Using protective coverings. (ii) Controlling areas over and around the vessels to eliminate harborages for pests. (iii) Checking on a regular basis for pests and pest infestation. (iv) Skimming the fermentation vessels, as necessary. 	<p>(3) Permit the taking of proper precautions to protect dietary ingredients or dietary supplements in outdoor bulk fermentation vessels by any effective means, including:</p> <ul style="list-style-type: none"> (i) Using protective coverings. (ii) Controlling areas over and around the vessels to eliminate harborages for pests. (iii) Checking on a regular basis for pests and pest infestation. (iv) Skimming the fermentation vessels, as necessary. 	<p>(g) Provide protection by any effective means against contamination of components, dietary ingredients, and dietary supplements in bulk fermentation vessels, including consideration of:</p> <p>(1) Use of protective coverings;</p> <p>(2) Placement in areas where you can eliminate harborages for pests over and around the vessels;</p> <p>(3) Placement in areas where you can check regularly for pests, pest infestation, filth or any other extraneous materials; and</p> <p>(4) Use of skimming equipment.</p>
	<p>(7) Provide, where necessary, adequate screening or other protection against pests.</p>	<p>(7) Provide, where necessary, adequate screening or other protection against pests.</p>	<p>(h) Use adequate screening or other protection against pests, where necessary.</p>

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<p>§ 211.63 Equipment design, size, and location.</p> <p>Equipment used in the manufacture, processing, packing, or holding of a drug product shall be of appropriate design, adequate size, and suitably located to facilitate operations for its intended use and for its cleaning and maintenance.</p>	<p>Subpart C—Equipment</p> <p>¶110.40 Equipment and utensils.</p> <p>(a) All plant equipment and utensils shall be so designed and of such material and workmanship as to be adequately cleanable, and shall be properly maintained.</p> <p>(d) Holding, conveying, and manufacturing systems, including gravimetric, pneumatic, closed, and automated systems, shall be of a design and construction that enables them to be maintained in an appropriate sanitary condition.</p>	<p>Equipment and Utensils</p> <p>(a) Design and construction.</p> <p>(1) All plant equipment and utensils shall be so designed and of such material and workmanship as to be adequately cleanable, and shall be properly maintained.</p> <p>(6) Holding, conveying, and manufacturing systems, including gravimetric, pneumatic, closed, and automated systems, shall be of a design and construction that enables them to be maintained in an appropriate clean condition.</p>	<p>Subpart D—Equipment and Utensils</p> <p>§ 111.25 <u>What requirements apply to the equipment and utensils you use?</u></p> <p>(a) (1) You must use equipment and utensils that are of appropriate design, construction, and workmanship to enable them to be suitable for their intended use and to be adequately cleaned and properly maintained. Equipment and utensils include, but are not limited to, the following:</p> <p>(i) Equipment used to hold or convey;</p> <p>(ii) Equipment used to measure;</p> <p>(iii) Equipment using compressed air or gas;</p> <p>iv) Equipment used to carry out processes in closed pipes and vessels; and</p> <p>(v) Equipment used in automatic, mechanical, or electronic systems.</p>
<p>§ 211.65 Equipment construction.</p> <p>(a) Equipment shall be constructed so that surfaces that contact components, in-process materials, or drug products shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements.</p> <p>(b) Any substances required for operation, such as lubricants or coolants, shall not come into contact with components, drug product containers, closures, in-process materials, or drug products so as to alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements.</p>	<p>The design, construction, and use of equipment and utensils shall preclude the adulteration of food with lubricants, fuel, metal fragments, contaminated water, or any other contaminants.</p>	<p>(2) The design, construction and use of equipment and utensils shall preclude the adulteration of raw materials, packaging materials, in-process materials or finished product with lubricants, fuel, metal fragments, contaminated water, or any other contaminants.</p>	<p>(2) You must use equipment and utensils of appropriate design and construction so that use will not result in the contamination of components, dietary ingredients, or dietary supplements with:</p> <p>(i) Lubricants;</p> <p>(ii) Fuel;</p> <p>(iii) Coolants;</p> <p>(iv) Metal or glass fragments;</p> <p>(v) Filth or any other extraneous material;</p> <p>(vi) Contaminated water; or</p> <p>(vii) Any other contaminants.</p>

PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)	Food cGMP (21 CFR Part 110)	Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)	Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)
	<p>All equipment should be so installed and maintained as to facilitate the cleaning of the equipment and of all adjacent spaces. Food-contact surfaces shall be corrosion-resistant when in contact with food. They shall be made of nontoxic materials and designed to withstand the environment of their intended use and the action of food, and, if applicable, cleaning compounds and sanitizing agents. Food-contact surfaces shall be maintained to protect food from being contaminated by any source, including unlawful indirect food additives.</p> <p>....(7) Equipment, containers, and utensils used to convey, hold, or store raw materials, work-in-process, rework, or food shall be constructed, handled, and maintained during manufacturing or storage in a manner that protects against contamination....</p>	<p>(3) All equipment should be so installed and maintained as to facilitate the cleaning of the equipment and of all adjacent spaces. Processing equipment and utensils shall be corrosion-resistant when in contact with raw materials, in-process or finished dietary product. They shall be made of nontoxic materials and designed to withstand the environment of their intended use and the action of dietary products, and, if applicable, cleaning compounds and sanitizing agents. Processing equipment and utensils shall be maintained to protect dietary products from being adulterated by any source.</p> <p>(12) Equipment, containers, and utensils used to convey, hold, or store raw materials, in-process material, rework, or finished product shall be constructed, handled, and maintained during manufacturing or storage in a manner that protects against contamination.</p>	<p>(3) All equipment and utensils you use must be:</p> <p>(i) Installed and maintained to facilitate cleaning the equipment, utensils, and all adjacent spaces;</p> <p>(ii) Corrosion-resistant if the equipment or utensils contact components, dietary ingredients, or dietary supplements;</p> <p>(iii) Made of nontoxic materials;</p> <p>(iv) Designed and constructed to withstand the environment of their intended use, the action of components, dietary ingredients, or dietary supplements, and, if applicable, cleaning compounds and sanitizing agents; and</p> <p>(v) Maintained to protect components, dietary ingredients, and dietary supplements from being contaminated by any source.</p>
	<p>(b) Seams on food-contact surfaces shall be smoothly bonded or maintained so as to minimize accumulation of food particles, dirt, and organic matter and thus minimize the opportunity for growth of microorganisms.</p>	<p>(4) Seams on utensils and processing equipment shall be smoothly bonded or maintained so as to minimize accumulation of product, dirt, and organic matter and thus minimize the opportunity for growth of microorganisms.</p>	<p>(4) Equipment and utensils you use must have seams that are smoothly bonded or maintained to minimize accumulation of component, dietary ingredient, or dietary supplement particles, dirt, filth, organic material, or any extraneous materials or contaminants to minimize the opportunity for growth of microorganisms.</p>
	<p>(c) Equipment that is in the manufacturing or food-handling area and that does not come into contact with food shall be so constructed that it can be kept in a clean condition.</p>	<p>(5) Equipment that is in the manufacturing or product handling area and that does not come into contact with a dietary product shall be so constructed that it can be kept in a clean condition.</p>	
	<p>(e) Each freezer and cold storage compartment used to store and hold food capable of supporting growth of microorganisms shall be fitted with an indicating thermometer, temperature-measuring device, or temperature-recording device so installed as to show the temperature accurately within the compartment, and should be fitted with an automatic control for regulating temperature or with an automatic alarm system to indicate a significant temperature change in a manual operation.</p>	<p>(7) Each freezer and cold storage compartment used to store and hold a dietary product capable of supporting growth of microorganisms shall be fitted with an indicating thermometer, temperature-measuring device, or temperature-recording device so installed as to show the temperature accurately within the compartment, and should be fitted with an automatic control for regulating temperature or with an automatic alarm system to indicate a significant temperature change in a manual operation.</p>	<p>(5) Each freezer and cold storage compartment you use to hold components, dietary ingredients, or dietary supplements:</p> <p>(i) Must be fitted with an indicating thermometer, temperature-measuring device, or temperature-recording device that shows the temperature accurately within the compartment; and</p> <p>(ii) Must have an automatic device for regulating temperature or an automatic alarm system to indicate a significant temperature change in a manual operation.</p>

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	<p>(f) Instruments and controls used for measuring, regulating, or recording temperatures, pH, acidity, water activity, or other conditions that control or prevent the growth of undesirable microorganisms in food shall be accurate and adequately maintained, and adequate in number for their designated uses.</p>	<p>(8) Instruments and controls used in the manufacture, processing, packing or holding dietary products, including instruments and controls used for measuring, regulating, or recording temperatures, pH, acidity, water activity, or other conditions that control or prevent the growth of undesirable microorganisms in such products shall be accurate and adequately maintained, and adequate in number for their designated uses.</p>	<p>(6) Instruments or controls used in the manufacturing, packaging, or holding of a dietary ingredient or dietary supplement, including but not limited to, instruments or controls you use to measure, regulate, or record temperatures, hydrogen ion concentration (pH), water activity, or other conditions that control or prevent the growth of microorganisms or other contamination must be:</p> <p>(i) Accurate and precise;</p> <p>(ii) Adequately maintained; and</p> <p>(iii) Adequate in number for their designated uses.</p>
	<p>(g) Compressed air or other gases mechanically introduced into food or used to clean food-contact surfaces or equipment shall be treated in such a way that food is not contaminated with unlawful indirect food additives.</p>	<p>(9) Compressed air or other gases mechanically introduced into a dietary product or used to clean equipment or utensils shall be treated in such a way that dietary ingredients or dietary supplements are not adulterated.</p>	<p>(7) Compressed air or other gases you introduce mechanically into or onto a component, dietary ingredient, dietary supplement, or contact surface or that you use to clean any contact surface must be treated in such a way that the component, dietary ingredient, dietary supplement, or contact surface is not contaminated.</p>
			<p>(b)(l) You must calibrate instruments and controls you use in manufacturing or testing a component, dietary ingredient, or dietary supplement.</p> <p>(2) You must calibrate before first use; and</p> <p>(i) As specified in writing by the manufacturer of the instrument and control, or</p> <p>(ii) At routine intervals or as otherwise necessary to ensure the accuracy and precision of the instrument and control.</p>
<p>§ 211.160 General requirements.</p> <p>Laboratory controls shall include:</p> <p>(4) The calibration of instruments, apparatus, gauges, and recording devices at suitable intervals in accordance with an established written program containing specific directions, schedules, limits for accuracy and precision, and provisions for remedial action in the event accuracy and/or precision limits are not met. Instruments, apparatus, gauges, and recording devices not meeting established specifications shall not be used.</p>			<p>(c) You must:</p> <p>(1) Establish a written procedure for calibrating instruments and controls you use in manufacturing or testing a component, dietary ingredient, or dietary supplement and document that the written procedure was followed each time a calibration is performed, or</p> <p>(2) Document, at the time of performance that the instrument and control calibration established in accordance with this section was performed.</p>

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			<p>(d) You must identify the following for calibrating instruments and controls in any written procedure or at the time of performance:</p> <p>(1) The instrument or control calibrated;</p> <p>(2) The date of calibration;</p> <p>(3) The reference standard used including the certification of accuracy of the known reference standard and a history of recertification of accuracy;</p> <p>(4) The calibration method used including appropriate limits for accuracy and precision of instruments and controls when calibrating;</p> <p>(5) The calibration reading or readings found; and</p> <p>(6) The recalibration method used if accuracy or precision or both accuracy and precision limits for instruments and controls were not met; and</p> <p>(7) The initials of the person who performed the calibration.</p>
			<p>(d) You must repair or replace instruments or controls that cannot be adjusted to agree with the reference standard.</p>

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<p>§ 211.67 Equipment cleaning and maintenance.</p> <p>(a) Equipment and utensils shall be cleaned, maintained, and sanitized at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, strength, quality, or purity of the drug product beyond the official or other established requirements.</p>	<p>¶110.80(b) Manufacturing operations.</p> <p>(1) Equipment and utensils and finished food containers shall be maintained in an acceptable condition through appropriate cleaning and sanitizing, as necessary. Insofar as necessary, equipment shall be taken apart for thorough cleaning....</p> <p>¶110.35 Sanitary operations.</p> <p>(a) General maintenance.</p> <p>....Cleaning and sanitizing of utensils and equipment shall be conducted in a manner that protects against contamination of food, food-contact surfaces, or food-packaging materials....</p> <p>(d) Sanitation of food-contact surfaces. All food-contact surfaces, including utensils and food-contact surfaces of equipment, shall be cleaned as frequently as necessary to protect against contamination of food.</p> <p>(1) Food-contact surfaces used for manufacturing or holding low-moisture food shall be in a dry, sanitary condition at the time of use. When the surfaces are wet-cleaned, they shall, when necessary, be sanitized and thoroughly dried before subsequent use.</p>	<p>(b) Sanitation of equipment and utensils.</p> <p>(9) Equipment and utensils and finished product containers shall be maintained in an acceptable condition through appropriate cleaning and sanitizing, as necessary. Insofar as necessary, equipment shall be taken apart for thorough cleaning.</p> <p>(1) Cleaning and sanitizing of utensils and equipment shall be conducted in a manner that protects against adulteration of raw materials, in-process or finished dietary product, processing equipment, utensils or packaging materials.</p> <p>(2) All utensils and processing equipment shall be cleaned as frequently as necessary to protect against product adulteration.</p> <p>(3) Utensils and processing equipment used for manufacturing or holding of dry dietary products shall be in a dry, sanitary condition at the time of use. When the surfaces are wet-cleaned, they shall, when necessary, be sanitized and thoroughly dried before subsequent use.</p>	<p>(e)(1) You must maintain, clean, and sanitize as necessary, all equipment, utensils, and any other contact surfaces that are used to manufacture, package, or hold components, dietary ingredients, or dietary supplements. Equipment and utensils must be taken apart as necessary for thorough maintenance, cleaning, and sanitizing.</p> <p>(2) You must ensure that all contact surfaces used for manufacturing or holding of low-moisture components, dietary ingredients, or dietary supplements are in a dry and sanitary condition at the time of use. When the surfaces are wet-cleaned, they must be sanitized, when necessary, and thoroughly dried before subsequent use.</p>
	<p>(2) In wet processing, when cleaning is necessary to protect against the introduction of microorganisms into food, all food-contact surfaces shall be cleaned and sanitized before use and after any interruption during which the food-contact surfaces may have become contaminated. Where equipment and utensils are used in a continuous production operation, the utensils and food-contact surfaces of the equipment shall be cleaned and sanitized as necessary.</p>	<p>(4) In wet processing, when cleaning is necessary to protect against the introduction of microorganisms into a dietary product, all utensils and processing equipment shall be cleaned and sanitized as appropriate before use and after any interruption during which the utensils or processing equipment may have become contaminated. Where equipment and utensils are used in a continuous production operation or in back-to-back operations involving different batches of the same products, the utensils and product-contact surfaces of the equipment shall be cleaned and sanitized as appropriate.</p>	<p>(3) If you use wet processing during manufacturing, you must clean and sanitize all contact surfaces, as necessary, to protect against the introduction of microorganisms into components, dietary ingredients, or dietary supplements. When cleaning and sanitizing is necessary, you must clean and sanitize all contact surfaces before use and after any interruption during which the contact surface may have become contaminated. If you use contact surfaces in a continuous production operation or in back-to-back operations involving different batches of the same dietary ingredient or dietary supplement, you must clean and sanitize the contact surfaces as necessary.</p>
	<p>(3) Non-food-contact surfaces of equipment used in the operation of food plants should be cleaned as frequently as necessary to protect against contamination of food.</p>	<p>(5) Non-product-contact surfaces of equipment should be cleaned as frequently as necessary to protect against product adulteration.</p>	<p>(4) You must clean surfaces that do not touch components, dietary ingredients, or dietary supplements as frequently as necessary to protect against contaminating components, dietary ingredients, or dietary supplements.</p>

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	<p>(4) Single-service articles (such as utensils intended for one-time use, paper cups, and paper towels) should be stored in appropriate containers and shall be handled, dispensed, used, and disposed of in a manner that protects against contamination of food or food-contact surfaces.</p>	<p>(6) Single-service articles (such as utensils intended for one-time use, paper cups, and paper towels) should be stored in appropriate containers and shall be handled, dispensed, used, and disposed of in a manner that protects against adulteration of dietary products, and contamination of utensils and processing equipment.</p>	<p>(5) Single-service articles (such as utensils intended for one-time use, paper cups, and paper towels) must be:</p> <p>(i) Stored in appropriate containers; and</p> <p>(ii) Handled, dispensed, used, and disposed of in a manner that protects against contamination of components, dietary ingredients, dietary supplements, or any contact surface.</p>
	<p>(5) Sanitizing agents shall be adequate and safe under conditions of use. Any facility, procedure, or machine is acceptable for cleaning and sanitizing equipment and utensils if it is established that the facility, procedure, or machine will routinely render equipment and utensils clean and provide adequate cleaning and sanitizing treatment.</p>	<p>(7) Sanitizing agents shall be adequate and safe under conditions of use. Any facility, procedure, or machine is acceptable for cleaning and sanitizing equipment and utensils if it is established that the facility, procedure, or machine will routinely render equipment and utensils clean and provide adequate cleaning and sanitizing treatment.</p>	<p>(6) Cleaning compounds and sanitizing agents must be adequate for intended use and safe under condition of use;</p>
	<p>(e) Storage and handling of cleaned portable equipment and utensils. Cleaned and sanitized portable equipment with food-contact surfaces and utensils should be stored in a location and manner that protects food-contact surfaces from contamination.</p>	<p>(8) Cleaned and sanitized portable equipment with product-contact surfaces and utensils should be stored in a location and manner that protects product-contact surfaces from contamination.</p>	<p>(7) You must store cleaned and sanitized portable equipment and utensils that have contact surfaces in a location and manner that protects them from contamination.</p>
<p>(b) Written procedures shall be established and followed for cleaning and maintenance of equipment, including utensils, used in the manufacture, processing, packing, or holding of a drug product. These procedures shall include, but are not necessarily limited to, the following:</p> <p>(1) Assignment of responsibility for cleaning and maintaining equipment;</p> <p>(2) Maintenance and cleaning schedules, including, where appropriate, sanitizing schedules;</p> <p>(3) A description in sufficient detail of the methods, equipment, and materials used in cleaning and maintenance operations, and the methods of disassembling and reassembling equipment as necessary to assure proper cleaning and maintenance;</p> <p>(4) Removal or obliteration of previous batch identification;</p> <p>(5) Protection of clean equipment from contamination prior to use;</p> <p>(6) Inspection of equipment for cleanliness immediately before use.</p> <p>(c) Records shall be kept of maintenance, cleaning, sanitizing, and inspection as specified in §§211.180 and 211.182.</p>		<p>(10) Written procedures shall be established and followed for cleaning and maintaining equipment and utensils used in the manufacture of dietary products.</p>	
			<p>(f) You must keep calibration records as required by this section in accordance with § 111.125.</p>

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<p>§ 211.68 Automatic, mechanical, and electronic equipment.</p> <p>(a) Automatic, mechanical, or electronic equipment or other types of equipment, including computers, or related systems that will perform a function satisfactorily, may be used in the manufacture, processing, packing, and holding of a drug product.</p>			<p>§ 111.30 What requirements apply to automatic, mechanical, or electronic equipment?</p> <p>(a) When you use automatic, mechanical, or electronic equipment to manufacture, package, label, and hold a dietary ingredient or dietary supplement, you must:</p> <p>(1) Design or select equipment to ensure that dietary ingredient or dietary supplement specifications are consistently achieved and</p> <p>(2) Determine the suitability of your equipment by ensuring that your equipment is capable of operating satisfactorily within the operating limits required by the process.</p>
<p>If such equipment is so used, it shall be routinely calibrated, inspected, or checked according to a written program designed to assure proper performance....</p> <p>(b) Appropriate controls shall be exercised over computer or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel. Input to and output from the computer or related system of formulas or other records or data shall be checked for accuracy. The degree and frequency of input/output verification shall be based on the complexity and reliability of the computer or related system. A backup file of data entered into the computer or related system shall be maintained except where certain data, such as calculations performed in connection with laboratory analysis, are eliminated by computerization or other automated processes. In such instances a written record of the program shall be maintained along with appropriate validation data. Hard copy or alternative systems, such as duplicates, tapes, or microfilm, designed to assure that backup data are exact and complete and that it is secure from alteration, inadvertent erasures, or loss shall be maintained.</p>			<p>(b) For any automatic, mechanical, or electronic equipment you use, you must:</p> <p>(1) Routinely calibrate, inspect, or check to ensure proper performance. Your quality control unit must approve these calibrations, inspections, or checks;</p> <p>(2) Make and keep written records of equipment calibrations, inspections, or checks;</p> <p>(3) Establish and use appropriate controls, to ensure that your quality control unit approves changes in the master manufacturing record, batch control records, packaging operations and label operations, or changes to other operations related to the equipment that you use and that only authorized personnel institute the changes;</p> <p>(4) Establish and use appropriate controls to ensure that the equipment functions in accordance with its intended use. These controls must be approved by your quality control unit; and</p> <p>(5) Make and keep backup file(s) of software programs and of data entered into your computer system. Your backup file (e.g., a hard copy of data you have entered, diskettes, tapes, microfilm, or compact disks) must be an exact and complete record of the data you entered. You must keep your backup software programs and data secure from alterations, inadvertent erasures, or equipment loss.</p>
<p>(a) ...Written records of those calibration checks and inspections shall be maintained.</p>			<p>(c) You must keep automatic, mechanical, or electronic equipment records required by this section in accordance with § 111.125.</p>

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<p>§ 211.72 Filters.</p> <p>Filters for liquid filtration used in the manufacture, processing, or packing of injectable drug products intended for human use shall not release fibers into such products. Fiber-releasing filters may not be used in the manufacture, processing, or packing of these injectable drug products unless it is not possible to manufacture such drug products without the use of such filters. If use of a fiber-releasing filter is necessary, an additional non-fiber-releasing filter of 0.22 micron maximum mean porosity (0.45 micron if the manufacturing conditions so dictate) shall subsequently be used to reduce the content of particles in the injectable drug product. Use of an asbestos-containing filter, with or without subsequent use of a specific non-fiber-releasing filter, is permissible only upon submission of proof to the appropriate bureau of the Food and Drug Administration that use of a non-fiber-releasing filter will, or is likely to, compromise the safety or effectiveness of the injectable drug product.</p>			
			<p>Subpart E--Production and Process Controls</p> <p><u>§ 111.35 What production and process controls must you use?</u></p> <p>(a) You must implement a system of production and process controls that covers all stages of manufacturing, packaging, labeling, and holding of the dietary ingredients and dietary supplements.</p> <p>(b) Your production and in-process control system must be designed to ensure that the dietary ingredient or dietary supplement is manufactured, packaged, and held in a manner that will prevent adulteration of the dietary ingredient or dietary supplement. The production and in-process control system must include all requirements of this subpart and must be reviewed and approved by the quality control unit.</p>
			<p>(c) You must use a quality control unit in your manufacturing, packaging, and label operations for producing the dietary ingredient or dietary supplement to ensure that these operations are performed in a manner that prevents adulteration and ensures that the dietary ingredient or dietary supplement meets specifications for identity, purity, quality, strength, and composition.</p>

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			<p>(d) Any substance, other than a "dietary ingredient" within the meaning of section 201(ff) of the Federal Food, Drug, and Cosmetic Act (the act), the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of the dietary ingredient or dietary supplement must be:</p> <p>(1) Authorized for use as a food additive under section 409 of the act; or</p> <p>(2) Authorized by a prior sanction consistent with § 170.3(l) of this chapter; or</p> <p>(3) If used as a color additive, subject to a listing that, by the terms of that listing, includes the use in a dietary supplement; or</p> <p>(4) Generally recognized as safe (GRAS) for use in a dietary ingredient or dietary supplement. Any claim that a substance is GRAS, other than a dietary ingredient within the meaning of section 201(ff) of the act, must be supported by a citation to the agency's regulations or by an explanation for why there is general recognition of safety of the use of the substance in a dietary ingredient or dietary supplement; and</p> <p>(5) Must comply with all other applicable statutory and regulatory requirements under the act</p>

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<p>§ 211.160 General requirements.</p> <p>(b) Laboratory controls shall include the establishment of scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity. Laboratory controls shall include:</p> <p>(1) Determination of conformance to appropriate written specifications for the acceptance of each lot within each shipment of components, drug product containers, closures, and labeling used in the manufacture, processing, packing, or holding of drug products. The specifications shall include a description of the sampling and testing procedures used. Samples shall be representative and adequately identified. Such procedures shall also require appropriate retesting of any component, drug product container, or closure that is subject to deterioration.</p> <p>(2) Determination of conformance to written specifications and a description of sampling and testing procedures for in-process materials. Such samples shall be representative and properly identified.</p> <p>(3) Determination of conformance to written descriptions of sampling procedures and appropriate specifications for drug products. Such samples shall be representative and properly identified.</p>			<p>(e) You must establish a specification for any point, step, or stage in the manufacturing process where control is necessary to prevent adulteration. Specifications must be established for:</p> <p>(1) The identity, purity, quality, strength, and composition of components, dietary ingredients, or dietary supplements that you receive;</p> <p>(2) The in-process controls in the master manufacturing record where control is necessary to ensure the identity, purity, quality, strength, and composition of dietary ingredients or dietary supplements;</p> <p>(3) The identity, purity, quality, strength, and composition of the dietary ingredient or dietary supplement that you manufacture; and</p>
<p>§ 211.94 Drug product containers and closures.</p> <p>(a) Drug product containers and closures shall not be reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the drug beyond the official or established requirements.</p> <p>(b) Container closure systems shall provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the drug product.</p> <p>(c) Drug product containers and closures shall be clean and, where indicated by the nature of the drug, sterilized and processed to remove pyrogenic properties to assure that they are suitable for their intended use.</p> <p>(d) Standards or specifications, methods of testing, and, where indicated, methods of cleaning, sterilizing, and processing to remove pyrogenic properties shall be written and followed for drug product containers and closures.</p>			<p>(4) The dietary ingredient or dietary supplement labels and the packaging that may come in contact with dietary ingredients and dietary supplements. The packaging must be safe and suitable for its intended use and comply with all other applicable statutory and regulatory requirements under the act and must not be reactive or absorptive so as to affect the safety of the dietary ingredient and dietary supplement.</p>

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<p>§ 211.110 Sampling and testing of in-process materials and drug products.</p> <p>(a) To assure batch uniformity and integrity of drug products, written procedures shall be established and followed that describe the in-process controls, and tests, or examinations to be conducted on appropriate samples of in-process materials of each batch. Such control procedures shall be established to monitor the output and to validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product. Such control procedures shall include, but are not limited to, the following, where appropriate:</p> <p>(1) Tablet or capsule weight variation;</p> <p>(2) Disintegration time;</p> <p>(3) Adequacy of mixing to assure uniformity and homogeneity;</p> <p>(4) Dissolution time and rate;</p> <p>(5) Clarity, completeness, or pH of solutions.</p> <p>(b) Valid in-process specifications for such characteristics shall be consistent with drug product final specifications and shall be derived from previous acceptable process average and process variability estimates where possible and determined by the application of suitable statistical procedures where appropriate. Examination and testing of samples shall assure that the drug product and in-process material conform to specifications.</p> <p>(c) In-process materials shall be tested for identity, strength, quality, and purity as appropriate, and approved or rejected by the quality control unit, during the production process, e.g., at commencement or completion of significant phases or after storage for long periods.</p> <p>(d) Rejected in-process materials shall be identified and controlled under a quarantine system designed to prevent their use in manufacturing or processing operations for which they are unsuitable.</p>			<p>(f) You must monitor the in-process control points, steps, or stages to ensure that specifications established under paragraph (e) of this section are met and to detect any unanticipated occurrence that may result in adulteration;</p>

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<p>§ 211.84 Testing and approval or rejection of components, drug product containers, and closures.</p> <p>(d) Samples shall be examined and tested as follows:</p> <p>(1) At least one test shall be conducted to verify the identity of each component of a drug product. Specific identity tests, if they exist, shall be used.</p> <p>(2) Each component shall be tested for conformity with all appropriate written specifications for purity, strength, and quality. In lieu of such testing by the manufacturer, a report of analysis may be accepted from the supplier of a component, provided that at least one specific identity test is conducted on such component by the manufacturer, and provided that the manufacturer establishes the reliability of the supplier's analyses through appropriate validation of the supplier's test results at appropriate intervals.</p> <p>(4) When appropriate, components shall be microscopically examined.</p> <p>§ 211.165 Testing and release for distribution.</p> <p>(a) For each batch of drug product, there shall be appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient, prior to release. Where sterility and/or pyrogen testing are conducted on specific batches of shortlived radiopharmaceuticals, such batches may be released prior to completion of sterility and/or pyrogen testing, provided such testing is completed as soon as possible.</p> <p>(b) There shall be appropriate laboratory testing, as necessary, of each batch of drug product required to be free of objectionable microorganisms.</p> <p>(c) Any sampling and testing plans shall be described in written procedures that shall include the method of sampling and the number of units per batch to be tested; such written procedure shall be followed.</p> <p>(d) Acceptance criteria for the sampling and testing conducted by the quality control unit shall be adequate to assure that batches of drug products meet each appropriate specification and appropriate statistical quality control criteria as a condition for their approval and release. The statistical quality control criteria shall include appropriate acceptance levels and/or appropriate rejection levels.</p>		<p>(7) (iv) Each lot of raw material shall undergo at least one test by the manufacturer to verify its identity. Such tests may include any appropriate test with sufficient specificity to determine identity, including chemical and laboratory tests, gross organoleptic analysis, microscopic identification, or analysis of constituent markers.</p> <p>(11) Written procedures shall be established and followed that describe appropriate tests, and/or examinations to be conducted that may be necessary to assure the purity, composition and quality of the finished product.</p>	<p>(g) You must ensure, through testing or examination, that each specification that you established under paragraph (e) of this section is met. Specific testing requirements are as follows:</p> <p>(1) You must test each finished batch of the dietary ingredient or dietary supplement produced before releasing for distribution to determine whether established specifications for identity, purity, quality, strength, and composition are met provided that there are scientifically valid analytical methods available to conduct such testing.</p> <p>(2) For any specification for identity, purity, quality, strength, or composition for which you document cannot be tested on the finished batch of a dietary ingredient or dietary supplement, because there is no scientifically valid analytical method available for such testing, then you must:</p> <p>(i) Perform testing on each shipment lot of components, dietary ingredients or dietary supplements received to determine whether such specification is met; and</p> <p>(ii) Perform testing in-process in accordance with the master manufacturing record where control is necessary to ensure the identity, purity, quality, strength, and composition of dietary ingredients or dietary supplements; and</p> <p>(3) Your quality control unit must determine when finished batch testing cannot be completed for any specification on the identity, purity, quality, strength, and composition of dietary ingredients or dietary supplements.</p>
<p>(e) The accuracy, sensitivity, specificity, and reproducibility of test methods employed by the firm shall be established and documented. Such validation and documentation may be accomplished in accordance with §211.194(a)(2).</p>			<p>(h) You must use an appropriate test or examination to determine whether your specifications are met. An appropriate test is one that is a scientifically valid analytical method.</p>

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			<p>(i) You must:</p> <p>(1) Establish corrective action plans for use when an established specification is not met;</p> <p>(2) Review the results of the monitoring required by this section and conduct a material review of any component, dietary ingredient, dietary supplement, packaging or label for which you establish a specification that is not met, or any unanticipated occurrence that adulterates or could result in adulteration of the component, dietary ingredient, dietary supplement, packaging, or label; and</p> <p>(3) Make a material disposition decision for any component, dietary ingredient, dietary supplement, packaging, or label:</p> <p>(i) If a component, dietary ingredient, dietary supplement, packaging, or label fails to meet specifications;</p> <p>(ii) If any step established in the master manufacturing record is not completed;</p> <p>(iii) If there is any unanticipated occurrence during the manufacturing operations that adulterates or may lead to adulteration of the component, dietary ingredient, dietary supplement, packaging, or label;</p> <p>(iv) If calibration of an instrument, or control suggests a problem that may have caused batches of, a dietary ingredient or dietary supplement to become adulterated; or</p> <p>(v) If a dietary ingredient or dietary supplement is returned.</p>

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<p>(f) Drug products failing to meet established standards or specifications and any other relevant quality control criteria shall be rejected. Reprocessing may be performed. Prior to acceptance and use, reprocessed material must meet appropriate standards, specifications, and any other relevant criteria.</p> <p>§ 211.84 Testing and approval or rejection of components, drug product containers, and closures.</p> <p>(e) Any lot of components, drug product containers, or closures that meets the appropriate written specifications of identity, strength, quality, and purity and related tests under paragraph (d) of this section may be approved and released for use. Any lot of such material that does not meet such specifications shall be rejected</p>	<p>¶110.80 Processes and controls.</p> <p>All food that has become contaminated to the extent that it is adulterated within the meaning of the act shall be rejected, or if permissible, treated or processed to eliminate the contamination.</p>	<p>(3) All product that has become contaminated to the extent that it is adulterated within the meaning of the act shall be rejected, or if permissible, treated or processed to eliminate the contamination.</p>	<p>(4) For any deviation, or unanticipated occurrence which resulted in or could lead to adulteration of the component, dietary ingredient, dietary supplement, packaging, or label</p> <p>(i) You must reject the component, dietary ingredient, dietary supplement, packaging, or label unless the quality control unit determines that in-process adjustments are possible to correct the deviation or occurrence;</p> <p>(ii) You must not reprocess a rejected component, dietary ingredient, or dietary supplement unless approved by the quality control unit; and</p> <p>(iii) You must not reprocess any component, dietary ingredient or dietary supplement if it is rejected because of contamination with microorganisms or other contaminants, such as heavy metals;</p>
			<p>(5) Have your quality control unit review and approve any material review and disposition decision described in paragraphs (i) (2) and (i) (3) of this section.</p>
			<p>(j) The person who conducts the material review and makes the disposition decision must, at the time of performance, document every material review and disposition decision in paragraph (i) of this section. The documentation must be included in the appropriate batch production record and must:</p> <p>(1) Identify the specific deviation from the specification or the unanticipated occurrence;</p> <p>(2) Describe your investigation into the cause of the deviation from the specification or the unanticipated occurrence;</p> <p>(3) Evaluate whether or not the deviation from the specification or unanticipated occurrence has resulted in or could lead to adulteration;</p> <p>(4) Identify the action(s) taken to correct and prevent a recurrence of the deviation or the unanticipated occurrence; and</p> <p>(5) Discuss what you did with the component, dietary ingredient, dietary supplement, packaging, or label.</p>

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<p>§ 211.84 Testing and approval or rejection of components, drug product containers, and closures.</p> <p>(d) Samples shall be examined and tested as follows:</p> <p>(6) Each lot of a component, drug product container, or closure that is liable to microbiological contamination that is objectionable in view of its intended use shall be subjected to microbiological tests before use.</p>	<p>(4) Raw materials, other ingredients, and rework susceptible to contamination with pests, undesirable microorganisms, or extraneous material shall comply with applicable Food and Drug Administration regulations, guidelines, and defect action levels for natural or unavoidable defects if a manufacturer wishes to use the materials in manufacturing food. Compliance with this requirement may be verified by any effective means, including purchasing the materials under a supplier's guarantee or certification, or examination of these materials for contamination.</p>	<p>(7) Raw material samples shall be examined and tested as follows:</p> <p>(i) Each lot of raw material, in-process material and rework that is liable to adulteration with filth, insect infestation or other visually evident extraneous material shall be examined against established specifications for such adulteration, and shall comply with any applicable Food and Drug Administration regulations, and guidelines. In lieu of such examination by the manufacturer, a guarantee or certification of examination may be accepted from the supplier of a component provided that the manufacturer establishes the reliability of the supplier's examination.</p> <p>(ii) Each lot of a raw material that is liable to microbiological contamination that is objectionable in view of its intended use shall be subjected to microbiological tests before use. Raw materials shall either not contain levels of microorganisms that may produce food poisoning or other disease in humans, or they shall be otherwise treated during manufacturing operations so that they no longer contain levels that would cause the product to be adulterated within the meaning of the act. In lieu of such testing by the manufacturer, a guarantee or certification of analysis may be accepted from the supplier of a component provided that the manufacturer establishes the reliability of the supplier's analyses.</p>	<p>(k) You must test or examine components, dietary ingredients, and dietary supplements for those types of contamination that may adulterate or may lead to adulteration. You must use an appropriate scientifically valid method for the test or examination. The types of contamination include, but are not limited to, the following:</p> <p>(1) Filth, insects, or other extraneous material;</p> <p>(2) Microorganisms; and</p> <p>(3) Toxic substances.</p> <p>(l) Tests in accordance with this section must include at least, one of the following:</p> <p>(1) Gross organoleptic analysis;</p> <p>(2) Microscopic analysis;</p> <p>(3) Chemical analysis; or</p> <p>(4) Other appropriate test.</p>
	<p>(3) Raw materials and other ingredients susceptible to contamination with aflatoxin or other natural toxins shall comply with current Food and Drug Administration regulations, guidelines, and action levels for poisonous or deleterious substances before these materials or ingredients are incorporated into finished food. Compliance with this requirement may be accomplished by purchasing raw materials and other ingredients under a supplier's guarantee or certification, or may be verified by analyzing these materials and ingredients for aflatoxins and other natural toxins.</p>	<p>(iii) Raw materials and other ingredients susceptible to adulteration with aflatoxin or other natural toxins shall comply with current Food and Drug Administration regulations, guidelines, and action levels for poisonous or deleterious substances before these materials or ingredients are incorporated into a finished dietary ingredient or dietary supplement. Compliance with this requirement may be accomplished by analyzing these materials and ingredients for aflatoxins and other natural toxins or, in lieu of such testing by the manufacturer, a guarantee or certification of analysis may be accepted from the supplier of a component provided that the manufacturer establishes the reliability of the supplier's analyses.</p>	

<p>PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p>Food cGMP (21 CFR Part 110)</p>	<p>Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p>Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
		<p>(b) Laboratory records. Laboratory records shall be maintained and shall include complete data derived from all specified tests.</p>	<p>(m) You must record results of all testing and examinations performed in accordance with this section. If a test or examination is performed on a batch production you must record the test or examination result in the batch production record in accordance with § 111.50(c) (10). Your records must document whether the testing and examination demonstrates that specifications are met.</p>

<p style="text-align: center;">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p style="text-align: center;">Food cGMP (21 CFR Part 110)</p>	<p style="text-align: center;">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p style="text-align: center;">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
			<p>(n) For any specification that is not met, you must conduct a material review and disposition decision under paragraph (i) of this section.</p>
<p>§ 211.194 Laboratory records.</p> <p>(a) Laboratory records shall include complete data derived from all tests necessary to assure compliance with established specifications and standards, including examinations and assays, as follows:</p> <p>(1) A description of the sample received for testing with identification of source (that is, location from where sample was obtained), quantity, lot number or other distinctive code, date sample was taken, and date sample was received for testing.</p> <p>(2) A statement of each method used in the testing of the sample. The statement shall indicate the location of data that establish that the methods used in the testing of the sample meet proper standards of accuracy and reliability as applied to the product tested. (If the method employed is in the current revision of the United States Pharmacopeia, National Formulary, Association of Official Analytical Chemists, Book of Methods,² or in other recognized standard references, or is detailed in an approved new drug application and the referenced method is not modified, a statement indicating the method and reference will suffice). The suitability of all testing methods used shall be verified under actual conditions of use.</p> <p>²Copies may be obtained from: Association of Official Analytical Chemists, 2200 Wilson Blvd., Suite 400, Arlington, VA 22201-3301.</p> <p>(3) A statement of the weight or measure of sample used for each test, where appropriate.</p> <p>(4) A complete record of all data secured in the course of each test, including all graphs, charts, and spectra from laboratory instrumentation, properly identified to show the specific component, drug product container, closure, in-process material, or drug product, and lot tested.</p> <p>(5) A record of all calculations performed in connection with the test, including units of measure, conversion factors, and equivalency factors.</p> <p>(6) A statement of the results of tests and how the results compare with established standards of identity, strength, quality, and purity for the component, drug product container, closure, in-process material, or drug product tested.</p> <p>(7) The initials or signature of the person who performs each test and the date(s) the tests were performed.</p> <p>(8) The initials or signature of a second person showing that the original records have been reviewed for accuracy, completeness, and compliance with established standards.</p>			<p>(o) You must make and retain records, in accordance with § 111.125, to ensure that you follow the requirements of this section. The records must include, but are not limited to:</p> <p>(1) The specifications established;</p> <p>(2) The actual results obtained during the monitoring operation;</p> <p>(3) Any deviation from specifications and any unanticipated occurrences;</p> <p>(4) Any corrective actions taken;</p> <p>(5) The disposition decisions and follow-up; and</p> <p>(6) The identity of the individual qualified by training and experience who investigated any deviation from specifications) or unanticipated occurrence and the identity of the individual from the quality control unit who reviewed the results of that investigation.</p>

<p>PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p>Food cGMP (21 CFR Part 110)</p>	<p>Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p>Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
<p>(b) Complete records shall be maintained of any modification of an established method employed in testing. Such records shall include the reason for the modification and data to verify that the modification produced results that are at least as accurate and reliable for the material being tested as the established method.</p> <p>(c) Complete records shall be maintained of any testing and standardization of laboratory reference standards, reagents, and standard solutions.</p> <p>(d) Complete records shall be maintained of the periodic calibration of laboratory instruments, apparatus, gauges, and recording devices required by §211.160(b)(4).</p> <p>(e) Complete records shall be maintained of all stability testing performed in accordance with §211.166.</p>			
	<p>Subpart E--Production and Process Controls</p> <p>¶110.80 Processes and controls.</p> <p>...Appropriate quality control operations shall be employed to ensure that food is suitable for human consumption and that food-packaging materials are safe and suitable...</p>	<p>Quality Control and Laboratory Operations</p> <p>Appropriate quality control operations shall be employed to assure that dietary products conform to appropriate standards of purity, quality and composition, and that packaging materials are safe and suitable for their intended purpose.</p>	<p>§ 111.37 <u>What requirements apply to quality control?</u></p> <p>(a) You must use a quality control unit to ensure that your manufacturing, packaging, label, and holding operations in the production of dietary ingredients and dietary supplements are performed in a manner that prevents adulteration and misbranding, including ensuring that dietary ingredients and dietary supplements meet specifications for identity, purity, quality, strength, and composition.</p>

<p align="center">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p align="center">Food cGMP (21 CFR Part 110)</p>	<p align="center">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p align="center">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
<p>§ 211.22 Responsibilities of quality control unit.</p> <p>(a) There shall be a quality control unit that shall have the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging material, labeling, and drug products, and the authority to review production records to assure that no errors have occurred or, if errors have occurred, that they have been fully investigated. The quality control unit shall be responsible for approving or rejecting drug products manufactured, processed, packed, or held under contract by another company.</p> <p>(c) The quality control unit shall have the responsibility for approving or rejecting all procedures or specifications impacting on the identity, strength, quality, and purity of the drug product.</p> <p>§ 211.160 General requirements.</p> <p>(a) The establishment of any specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms required by this subpart, including any change in such specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms, shall be drafted by the appropriate organizational unit and reviewed and approved by the quality control unit. The requirements in this subpart shall be followed and shall be documented at the time of performance. Any deviation from the written specifications, standards, sampling plans, test procedures, or other laboratory control mechanisms shall be recorded and justified.</p>		<p>(a) Quality control unit.</p> <p>(1) There shall be a quality control unit that has the responsibility and authority to:</p> <p>(i) Approve or reject all procedures, specifications, controls, tests and examinations, or deviations from them, that impact the purity, quality and composition of a dietary ingredient or dietary supplement; and</p> <p>(ii) Approve or reject all raw materials, packaging materials, labeling, and finished dietary products, including products manufactured, processed, packed, or held under contract by another company, based on adequate determination of conformance to established specifications; and</p> <p>(iii) Assure that completed production records are reviewed as appropriate. Quality control shall be responsible for evaluation of errors committed in the manufacture of a product and shall have the final authority to determine if the error may be corrected in such manner that the product can be approved for distribution or must be destroyed. Such evaluations and their resolution must be documented and maintained with and/or cross-referenced in the batch production record.</p>	<p>(b) Your quality control unit must do the following:</p> <p>(1) Approve or reject all processes, specifications, controls, tests, and examinations, and deviations from or modifications to them, that may affect the identity, purity, quality, strength, and composition of a dietary ingredient or dietary supplement;</p> <p>(2) Determine whether all components, dietary ingredients dietary supplements, packaging, and labels conform to specifications;</p> <p>(3) Approve or reject all components, dietary ingredients, dietary supplements, packaging and labels;</p> <p>(4) Review and approve all master manufacturing records and all modifications to the master manufacturing records;</p> <p>(5) Review and approve all batch production-related records which include, but are not limited to, cross-referencing receiving and batch production records, approval of a material review and disposition decision, approval for reprocessing, and reject all components, dietary ingredients packaging, and labels; approve all master manufacturing records and the master manufacturing records; approval for releasing for distribution;</p> <p>(6) Review and approve all processes for calibrating instruments or controls;</p> <p>(7) Review all records for calibration of instruments, apparatus, gauges, and recording devices;</p> <p>(8) Review all records for equipment calibrations, inspections, and checks;</p> <p>(9) Review and approve all laboratory control processes, and testing results;</p> <p>(10) Review and approve all packaging and label records which include, but are not limited to, cross-referencing receiving and batch production records, approval for repackaging and relabeling, and approval for releasing for distribution;</p>

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<p>§ 211.84 Testing and approval or rejection of components, drug product containers, and closures.</p> <p>(b) Representative samples of each shipment of each lot shall be collected for testing or examination. The number of containers to be sampled, and the amount of material to be taken from each container, shall be based upon appropriate criteria such as statistical criteria for component variability, confidence levels, and degree of precision desired, the past quality history of the supplier, and the quantity needed for analysis and reserve where required by §211.170.</p> <p>(c) Samples shall be collected in accordance with the following procedures:</p> <p>(1) The containers of components selected shall be cleaned where necessary, by appropriate means.</p> <p>(2) The containers shall be opened, sampled, and resealed in a manner designed to prevent contamination of their contents and contamination of other components, drug product containers, or closures.</p> <p>(3) Sterile equipment and aseptic sampling techniques shall be used when necessary.</p> <p>(4) If it is necessary to sample a component from the top, middle, and bottom of its container, such sample subdivisions shall not be composited for testing.</p> <p>(5) Sample containers shall be identified so that the following information can be determined: name of the material sampled, the lot number, the container from which the sample was taken, the date on which the sample was taken, and the name of the person who collected the sample.</p> <p>(6) Containers from which samples have been taken shall be marked to show that samples have been removed from them.</p>			<p>(11) Collect representative samples of:</p> <p>(i) Each shipment lot of components, dietary ingredients, dietary supplements, packaging, and labels received to determine whether the component, dietary ingredient, dietary supplement, packaging, or labels meet specifications;</p>

<p>PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p>Food cGMP (21 CFR Part 110)</p>	<p>Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p>Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
			<p>(ii) In process materials at points, steps, or stages, in the manufacturing process as specified in the, master manufacturing record where control is necessary to ensure the identity, purity, quality, strength, and composition of dietary ingredients or dietary supplements;</p> <p>(iii) Each batch of dietary ingredient or dietary supplement manufactured to determine, before releasing for distribution, whether the dietary ingredient or dietary supplement meets its specifications for identity, purity, quality, strength, and composition; and</p> <p>(iv) Each batch of packaged and labeled dietary ingredients or dietary supplements to determine that you used the packaging specified in the master manufacturing record and applied the label specified in the master manufacturing record.</p>
			<p>(12) Keep the reserve samples for 3 years from the date of manufacture for use in appropriate investigations including, but not limited to, consumer complaint investigations to determine, for example, whether the dietary ingredient or dietary supplement associated with a consumer complaint failed to meet any of its specifications for identity, purity, quality, strength, and composition. The reserve samples must:</p> <p>(i) Be identified with the batch or lot number; and</p> <p>(ii) Consist of at least twice the quantity necessary for tests.</p>

<p>PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p>Food cGMP (21 CFR Part 110)</p>	<p>Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p>Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
			<p>(13) Perform appropriate tests and examinations of:</p> <p>(i) Components, dietary ingredients, dietary supplements, packaging, and labels received to ensure that they meet specifications;</p> <p>(ii) Dietary ingredient and dietary supplement batch production at points, steps, or stages identified in the master manufacturing record where control is necessary to prevent adulteration;</p> <p>(iii) Dietary ingredients and dietary supplements that you manufacture to ensure that they meet specifications; and</p> <p>(iv) Packaged and labeled dietary ingredients and dietary supplements to ensure that you used the packaging specified in the master manufacturing record and you applied the label specified in the master manufacturing record.</p>
			<p>(14) Review and approve all material review and disposition decisions; and</p>
			<p>(15) Approve the reprocessing or distribution of returned dietary ingredients or dietary supplements.</p>
			<p>(c) Your quality control unit must establish and maintain documentation at the time of performance that it performed the review, approval, or rejection requirements of this section by recording the following:</p> <p>(1) Date the required review, approval, or rejection was performed; and</p> <p>(2) Signature of the person performing the requirement.</p>
<p>§ 211.22 Responsibilities of quality control unit.</p> <p>(d) The responsibilities and procedures applicable to the quality control unit shall be in writing; such written procedures shall be followed.</p>		<p>(3) The responsibilities and procedures applicable to the quality control unit shall be established in writing and followed.</p>	
			<p>(d) You must keep quality control records in accordance with § 111.125.</p>

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<p>§ 211.137 Expiration dating.</p> <p>(a) To assure that a drug product meets applicable standards of identity, strength, quality, and purity at the time of use, it shall bear an expiration date determined by appropriate stability testing described in §211.166.</p> <p>(b) Expiration dates shall be related to any storage conditions stated on the labeling, as determined by stability studies described in §211.166.</p> <p>(c) If the drug product is to be reconstituted at the time of dispensing, its labeling shall bear expiration information for both the reconstituted and unreconstituted drug products.</p> <p>(d) Expiration dates shall appear on labeling in accordance with the requirements of §201.17 of this chapter.</p>		<p>(c) Expiration dating.</p> <p>(1) Whenever a dietary ingredient or dietary supplement bears an expiration date, such date shall be supported by data and rationale to reasonably assure that the product meets established specifications at the expiration date.</p>	
<p>(e) Homeopathic drug products shall be exempt from the requirements of this section.</p> <p>(f) Allergenic extracts that are labeled "No U.S. Standard of Potency" are exempt from the requirements of this section.</p> <p>(g) New drug products for investigational use are exempt from the requirements of this section, provided that they meet appropriate standards or specifications as demonstrated by stability studies during their use in clinical investigations. Where new drug products for investigational use are to be reconstituted at the time of dispensing, their labeling shall bear expiration information for the reconstituted drug product.</p> <p>(h) Pending consideration of a proposed exemption, published in the Federal Register of September 29, 1978, the requirements in this section shall not be enforced for human OTC drug products if their labeling does not bear dosage limitations and they are stable for at least 3 years as supported by appropriate stability data.</p>			

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<p>§ 211.166 Stability testing.</p> <p>(a) There shall be a written testing program designed to assess the stability characteristics of drug products. The results of such stability testing shall be used in determining appropriate storage conditions and expiration dates. The written program shall be followed and shall include:</p> <p>(1) Sample size and test intervals based on statistical criteria for each attribute examined to assure valid estimates of stability;</p> <p>(2) Storage conditions for samples retained for testing;</p> <p>(3) Reliable, meaningful, and specific test methods;</p> <p>(4) Testing of the drug product in the same container-closure system as that in which the drug product is marketed;</p> <p>(5) Testing of drug products for reconstitution at the time of dispensing (as directed in the labeling) as well as after they are reconstituted.</p> <p>(b) An adequate number of batches of each drug product shall be tested to determine an appropriate expiration date and a record of such data shall be maintained. Accelerated studies, combined with basic stability information on the components, drug products, and container-closure system, may be used to support tentative expiration dates provided full shelf life studies are not available and are being conducted. Where data from accelerated studies are used to project a tentative expiration date that is beyond a date supported by actual shelf life studies, there must be stability studies conducted, including drug product testing at appropriate intervals, until the tentative expiration date is verified or the appropriate expiration date determined.</p>		<p>(2) Appropriate accelerated stability studies or data from similar product formulations may be used for an initial determination of shelf life. Product shelf life shall be confirmed and may be extended on the basis of real time studies on product stored under labeled storage conditions.</p>	
<p>(c) For homeopathic drug products, the requirements of this section are as follows:</p> <p>(1) There shall be a written assessment of stability based at least on testing or examination of the drug product for compatibility of the ingredients, and based on marketing experience with the drug product to indicate that there is no degradation of the product for the normal or expected period of use.</p> <p>(2) Evaluation of stability shall be based on the same container-closure system in which the drug product is being marketed.</p> <p>(d) Allergenic extracts that are labeled "No U.S. Standard of Potency" are exempt from the requirements of this section.</p>			

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<p>§ 211.167 Special testing requirements.</p> <p>(a) For each batch of drug product purporting to be sterile and/or pyrogen-free, there shall be appropriate laboratory testing to determine conformance to such requirements. The test procedures shall be in writing and shall be followed.</p> <p>(b) For each batch of ophthalmic ointment, there shall be appropriate testing to determine conformance to specifications regarding the presence of foreign particles and harsh or abrasive substances. The test procedures shall be in writing and shall be followed.</p> <p>(c) For each batch of controlled-release dosage form, there shall be appropriate laboratory testing to determine conformance to the specifications for the rate of release of each active ingredient. The test procedures shall be in writing and shall be followed.</p>			
<p>§ 211.82 Receipt and storage of untested components, drug product containers, and closures.</p> <p>(a) Upon receipt and before acceptance, each container or grouping of containers of components, drug product containers, and closures shall be examined visually for appropriate labeling as to contents, container damage or broken seals, and contamination.</p> <p>(b) Components, drug product containers, and closures shall be stored under quarantine until they have been tested or examined, as appropriate, and released. Storage within the area shall conform to the requirements of §211.80.</p> <p>§ 211.84 Testing and approval or rejection of components, drug product containers, and closures.</p> <p>(d) (5) Each lot of a component, drug product container, or closure that is liable to contamination with filth, insect infestation, or other extraneous adulterant shall be examined against established specifications for such contamination.</p>	<p>¶110.80 (a) Raw materials and other ingredients.</p> <p>...Containers and carriers of raw materials should be inspected on receipt to ensure that their condition has not contributed to the contamination or deterioration of food.</p>	<p>(c) Handling and storage of raw materials, in-process materials and rework.</p> <p>...Containers of raw materials should be inspected on receipt to assure that their condition has not contributed to the adulteration or deterioration of the contents.</p> <p>(2) Written procedures shall be established and followed describing in sufficient detail the control procedures employed for the receipt, storage, handling, sampling, examination, and/or testing that may be necessary to assure the identity of labeling and the appropriate identity, cleanliness and quality characteristics of packaging materials for dietary products.</p>	<p>§ 111.40 What requirements apply to components, dietary ingredients, dietary supplements, packaging, and labels you receive?</p> <p>(a) For components, dietary ingredients, or dietary supplements you receive, you must:</p> <p>(1) Visually examine each container or grouping of containers in a shipment for appropriate content label, container, damage, or broken seals to determine whether the container condition has resulted in contamination or deterioration of the components, dietary ingredients, or dietary supplement;</p>
			<p>(2) Visually examine the supplier's invoice, guarantee, or certification to ensure that the components, dietary ingredients, or dietary supplements are consistent with your purchase order and perform testing, as needed, to determine whether specifications are met.</p>

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<p>§ 211.84 Testing and approval or rejection of components, drug product containers, and closures.</p> <p>(a) Each lot of components, drug product containers, and closures shall be withheld from use until the lot has been sampled, tested, or examined, as appropriate, and released for use by the quality control unit.</p>			<p>(3) Quarantine components, dietary ingredients, or dietary supplements until your quality control unit reviews the supplier's invoice, guarantee, or certification and performs testing, as needed, of a representative sample to determine that specifications are met. If specifications are not met, you must conduct a material review and make a disposition decision. Your quality control unit must approve and release the components, dietary ingredients, and dietary supplements from quarantine before you use them;</p>
<p>§ 211.80 General requirements.</p> <p>(d) Each container or grouping of containers for components or drug product containers, or closures shall be identified with a distinctive code for each lot in each shipment received. This code shall be used in recording the disposition of each lot. Each lot shall be appropriately identified as to its status (i.e., quarantined, approved, or rejected).</p>		<p>(6) Each lot of raw material shall be identified with a distinctive lot number and shall be appropriately controlled according to its status (e.g. quarantined, approved, rejected).</p>	<p>(4) Identify each lot of components, dietary ingredients, or dietary supplements in a shipment in a manner that allows you to trace the shipment to the supplier, the date received, the name of the component or dietary supplement, and the status (e.g., quarantined, approved, or rejected) and to trace the shipment lot to the dietary ingredient or dietary supplement manufactured and distributed. You must use this unique identifier whenever you record the disposition of each shipment lot received; and</p>
<p>(b) Components and drug product containers and closures shall at all times be handled and stored in a manner to prevent contamination.</p> <p>(c) Bagged or boxed components of drug product containers, or closures shall be stored off the floor and suitably spaced to permit cleaning and inspection.</p>	<p>¶110.80 (a) Raw materials and other ingredients.</p> <p>(1) Raw materials and other ingredients shall be inspected and segregated or otherwise handled as necessary to ascertain that they are clean and suitable for processing into food and shall be stored under conditions that will protect against contamination and minimize deterioration.</p> <p>(7) Liquid or dry raw materials and other ingredients received and stored in bulk form shall be held in a manner that protects against contamination.</p> <p>(5) Raw materials, other ingredients, and rework shall be held in bulk, or in containers designed and constructed so as to protect against contamination and shall be held at such temperature and relative humidity and in such a manner as to prevent the food from becoming adulterated within the meaning of the act. Material scheduled for rework shall be identified as such.</p>	<p>(1) Raw materials, in-process materials and rework shall be inspected and segregated or otherwise handled as necessary to ascertain that they are clean and suitable for processing into dietary products and shall be stored under conditions that will protect against adulteration and minimize deterioration.</p> <p>(1)...Liquid or dry raw materials and other ingredients received and stored in bulk form shall be held in a manner that protects against contamination.</p> <p>(3) Raw materials, in-process materials, and rework shall be held in bulk, or in containers designed and constructed so as to protect against adulteration and shall be held at such temperature and relative humidity and in such a manner as to prevent a dietary ingredient or dietary supplement from becoming adulterated within the meaning of the act. Material scheduled for rework shall be identified as such.</p>	<p>(5) Hold components, dietary ingredients, or dietary supplements under conditions that will protect against contamination, deterioration, and avoid mixups.</p>
	<p>(6) Frozen raw materials and other ingredients shall be kept frozen. If thawing is required prior to use, it shall be done in a manner that prevents the raw materials and other ingredients from becoming adulterated within the meaning of the act.</p>	<p>(4) Frozen raw materials and other ingredients shall be kept frozen. If thawing is required prior to use, it shall be done in a manner that prevents the raw materials and other ingredients from becoming adulterated within the meaning of the act.</p>	

<p align="center">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p align="center">Food cGMP (21 CFR Part 110)</p>	<p align="center">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p align="center">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
<p>§ 211.80 General requirements.</p> <p>(a) There shall be written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, testing, and approval or rejection of components and drug product containers and closures; such written procedures shall be followed.</p>		<p>(5) Written procedures shall be established and followed describing the receipt, identification, examination, handling, sampling, testing and approval or rejection of raw materials.</p>	
<p>§ 211.82 Receipt and storage of untested components, drug product containers, and closures.</p> <p>(a) Upon receipt and before acceptance, each container or grouping of containers of components, drug product containers, and closures shall be examined visually for appropriate labeling as to contents, container damage or broken seals, and contamination.</p> <p>(b) Components, drug product containers, and closures shall be stored under quarantine until they have been tested or examined, as appropriate, and released. Storage within the area shall conform to the requirements of §211.80.</p> <p>§ 211.84 Testing and approval or rejection of components, drug product containers, and closures.</p> <p>(d) (5) Each lot of a component, drug product container, or closure that is liable to contamination with filth, insect infestation, or other extraneous adulterant shall be examined against established specifications for such contamination.</p>			<p>(b) For packaging and labels you receive, you must:</p> <p>(1) Visually examine each container or grouping of containers in a shipment for appropriate content label, container damage, or broken seals to determine whether the container condition has resulted in contamination or deterioration of the packaging and labels;</p>
<p>(d) (3) Containers and closures shall be tested for conformance with all appropriate written procedures. In lieu of such testing by the manufacturer, a certificate of testing may be accepted from the supplier, provided that at least a visual identification is conducted on such containers/closures by the manufacturer and provided that the manufacturer establishes the reliability of the supplier's test results through appropriate validation of the supplier's test results at appropriate intervals.</p>			<p>(2) Quarantine packaging and labels until your quality control unit tests or examines a representative sample to determine that specifications are met. You must conduct at least a visual identification on the containers and closures. If specifications are not met, you must conduct a material review and make a disposition decision. Your quality control unit must approve and release packaging and labels from quarantine before you use them;</p>
<p>§ 211.80 General requirements.</p> <p>(d) Each container or grouping of containers for components or drug product containers, or closures shall be identified with a distinctive code for each lot in each shipment received. This code shall be used in recording the disposition of each lot. Each lot shall be appropriately identified as to its status (i.e., quarantined, approved, or rejected).</p>			<p>(3) Identify each shipment lot of packaging and labels in a manner that allows you to trace the shipment lot to the supplier, the date received, the name of the packaging and label and the status (e.g., quarantined, approved, or rejected) and to trace the shipment lot to the dietary ingredient or dietary supplement manufactured and distributed. You must use this unique identifier whenever you record the disposition of each shipment lot received; and</p>

PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)	Food cGMP (21 CFR Part 110)	Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)	Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)
<p>(b) Components and drug product containers and closures shall at all times be handled and stored in a manner to prevent contamination.</p> <p>(c) Bagged or boxed components of drug product containers, or closures shall be stored off the floor and suitably spaced to permit cleaning and inspection.</p>			<p>(4) Hold packaging and labels under conditions that will protect against contamination, deterioration, and avoid mixups.</p>

<p align="center">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p align="center">Food cGMP (21 CFR Part 110)</p>	<p align="center">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p align="center">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
<p>§ 211.122 Materials examination and usage criteria.</p> <p>(a) There shall be written procedures describing in sufficient detail the receipt, identification, storage, handling, sampling, examination, and/or testing of labeling and packaging materials; such written procedures shall be followed. Labeling and packaging materials shall be representatively sampled, and examined or tested upon receipt and before use in packaging or labeling of a drug product.</p> <p>(b) Any labeling or packaging materials meeting appropriate written specifications may be approved and released for use. Any labeling or packaging materials that do not meet such specifications shall be rejected to prevent their use in operations for which they are unsuitable.</p> <p>(c) Records shall be maintained for each shipment received of each different labeling and packaging material indicating receipt, examination or testing, and whether accepted or rejected.</p>			
<p>§ 211.184 Component, drug product container, closure, and labeling records.</p> <p>These records shall include the following:</p> <p>(a) The identity and quantity of each shipment of each lot of components, drug product containers, closures, and labeling; the name of the supplier; the supplier's lot number(s) if known; the receiving code as specified in §211.80; and the date of receipt. The name and location of the prime manufacturer, if different from the supplier, shall be listed if known.</p> <p>(b) The results of any test or examination performed (including those performed as required by §211.82(a), §211.84(d), or §211.122(a)) and the conclusions derived therefrom.</p> <p>(c) An individual inventory record of each component, drug product container, and closure and, for each component, a reconciliation of the use of each lot of such component. The inventory record shall contain sufficient information to allow determination of any batch or lot of drug product associated with the use of each component, drug product container, and closure.</p> <p>(d) Documentation of the examination and review of labels and labeling for conformity with established specifications in accord with §§211.122(c) and 211.130(c).</p> <p>(e) The disposition of rejected components, drug product containers, closure, and labeling.</p>			<p>(c) (1) The person who performs the component, dietary ingredient, dietary supplement, packaging, or label requirements of this section must document, at the time of performance, that the requirements were followed. The documentation must include, but not be limited to:</p> <p>(i) The date that the components, dietary ingredients, dietary supplements, packaging, or labels were received;</p> <p>(ii) The signature of the person performing the requirement;</p> <p>(iii) Any test results; and</p> <p>(iv) Any material review and disposition decision you conducted in accordance with §111.35(i) and disposition of any rejected material under S 111.74.</p> <p>(2) You must keep component, dietary supplement, packaging, and label receiving records in accordance with § 111.125.</p>

<p align="center">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p align="center">Food cGMP (21 CFR Part 110)</p>	<p align="center">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p align="center">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
<p>§ 211.186 Master production and control records.</p> <p>(a) To assure uniformity from batch to batch, master production and control records for each drug product, including each batch size thereof, shall be prepared, dated, and signed (full signature, handwritten) by one person and independently checked, dated, and signed by a second person. The preparation of master production and control records shall be described in a written procedure and such written procedure shall be followed.</p>		<p>Production and Process Controls</p> <p>(a) Master production and control records.</p> <p>(1) To assure uniformity from batch to batch, a master production and control record shall be prepared for the manufacture of each dietary ingredient and dietary supplement, ...</p>	<p>§ 111.45 What requirements apply to establishing a master manufacturing record?</p> <p>(a) You must prepare and follow a written master manufacturing record for each type of dietary ingredient or dietary supplement that you manufacture and for each batch size to ensure uniformity from batch to batch. The master manufacturing record must:</p> <p>(1) Identify specifications for the points, steps, or stages in the manufacturing process where control is necessary to prevent adulteration; and</p> <p>(2) Establish controls and procedures to ensure that each batch of dietary ingredient or dietary supplement manufactured meets those specifications.</p>
<p>(b) Master production and control records shall include:</p> <p>(1) The name and strength of the product and a description of the dosage form;</p>		<p>Master production and control records shall include, as appropriate:</p>	<p>(b) The master manufacturing record must include the following information:</p> <p>(1) The name of the dietary ingredient or dietary supplement to be manufactured and the strength, concentration, weight, or measure of each dietary ingredient for each batch size;</p>
<p>(3) A complete list of components designated by names or codes sufficiently specific to indicate any special quality characteristic;</p>		<p>(i) A complete list of raw materials used in the manufacture of a dietary product, designated by names or codes sufficiently specific to indicate any special quality characteristic(s).</p>	<p>(2) A complete list of components to be used;</p>
<p>(4) An accurate statement of the weight or measure of each component, using the same weight system (metric, avoirdupois, or apothecary) for each component. Reasonable variations may be permitted, however, in the amount of components necessary for the preparation in the dosage form, provided they are justified in the master production and control records;</p> <p>§ 211.101 Charge-in of components.</p> <p>(a) The batch shall be formulated with the intent to provide not less than 100 percent of the labeled or established amount of active ingredient.</p>		<p>(ii) An accurate statement of the weight or measure of each raw material used in the manufacture of a dietary product. Each batch shall be formulated with the intent to provide not less than 100 percent of each claimed dietary ingredient.</p>	<p>(3) An accurate statement of the weight or measure of each component to be used;</p>

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<p>§ 211.186 Master production and control records.</p> <p>(b) (2) The name and weight or measure of each active ingredient per dosage unit or per unit of weight or measure of the drug product, and a statement of the total weight or measure of any dosage unit;</p>		<p>(iii) For dietary supplements, the name and weight or measure of each dietary ingredient per unit or portion or per unit of weight or measure of the supplement.</p>	<p>(4) The identity and, weight or measure of each dietary ingredient that will be declared on the Supplement Facts label and the identity of each ingredient that will be declared on the ingredients list of the dietary supplement in compliance with section 403(s) of the Federal Food, Drug, and Cosmetic Act;</p>
<p>(5) A statement concerning any calculated excess of component;</p>		<p>(iv) A statement concerning any calculated excess of dietary ingredient contained in a dietary supplement.</p>	<p>(5) A statement that explains any intentional excess amount of a dietary ingredient;</p>
		<p>(v) A statement of the total weight or measure of any dietary supplement unit.</p>	
<p>(6) A statement of theoretical weight or measure at appropriate phases of processing;</p> <p>(7) A statement of theoretical yield, including the maximum and minimum percentages of theoretical yield beyond which investigation according to §211.192 is required;</p>		<p>(vi) A statement of theoretical weight or measure of a dietary ingredient or dietary supplement expected at the conclusion of manufacture, including the maximum and minimum percentages of theoretical yield beyond which investigation is required.</p>	<p>(6) A statement of theoretical yield of a manufactured dietary ingredient or dietary supplement expected at each point, step, or stage of the manufacturing process where control is needed to prevent adulteration, and the expected yield when you finish manufacturing the dietary ingredient or dietary supplement, including the maximum and minimum percentages of theoretical yield beyond which a deviation investigation of a batch is performed and material review is conducted and disposition decision is made;</p>
<p>(8) A description of the drug product containers, closures, and packaging materials, including a specimen or copy of each label and all other labeling signed and dated by the person or persons responsible for approval of such labeling;</p>		<p>(vii) A description of the product container(s), closure(s), and other packaging materials, including positive identification of all labeling used.</p>	<p>(7) A description of packaging and a copy of the label to be used; and</p>

<p style="text-align: center;">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p style="text-align: center;">Food cGMP (21 CFR Part 110)</p>	<p style="text-align: center;">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p style="text-align: center;">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
<p>(9) Complete manufacturing and control instructions, sampling and testing procedures, specifications, special notations, and precautions to be followed.</p>		<p>(viii) Manufacturing and control instructions, designed to assure that the dietary product has the purity, composition and quality it is represented to possess.</p>	<p>(8) Written instructions including, but not limited to, the following:</p> <p>(i) Specifications for each point, step, or stage in manufacturing the dietary ingredient or dietary supplement necessary to prevent adulteration;</p> <p>(ii) Sampling and testing procedures;</p> <p>(iii) Specific actions necessary to perform and verify points, steps, or stages, necessary to meet specifications and otherwise prevent adulteration, including, but not limited to, one person weighing or measuring a component and another person verifying the weight or measure and one person adding the component and another person verifying the addition;</p> <p>(iv) Special notations and precautions to be followed; and</p> <p>(v) Corrective action plans for use when a specification is not met.</p>
		<p>(a) (1) ... and shall be reviewed and approved by the quality control unit.</p>	<p>(c) You must have the quality control unit review and approve each master manufacturing record and any modifications to a master manufacturing record.</p>
			<p>(d) You must keep master manufacturing records in accordance with § 111.125.</p>
<p>§ 211.188 Batch production and control records.</p> <p>Batch production and control records shall be prepared for each batch of drug product produced and shall include complete information relating to the production and control of each batch.</p>		<p>(b) Batch production and control records.</p> <p>(1) Individual batch production and control records shall be prepared and followed for each batch of dietary product produced and shall include complete information relating to the production and control of each batch.</p>	<p>§ 111.50 <u>What requirements apply to establishing a batch production record?</u></p> <p>(a) You must prepare a batch production record every time you manufacture a batch of a dietary ingredient or dietary supplement and the batch production record must include complete information relating to the production and control of each batch.</p>
<p>§ 211.188 Batch production and control records. (Cont.)</p> <p>These records shall include:</p> <p>(a) An accurate reproduction of the appropriate master production or control record, checked for accuracy, dated, and signed;</p> <p>(b) Documentation that each significant step in the manufacture, processing, packing, or holding of the batch was accomplished, including:</p>		<p>(2) These records shall be an accurate reproduction of the appropriate master production and control record and shall include documentation that each significant step in the manufacture, processing, packing, or holding of the batch was accomplished, including:</p>	<p>(b) Your batch production record must accurately follow the appropriate master manufacturing record and you must perform each step in producing the batch.</p> <p>(c) The batch production record must include, but is not limited to, the following information:</p>
			<p>(1) The batch, lot, or control number,</p>

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(1) Dates;		(i) Dates;	<p>(2) Documentation at the time of performance, showing the date on which each step of the master manufacturing record was performed, and the initials of the persons performing each step, including but not limited to:</p> <p>(i) The person responsible for weighing or measuring each component used in the batch; and</p> <p>(ii) The person responsible for adding the component to the batch.</p>
(2) Identity of individual major equipment and lines used;		(ii) Identity of individual major equipment and lines used;	(3) The identity of equipment and processing lines used in producing the batch;
<p>§ 211.182 Equipment cleaning and use log.</p> <p>A written record of major equipment cleaning, maintenance (except routine maintenance such as lubrication and adjustments), and use shall be included in individual equipment logs that show the date, time, product, and lot number of each batch processed. If equipment is dedicated to manufacture of one product, then individual equipment logs are not required, provided that lots or batches of such product follow in numerical order and are manufactured in numerical sequence. In cases where dedicated equipment is employed, the records of cleaning, maintenance, and use shall be part of the batch record. The persons performing and double-checking the cleaning and maintenance shall date and sign or initial the log indicating that the work was performed. Entries in the log shall be in chronological order.</p>		<p>Equipment and Utensils</p> <p>(b) Sanitation of equipment and utensils.</p> <p>(11) A written record of major equipment cleaning and use shall be maintained in individual equipment logs that show the date, product and lot number of each batch processed. The persons performing the cleaning shall record in the log that the work was performed. Entries in the log should be in chronological order.</p>	<p>4) The date and time of the maintenance, cleaning, and sanitizing of the equipment and processing lines used in producing the batch;</p>
<p>§ 211.188 Batch production and control records. (Cont.)</p> <p>(6) Inspection of the packaging and labeling area before and after use;</p>		(vi) Inspection of the packaging and labeling area;	
(3) Specific identification of each batch of component or in-process material used;		(iii) Specific identification, including lot number, of each raw material or in-process material used;	(5) The shipment lot unique identifier of each component, dietary ingredient, dietary supplement, packaging, and label used;
(4) Weights and measures of components used in the course of processing;		(iv) Weight or measure of each raw material used in the course of processing;	(6) The identity and weight or measure of each component used;
(11) Identification of the persons performing and directly supervising or checking each significant step in the operation;			(7) The initials at the time of performance or at the completion of the batch of the person responsible for verifying the weight or measure of each component used in the batch;
(11) Identification of the persons performing and directly supervising or checking each significant step in the operation;			(8) The initials at the time of performance or at the completion of the batch of the person responsible for verifying the addition of components to the batch;

PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)	Food cGMP (21 CFR Part 110)	Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)	Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)
<p>(7) A statement of the actual yield and a statement of the percentage of theoretical yield at appropriate phases of processing;</p> <p>§ 211.103 Calculation of yield.</p> <p>Actual yields and percentages of theoretical yield shall be determined at the conclusion of each appropriate phase of manufacturing, processing, packaging, or holding of the drug product. Such calculations shall be performed by one person and independently verified by a second person.</p>		<p>(vii) A statement of the actual yield at the conclusion of manufacture and a statement of the percentage of theoretical yield, as appropriate;</p>	<p>(9) A statement of the actual yield and a statement of the percentage of theoretical yield at appropriate phases of processing;</p>
<p>§ 211.188 Batch production and control records. (Cont.)</p> <p>(5) In-process and laboratory control results;</p>		<p>(v) Quality control results;</p>	<p>(10) The actual test results for any testing performed during the batch production;</p>
			<p>(11) Documentation that the dietary ingredient and dietary supplement meets specifications;</p>
<p>(8) Complete labeling control records, including specimens or copies of all labeling used;</p>		<p>(viii) Label control records, including specimens, copies or records of all labels used;</p>	<p>(12) Copies of all container labels used and the results of examinations conducted during the label operation to ensure that the containers have the correct label;</p>
<p>(9) Description of drug product containers and closures;</p>		<p>(ix) Description of product containers and closures used;</p>	
<p>(12) Any investigation made according to §211.192.</p>		<p>(x) Any special notes of investigations or deviations from the described process.</p>	<p>(13) Any documented material review and disposition decision in accordance with § 111.35(j); and</p>
			<p>(14) Signature of the quality control unit to document batch production record review and any approval for reprocessing or repackaging.</p>
<p>(10) Any sampling performed;</p>			
<p>(13) Results of examinations made in accordance with §211.134.</p>			

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<p>§ 211.111 Time limitations on production.</p> <p>When appropriate, time limits for the completion of each phase of production shall be established to assure the quality of the drug product. Deviation from established time limits may be acceptable if such deviation does not compromise the quality of the drug product. Such deviation shall be justified and documented.</p>			
<p>§ 211.192 Production record review.</p> <p>All drug product production and control records, including those for packaging and labeling, shall be reviewed and approved by the quality control unit to determine compliance with all established, approved written procedures before a batch is released or distributed. Any unexplained discrepancy (including a percentage of theoretical yield exceeding the maximum or minimum percentages established in master production and control records) or the failure of a batch or any of its components to meet any of its specifications shall be thoroughly investigated, whether or not the batch has already been distributed. The investigation shall extend to other batches of the same drug product and other drug products that may have been associated with the specific failure or discrepancy. A written record of the investigation shall be made and shall include the conclusions and followup.</p>		<p>(3) Any deviation from written, approved specifications, standards, test procedures or other laboratory control mechanisms shall be recorded and justified.</p>	<p>(d) The quality control unit must review in accordance with § 111.37 (b) (5) the batch production record established in paragraph (c) of this section.</p> <p>(1) If a batch deviates from the master manufacturing record, including any deviation from specifications, the quality control unit must conduct a material review and make a disposition decision and record any decision in the batch production record.</p> <p>(2) The quality control unit must not approve and release for distribution any batch of dietary ingredient or dietary supplement that does not meet all specifications.</p>
<p>§ 211.100 Written procedures; deviations.</p> <p>(a) There shall be written procedures for production and process control designed to assure that the drug products have the identity, strength, quality, and purity they purport or are represented to possess. Such procedures shall include all requirements in this subpart. These written procedures, including any changes, shall be drafted, reviewed, and approved by the appropriate organizational units and reviewed and approved by the quality control unit.</p> <p>(b) Written production and process control procedures shall be followed in the execution of the various production and process control functions and shall be documented at the time of performance. Any deviation from the written procedures shall be recorded and justified.</p>			<p>(e) The quality control unit must document in accordance with § 111.37(c) the review performed in accordance with paragraph (d) of this section and it must be documented at the time of performance. The review and documentation must include, but is not limited to, the following:</p> <p>(1) Review of component, dietary ingredient, and dietary supplement receiving records including review of testing and examination results;</p> <p>(2) Identification of any deviation from the master manufacturing record that may have caused a batch or any of its components to fail to meet specifications identified in the master production record;</p> <p>(3) Records of investigations, conclusions, and corrective actions performed in accordance with paragraph (d) of this section; and</p> <p>(4) The identity of the person qualified by training and experience who performed the investigation in accordance with paragraph (d) of this section.</p>

<p style="text-align: center;">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p style="text-align: center;">Food cGMP (21 CFR Part 110)</p>	<p style="text-align: center;">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p style="text-align: center;">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
			<p>(f) You must not reprocess a batch that deviates from the master manufacturing record unless approved by the quality control unit. You must not reprocess a dietary ingredient or dietary supplement if it is rejected because of contamination with microorganisms of public health significance or other contaminants, such as heavy metals;</p>
			<p>(g) Any batch of dietary ingredient or dietary supplement that is reprocessed must meet all specifications for the batch of dietary ingredient or dietary supplement and be evaluated and approved by the quality control unit before releasing for distribution. The results of the reevaluation by the quality control unit must be documented in the batch production record; and</p>
<p>§ 211.170 Reserve samples.</p> <p>(b) An appropriately identified reserve sample that is representative of each lot or batch of drug product shall be retained and stored under conditions consistent with product labeling. The reserve sample shall be stored in the same immediate container-closure system in which the drug product is marketed or in one that has essentially the same characteristics. The reserve sample consists of at least twice the quantity necessary to perform all the required tests, except those for sterility and pyrogens...</p> <p>The retention time is as follows:</p> <p>(1) For a drug product other than those described in paragraphs (b) (2) and (3) of this section, the reserve sample shall be retained for 1 year after the expiration date of the drug product.</p> <p>(3) For an OTC drug product that is exempt for bearing an expiration date under §211.137, the reserve sample must be retained for 3 years after the lot or batch of drug product is distributed.</p>			<p>(h) You must collect representative reserve samples of each batch of dietary ingredient or dietary supplement and keep the reserve samples for 3 years from the date of manufacture for use in appropriate investigations including, but not limited to, consumer complaint investigations to determine whether, for example, the dietary ingredient or dietary supplement associated with a consumer complaint failed to meet any of its specifications for identity, purity, quality, strength, and composition.</p>
			<p>(i) You must keep batch production records in accordance with § 111.125.</p>

<p style="text-align: center;">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p style="text-align: center;">Food cGMP (21 CFR Part 110)</p>	<p style="text-align: center;">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p style="text-align: center;">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
<p>§ 211.22 Responsibilities of quality control unit.</p> <p>(b) Adequate laboratory facilities for the testing and approval (or rejection) of components, drug product containers, closures, packaging materials, in-process materials, and drug products shall be available to the quality control unit.</p>		<p>(2) Adequate laboratory facilities should be available, as needed, to the quality control unit.</p>	<p>§ 111.60 <u>What requirements apply to laboratory operations?</u></p> <p>(a) You must use adequate laboratory facilities to perform whatever testing and examinations are necessary to determine that components, dietary ingredients, and dietary supplements received meet specifications; that specifications are met during in-process, as specified in the master manufacturing record; and that dietary ingredients and dietary supplements manufactured meet specifications.</p>

<p>PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p>Food cGMP (21 CFR Part 110)</p>	<p>Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p>Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
			<p>(b)(1) You must establish and follow laboratory control processes that are approved by the quality control unit. Laboratory control processes must include, but are not limited to, the following:</p> <ul style="list-style-type: none"> (i) Use of criteria for selecting appropriate examination and testing methods; (ii) Use of criteria for establishing appropriate specifications; and (iii) Use of sampling plans for obtaining representative samples of: <ul style="list-style-type: none"> (A) Components, dietary ingredients, and dietary supplements received to determine whether specifications are met; (B) In-process materials during the batch manufacturing when testing or examination is required in the master manufacturing record; (C) Each batch of dietary ingredient or dietary supplement manufactured to determine that the dietary ingredient or dietary supplement meets specifications; (D) Packaging and labels received to determine that the materials meet specifications; and (E) Each batch of packaged and labeled dietary ingredients or dietary supplements to ensure that the label specified in the master manufacturing record has been applied. (iv) Use of criteria for selecting standard reference materials used in performing tests and examinations; (v) Use of appropriate test method validations; and (vi) Use of test methods and, examinations in accordance with established criteria, <p>(2) The person who conducts the testing and examination at the time of performance must document that laboratory examination results.</p> <p>(3) You must keep laboratory examination and testing records in accordance with § 111.125.</p>
			<p>(c) You must verify that the laboratory examination and testing methodologies are appropriate for their intended use.</p>
			<p>(d) You must identify and use the appropriate validated testing method for each established specification for which testing is required to determine whether the specification is met.</p>

<p>PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p>Food cGMP (21 CFR Part 110)</p>	<p>Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p>Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
			<p>§ 111.65 What requirements apply to manufacturing operations?</p> <p>(a) You must design or select manufacturing processes to ensure that dietary ingredient or dietary specifications are consistently achieved.</p>
	<p>¶110.80 Processes and controls.</p> <p>All operations in the receiving, inspecting, transporting, segregating, preparing, manufacturing, packaging, and storing of food shall be conducted in accordance with adequate sanitation principles...</p>	<p>(d) Manufacturing operations.</p> <p>(1) All operations in the receiving, inspecting, transporting, segregating, preparing, manufacturing, packaging, and storing of dietary products shall be conducted in accordance with adequate sanitation principles.</p>	<p>(b) You must conduct all manufacturing operations in accordance with adequate sanitation principles.</p>
	<p>...All reasonable precautions shall be taken to ensure that production procedures do not contribute contamination from any source. Chemical, microbial, or extraneous-material testing procedures shall be used where necessary to identify sanitation failures or possible food contamination.</p>	<p>(2) All reasonable precautions shall be taken to assure that production procedures do not contribute adulteration from any source. Chemical, microbial, or extraneous-material testing procedures shall be used where necessary to identify sanitation failures or possible product adulteration.</p>	<p>(c) You must take all the necessary precautions during the manufacture of a dietary ingredient or dietary supplement to prevent contamination of components, dietary ingredients, or dietary supplements. These precautions include, but are not limited to:</p>
<p>§ 211.113 Control of microbiological contamination.</p> <p>(a) Appropriate written procedures, designed to prevent objectionable microorganisms in drug products not required to be sterile, shall be established and followed.</p> <p>(b) Appropriate written procedures, designed to prevent microbiological contamination of drug products purporting to be sterile, shall be established and followed. Such procedures shall include validation of any sterilization process.</p>	<p>¶110.80(b) Manufacturing operations.</p> <p>...(2) All food manufacturing, including packaging and storage, shall be conducted under such conditions and controls as are necessary to minimize the potential for the growth of microorganisms, or for the contamination of food.</p>	<p>(4) All product manufacturing, including packaging and storage, shall be conducted under such conditions and controls as are necessary to minimize the potential for the growth of microorganisms, or for the adulteration of raw materials, in-process materials and finished product.</p>	<p>(1) Performing manufacturing operations under conditions and controls that protect against the potential for growth of microorganisms and the potential for contamination;</p>
	<p>(1)...Raw materials shall be washed or cleaned as necessary to remove soil or other contamination.</p>	<p>(2) Raw agricultural materials that contain soil or other contaminants shall be washed or cleaned as necessary.</p>	<p>(2) Washing or cleaning components that contain soil or other contaminants;</p>
	<p>(1)...Water used for washing, rinsing, or conveying food shall be safe and of adequate sanitary quality. Water may be reused for washing, rinsing, or conveying food if it does not increase the level of contamination of the food.</p>	<p>(2)... Water used for washing, rinsing, or conveying raw agricultural materials shall be safe and of adequate sanitary quality. Notwithstanding the general requirement for potable water, water may be reused for washing, rinsing, or conveying raw agricultural materials if it does not increase the level of contamination of the such materials.</p>	<p>(3) Using water that meets the National Primary Drinking Water regulations or, where necessary, higher sanitary quality and that complies with all applicable Federal, State, and local regulations for water that is used in the manufacturing operation. If you reuse water that was used to wash components to remove soil or contaminants, the reused water must be safe and of adequate sanitary quality so that it does not become a source of contamination;</p>
			<p>(4) Performing chemical, microbiological, or other testing as necessary to prevent the use of contaminated components, dietary ingredients, and dietary supplements;</p>

<p style="text-align: center;">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p style="text-align: center;">Food cGMP (21 CFR Part 110)</p>	<p style="text-align: center;">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p style="text-align: center;">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
	<p>(2) Raw materials and other ingredients shall either not contain levels of microorganisms that may produce food poisoning or other disease in humans, or they shall be pasteurized or otherwise treated during manufacturing operations so that they no longer contain levels that would cause the product to be adulterated within the meaning of the act. Compliance with this requirement may be verified by any effective means, including purchasing raw materials and other ingredients under a supplier's guarantee or certification.</p> <p>One way to comply with this requirement is careful monitoring of physical factors such as time, temperature, humidity, a_w, pH, pressure, flow rate, and manufacturing operations such as freezing, dehydration, heat processing, acidification, and refrigeration to ensure that mechanical breakdowns, time delays, temperature fluctuations, and other factors do not contribute to the decomposition or contamination of food.</p> <p>(4) Measures such as sterilizing, irradiating, pasteurizing, freezing, refrigerating, controlling pH or controlling a_w that are taken to destroy or prevent the growth of undesirable microorganisms, particularly those of public health significance, shall be adequate under the conditions of manufacture, handling, and distribution to prevent food from being adulterated within the meaning of the act.</p> <p>(14) Food such as, but not limited to, dry mixes, nuts, intermediate moisture food, and dehydrated food, that relies on the control of a_w for preventing the growth of undesirable microorganisms shall be processed to and maintained at a safe moisture level. Compliance with this requirement may be accomplished by any effective means, including employment of one or more of the following practices:</p> <ul style="list-style-type: none"> (i) Monitoring the a_w of food. (ii) Controlling the soluble solids-water ratio in finished food. (iii) Protecting finished food from moisture pickup, by use of a moisture barrier or by other means, so that the a_w of the food does not increase to an unsafe level. 	<p>(5) Measures such as sterilizing, irradiating, pasteurizing, freezing, refrigerating, controlling pH or controlling water activity (a_w) that are taken to destroy or prevent the growth of undesirable microorganisms, particularly those of public health significance, shall be adequate under the conditions of manufacture, handling, and distribution to prevent dietary products from being adulterated within the meaning of the act.</p> <p>(15) Intermediate or dehydrated dietary products that rely on the control of water activity (a_w) for preventing the growth of undesirable microorganisms shall be processed to and maintained at a safe moisture level. Compliance with this requirement may be accomplished by any effective means, including employment of one or more of the following practices:</p> <ul style="list-style-type: none"> (i) Monitoring the water activity (a_w) of the material. (ii) Controlling the soluble solids-water ratio in finished product. (iii) Protecting finished product from moisture pickup, by use of a moisture barrier or by other means, so that the water activity (a_w) of the product does not increase to an unsafe level. 	<p>(5) Sterilizing, pasteurizing, freezing, refrigerating controlling hydrogen-ion concentration (pH), controlling humidity, controlling water activity (A_w), or using any other effective means to remove, destroy, or prevent the growth of microorganisms and prevent decomposition;</p>

PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)	Food cGMP (21 CFR Part 110)	Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)	Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)
	<p>(15) Food such as, but not limited to, acid and acidified food, that relies principally on the control of pH for preventing the growth of undesirable microorganisms shall be monitored and maintained at a pH of 4.6 or below. Compliance with this requirement may be accomplished by any effective means, including employment of one or more of the following practices:</p> <ul style="list-style-type: none"> (i) Monitoring the pH of raw materials, food in process, and finished food. (ii) Controlling the amount of acid or acidified food added to low-acid food. 	<p>(16) Dietary ingredients and dietary supplements that rely principally on the control of pH for preventing the growth of undesirable microorganisms shall be monitored and maintained at an appropriate pH. Compliance with this requirement may be accomplished by any effective means, including employment of one or more of the following practices:</p> <ul style="list-style-type: none"> (i) Monitoring the pH of raw materials, in process material, and finished product. (ii) Controlling the amount of acid added to the product 	
	<p>(3) Food that can support the rapid growth of undesirable microorganisms, particularly those of public health significance, shall be held in a manner that prevents the food from becoming adulterated within the meaning of the act. Compliance with this requirement may be accomplished by any effective means, including:</p> <ul style="list-style-type: none"> (i) Maintaining refrigerated foods at 45°F (7.2°C) or below as appropriate for the particular food involved. (ii) Maintaining frozen foods in a frozen state. (iii) Maintaining hot foods at 140°F (60°C) or above. (iv) Heat treating acid or acidified foods to destroy mesophilic micro-organisms when those foods are to be held in hermetically sealed containers at ambient temperatures. 		<p>(6) Holding components, dietary ingredients, and dietary supplements that can support the rapid growth of microorganisms of public health significance in a manner that prevents the components, dietary ingredients, and dietary supplements from becoming adulterated;</p>
			<p>(7) Identifying and holding any components, dietary ingredients, or dietary supplements, for which a material review and disposition decision is required, in a manner that protects the components, dietary ingredients, or dietary supplements against contamination and mixups;</p>

PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)	Food cGMP (21 CFR Part 110)	Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)	Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)
	<p>(10) Mechanical manufacturing steps such as washing, peeling, trimming, cutting, sorting and inspecting, mashing, dewatering, cooling, shredding, extruding, drying, whipping, defatting, and forming shall be performed so as to protect food against contamination. Compliance with this requirement may be accomplished by providing adequate physical protection of food from contaminants that may drip, drain, or be drawn into the food. Protection may be provided by adequate cleaning and sanitizing of all food-contact surfaces, and by using time and temperature controls at and between each manufacturing step.</p>	<p>(13) Mechanical manufacturing steps such as cutting, sorting, inspecting, shredding, drying, grinding, blending and sifting shall be performed so as to protect dietary ingredients and dietary supplements against adulteration. Compliance with this requirement may be accomplished by providing adequate physical protection of dietary products from contact with adulterants. Protection may be provided by adequate cleaning and sanitizing of all processing equipment between each manufacturing step.</p>	<p>(8) Performing mechanical manufacturing steps (such as cutting, sorting, inspecting, shredding, drying, grinding, blending, and sifting) by any effective means to protect the dietary ingredients or dietary supplements against contamination. Such steps must include consideration of:</p> <ul style="list-style-type: none"> (i) Cleaning and sanitizing contact surfaces; (ii) Using temperature controls; and (iii) Using time controls.
	<p>...(8) Effective measures shall be taken to protect against the inclusion of metal or other extraneous material in food. Compliance with this requirement may be accomplished by using sieves, traps, magnets, electronic metal detectors, or other suitable effective means.</p>	<p>(9) Effective measures shall be taken as necessary to protect against the inclusion of metal or other extraneous material in product. Compliance with this requirement may be accomplished by using sieves, traps, magnets, electronic metal detectors, or other suitable effective means.</p>	<p>(9) Using effective measures to protect against the inclusion of metal or other foreign material in components, dietary ingredients, or dietary supplements. Compliance with this requirement must include consideration of the use of:</p> <ul style="list-style-type: none"> (i) Filters or strainers; (ii) Traps; (iii) Magnets; or (iv) Electronic metal detectors.

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<p>§ 211.105 Equipment identification.</p> <p>(a) All compounding and storage containers, processing lines, and major equipment used during the production of a batch of a drug product shall be properly identified at all times to indicate their contents and, when necessary, the phase of processing of the batch.</p> <p>(b) Major equipment shall be identified by a distinctive identification number or code that shall be recorded in the batch production record to show the specific equipment used in the manufacture of each batch of a drug product. In cases where only one of a particular type of equipment exists in a manufacturing facility, the name of the equipment may be used in lieu of a distinctive identification number or code.</p>		<p>(8) All raw material containers, compounding and storage containers, processing lines and major equipment used during the production of a batch shall be properly identified at all times to indicate their contents and when necessary, the phase of processing of the batch.</p>	<p>(10) Segregating and identifying all containers for a specific batch of dietary ingredients or dietary supplements to identify their contents and, where necessary, the phase of manufacturing; and</p> <p>(11) Identifying all processing lines and major equipment used during manufacturing to indicate their contents including the name of the dietary ingredient or dietary supplement and the specific batch or lot number and, when necessary, the phase of manufacturing.</p>
<p>§ 211.115 Reprocessing.</p> <p>(a) Written procedures shall be established and followed prescribing a system for reprocessing batches that do not conform to standards or specifications and the steps to be taken to insure that the reprocessed batches will conform with all established standards, specifications, and characteristics.</p> <p>(b) Reprocessing shall not be performed without the review and approval of the quality control unit.</p>	<p>(9)...If the adulterated food is capable of being reconditioned, it shall be reconditioned using a method that has been proven to be effective or it shall be reexamined and found not to be adulterated within the meaning of the act before being incorporated into other food.</p>	<p>(12) Written procedures shall be established and followed prescribing the method for reprocessing batches or operational start-up materials that do not conform to finished goods standards or specifications. Finished goods manufactured using such materials shall meet all established purity, composition and quality standards.</p>	<p>(d) You must conduct a material review and make a disposition decision in accordance with § 111.35(i) for any component, dietary ingredient, or dietary supplement that fails to meet specifications or that is or may be adulterated. If the material review and disposition decision allows you to reprocess the component, dietary ingredient, or dietary supplement, you must retest or reexamine the component, dietary ingredient, or dietary supplement to ensure that it meets specifications and is approved by the quality control unit.</p>
<p>§ 211.86 Use of approved components, drug product containers, and closures.</p> <p>Components, drug product containers, and closures approved for use shall be rotated so that the oldest approved stock is used first. Deviation from this requirement is permitted if such deviation is temporary and appropriate.</p>		<p>(8) Approved raw materials shall be rotated so that the oldest approved stock is used first. Deviation from this requirement is permitted if such deviation is temporary and appropriate.</p>	
<p>§ 211.87 Retesting of approved components, drug product containers, and closures.</p> <p>Components, drug product containers, and closures shall be retested or reexamined, as appropriate, for identity, strength, quality, and purity and approved or rejected by the quality control unit in accordance with §211.84 as necessary, e.g., after storage for long periods or after exposure to air, heat or other conditions that might adversely affect the component, drug product container, or closure.</p>		<p>(9) Raw materials shall be retested or reexamined and approved or rejected by the quality control after a specified time in storage or after exposure to air, heat, or other conditions that are likely to adversely affect the purity, quality or composition of the raw material.</p>	

PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)	Food cGMP (21 CFR Part 110)	Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)	Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)
	<p>(11) Heat blanching, when required in the preparation of food, should be effected by heating the food to the required temperature, holding it at this temperature for the required time, and then either rapidly cooling the food or passing it to subsequent manufacturing without delay. Thermophilic growth and contamination in blanchers should be minimized by the use of adequate operating temperatures and by periodic cleaning. Where the blanched food is washed prior to filling, water used shall be safe and of adequate sanitary quality.</p>	<p>(14) Heat blanching, when required in the preparation of a dietary product, should be effected by heating the product to the required temperature, holding it at this temperature for the required time, and then either rapidly cooling the material or passing it to subsequent manufacturing without delay. Thermophilic growth and contamination in blanchers should be minimized by the use of adequate operating temperatures and by periodic cleaning. Where the blanched product is washed prior to filling, potable water shall be used.</p>	
	<p>(12) Batters, breading, sauces, gravies, dressings, and other similar preparations shall be treated or maintained in such a manner that they are protected against contamination. Compliance with this requirement may be accomplished by any effective means, including one or more of the following:</p> <ul style="list-style-type: none"> (i) Using ingredients free of contamination. (ii) Employing adequate heat processes where applicable. (iii) Using adequate time and temperature controls. (iv) Providing adequate physical protection of components from contaminants that may drip, drain, or be drawn to them. (v) Cooling to an adequate temperature during manufacturing. (vi) Disposing of batters at appropriate intervals to protect against the growth of microorganisms. 		
	<p>(16) When ice is used in contact with food, it shall be made from water that is safe and of adequate sanitary quality, and shall be used only if it has been manufactured in accordance with current good manufacturing practice as outlined in this part.</p>	<p>(17) When ice is used in contact with dietary products, it shall be made from potable water, and shall be used only if it has been manufactured in accordance with current good manufacturing practice as outlined in 21 CFR Part 110.</p>	
	<p>(17) Food manufacturing areas and equipment used for manufacturing human food should not be used to manufacture nonhuman food grade animal food or inedible products, unless there is no reasonable possibility for the contamination of the human food.</p>		

PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)	Food cGMP (21 CFR Part 110)	Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)	Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)
<p>§ 211.101 Charge-in of components.</p> <p>Written production and control procedures shall include the following, which are designed to assure that the drug products produced have the identity, strength, quality, and purity they purport or are represented to possess:</p> <p>(b) Components for drug product manufacturing shall be weighed, measured, or subdivided as appropriate. If a component is removed from the original container to another, the new container shall be identified with the following information:</p> <p>(1) Component name or item code;</p> <p>(2) Receiving or control number;</p> <p>(3) Weight or measure in new container;</p> <p>(4) Batch for which component was dispensed, including its product name, strength, and lot number.</p> <p>(c) Weighing, measuring, or subdividing operations for components shall be adequately supervised. Each container of component dispensed to manufacturing shall be examined by a second person to assure that:</p> <p>(1) The component was released by the quality control unit;</p> <p>(2) The weight or measure is correct as stated in the batch production records;</p> <p>(3) The containers are properly identified.</p> <p>(d) Each component shall be added to the batch by one person and verified by a second person.</p>			

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<p>§ 211.130 Packaging and labeling operations.</p> <p>There shall be written procedures designed to assure that correct labels, labeling, and packaging materials are used for drug products; such written procedures shall be followed. These procedures shall incorporate the following features:</p> <p>(a) Prevention of mixups and cross-contamination by physical or spatial separation from operations on other drug products.</p> <p>(b) Identification and handling of filled drug product containers that are set aside and held in unlabeled condition for future labeling operations to preclude mislabeling of individual containers, lots, or portions of lots. Identification need not be applied to each individual container but shall be sufficient to determine name, strength, quantity of contents, and lot or control number of each container.</p> <p>(d) Examination of packaging and labeling materials for suitability and correctness before packaging operations, and documentation of such examination in the batch production record.</p> <p>(e) Inspection of the packaging and labeling facilities immediately before use to assure that all drug products have been removed from previous operations. Inspection shall also be made to assure that packaging and labeling materials not suitable for subsequent operations have been removed. Results of inspection shall be documented in the batch production records.</p>	<p>(13) Filling, assembling, packaging, and other operations shall be performed in such a way that the food is protected against contamination. Compliance with this requirement may be accomplished by any effective means, including:</p> <p>(i) Use of a quality control operation in which the critical control points are identified and controlled during manufacturing.</p> <p>(ii) Adequate cleaning and sanitizing of all food-contact surfaces and food containers.</p> <p>(iii) Using materials for food containers and food-packaging materials that are safe and suitable, as defined in ¶130.3(d) of this chapter.</p> <p>(iv) Providing physical protection from contamination, particularly airborne contamination.</p> <p>(v) Using sanitary handling procedures.</p>	<p>(e) Packaging and labeling operations.</p> <p>(1) Filling, assembling, packaging, and other operations shall be performed in such a way that dietary products are protected against adulteration. Compliance with this requirement may be accomplished by any effective means, including:</p> <p>(i) Adequate cleaning and sanitizing of all filling and packaging equipment, utensils and product containers, as appropriate.</p> <p>(ii) Using materials for product containers and packaging materials that are safe and suitable.</p> <p>(iii) Providing physical protection from adulteration, particularly airborne contamination.</p> <p>(iv) Using sanitary handling procedures.</p>	<p>§ 111.70 What requirements apply to packaging and label operations?</p> <p>(a) You must take necessary actions to ensure that each packaging container for holding dietary ingredients or dietary supplements meets specifications so that the condition of the packaging container will not contaminate your dietary ingredients or dietary supplements nor cause them to deteriorate;</p> <p>(b) You must fill, assemble, package, and perform other related operations in a way that protects your dietary ingredients or dietary supplements against adulteration and misbranding. You must do this using any effective means, including but not limited to, the following:</p> <p>(1) Cleaning and sanitizing all filling and packaging equipment, utensils, and dietary ingredient or dietary supplement containers, as appropriate;</p> <p>(2) Protecting manufactured dietary ingredients and dietary supplements from contamination, particularly airborne contamination;</p> <p>(3) Using sanitary handling procedures;</p>
<p>§ 211.122 Materials examination and usage criteria.</p> <p>(d) Labels and other labeling materials for each different drug product, strength, dosage form, or quantity of contents shall be stored separately with suitable identification. Access to the storage area shall be limited to authorized personnel.</p>		<p>(3) For dietary supplements, labels and other labeling materials for each different product type, strength, or quantity of contents shall be stored separately with suitable identification.</p>	<p>(4) Establishing physical or spatial separation of packaging and labels from operations on other dietary ingredients and dietary supplements to prevent mixups;</p>
			<p>(5) Identifying, by any effective means, filled dietary ingredient or dietary supplement containers that are set aside and held in unlabeled condition for future label operations, to prevent mixups;</p>
<p>§ 211.130 Packaging and labeling operations.</p> <p>(c) Identification of the drug product with a lot or control number that permits determination of the history of the manufacture and control of the batch.</p>		<p>(6) Dietary ingredient and dietary supplement packages shall be identified with a lot number that permits determination of the history of the manufacture and control of the batch.</p>	<p>(6) Identifying the dietary ingredient or dietary supplement with a batch, lot, or control number that can be used to determine the manufacturing history and control of the batch;</p>

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<p>§ 211.134 Drug product inspection.</p> <p>(a) Packaged and labeled products shall be examined during finishing operations to provide assurance that containers and packages in the lot have the correct label.</p> <p>(b) A representative sample of units shall be collected at the completion of finishing operations and shall be visually examined for correct labeling.</p> <p>(c) Results of these examinations shall be recorded in the batch production or control records.</p>		<p>(7) Packaged and labeled dietary supplements shall be examined to provide assurance that containers and packages in the lot have the correct label and lot number. Products not meeting specifications shall be rejected by the quality control unit.</p>	<p>(7) Examining a representative sample of each batch of the packaged and labeled dietary ingredient or dietary supplement to ensure that the dietary ingredient or dietary supplement meets specifications and that the label specified in the master manufacturing record has been applied; and</p>
<p>§ 211.122 Materials examination and usage criteria.</p> <p>(e) Obsolete and outdated labels, labeling, and other packaging materials shall be destroyed.</p>		<p>(4) Obsolete labels, labeling, and other packaging materials for dietary products shall be destroyed.</p>	<p>(8) Suitably disposing of labels and other packaging for dietary ingredients or dietary supplements that are obsolete or incorrect to ensure that they are not used in any future packaging and label operations.</p>
<p>(f) Use of gang-printed labeling for different drug products, or different strengths or net contents of the same drug product, is prohibited unless the labeling from gang-printed sheets is adequately differentiated by size, shape, or color.</p>			
<p>(g) If cut labeling is used, packaging and labeling operations shall include one of the following special control procedures:</p> <p>(1) Dedication of labeling and packaging lines to each different strength of each different drug product;</p> <p>(2) Use of appropriate electronic or electromechanical equipment to conduct a 100-percent examination for correct labeling during or after completion of finishing operations; or</p> <p>(3) Use of visual inspection to conduct a 100-percent examination for correct labeling during or after completion of finishing operations for hand-applied labeling. Such examination shall be performed by one person and independently verified by a second person.</p>			
<p>(h) Printing devices on, or associated with, manufacturing lines used to imprint labeling upon the drug product unit label or case shall be monitored to assure that all imprinting conforms to the print specified in the batch production record.</p>			
			<p>(c) You must conduct a material review and make a disposition decision of any packaged and labeled dietary ingredients or dietary supplements that do not meet specifications.</p>
			<p>(d) You must only repackage or relabel dietary ingredients or dietary supplements after the quality control unit has approved and documented such repackaging or relabeling.</p>

<p style="text-align: center;">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p style="text-align: center;">Food cGMP (21 CFR Part 110)</p>	<p style="text-align: center;">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p style="text-align: center;">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
			<p>(e) You must retest or reexamine any repackaged or relabeled dietary ingredients or dietary supplements. They must meet all specifications and the quality control unit must approve or reject their release for distribution.</p>
<p>§ 211.125 Labeling issuance.</p> <p>(a) Strict control shall be exercised over labeling issued for use in drug product labeling operations.</p> <p>(b) Labeling materials issued for a batch shall be carefully examined for identity and conformity to the labeling specified in the master or batch production records.</p> <p>(c) Procedures shall be used to reconcile the quantities of labeling issued, used, and returned, and shall require evaluation of discrepancies found between the quantity of drug product finished and the quantity of labeling issued when such discrepancies are outside narrow preset limits based on historical operating data. Such discrepancies shall be investigated in accordance with §211.192. Labeling reconciliation is waived for cut or roll labeling if a 100-percent examination for correct labeling is performed in accordance with §211.122(g)(2).</p>		<p>(5) Written procedures shall be established and followed to assure that correct labels, labeling, and packaging materials are issued and used for dietary products.</p>	<p>(f) (1) You must control the issuance and use of packaging, and labels and reconciliation of any issuance and use discrepancies; and</p> <p>(2) You must examine, before packaging operations, packaging and labels for each batch of dietary ingredient or dietary supplement to ensure that the label and packaging conform to the master manufacturing record.</p>
<p>(d) All excess labeling bearing lot or control numbers shall be destroyed.</p> <p>(e) Returned labeling shall be maintained and stored in a manner to prevent mixups and provide proper identification</p> <p>(f) Procedures shall be written describing in sufficient detail the control procedures employed for the issuance of labeling; such written procedures shall be followed.</p>			
			<p>(g) The person that performs the requirements of this section must document at the time of performance that the requirements are performed including, but not limited to, documentation in the batch-production record of:</p> <p>(1) The identity and quantity of the packaging and labels used and reconciliation of any discrepancies between issuance and use;</p> <p>(2) The examination conducted, in accordance with paragraph (b)(7) of this section;</p> <p>(3) The conclusions you reached from retests conducted in accordance with paragraph (e) of this section; and</p> <p>(4) Any material reviews and disposition decisions for packaging and labels.</p>

<p style="text-align: center;">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p style="text-align: center;">Food cGMP (21 CFR Part 110)</p>	<p style="text-align: center;">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p style="text-align: center;">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
			<p>(h) You must keep packaging and label operations records required under this section in accordance with § 111.125.</p>
<p>§ 211.132 Tamper-evident packaging requirements for over-the-counter (OTC) human drug products.</p> <p>(a) <i>General.</i> The Food and Drug Administration has the authority under the Federal Food, Drug, and Cosmetic Act (the act) to establish a uniform national requirement for tamper-evident packaging of OTC drug products that will improve the security of OTC drug packaging and help assure the safety and effectiveness of OTC drug products. An OTC drug product (except a dermatological, dentifrice, insulin, or lozenge product) for retail sale that is not packaged in a tamper-resistant package or that is not properly labeled under this section is adulterated under section 501 of the act or misbranded under section 502 of the act, or both.</p>			
<p>(b) <i>Requirements for tamper-evident package.</i></p> <p>(1) Each manufacturer and packer who packages an OTC drug product (except a dermatological, dentifrice, insulin, or lozenge product) for retail sale shall package the product in a tamper-evident package, if this product is accessible to the public while held for sale. A tamper-evident package is one having one or more indicators or barriers to entry which, if breached or missing, can reasonably be expected to provide visible evidence to consumers that tampering has occurred. To reduce the likelihood of successful tampering and to increase the likelihood that consumers will discover if a product has been tampered with, the package is required to be distinctive by design or by the use of one or more indicators or barriers to entry that employ an identifying characteristic (e.g., a pattern, name, registered trademark, logo, or picture). For purposes of this section, the term "distinctive by design" means the packaging cannot be duplicated with commonly available materials or through commonly available processes. A tamper-evident package may involve an immediate-container and closure system or secondary-container or carton system or any combination of systems intended to provide a visual indication of package integrity. The tamper-evident feature shall be designed to and shall remain intact when handled in a reasonable manner during manufacture, distribution, and retail display.</p> <p>(2) In addition to the tamper-evident packaging feature described in paragraph (b)(1) of this section, any two-piece, hard gelatin capsule covered by this section must be sealed using an acceptable tamper-evident technology.</p>			

<p style="text-align: center;">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p style="text-align: center;">Food cGMP (21 CFR Part 110)</p>	<p style="text-align: center;">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p style="text-align: center;">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
<p>(c) <i>Labeling.</i></p> <p>(1) In order to alert consumers to the specific tamper-evident feature(s) used, each retail package of an OTC drug product covered by this section (except ammonia inhalant in crushable glass ampules, containers of compressed medical oxygen, or aerosol products that depend upon the power of a liquefied or compressed gas to expel the contents from the container) is required to bear a statement that:</p> <p style="padding-left: 40px;">(i) Identifies all tamper-evident feature(s) and any capsule sealing technologies used to comply with paragraph (b) of this section;</p> <p style="padding-left: 40px;">(ii) Is prominently placed on the package; and</p> <p style="padding-left: 40px;">(iii) Is so placed that it will be unaffected if the tamper-evident feature of the package is breached or missing.</p> <p>(2) If the tamper-evident feature chosen to meet the requirements in paragraph (b) of this section uses an identifying characteristic, that characteristic is required to be referred to in the labeling statement. For example, the labeling statement on a bottle with a shrink band could say "For your protection, this bottle has an imprinted seal around the neck."</p>			
<p>(d) <i>Request for exemptions from packaging and labeling requirements.</i> A manufacturer or packer may request an exemption from the packaging and labeling requirements of this section. A request for an exemption is required to be submitted in the form of a citizen petition under §10.30 of this chapter and should be clearly identified on the envelope as a "Request for Exemption from the Tamper-Evident Packaging Rule." The petition is required to contain the following:</p> <p>(1) The name of the drug product or, if the petition seeks an exemption for a drug class, the name of the drug class, and a list of products within that class.</p> <p>(2) The reasons that the drug product's compliance with the tamper-evident packaging or labeling requirements of this section is unnecessary or cannot be achieved.</p> <p>(3) A description of alternative steps that are available, or that the petitioner has already taken, to reduce the likelihood that the product or drug class will be the subject of malicious adulteration.</p> <p>(4) Other information justifying an exemption.</p>			

<p align="center">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p align="center">Food cGMP (21 CFR Part 110)</p>	<p align="center">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p align="center">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
<p>(e) <i>OTC drug products subject to approved new drug applications.</i> Holders of approved new drug applications for OTC drug products are required under §314.70 of this chapter to provide the agency with notification of changes in packaging and labeling to comply with the requirements of this section. Changes in packaging and labeling required by this regulation may be made before FDA approval, as provided under §314.70(c) of this chapter. Manufacturing changes by which capsules are to be sealed require prior FDA approval under §314.70(b) of this chapter.</p>			
<p>(f) <i>Poison Prevention Packaging Act of 1970.</i> This section does not affect any requirements for "special packaging" as defined under §310.3(l) of this chapter and required under the Poison Prevention Packaging Act of 1970.</p>			
			<p><u>§ 111.72 What requirements apply to packaging of iron-containing dietary supplements?</u></p> <p>(a) The use of iron and iron salts as iron sources in dietary supplements offered in solid oral dosage form (e.g., tablets or capsules), and containing 30 milligrams or more of iron per dosage unit, is safe and in accordance with current good manufacturing practice only when such supplements are packaged in unit-dose packaging. "Unitdose packaging" means a method of packaging a product into a nonreusable container designed to hold a single dosage unit intended for administration directly from that container, irrespective of whether the recommended dose is one or more than one of these units. The term "dosage unit" means the individual physical unit of the product (e.g., tablets or capsules). Iron-containing dietary supplements that are subject to this regulation are also subject to child-resistant special packaging requirements in 16 CFR parts 1700, 1701, and 1702.</p> <p>(b)(1) Dietary supplements offered in solid oral dosage form (e.g., tablets or capsules), and containing 30 milligrams or more of iron per dosage unit, are exempt from the provisions of paragraph (a) of this section until January 15, 1998, if the sole source of iron in the dietary supplement is carbonyl iron that meets the specifications of § 184.1375 of this chapter.</p> <p>(2) If the temporary exemption is not extended or made permanent, such dietary supplements shall be in compliance with the provisions of paragraph (a) of this section on or before July 15, 1998.</p>

<p align="center">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p align="center">Food cGMP (21 CFR Part 110)</p>	<p align="center">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p align="center">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
<p>§ 211.89 Rejected components, drug product containers, and closures.</p> <p>Rejected components, drug product containers, and closures shall be identified and controlled under a quarantine system designed to prevent their use in manufacturing or processing operations for which they are unsuitable.</p>	<p>(9) Food, raw materials, and other ingredients that are adulterated within the meaning of the act shall be disposed of in a manner that protects against the contamination of other food...</p>	<p>(10) Rejected raw materials, shall be identified and controlled under a system that prevents their use in manufacturing or processing operations for which they are unsuitable.</p> <p>(10) Dietary products, raw materials, and in-process materials that are rejected or adulterated within the meaning of the act shall be identified, stored and disposed of in a manner that protects against the adulteration of other products.</p>	<p>§ 111.74 What requirements apply to rejected components, dietary ingredients, dietary supplements, packaging, and labels?</p> <p>You must clearly identify, hold, and control under a quarantine system any component, dietary ingredient, dietary supplement, packaging, and label that is rejected and unsuitable for use in manufacturing, packaging, or label operations.</p>
<p>§ 211.142 Warehousing procedures.</p> <p>Written procedures describing the warehousing of drug products shall be established and followed. They shall include:</p> <p>(a) Quarantine of drug products before release by the quality control unit.</p> <p>(b) Storage of drug products under appropriate conditions of temperature, humidity, and light so that the identity, strength, quality, and purity of the drug products are not affected.</p>	<p>¶110.93 Warehousing and distribution.</p> <p>Storage and transportation of finished food shall be under conditions that will protect food against physical, chemical, and microbial contamination as well as against deterioration of the food and the container.</p>	<p>Warehousing, Distribution and Post-Distribution Procedures</p> <p>(a) Storage and distribution.</p> <p>(1) Storage and transportation of finished product shall be under conditions that will protect product against physical, chemical, and microbial adulteration as well as against deterioration of the product and the container.</p>	<p>Subpart F--Holding and Distributing</p> <p>§ 111.80 What requirements apply to holding components dietary ingredients, dietary supplements, packaging and labels?</p> <p>(a) You must hold components, dietary ingredients, and dietary supplements under appropriate conditions of temperature, humidity, and light so that the identity, purity, quality, strength, and composition of the components, dietary ingredients, and dietary supplements are not affected.</p>
			<p>(b) You must hold packaging and labels under appropriate conditions of temperature, humidity, and light so that the quality of the packaging and labels are not affected.</p>
	<p>(6) Effective measures shall be taken to protect finished food from contamination by raw materials, other ingredients, or refuse. When raw materials, other ingredients, or refuse are unprotected, they shall not be handled simultaneously in a receiving, loading, or shipping area if that handling could result in contaminated food. Food transported by conveyor shall be protected against contamination as necessary.</p>	<p>(7) Effective measures shall be taken to protect finished dietary ingredients and dietary supplements from adulteration by raw materials, in-process materials or refuse. When raw materials, in-process materials or refuse are unprotected, they shall not be handled simultaneously in a receiving, loading, or shipping area if that handling could result in adulterated dietary products. Dietary ingredients and dietary supplements transported by conveyor shall be protected against adulteration as necessary.</p>	<p>(c) You must hold components, dietary ingredients, dietary supplements, packaging, and labels under conditions that do not lead to the mixup, contamination, or deterioration of components, dietary ingredients, dietary supplements, packaging, and labels.</p>
	<p>(5) Work-in-process shall be handled in a manner that protects against contamination.</p>	<p>(6) Work-in-process shall be handled in a manner that protects against adulteration.</p>	<p>Sec. 111.82 What requirements apply to holding in-process material?</p> <p>(a) You must identify and hold in-process material under conditions that will protect them against mixup, contamination, and deterioration</p>
			<p>(b) You must hold in process material under appropriate conditions of temperature, humidity, and light.</p>

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<p>§ 211.170 Reserve samples.</p> <p>(a) An appropriately identified reserve sample that is representative of each lot in each shipment of each active ingredient shall be retained. The reserve sample consists of at least twice the quantity necessary for all tests required to determine whether the active ingredient meets its established specifications, except for sterility and pyrogen testing. The retention time is as follows:</p> <p>(1) For an active ingredient in a drug product other than those described in paragraphs (a) (2) and (3) of this section, the reserve sample shall be retained for 1 year after the expiration date of the last lot of the drug product containing the active ingredient.</p>			<p>§ 111.83 <u>What requirements apply to holding reserve samples of components, dietary ingredients and dietary supplements?</u></p> <p>(a) For any reserve samples of components or dietary ingredients you collect, you must hold such reserve samples in a manner that protects against contamination and deterioration:</p>
<p>(2) For an active ingredient in a radioactive drug product, except for nonradioactive reagent kits, the reserve sample shall be retained for:</p> <p>(i) Three months after the expiration date of the last lot of the drug product containing the active ingredient if the expiration dating period of the drug product is 30 days or less; or</p> <p>(ii) Six months after the expiration date of the last lot of the drug product containing the active ingredient if the expiration dating period of the drug product is more than 30 days.</p> <p>(3) For an active ingredient in an OTC drug product that is exempt from bearing an expiration date under §211.137, the reserve sample shall be retained for 3 years after distribution of the last lot of the drug product containing the active ingredient.</p>			

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<p>(b) An appropriately identified reserve sample that is representative of each lot or batch of drug product shall be retained and stored under conditions consistent with product labeling. The reserve sample shall be stored in the same immediate container-closure system in which the drug product is marketed or in one that has essentially the same characteristics. The reserve sample consists of at least twice the quantity necessary to perform all the required tests, except those for sterility and pyrogens. Except for those for drug products described in paragraph (b)(2) of this section, reserve samples from representative sample lots or batches selected by acceptable statistical procedures shall be examined visually at least once a year for evidence of deterioration unless visual examination would affect the integrity of the reserve sample. Any evidence of reserve sample deterioration shall be investigated in accordance with §211.192. The results of the examination shall be recorded and maintained with other stability data on the drug product. Reserve samples of compressed medical gases need not be retained. The retention time is as follows:</p> <p>(1) For a drug product other than those described in paragraphs (b) (2) and (3) of this section, the reserve sample shall be retained for 1 year after the expiration date of the drug product.</p> <p>(3) For an OTC drug product that is exempt for bearing an expiration date under §211.137, the reserve sample must be retained for 3 years after the lot or batch of drug product is distributed.</p>		<p>(b) Reserve samples. An appropriately identified reserve sample that is representative of each batch of a dietary product should be retained and stored under conditions consistent with the product labeling until at least one year after the expiration date, or if no expiration date is identified on the product, for at least three years after the date of manufacture. The reserve sample should be stored in the same immediate container-closure system in which the finished product is marketed or in one that provides similar protection. The reserve sample shall consist of at least twice the quantity necessary to perform all the required tests.</p>	<p>(b) You must hold reserve samples of dietary supplements in a manner that protects against contamination and deterioration. This includes, but is not limited to:</p> <p>(1) Holding the reserve samples under conditions of use recommended or suggested in the label of the dietary supplement and, if no conditions of use are recommended or suggested in the label, then under ordinary conditions of use; and</p> <p>(2) Using the same container-closure system in which the dietary supplement is marketed or in one that provides the same level of protection against contamination or deterioration.</p>
<p>(2) For a radioactive drug product, except for nonradioactive reagent kits, the reserve sample shall be retained for:</p> <p>(i) Three months after the expiration date of the drug product if the expiration dating period of the drug product is 30 days or less; or</p> <p>(ii) Six months after the expiration date of the drug product if the expiration dating period of the drug product is more than 30 days.</p>			

PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)	Food cGMP (21 CFR Part 110)	Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)	Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)
<p>§ 211.173 Laboratory animals.</p> <p>Animals used in testing components, in-process materials, or drug products for compliance with established specifications shall be maintained and controlled in a manner that assures their suitability for their intended use. They shall be identified, and adequate records shall be maintained showing the history of their use.</p>			
<p>§ 211.176 Penicillin contamination.</p> <p>If a reasonable possibility exists that a non-penicillin drug product has been exposed to cross-contamination with penicillin, the non-penicillin drug product shall be tested for the presence of penicillin. Such drug product shall not be marketed if detectable levels are found when tested according to procedures specified in 'Procedures for Detecting and Measuring Penicillin Contamination in Drugs,' which is incorporated by reference. Copies are available from the Division of Research and Testing (HFD-470), Center for Drug Evaluation and Research, Food and Drug Administration, 200 C St. SW., Washington, DC 20204, or available for inspection at the Office of the Federal Register, 800 North Capitol Street, NW., suite 700, Washington, DC 20408.</p>			

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<p>§ 211.204 Returned drug products. Returned drug products shall be identified as such and held. If the conditions under which returned drug products have been held, stored, or shipped before or during their return, or if the condition of the drug product, its container, carton, or labeling, as a result of storage or shipping, casts doubt on the safety, identity, strength, quality or purity of the drug product, the returned drug product shall be destroyed unless examination, testing, or other investigations prove the drug product meets appropriate standards of safety, identity, strength, quality, or purity. A drug product may be reprocessed provided the subsequent drug product meets appropriate standards, specifications, and characteristics. Records of returned drug products shall be maintained and shall include the name and label potency of the drug product dosage form, lot number (or control number or batch number), reason for the return, quantity returned, date of disposition, and ultimate disposition of the returned drug product. If the reason for a drug product being returned implicates associated batches, an appropriate investigation shall be conducted in accordance with the requirements of §211.192. Procedures for the holding, testing, and reprocessing of returned drug products shall be in writing and shall be followed.</p> <p>§ 211.208 Drug product salvaging. Drug products that have been subjected to improper storage conditions including extremes in temperature, humidity, smoke, fumes, pressure, age, or radiation due to natural disasters, fires, accidents, or equipment failures shall not be salvaged and returned to the marketplace. Whenever there is a question whether drug products have been subjected to such conditions, salvaging operations may be conducted only if there is (a) evidence from laboratory tests and assays (including animal feeding studies where applicable) that the drug products meet all applicable standards of identity, strength, quality, and purity and (b) evidence from inspection of the premises that the drug products and their associated packaging were not subjected to improper storage conditions as a result of the disaster or accident. Organoleptic examinations shall be acceptable only as supplemental evidence that the drug products meet appropriate standards of identity, strength, quality, and purity. Records including name, lot number, and disposition shall be maintained for drug products subject to this section.</p>		<p>(e) Returned products. Returned dietary products shall be identified as such and held. If the conditions under which returned dietary products have been held, stored, or shipped before or during their return, or if the condition of the product, its container, carton, or labeling as a result of storage or shipping, casts doubt on the purity, composition or quality of the product, the returned product shall be destroyed unless examination, testing or other investigations prove the product meets appropriate standards of purity, composition and quality. A product may be reprocessed provided the subsequent product meets appropriate specifications. Records pertaining to returned products that are subsequently reprocessed and/or redistributed shall be maintained and shall include the name and description of the product, lot number, reason for the return, quantity returned, date of disposition, and ultimate disposition of the returned product.</p> <p>(f) Product salvaging. Dietary products that have been subjected to improper storage conditions including extremes in temperature, humidity, smoke, fumes, pressure, age, or radiation due to natural disasters, fires, accidents, or equipment failures shall not be salvaged and returned to the marketplace. Whenever there is a question whether products have been subjected to such conditions, salvaging operations may be conducted only if there is (a) evidence from laboratory tests that the products meet all applicable standards of purity, quality and composition, and (b) evidence from inspection of the premises that the products and their associated packaging were not subjected to improper storage conditions as a result of the disaster or accident. Records including name, lot number, and disposition shall be maintained for products subject to this section.</p>	<p>§ 111.85 What requirements apply to returned dietary ingredients or dietary supplements?</p> <p>(a) You must identify and quarantine returned dietary ingredients or dietary supplements until the quality control unit conducts a material review and makes a disposition decision.</p> <p>(b) You must not salvage returned dietary ingredients and dietary supplements, unless:</p> <p>(1) Evidence from their packaging (or, if possible, an inspection of the premises, where the dietary ingredients and dietary supplements were held) indicates that the dietary ingredients and dietary supplements were not subjected to improper storage conditions; and</p> <p>(2) Tests demonstrate that the dietary ingredients or dietary supplements meet all specifications for identity, purity, quality, strength, and composition.</p> <p>(c) You must destroy or suitably dispose of the returned dietary ingredients or dietary supplements if such dietary ingredients or dietary supplements do not meet specifications for identity, purity, quality, strength, and composition, unless the quality control unit conducts a material review and makes a disposition decision to allow reprocessing.</p> <p>(d) If the reason for a dietary ingredient or a dietary supplement being returned implicates associated batches, you must conduct an investigation of your manufacturing processes and those other batches to determine compliance with specifications.</p> <p>(e) You must establish and keep records for this section on the material review and disposition decision and any testing conducted to determine compliance with established specifications in the master manufacturing record for the type of dietary ingredient or dietary supplement that was returned.</p> <p>(f) You must keep returned dietary ingredient and dietary supplement records in accordance with § 111.125.</p>

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			<p>§ 111.90 What requirements apply to distributing dietary ingredients or dietary supplements?</p> <p>Distribution of dietary ingredients and dietary supplements must be under conditions that will protect the dietary ingredients and dietary supplements against contamination and deterioration.</p>
<p>§ 211.150 Distribution procedures.</p> <p>Written procedures shall be established, and followed, describing the distribution of drug products. They shall include:</p> <p>(a) A procedure whereby the oldest approved stock of a drug product is distributed first. Deviation from this requirement is permitted if such deviation is temporary and appropriate.</p>			
<p>(b) A system by which the distribution of each lot of drug product can be readily determined to facilitate its recall if necessary.</p> <p>§ 211.196 Distribution records.</p> <p>Distribution records shall contain the name and strength of the product and description of the dosage form, name and address of the consignee, date and quantity shipped, and lot or control number of the drug product. For compressed medical gas products, distribution records are not required to contain lot or control numbers.</p>		<p>(2) Adequate distribution records shall be maintained and retained by the manufacturer at least one year beyond expected product shelf life, whereby an effective product recall can be achieved should one become necessary.</p>	

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<p>§ 211.198 Complaint files.</p> <p>(a) Written procedures describing the handling of all written and oral complaints regarding a drug product shall be established and followed. Such procedures shall include provisions for review by the quality control unit, of any complaint involving the possible failure of a drug product to meet any of its specifications and, for such drug products, a determination as to the need for an investigation in accordance with §211.192. Such procedures shall include provisions for review to determine whether the complaint represents a serious and unexpected adverse drug experience which is required to be reported to the Food and Drug Administration in accordance with §310.305 of this chapter.</p>		<p>(d) Complaint files.</p> <p>(1) Written procedures describing the handling of all written and oral complaints regarding a dietary product shall be established and followed. Such procedures shall include provisions for review by the quality control unit of any complaint involving the possible failure of a product to meet any of its specifications and, for such products, a determination as to the need for an investigation.</p>	<p>Subpart G--Consumer Complaints</p> <p>§ 111.95 <u>What requirements apply to consumer complaints?</u></p> <p>(a) A qualified person must review all consumer complaints to determine whether the consumer complaint involves a possible failure of a dietary ingredient or dietary supplement to meet any of its specifications, or any other requirements of this part, including those specifications and other requirements that, if not met, may result in a possible risk of illness or injury.</p> <p>(b) Your quality control unit must review all consumer complaints involving the possible failure of a dietary ingredient or dietary supplement to meet any of its specifications, or any other requirements of this part, including those specifications and other requirements that, if not met, may result in a possible risk of illness or injury, to determine whether there is a need to investigate the consumer complaint.</p> <p>(c) Your quality control unit must investigate a consumer complaint when there is a reasonable possibility of a relationship between the quality of a dietary supplement and an adverse event.</p> <p>(d) Your quality control unit's investigation of a consumer complaint must include the batch records associated with the dietary ingredient or dietary supplement involved in the consumer complaint. Your quality control unit must extend the investigation to other batches of dietary ingredients or dietary supplements that may have been associated with an adverse event.</p>

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<p>(b) A written record of each complaint shall be maintained in a file designated for drug product complaints. The file regarding such drug product complaints shall be maintained at the establishment where the drug product involved was manufactured, processed, or packed, or such file may be maintained at another facility if the written records in such files are readily available for inspection at that other facility. Written records involving a drug product shall be maintained until at least 1 year after the expiration date of the drug product, or 1 year after the date that the complaint was received, whichever is longer. In the case of certain OTC drug products lacking expiration dating because they meet the criteria for exemption under §211.137, such written records shall be maintained for 3 years after distribution of the drug product.</p>		<p>(2) A written record of each complaint shall be maintained, until at least 1 year after the expiration date of the product, or 1 year after the date that the complaint was received, whichever is longer.</p> <p>(4) Where an investigation is conducted, the written record shall include the findings of the investigation and follow-up action taken.</p>	<p>(e) You must make and keep a written record of every consumer complaint that is related to good manufacturing practices. For the purposes of the regulations in this part, a consumer complaint about product quality may or may not include concerns about a possible hazard, to health. However, a consumer complaint does not include an adverse event, illness, or injury related to the safety of a particular dietary ingredient independent of whether the product is produced under good manufacturing practices.</p>
<p>(1) The written record shall include the following information, where known: the name and strength of the drug product, lot number, name of complainant, nature of complaint, and reply to complainant.</p>		<p>(3) The written record shall include, where known: the name and description of the product, lot number, name of complainant, nature of complaint, and reply to complainant, if any.</p>	<p>The consumer complaint written record must include, but is not limited to, the following:</p> <p>(1) The name and description of the dietary ingredient or dietary supplement;</p> <p>(2) The batch or lot number of the dietary supplement, if available;</p> <p>(3) The name of the complainant, if available;</p> <p>(4) The nature of the complaint including how the consumer used the product;</p> <p>(5) The reply to the complainant if any; and</p> <p>(6) Findings of the investigation and follow-up action taken when an investigation is performed.</p>
<p>(2) Where an investigation under §211.192 is conducted, the written record shall include the findings of the investigation and followup. The record or copy of the record of the investigation shall be maintained at the establishment where the investigation occurred in accordance with §211.180(c).</p> <p>(3) Where an investigation under §211.192 is not conducted, the written record shall include the reason that an investigation was found not to be necessary and the name of the responsible person making such a determination.</p>			<p>(f)(1) The person who performs the requirements in accordance with this section must document at the time of performance that the requirement was performed.</p> <p>(2) You must keep consumer complaint records in accordance with § 111.125.</p>

<p align="center">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p align="center">Food cGMP (21 CFR Part 110)</p>	<p align="center">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p align="center">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
<p>§ 211.180 General requirements.</p> <p>(a) Any production, control, or distribution record that is required to be maintained in compliance with this part and is specifically associated with a batch of a drug product shall be retained for at least 1 year after the expiration date of the batch or, in the case of certain OTC drug products lacking expiration dating because they meet the criteria for exemption under §211.137, 3 years after distribution of the batch.</p> <p>(b) Records shall be maintained for all components, drug product containers, closures, and labeling for at least 1 year after the expiration date or, in the case of certain OTC drug products lacking expiration dating because they meet the criteria for exemption under §211.137, 3 years after distribution of the last lot of drug product incorporating the component or using the container, closure, or labeling.</p>		<p>(c) Records retention.</p> <p>(1) Any laboratory, production, control or distribution record specifically associated with a batch of product shall be retained for at least one year after the expiration date of the batch, or if no expiration date is identified on the product, for at least three years after the date of manufacture.</p> <p>(2) Raw material records shall be maintained for at least one year after the expiration date of the last batch of product incorporating the raw material, or if no expiration date is identified on the product, for at least three years after the date of manufacture of the finished product.</p>	<p>Subpart H--Records and Recordkeeping</p> <p>§ 111.125 What requirements apply to recordkeeping?</p> <p>(a) You must keep written records required by this part for 3 years beyond the date of manufacture of the last batch of dietary ingredients or dietary supplements associated with those records.</p>
<p>(c) All records required under this part, or copies of such records, shall be readily available for authorized inspection during the retention period at the establishment where the activities described in such records occurred. These records or copies thereof shall be subject to photocopying or other means of reproduction as part of such inspection. Records that can be immediately retrieved from another location by computer or other electronic means shall be considered as meeting the requirements of this paragraph.</p> <p>d) Records required under this part may be retained either as original records or as true copies such as photocopies, microfilm, microfiche, or other accurate reproductions of the original records. Where reduction techniques, such as microfilming, are used, suitable reader and photocopying equipment shall be readily available.</p>			<p>(b) Records required under this part must be kept as original records, as true copies (such as photocopies, microfilm, microfiche, or other accurate reproductions of the original records), or as electronic records. If you use reduction techniques, such as microfilming, you must make suitable reader and photocopying equipment readily available to FDA. All electronic records must comply with part 11 of this chapter.</p> <p>(c) You must have all records required under this part, or copies of such records, readily available during the retention period for authorized inspection and copying by FDA when requested.</p>
<p>(e) Written records required by this part shall be maintained so that data therein can be used for evaluating, at least annually, the quality standards of each drug product to determine the need for changes in drug product specifications or manufacturing or control procedures. Written procedures shall be established and followed for such evaluations and shall include provisions for:</p> <p>(1) A review of a representative number of batches, whether approved or rejected, and, where applicable, records associated with the batch.</p> <p>(2) A review of complaints, recalls, returned or salvaged drug products, and investigations conducted under §211.192 for each drug product.</p>			

<p align="center">PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)</p>	<p align="center">Food cGMP (21 CFR Part 110)</p>	<p align="center">Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)</p>	<p align="center">Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)</p>
<p>(f) Procedures shall be established to assure that the responsible officials of the firm, if they are not personally involved in or immediately aware of such actions, are notified in writing of any investigations conducted under §§211.198, 211.204, or 211.208 of these regulations, any recalls, reports of inspectional observations issued by the Food and Drug Administration, or any regulatory actions relating to good manufacturing practices brought by the Food and Drug Administration</p>			
	<p align="center">Subpart G--Defect Action Levels</p> <p>¶110.110 Natural or unavoidable defects in food for human use that present no health hazard. (a) Some foods, even when produced under current good manufacturing practice, contain natural or unavoidable defects that at low levels are not hazardous to health. The Food and Drug Administration establishes maximum levels for these defects in foods produced under current good manufacturing practice and uses these levels in deciding whether to recommend regulatory action.</p>	<p>(g) Defect Action Levels.</p> <p>(1) Some dietary ingredients and dietary supplements, even when produced under current good manufacturing practice, contain natural or unavoidable defects that at low levels are not hazardous to health. The Food and Drug Administration establishes maximum levels for these defects in dietary products produced under current good manufacturing practice and uses these levels in deciding whether to recommend regulatory action.</p>	
	<p>(b) Defect action levels are established for foods whenever it is necessary and feasible to do so. These levels are subject to change upon the development of new technology or the availability of new information.</p>	<p>(2) Defect action levels are established for dietary products whenever it is necessary and feasible to do so. These levels are subject to change upon the development of new technology or the availability of new information.</p>	
			<p><i>PART 112--RESTRICTIONS, FOR SUBSTANCES USED IN DIETARY SUPPLEMENTS</i></p> <p>Subpart A--General Provisions [Reserved]</p> <p>Subpart B--New Dietary Ingredients [Reserved]</p> <p>Subpart C--Restricted Dietary Ingredients [Reserved]</p>
	<p>(c) Compliance with defect action levels does not excuse violation of the requirement in section 402(a)(4) of the act that food not be prepared, packed, or held under unsanitary conditions or the requirements in this part that food manufacturers, distributors, and holders shall observe current good manufacturing practice. Evidence indicating that such a violation exists causes the food to be adulterated within the meaning of the act, even though the amounts of natural or unavoidable defects are lower than the currently established defect action levels. The manufacturer, distributor, and holder of food shall at all times utilize quality control operations that reduce natural or unavoidable defects to the lowest level currently feasible.</p>	<p>(3) Compliance with defect action levels does not excuse violation of the requirement in section 402(a)(4) of the act that dietary products not be prepared, packed, or held under unsanitary conditions or the requirements in this part that dietary product manufacturers, distributors, and holders shall observe current good manufacturing practice. Evidence indicating that such a violation exists causes a dietary product to be adulterated within the meaning of the act, even though the amounts of natural or unavoidable defects are lower than the currently established defect action levels. The manufacturer, distributor, and holder of a dietary product shall at all times utilize quality control operations that reduce natural or unavoidable defects to the lowest level currently feasible.</p>	

PHARMACEUTICAL cGMP (21 CFR Part 210 & 211)	Food cGMP (21 CFR Part 110)	Advanced Notice of Proposed Rulemaking (ANPR) (FR: 2-6-97)	Proposed cGMP for Dietary Ingredients and Dietary Supplements (FR: 3-13-03)
	<p>(d) The mixing of a food containing defects above the current defect action level with another lot of food is not permitted and renders the final food adulterated within the meaning of the act, regardless of the defect level of the final food.</p>	<p>(4) The mixing of a dietary ingredient or dietary supplement containing defects above the current defect action level with another lot of dietary ingredient or dietary supplement is not permitted and renders the final product adulterated within the meaning of the act, regardless of the defect level of the final product.</p>	
	<p>(e) A compilation of the current defect action levels for natural or unavoidable defects in food for human use that present no health hazard may be obtained upon request from the Industry Programs Branch (HFF-326), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 200 C St. SW., Washington, DC 20204.</p>	<p>(5) A compilation of the current defect action levels for natural or unavoidable defects in dietary products that present no health hazard may be obtained upon request from the Industry Programs Branch (HFF-326), Center for Food Safety and Applied Nutrition, Food and Drug Administration, 200 C St. SW., Washington, DC 20204.</p>	