D1. Definitions

US laws and regulations establish specialized definitions for various words and phrases, which are key to proper understanding of the applicable legal and regulatory requirements; in addition, some terms are unique to the botanical industry and may be unfamiliar to most English speakers.

The entries below define what is meant by various terms used in the document. Where quotation marks are used within the definitions, these indicate other terms with specialized meanings whose definitions are also provided here and should be consulted.

"Adulterated," when used in reference to "food," is defined by U.S. law[1] to mean the food meets one of the following conditions: (a) the food bears or contains any poisonous or deleterious substance which may render it injurious to health, except if the substance is not an added substance such food is not considered adulterated if the quantity of such substance in such food does not ordinarily render it injurious to health; (b) the food bears or contains any added poisonous or added deleterious substance that is unsafe; (c) the food consists in whole or in part of any filthy, putrid, or decomposed substance, or if it is otherwise unfit for food; (d) the food has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health; or (e) the food is a dietary supplement that has been prepared, packed, or held under conditions that do not comply with 21 CFR Part 111; or (f) the food meets various other technical provisions that U.S. law deems to be adulterated.[2]

"Botanical" as used in U.S. laws and regulations means any plant, fungus, or alga.[3]

"Botanical material" as used in this document refers to roots, rhizomes, leaves, stems, flowers, seeds, fruit, or other botanical structures or combinations of botanical structures that have been, or will be, harvested, handled, packed, stored, or processed.

"Covered activity" for purposes of 21 CFR Part 112 (i.e., the regulations applicable to growing and "harvesting" of "covered produce") is defined by FDA as growing, harvesting, "packing," or "holding" "covered produce" on a "farm." Covered activities include "manufacturing/processing" of covered produce on a farm, but only to the extent that such activities are performed on "raw agricultural commodities" and only to the extent that such activities are within the meaning of farm as defined by FDA. For produce that is exempted from Part 112 under 21 CFR § 112.2(b) because it receives commercial processing that will remove microbiological hazards, covered activities also include

[1] 21 U.S.C. § 342.

[2] See the full text of 21 U.S.C. § 342 for a complete list of the conditions that render food adulterated.

[3] For example, 21 CFR § 101.36(h) states in part, "The common or usual name of ingredients of dietary supplements that are botanicals (including fungi and algae) shall be…."

providing the written assurances required therein; acting consistently with those assurances; and documenting actions taken in compliance with those assurances.[4]

"Covered produce" is defined by FDA as "produce" that is subject to the requirements of 21 CFR Part 112 in accordance with §§112.1 and 112.2; the term refers to the harvestable or harvested part of the crop.[5] Basically, covered produce consists of fruits and vegetables or other produce, or mixtures thereof, that meet all of the following criteria: (a) they are intended for use as "food"; (b) they are "raw agricultural commodities"; (c) they are grown in the U.S. or will be imported to the US; and (d) FDA believes they are commonly eaten raw and therefore require special agricultural controls to ensure food safety (i.e., they are not excluded under 21 CFR § 112.2).[6] Covered produce does not include crops that meet any of the following criteria: They are (a) intended for non-food purposes (e.g., for biofuels, pharmaceuticals, clothing, household products, cosmetics, etc.); (b) grown outside the U.S. and will not be imported to the US; (c) in the FDA's list at 21 CFR § 112.2(a)(1) of produce rarely eaten raw (e.g., asparagus, winter squash, potatoes); (d) not raw agricultural commodities (i.e., they have been processed beyond their raw or natural state); or (e) produced by an individual for personal consumption or consumption on the same "farm" where they are grown or another farm under the same management.[7]

"Dietary ingredient" is defined under U.S. law as an ingredient in a "dietary supplement" that is a vitamin; mineral; herb or other botanical; amino acid; a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or a concentrate, metabolite, constituent, extract, or combination of any of these.[8]

"Dietary supplement" is defined under U.S. law as a "food" product (other than tobacco) intended to supplement the diet that bears or contains one or more "dietary ingredients"; is intended for ingestion typically in tablet, capsule, powder, softgel, gelcap, or liquid form; is not represented for use as a conventional food or as a sole item of a meal or the diet; and is labeled as a dietary supplement.[9]

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[4] The definition of "covered activity" under FDA regulations contains additional details. For the complete definition see 21 CFR § 112.3.

[5] 21 CFR § 112.3. See also Appendix 1 for more information.

[6] See additional details in 21 CFR § 112.1. In particular, it is to be noted that the list of examples of crops that are covered by Part 112 (i.e., that are not included on the list of "rarely consumed raw" crops that are exempt from Part 112) includes various crops that many people may assume are customarily cooked before eating, such as artichokes.

[7] See additional details in 21 CFR § 112.2, including the list of botanical crops that FDA considers to be "rarely consumed raw."

[8] 21 U.S.C. § 321 (ff).

[9] The definition of "dietary supplement" under U.S. law contains additional details. For the complete definition see 21 U.S.C. § 321 (ff).

"Facility" is defined under FDA regulations[10] as any establishment, structure, or structures under one ownership at one general physical location, or, in the case of a mobile facility, traveling to multiple locations, that "manufactures/processes," "packs," or "holds" "food" for consumption in the United States. Transport vehicles are not facilities if they hold food only in the usual course of business as carriers. A facility may consist of one or more contiguous structures, and a single building may house more than one distinct facility if the facilities are under separate ownership. The private residence of an individual is not a facility. Nonbottled water drinking water collection and distribution establishments and their structures are not facilities.

> (1) *Domestic facility* means any facility located in any State or Territory of the United States, the District of Columbia, or the Commonwealth of Puerto Rico that manufactures/processes, packs, or holds food for consumption in the United States.
>
> (2) *Foreign facility* means a facility other than a "domestic facility" that manufactures/processes, packs, or holds food for consumption in the United States.

"Farm" is defined by FDA regulation as the two types of operations enumerated below.[11] Under these definitions, farm includes both operations that grow crops and operations that merely "harvest" crops (i.e., wild collecting operations).

> (1) Primary production farm. A "primary production farm" is an operation under one management in one general (but not necessarily contiguous) physical location devoted to the growing of crops, the harvesting of crops, the raising of animals (including seafood), or any combination of these activities. The term farm includes operations that, in addition to these activities:
>
> > (i) "Pack" or "hold" "raw agricultural commodities";
> >
> > (ii) Pack or hold "processed food," provided that all processed food used in such activities is either consumed on that farm or another farm under the same management, or is processed food identified in paragraph (1)(iii)(B)(1) of this definition; and
> >
> > (iii) "Manufacture/process" food, provided that:
> >
> > (A) All food used in such activities is consumed on that farm or another farm under the same management; or

[10] 21 CFR § 1.227.

[11] 21 CFR § 1.227 and 21 CFR § 112.3.

(B) Any manufacturing/processing of food that is not consumed on that farm or another farm under the same management consists only of:

(1) Drying/dehydrating "raw agricultural commodities" to create a distinct commodity (such as drying/dehydrating grapes to produce raisins), and "packaging" and "labeling" such commodities, without additional manufacturing/processing (an example of additional manufacturing/processing is slicing);

(2) Treatment to manipulate the ripening of raw agricultural commodities (such as by treating produce with ethylene gas), and packaging and labeling treated raw agricultural commodities, without additional manufacturing/processing; and

(3) Packaging and labeling raw agricultural commodities, when these activities do not involve additional manufacturing/processing (an example of additional manufacturing/processing is irradiation).

(2) Secondary activities farm. A "secondary activities farm" is an operation, not located on a "primary production farm," devoted to harvesting (such as hulling or shelling), packing, and/or "holding" of raw agricultural commodities, provided that the primary production farm(s) that grows, harvests, and/or raises the majority of the raw agricultural commodities harvested, packed, and/or held by the secondary activities farm owns, or jointly owns, a majority interest in the secondary activities farm. A secondary activities farm may also conduct those additional activities allowed on a primary production farm as described in paragraphs (1)(ii) and (iii) of this definition.

"Farm mixed-type facility" is a "farm" that engages in both activities that are exempt from food facility registration[12] and activities that are outside the farm definition and therefore require the establishment to be registered with FDA.

"FDA" means the U.S. Food and Drug Administration.

"Food" is defined under U.S. law as (1) articles used for food or drink for man or other animals; (2) chewing gum; (3) articles used for components of any such article.[13] Under FDA regulations, food includes seeds and beans used to grow sprouts.[14] Examples of food include: Fruits, vegetables, fish, dairy products, eggs, "raw agricultural commodities" for use as food or as components of food, animal feed (including pet food), food and feed ingredients, food and feed additives, "dietary supplements" and

[12] See Appendix 3.

[13] 21 U.S.C. § 321 (f).

[14] 21 CFR § 112.3.

"dietary ingredients," infant formula, beverages (including alcoholic beverages and bottled water), live food animals, bakery goods, snack foods, candy, and canned foods.[15]

"Food processing," for purposes of this document, describes operations that are subject to FDA food regulations (e.g., 21 CFR Part 117) and that require the facility in which the operations occur to be registered with FDA as a food facility.[16]

"Garbling" means separating the target plant part from extraneous matter, such as dirt, other plant parts, etc.

"Harvesting" is defined under FDA regulations[17] as activities that are traditionally performed on "farms" for the purpose of removing "raw agricultural commodities" from the place they were grown or raised and preparing them for use as "food." Harvesting is limited to activities performed on raw agricultural commodities, or on "processed foods" created by drying/dehydrating a raw agricultural commodity without additional "manufacturing/processing," on a farm.[18] Harvesting does not include activities that transform a raw agricultural commodity into a "processed food." Examples of harvesting include cutting (or otherwise separating) the edible portion of the raw agricultural commodity from the crop plant and removing or trimming part of the raw agricultural commodity (e.g., foliage, husks, roots or stems). Examples of harvesting also include cooling, field coring, filtering, gathering, hulling, shelling, sifting, threshing, trimming of outer leaves of, and washing raw agricultural commodities grown on a farm.

"Herbarium" means a collection of plant samples and associated data preserved for study over the long term.

"Holding" is defined under FDA regulations[19] as storage of "food," and also includes activities performed incidental to storage of a food (e.g., activities performed for the safe or effective storage of that food, such as fumigating food during storage, and drying/dehydrating "raw agricultural commodities" when the drying/dehydrating does not create a distinct commodity (such as drying/dehydrating hay or alfalfa)). Holding also includes activities performed as a practical necessity for the distribution of that food (such as blending of the same raw agricultural commodity and breaking down pallets), but does not

[15] 21 CFR § 1.227.

[16] See Appendix 3 for more information about facility registration.

[17] 21 CFR § 1.227, 21 CFR § 112.3 and 21 CFR § 117.3.

[18] Activities that are considered "harvesting" when performed on the farm where the crop was grown, may constitute "manufacturing/processing" when performed at a different location by a different company. For example, if apples are washed on the same farm where they were grown, this is a harvesting activity; however, if the apples are sold to a different company which then washes them, this is a manufacturing/processing activity.

[19] 21 CFR § 1.227, 21 CFR § 112.3 and 21 CFR § 117.3.

include activities that transform a raw agricultural commodity into a "processed food." Holding facilities could include warehouses, cold storage facilities, storage silos, grain elevators, and liquid storage tanks.

"Label" (when used as a noun) is defined under U.S. laws and regulations as a display of written, printed, or graphic matter upon the immediate container of any article, or any such matter affixed to any consumer commodity or affixed to or appearing upon a package containing any consumer commodity.[20]

"Labeling" (when used as a noun) is defined under U.S. laws and regulations as all "labels" and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers, or (2) accompanying such article at any time while such article is in interstate commerce or held for sale after shipment or delivery in interstate commerce.[21]

"Labeling" (when used as a verb) means the activity of applying "labels" or "labeling" to an article or its immediate containers or wrappers.

"Manufacturing/processing" is defined under FDA regulations[22] as making "food" from one or more ingredients, or synthesizing, preparing, treating, modifying or manipulating food, including food crops or ingredients. Examples of manufacturing/processing activities include: Baking, boiling, bottling, canning, cooking, cooling, cutting, distilling, drying/dehydrating "raw agricultural commodities" to create a distinct commodity (such as drying/dehydrating grapes to produce raisins), evaporating, eviscerating, extracting juice, formulating, freezing, grinding, homogenizing, "labeling," milling, mixing, "packaging" (including modified atmosphere packaging), pasteurizing, peeling, rendering, treating to manipulate ripening, trimming, washing, or waxing. For "farms" and "farm mixed-type" facilities, manufacturing/processing does not include activities that are part of "harvesting," "packing," or "holding."

> See also the definition of "processed food" below, for an important distinction between "processing" and "manufacturing/processing."

"Packaging" (when used as a verb) is a "manufacturing/processing" activity in which food is placed into a container that directly contacts the food and that the consumer receives. Placing "raw agricultural commodities" into retail packages on a "farm" or "farm mixed-type facility" is exempt from the food processing regulations in Part 117 unless (a) additional manufacturing/processing that is outside the farm definition is also performed, or (b) raw agricultural commodities that are "produce" as defined in

[20] 21 U.S.C. § 321 (k); 21 CFR 1.3.

[21] 21 U.S.C. § 321 (m); 21 CFR 1.3.

[22] 21 CFR § 112.3 and 21 CFR § 117.3.

Part 112 are dehydrated to create a distinct commodity, in which case Part 117 Subpart B applies to the packaging, "packing," and "holding" of the dried commodities.[23]

"Packing" is defined under FDA regulations[24] as placing "food" into a container other than "packaging" the food and also includes activities performed incidental to packing of a food (e.g., activities performed for the safe or effective packing of that food (such as sorting, culling, grading, and weighing or conveying incidental to packing or re-packing)), but does not include activities that transform a "raw agricultural commodity" into a "processed food." Packing includes, for example, placing immediate packages of food (e.g., individual bottles labeled for retail sale) into secondary packages that will not be received by the consumer (such as cases, master packs, etc.).

"Pesticide" is defined under U.S. law as any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest; any substance or mixture of substances intended for use as a plant regulator, defoliant, or desiccant; and nitrogen stabilizers.[25] Pesticides include herbicides, fungicides, and insecticides as well as other substances.

"Processed food" is defined under U.S. law as any human or animal "food" other than a "raw agricultural commodity," and (according to FDA's interpretation of this legal definition) includes any raw agricultural commodity that has been subject to "manufacturing/processing" *that alters the general state of the commodity or creates a distinct commodity,* such as canning, cooking, freezing dehydration, or milling. In contrast, minor manufacturing/processing that does not alter the general state of the commodity or create a distinct commodity, such as coloring, washing, or waxing, does not (according to FDA's interpretation) transform the raw agricultural commodity into a processed food. [26]

Under the FDA interpretation of this provision, dehydration transforms a raw agricultural commodity into a processed food only if the drying "creates a new commodity," i.e., if the crop is normally traded in fresh form then dehydration of it constitutes manufacturing/processing. For example, fresh apples are a raw agricultural commodity while dried apples are a processed food. In contrast, dehydration of

[23] Compliance with this last requirement may be achieved by complying with Part 117 Subpart B or with the applicable requirements for packing and holding in Part 112.

[24] 21 CFR § 1.227, 21 CFR § 112.3 and 21 CFR § 117.3.

[25] The definition of "pesticide" under U.S. law contains additional details. For the complete definition see 7 U.S.C. § 136 (u).

[26] The precise legal definition given in 21 U.S.C. § 321 (gg) is as follows: "The term 'processed food' means any food other than a raw agricultural commodity and includes any raw agricultural commodity that has been subject to processing, such as canning, cooking, freezing, dehydration, or milling." This use of the term "processing" is different from the term "manufacturing/processing" as defined in FDA regulations. In the preamble to the proposed Produce Safety rule (78 FR 3540, 2013), FDA explains that manufacturing/processing includes nearly any type of food manipulation, even minor steps such as coloring, washing or waxing, but that a raw agricultural commodity is transformed into a processed food only if the manufacturing/processing alters the general state of the commodity or creates a new or distinct commodity.

commodities normally traded in dried form does not transform the commodity into a processed food (e.g., dried allspice berries and dried cinnamon bark remain raw agricultural commodities even though they have been dehydrated).[27]

"Processed botanical" for purposes of this document means any (food or non-food) "raw agricultural commodity" that has been subject to "manufacturing/processing" that alters the general state of the commodity or creates a distinct commodity, such as size reduction or extraction, or dehydration if the commodity is not normally traded in dried form.

"Produce" is defined under FDA regulations[28] as any fruit or vegetable (including mixes of intact fruits and vegetables) and includes mushrooms, sprouts (irrespective of seed source), peanuts, tree nuts, and herbs. A fruit is the edible reproductive body of a seed plant or tree nut (such as apple, orange, and almond) such that fruit means the harvestable or harvested part of a plant developed from a flower. A vegetable is the edible part of an herbaceous plant[29] (such as cabbage or potato) or fleshy fruiting body of a fungus (such as white button or shiitake) grown for an edible part such that vegetable means the harvestable or harvested part of any plant or fungus whose fruit, fleshy fruiting bodies, seeds, roots, tubers, bulbs, stems, leaves, or flower parts are used as "food" and includes mushrooms, sprouts, and herbs (such as basil or cilantro). Produce does not include food grains meaning the small, hard fruits or seeds of arable crops, or the crops bearing these fruits or seeds, that are primarily grown and processed for use as meal, flour, baked goods, cereals and oils rather than for direct consumption as small, hard

[27] The distinction between (a) drying a harvested food crop and thereby creating a distinct commodity from the fresh material (e.g., drying grapes into raisins) versus (b) drying a harvested food crop without creating a distinct commodity (e.g., the drying of hay or grains) stems from the 1998 Joint EPA/ FDA Policy Interpretation (63 FR 54532**,** 1998). The U.S. Environmental Protection Agency (EPA) and FDA created this distinction for purposes of implementing the U.S. Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) of 1996. Under this interpretation, if the dried material is a distinct commodity from the fresh commodity then it is a processed food; if the dried material is not a distinct commodity from the fresh commodity then it remains a raw agricultural commodity. The distinction was carried forward into the FDA regulations implementing FSMA (see for example the definitions of "farm," "harvesting," and "holding" in 21 CFR Part 112 and 21 CFR Part 117, and the preambles at 80 FR 74385, 2015; 80 FR 74395-34398, 2015; and 78 FR 3540, 2013).

[28] 21 CFR § 112.3.

[29] The Merriam-Webster dictionary defines "herbaceous" as either "of, relating to, or having the characteristics of an herb"; or "of a stem: having little or no woody tissue and persisting usually for a single growing season; or "having the texture, color, or appearance of a leaf" (https://www.merriam-webster.com/dictionary/herbaceous, accessed 12/02/2016). TheFreeDictionary.com defines "herbaceous plant" as "a plant lacking a permanent woody stem" (http://www.thefreedictionary.com/herbaceous+plant, accessed 12/02/2016) and Wikipedia defines "herbaceous plants" as "plants that have no persistent woody stem above ground" (https://en.wikipedia.org/wiki/Herbaceous_plant, accessed 12/02/2016). It is unclear which of these meanings FDA intends. "Of, relating to, or having the characteristics of an herb" and "having the texture, color, or appearance of a leaf" do not fit, since the examples given by FDA (cabbage, potatoes) are not "herbs" and potatoes are not leaves. It seems FDA intends to limit the definition of "vegetable" to non-woody plants, but this leads to additional contradictions because FDA lists "oregano" (a woody plant) in the definition of "covered produce."

fruits or seeds (including cereal grains, pseudo cereals, oilseeds and other plants used in the same fashion). Examples of food grains include barley, dent- or flint-corn, sorghum, oats, rice, rye, wheat, amaranth, quinoa, buckwheat, and oilseeds (e.g., cotton seed, flax seed, rapeseed, soybean, and sunflower seed).[30]

"Raw agricultural commodity" is defined under U.S. law as any human or animal "food" in its raw or natural state, including all fruits that are washed, colored, otherwise treated in their unpeeled natural form prior to marketing.[31] For purposes of this document, raw agricultural commodity also refers to non-food botanical crops in their raw or natural state. The natural state of a raw agricultural commodity may include being dried, but only if the commodity is normally traded in dried form (e.g., pinto beans). Dehydration of a raw agricultural commodity that is a food normally traded in fresh form (e.g., blueberries) transforms it into a "processed food."

"Rossing" means separating the outer bark from the inner bark.

"Voucher specimen" means an individual specimen plant including the aboveground structures (e.g., leaves, stems, flowers, fruits) and belowground structures when possible, that is representative of the harvested crop and which is documented, expertly identified, pressed, dried, labeled, and maintained in storage for future reference.

[30] Although it is not stated in the definition, FDA clarifies in the preamble to the rule that "algae" are excluded from the definition of produce. (80 FR 74385, November 27, 2015)

[31] 21 U.S.C. § 321 (r).

Appendix 1: Covered produce subject to 21 CFR Part 112

Botanical food crops are required to be cultivated or collected in accordance with 21 CFR Part 112 if they meet the definition of "covered produce." The following provisions of 21 CFR Part 112 explain what is, and is not, "covered produce."

FDA has issued Draft Guidance for Industry: Classification of Activities as Harvesting, Packing, Holding, or Manufacturing/Processing for Farms and Facilities (Aug. 2016) which is available on the FDA website. https://www.fda.gov/food/guidanceregulation/guidancedocumentsregulatoryinformation/ucm517567.htm

Application of FDA's regulations is fact specific and those using this document should consult with counsel or experienced consultants regarding their application to specific facts. FDA has established a portal for asking questions regarding the application of the Food Safety Modernization Act and its regulations. https://www.fda.gov/Food/GuidanceRegulation/FSMA/ucm459719.htm

Title 21: Food and Drugs
PART 112—STANDARDS FOR THE GROWING, HARVESTING, PACKING, AND HOLDING OF PRODUCE FOR HUMAN CONSUMPTION
Subpart A—General Provisions

§112.1 What food is covered by this part?

(a) Unless it is excluded from this part under §112.2, food that is produce within the meaning of this part and that is a raw agricultural commodity (RAC) is covered by this part. This includes a produce RAC that is grown domestically and a produce RAC that will be imported or offered for import in any State or territory of the United States, the District of Columbia, or the Commonwealth of Puerto Rico.

(b) For the purpose of this part and subject to the exemptions and qualified exemptions therein, covered produce includes all of the following:

(1) Fruits and vegetables such as almonds, apples, apricots, apriums, Artichokes-globe-type, Asian pears, avocados, babacos, bananas, Belgian endive, blackberries, blueberries, boysenberries, brazil nuts, broad beans, broccoli, Brussels sprouts, burdock, cabbages, Chinese cabbages (Bok Choy, mustard, and Napa), cantaloupes, carambolas, carrots, cauliflower, celeriac, celery, chayote fruit, cherries (sweet), chestnuts, chicory (roots and tops), citrus (such as clementine, grapefruit, lemons, limes, mandarin, oranges, tangerines, tangors, and uniq fruit), cowpea beans, cress-garden, cucumbers, curly endive, currants, dandelion leaves, fennel-Florence, garlic, genip, gooseberries, grapes, green beans, guavas, herbs (such as basil, chives, cilantro, oregano, and parsley), honeydew, huckleberries, Jerusalem artichokes, kale, kiwifruit, kohlrabi, kumquats, leek, lettuce, lychees, macadamia nuts, mangos, other melons (such as Canary, Crenshaw and Persian), mulberries, mushrooms, mustard greens, nectarines,

onions, papayas, parsnips, passion fruit, peaches, pears, peas, peas-pigeon, peppers (such as bell and hot), pine nuts, pineapples, plantains, plums, plumcots, quince, radishes, raspberries, rhubarb, rutabagas, scallions, shallots, snow peas, soursop, spinach, sprouts (such as alfalfa and mung bean), strawberries, summer squash (such as patty pan, yellow and zucchini), sweetsop, Swiss chard, taro, tomatoes, turmeric, turnips (roots and tops), walnuts, watercress, watermelons, and yams; and

(2) Mixes of intact fruits and vegetables (such as fruit baskets).

§112.2 What produce is not covered by this part?

(a) The following produce is not covered by this part:

(1) Produce that is rarely consumed raw, specifically the produce on the following exhaustive list: Asparagus; beans, black; beans, great Northern; beans, kidney; beans, lima; beans, navy; beans, pinto; beets, garden (roots and tops); beets, sugar; cashews; cherries, sour; chickpeas; cocoa beans; coffee beans; collards; corn, sweet; cranberries; dates; dill (seeds and weed); eggplants; figs; ginger; hazelnuts; horseradish; lentils; okra; peanuts; pecans; peppermint; potatoes; pumpkins; squash, winter; sweet potatoes; and water chestnuts.

(2) Produce that is produced by an individual for personal consumption or produced for consumption on the farm or another farm under the same management; and

(3) Produce that is not a raw agricultural commodity.

(b) Produce is eligible for exemption from the requirements of this part (except as noted in paragraphs (b)(1), (2), and (3) of this section) under the following conditions:

(1) The produce receives commercial processing that adequately reduces the presence of microorganisms of public health significance. Examples of commercial processing that adequately reduces the presence of microorganisms of public health significance are processing in accordance with the requirements of part 113, 114, or 120 of this chapter, treating with a validated process to eliminate spore-forming microorganisms (such as processing to produce tomato paste or shelf-stable tomatoes), and processing such as refining, distilling, or otherwise manufacturing/processing produce into products such as sugar, oil, spirits, wine, beer or similar products; and

(2) You must disclose in documents accompanying the produce, in accordance with the practice of the trade, that the food is “not processed to adequately reduce the presence of microorganisms of public health significance;” and

(3) You must either:

(i) Annually obtain written assurance, subject to the requirements of paragraph (b)(6) of this section, from the customer that performs the commercial processing described in paragraph (b)(1) of this section that the customer has established and is following procedures (identified in the written assurance) that adequately reduce the presence of microorganisms of public health significance; or

(ii) Annually obtain written assurance, subject to the requirements of paragraph (b)(6) of this section, from your customer that an entity in the distribution chain subsequent to the customer will perform commercial processing described in paragraph (b)(1) of this section and that the customer:

(A) Will disclose in documents accompanying the food, in accordance with the practice of the trade, that the food is "not processed to adequately reduce the presence of microorganisms of public health significance"; and

(B) Will only sell to another entity that agrees, in writing, it will either:

(*1*) Follow procedures (identified in a written assurance) that adequately reduce the presence of microorganisms of public health significance; or

(*2*) Obtain a similar written assurance from its customer that the produce will receive commercial processing described in paragraph (b)(1) of this section, and that there will be disclosure in documents accompanying the food, in accordance with the practice of the trade, that the food is "not processed to adequately reduce the presence of microorganisms of public health significance"; and

(4) You must establish and maintain documentation of your compliance with applicable requirements in paragraphs (b)(2) and (3) in accordance with the requirements of subpart O of this part, including:

(i) Documents containing disclosures required under paragraph (b)(2) of this section; and

(ii) Annual written assurances obtained from customers required under paragraph (b)(3) of this section; and

(5) The requirements of this subpart and subpart Q of this part apply to such produce; and

(6) An entity that provides a written assurance under §112.2(b)(3)(i) or (ii) must act consistently with the assurance and document its actions taken to satisfy the written assurance.

§112.3 What definitions apply to this part?

…

Covered produce means produce that is subject to the requirements of this part in accordance with §§112.1 and 112.2. The term "covered produce" refers to the harvestable or harvested part of the crop.

…

Produce means any fruit or vegetable (including mixes of intact fruits and vegetables) and includes mushrooms, sprouts (irrespective of seed source), peanuts, tree nuts, and herbs. A fruit is the edible reproductive body of a seed plant or tree nut (such as apple, orange, and almond) such that fruit means the harvestable or harvested part of a plant developed from a flower. A vegetable is the edible part of an herbaceous plant (such as cabbage or potato) or fleshy fruiting body of a fungus (such as white button or shiitake) grown for an edible part such that vegetable means the harvestable or harvested

part of any plant or fungus whose fruit, fleshy fruiting bodies, seeds, roots, tubers, bulbs, stems, leaves, or flower parts are used as food and includes mushrooms, sprouts, and herbs (such as basil or cilantro). Produce does not include food grains meaning the small, hard fruits or seeds of arable crops, or the crops bearing these fruits or seeds, that are primarily grown and processed for use as meal, flour, baked goods, cereals and oils rather than for direct consumption as small, hard fruits or seeds (including cereal grains, pseudo cereals, oilseeds and other plants used in the same fashion). Examples of food grains include barley, dent- or flint-corn, sorghum, oats, rice, rye, wheat, amaranth, quinoa, buckwheat, and oilseeds (*e.g.,* cotton seed, flax seed, rapeseed, soybean, and sunflower seed).

…

Appendix 2: Farms exempt from 21 CFR Part 112

Farms that grow or collect "covered produce" may nevertheless be exempt from the requirements of Part 112, if they meet certain criteria as set forth below.

Title 21: Food and Drugs

PART 112—STANDARDS FOR THE GROWING, HARVESTING, PACKING, AND HOLDING OF PRODUCE FOR HUMAN CONSUMPTION

Subpart A—General Provisions

§112.3 What definitions apply to this part?

…

Covered produce means produce that is subject to the requirements of this part in accordance with §§112.1 and 112.2. The term "covered produce" refers to the harvestable or harvested part of the crop.

…

Produce means any fruit or vegetable (including mixes of intact fruits and vegetables) and includes mushrooms, sprouts (irrespective of seed source), peanuts, tree nuts, and herbs. A fruit is the edible reproductive body of a seed plant or tree nut (such as apple, orange, and almond) such that fruit means the harvestable or harvested part of a plant developed from a flower. A vegetable is the edible part of an herbaceous plant (such as cabbage or potato) or fleshy fruiting body of a fungus (such as white button or shiitake) grown for an edible part such that vegetable means the harvestable or harvested part of any plant or fungus whose fruit, fleshy fruiting bodies, seeds, roots, tubers, bulbs, stems, leaves, or flower parts are used as food and includes mushrooms, sprouts, and herbs (such as basil or cilantro). Produce does not include food grains meaning the small, hard fruits or seeds of arable crops, or the crops bearing these fruits or seeds, that are primarily grown and processed for use as meal, flour, baked goods, cereals and oils rather than for direct consumption as small, hard fruits or seeds (including cereal grains, pseudo cereals, oilseeds and other plants used in the same fashion). Examples of food grains include barley, dent- or flint-corn, sorghum, oats, rice, rye, wheat, amaranth, quinoa, buckwheat, and oilseeds (*e.g.,* cotton seed, flax seed, rapeseed, soybean, and sunflower seed).

…

Qualified end-user, with respect to a food, means the consumer of the food (where the term consumer does not include a business); or a restaurant or retail food establishment (as those terms are defined in §1.227) that is located:

(1) In the same State or the same Indian reservation as the farm that produced the food; or

(2) Not more than 275 miles from such farm.

…

§112.4 Which farms are subject to the requirements of this part?

(a) Except as provided in paragraph (b) of this section, a farm or farm mixed-type facility with an average annual monetary value of produce (as "produce" is defined in §112.3(c)) sold during the previous 3-year period of more than $25,000 (on a rolling basis), adjusted for inflation using 2011 as the baseline year for calculating the adjustment, is a "covered farm" subject to this part. Covered farms subject to this part must comply with all applicable requirements of this part when conducting a covered activity on covered produce.

(b) A farm is not a covered farm if it satisfies the requirements in §112.5 and we have not withdrawn the farm's exemption in accordance with the requirements of subpart R of this part.

§112.5 Which farms are eligible for a qualified exemption and associated modified requirements based on average monetary value of all food sold and direct farm marketing?

(a) A farm is eligible for a qualified exemption and associated modified requirements in a calendar year if:

(1) During the previous 3-year period preceding the applicable calendar year, the average annual monetary value of the food (as defined in §112.3(c)) the farm sold directly to qualified end-users (as defined in §112.3(c)) during such period exceeded the average annual monetary value of the food the farm sold to all other buyers during that period; and

(2) The average annual monetary value of all food (as defined in §112.3(c)) the farm sold during the 3-year period preceding the applicable calendar year was less than $500,000, adjusted for inflation.

(b) For the purpose of determining whether the average annual monetary value of all food sold during the 3-year period preceding the applicable calendar year was less than $500,000, adjusted for inflation, the baseline year for calculating the adjustment for inflation is 2011.

Appendix 3: Food facility registration requirements

The following are the FDA regulations that govern which farms and other operations must register with FDA as a food processing facility.

Title 21: Food and Drugs

PART 1—GENERAL ENFORCEMENT REGULATIONS

Subpart H—Registration of Food Facilities

§1.225 Who must register under this subpart?

(a) You must register your facility under this subpart if you are the owner, operator, or agent in charge of either a domestic or foreign facility, as defined in this subpart, and your facility is engaged in the manufacturing/processing, packing, or holding of food for consumption in the United States, unless your facility qualifies for one of the exemptions in §1.226.

(b) If you are an owner, operator, or agent in charge of a domestic facility, you must register your facility whether or not the food from the facility enters interstate commerce.

(c) If you are the owner, operator, or agent in charge of a facility, you may authorize an individual to register your facility on your behalf.

§1.226 Who does not have to register under this subpart?

This subpart does not apply to the following facilities:

(a) A foreign facility, if food from such facility undergoes further manufacturing/processing (including packaging) by another facility outside the United States. A facility is not exempt under this provision if the further manufacturing/processing (including packaging) conducted by the subsequent facility consists of adding labeling or any similar activity of a *de minimis* nature;

(b) Farms;[32]

(c) Retail food establishments;

(d) Restaurants;

(e) Nonprofit food establishments in which food is prepared for, or served directly to, the consumer;

[32] Note however that if a farm performs food processing operations beyond what is permitted in the "farm" definition, the farm is classed as a "farm mixed-type facility" and is required to register as a food processing facility.

(f) Fishing vessels, including those that not only harvest and transport fish but also engage in practices such as heading, eviscerating, or freezing intended solely to prepare fish for holding on board a harvest vessel. However, those fishing vessels otherwise engaged in processing fish are subject to this subpart. For the purposes of this section, "processing" means handling, storing, preparing, shucking, changing into different market forms, manufacturing, preserving, packing, labeling, dockside unloading, holding, or heading, eviscerating, or freezing other than solely to prepare fish for holding on board a harvest vessel;

(g) Facilities that are regulated exclusively, throughout the entire facility, by the U.S. Department of Agriculture under the Federal Meat Inspection Act (21 U.S.C. 601 *et seq.*), the Poultry Products Inspection Act (21 U.S.C. 451 *et seq.*), or the Egg Products Inspection Act (21 U.S.C. 1031 *et seq.*);

§1.227 What definitions apply to this subpart?

…

Facility means any establishment, structure, or structures under one ownership at one general physical location, or, in the case of a mobile facility, traveling to multiple locations, that manufactures/processes, packs, or holds food for consumption in the United States. Transport vehicles are not facilities if they hold food only in the usual course of business as carriers. A facility may consist of one or more contiguous structures, and a single building may house more than one distinct facility if the facilities are under separate ownership. The private residence of an individual is not a facility. Nonbottled water drinking water collection and distribution establishments and their structures are not facilities.

(1) *Domestic facility* means any facility located in any State or Territory of the United States, the District of Columbia, or the Commonwealth of Puerto Rico that manufactures/processes, packs, or holds food for consumption in the United States.

(2) *Foreign facility* means a facility other than a domestic facility that manufactures/processes, packs, or holds food for consumption in the United States.

…

Appendix 4: Exemptions from 21 CFR Part 117

21 CFR Part 117 establishes good manufacturing practice regulations intended to assure food safety. However, food facilities are exempted from parts of Part 117 under certain circumstances, such as (a) if other good manufacturing practice regulations already apply; (b) if the facility is a small or very small business that is a farm mixed-type facility performing what FDA deems to be low-risk activities; or (c) if the foods involved are inherently low risk (e.g., alcoholic beverages; packaged shelf-stable foods; dried agricultural commodities).

Title 21: Food and Drugs

PART 117—CURRENT GOOD MANUFACTURING PRACTICE, HAZARD ANALYSIS, AND RISK-BASED PREVENTIVE CONTROLS FOR HUMAN FOOD
Subpart A—General Provisions

§117.3 Definitions

…

Qualified end-user, with respect to a food, means the consumer of the food (where the term consumer does not include a business); or a restaurant or retail food establishment (as those terms are defined in §1.227 of this chapter) that:

(1) Is located:

(i) In the same State or the same Indian reservation as the qualified facility that sold the food to such restaurant or establishment; or

(ii) Not more than 275 miles from such facility; and

(2) Is purchasing the food for sale directly to consumers at such restaurant or retail food establishment.

Qualified facility means (when including the sales by any subsidiary; affiliate; or subsidiaries or affiliates, collectively, of any entity of which the facility is a subsidiary or affiliate) a facility that is a very small business as defined in this part, or a facility to which both of the following apply:

(1) During the 3-year period preceding the applicable calendar year, the average annual monetary value of the food manufactured, processed, packed or held at such facility that is sold directly to qualified end-users (as defined in this part) during such period exceeded the average annual monetary value of the food sold by such facility to all other purchasers; and

(2) The average annual monetary value of all food sold during the 3-year period preceding the applicable calendar year was less than $500,000, adjusted for inflation.

…

§117.5 Exemptions

(a) Except as provided by subpart E[33] of this part, subparts C[34] and G[35] of this part do not apply to a qualified facility. Qualified facilities are subject to the modified requirements in §117.201.

(b) Subparts C and G of this part do not apply with respect to activities that are subject to part 123 of this chapter (Fish and Fishery Products) at a facility if you are required to comply with, and are in compliance with, part 123 of this chapter with respect to such activities.

(c) Subparts C and G of this part do not apply with respect to activities that are subject to part 120 of this chapter (Hazard Analysis and Critical Control Point (HACCP) Systems)[36] at a facility if you are required to comply with, and are in compliance with, part 120 of this chapter with respect to such activities.

(d)(1) Subparts C and G of this part do not apply with respect to activities that are subject to part 113 of this chapter (Thermally Processed Low-Acid Foods Packaged in Hermetically Sealed Containers) at a facility if you are required to comply with, and are in compliance with, part 113 of this chapter with respect to such activities.

(2) The exemption in paragraph (d)(1) of this section is applicable only with respect to the microbiological hazards that are regulated under part 113 of this chapter.

(e) Subparts C and G do not apply to any facility with regard to the manufacturing, processing, packaging, or holding of a dietary supplement that is in compliance with the requirements of part 111 of this chapter (Current Good Manufacturing Practice in Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements) and section 761 of the Federal Food, Drug, and Cosmetic Act (Serious Adverse Event Reporting for Dietary Supplements).

(f) Subparts C and G of this part do not apply to activities of a facility that are subject to section 419 of the Federal Food, Drug, and Cosmetic Act (Standards for Produce Safety).[37]

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[33] Subpart E establishes procedures for revoking a facility's status as a "qualified facility" that enjoys exemptions from Part 117.

[34] Subpart C establishes requirements for hazard analysis and risk-based preventive controls, similar to "HACCP" systems used by food regulators in other countries.

[35] Subpart G establishes requirements for creating a program to control the facility's supply chain.

[36] Part 120 establishes requirements for HACCP-based food safety controls in the processing of juices (e.g., fruit juice).

[37] This means that farm activities performed on covered produce at a farm mixed-type facility are exempt from Part 117 Subparts C and G.

(g)(1) The exemption in paragraph (g)(3)[38] of this section applies to packing or holding of processed foods on a farm mixed-type facility, except for processed foods produced by drying/dehydrating raw agricultural commodities to create a distinct commodity (such as drying/dehydrating grapes to produce raisins, and drying/dehydrating fresh herbs to produce dried herbs), and packaging and labeling such commodities, without additional manufacturing/processing (such as chopping and slicing), the packing and holding of which are within the "farm" definition in §1.227 of this chapter. Activities that are within the "farm" definition, when conducted on a farm mixed-type facility, are not subject to the requirements of subparts C and G of this part and therefore do not need to be specified in the exemption.

(2) For the purposes of paragraphs (g)(3) and (h)(3) of this section, the following terms describe the foods associated with the activity/food combinations. Several foods that are fruits or vegetables are separately considered for the purposes of these activity/food combinations (*i.e.,* coffee beans, cocoa beans, fresh herbs, peanuts, sugarcane, sugar beets, tree nuts, seeds for direct consumption) to appropriately address specific hazards associated with these foods and/or processing activities conducted on these foods.

(i) *Dried/dehydrated fruit and vegetable products* includes only those processed food products such as raisins and dried legumes made without additional manufacturing/processing beyond drying/dehydrating, packaging, and/or labeling.

(ii) *Other fruit and vegetable products* includes those processed food products that have undergone one or more of the following processes: acidification, boiling, canning, coating with things other than wax/oil/resin, cooking, cutting, chopping, grinding, peeling, shredding, slicing, or trimming. Examples include flours made from legumes (such as chickpea flour), pickles, and snack chips made from potatoes or plantains. Examples also include dried fruit and vegetable products made with additional manufacturing/processing (such as dried apple slices; pitted, dried plums, cherries, and apricots; and sulfited raisins). This category does not include dried/dehydrated fruit and vegetable products made without additional manufacturing/processing as described in paragraph (g)(2)(i) of this section. This category also does not include products that require time/temperature control for safety (such as fresh-cut fruits and vegetables).

(iii) *Peanut and tree nut products* includes processed food products such as roasted peanuts and tree nuts, seasoned peanuts and tree nuts, and peanut and tree nut flours.

(iv) *Processed seeds for direct consumption* include processed food products such as roasted pumpkin seeds, roasted sunflower seeds, and roasted flax seeds.

(v) *Dried/dehydrated herb and spice products* includes only processed food products such as dried intact herbs made without additional manufacturing/processing beyond drying/dehydrating, packaging, and/or labeling.

(vi) *Other herb and spice products* includes those processed food products such as chopped fresh herbs, chopped or ground dried herbs (including tea), herbal extracts (*e.g.,* essential oils, extracts containing more than 20 percent ethanol, extracts containing more than 35 percent glycerin), dried

[38] This provision (g) establishes exemptions from Subparts C and G of Part 117 for the packing and holding of certain processed foods when performed by small or very small businesses that are farm mixed-type facilities.

herb- or spice-infused honey, and dried herb- or spice-infused oils and/or vinegars. This category does not include dried/dehydrated herb and spice products made without additional manufacturing/processing beyond drying/dehydrating, packaging, and/or labeling as described in paragraph (g)(2)(v) of this section. This category also does not include products that require time/temperature control for safety, such as fresh herb-infused oils.

(vii) *Grains* include barley, dent- or flint-corn, sorghum, oats, rice, rye, wheat, amaranth, quinoa, buckwheat and oilseeds for oil extraction (such as cotton seed, flax seed, rapeseed, soybeans, and sunflower seed).

(viii) *Milled grain products* include processed food products such as flour, bran, and corn meal.

(ix) *Baked goods* include processed food products such as breads, brownies, cakes, cookies, and crackers. This category does not include products that require time/temperature control for safety, such as cream-filled pastries.

(x) *Other grain products* include processed food products such as dried cereal, dried pasta, oat flakes, and popcorn. This category does not include milled grain products as described in paragraph (g)(2)(viii) of this section or baked goods as described in paragraph (g)(2)(ix) of this section.

(3) Subparts C and G of this part do not apply to on-farm packing or holding of food by a small or very small business, and §117.201 does not apply to on-farm packing or holding of food by a very small business, if the only packing and holding activities subject to section 418 of the Federal Food, Drug, and Cosmetic Act that the business conducts are the following low-risk packing or holding activity/food combinations—*i.e.,* packing (or re-packing) (including weighing or conveying incidental to packing or re-packing); sorting, culling, or grading incidental to packing or storing; and storing (ambient, cold and controlled atmosphere) of:

(i) Baked goods (*e.g.,* bread and cookies);

(ii) Candy (*e.g.,* hard candy, fudge, maple candy, maple cream, nut brittles, taffy, and toffee);

(iii) Cocoa beans (roasted);

(iv) Cocoa products;

(v) Coffee beans (roasted);

(vi) Game meat jerky;

(vii) Gums, latexes, and resins that are processed foods;

(viii) Honey (pasteurized);

(ix) Jams, jellies, and preserves;

(x) Milled grain products (*e.g.,* flour, bran, and corn meal);

(xi) Molasses and treacle;

(xii) Oils (*e.g.,* olive oil and sunflower seed oil);

(xiii) Other fruit and vegetable products (*e.g.,* flours made from legumes; pitted, dried fruits; sliced, dried apples; snack chips);

(xiv) Other grain products (*e.g.,* dried pasta, oat flakes, and popcorn);

(xv) Other herb and spice products (*e.g.,* chopped or ground dried herbs, herbal extracts);

(xvi) Peanut and tree nut products (*e.g.,* roasted peanuts and tree nut flours);

(xvii) Processed seeds for direct consumption (*e.g.,* roasted pumpkin seeds);

(xviii) Soft drinks and carbonated water;

(xix) Sugar;

(xx) Syrups (*e.g.,* maple syrup and agave syrup);

(xxi) Trail mix and granola;

(xxii) Vinegar; and

(xxiii) Any other processed food that does not require time/temperature control for safety (e.g., vitamins, minerals, and dietary ingredients (*e.g.,* bone meal) in powdered, granular, or other solid form).

(h)(1) The exemption in paragraph (h)(3)[39] of this section applies to manufacturing/processing of foods on a farm mixed-type facility, except for manufacturing/processing that is within the "farm" definition in §1.227 of this chapter. Drying/dehydrating raw agricultural commodities to create a distinct commodity (such as drying/dehydrating grapes to produce raisins, and drying/dehydrating fresh herbs to produce dried herbs), and packaging and labeling such commodities, without additional manufacturing/processing (such as chopping and slicing), are within the "farm" definition in §1.227 of this chapter. In addition, treatment to manipulate ripening of raw agricultural commodities (such as by treating produce with ethylene gas), and packaging and labeling the treated raw agricultural commodities, without additional manufacturing/processing, is within the "farm" definition. In addition, coating intact fruits and vegetables with wax, oil, or resin used for the purpose of storage or transportation is within the "farm" definition. Activities that are within the "farm" definition, when conducted on a farm mixed-type facility, are not subject to the requirements of subparts C and G of this part and therefore do not need to be specified in the exemption.

[39] This provision (h) establishes exemptions from Subparts C and G of Part 117 for the manufacturing/processing of certain foods when performed by small or very small businesses that are farm mixed-type facilities.

(2) The terms in paragraph (g)(2) of this section describe certain foods associated with the activity/food combinations in paragraph (h)(3) of this section.

(3) Subparts C and G of this part do not apply to on-farm manufacturing/processing activities conducted by a small or very small business for distribution into commerce, and §117.201 does not apply to on-farm manufacturing/processing activities conducted by a very small business for distribution into commerce, if the only manufacturing/processing activities subject to section 418 of the Federal Food, Drug, and Cosmetic Act that the business conducts are the following low-risk manufacturing/processing activity/food combinations:

(i) Boiling gums, latexes, and resins;

(ii) Chopping, coring, cutting, peeling, pitting, shredding, and slicing acid fruits and vegetables that have a pH less than 4.2 (*e.g.,* cutting lemons and limes), baked goods (*e.g.,* slicing bread), dried/dehydrated fruit and vegetable products (*e.g.,* pitting dried plums), dried herbs and other spices (*e.g.,* chopping intact, dried basil), game meat jerky, gums/latexes/resins, other grain products (*e.g.,* shredding dried cereal), peanuts and tree nuts, and peanut and tree nut products (*e.g.,* chopping roasted peanuts);

(iii) Coating dried/dehydrated fruit and vegetable products (*e.g.,* coating raisins with chocolate), other fruit and vegetable products except for non-dried, non-intact fruits and vegetables (*e.g.,* coating dried plum pieces, dried pitted cherries, and dried pitted apricots with chocolate are low-risk activity/food combinations but coating apples on a stick with caramel is not a low-risk activity/food combination), other grain products (*e.g.,* adding caramel to popcorn or adding seasonings to popcorn provided that the seasonings have been treated to significantly minimize pathogens, peanuts and tree nuts (*e.g.,* adding seasonings provided that the seasonings have been treated to significantly minimize pathogens), and peanut and tree nut products (*e.g.,* adding seasonings provided that the seasonings have been treated to significantly minimize pathogens));

(iv) Drying/dehydrating (that includes additional manufacturing or is performed on processed foods) other fruit and vegetable products with pH less than 4.2 (*e.g.,* drying cut fruit and vegetables with pH less than 4.2), and other herb and spice products (*e.g.,* drying chopped fresh herbs, including tea);

(v) Extracting (including by pressing, by distilling, and by solvent extraction) dried/dehydrated herb and spice products (*e.g.,* dried mint), fresh herbs (*e.g.,* fresh mint), fruits and vegetables (*e.g.,* olives, avocados), grains (*e.g.,* oilseeds), and other herb and spice products (*e.g.,* chopped fresh mint, chopped dried mint);

(vi) Freezing acid fruits and vegetables with pH less than 4.2 and other fruit and vegetable products with pH less than 4.2 (*e.g.,* cut fruits and vegetables);

(vii) Grinding/cracking/crushing/milling baked goods (*e.g.,* crackers), cocoa beans (roasted), coffee beans (roasted), dried/dehydrated fruit and vegetable products (*e.g.,* raisins and dried legumes), dried/dehydrated herb and spice products (*e.g.,* intact dried basil), grains (*e.g.,* oats, rice, rye, wheat), other fruit and vegetable products (*e.g.,* dried, pitted dates), other grain products (*e.g.,* dried cereal), other herb and spice products (*e.g.,* chopped dried herbs), peanuts and tree nuts, and peanut and tree nut products (*e.g.,* roasted peanuts);

(viii) Labeling baked goods that do not contain food allergens, candy that does not contain food allergens, cocoa beans (roasted), cocoa products that do not contain food allergens), coffee beans (roasted), game meat jerky, gums/latexes/resins that are processed foods, honey (pasteurized), jams/jellies/preserves, milled grain products that do not contain food allergens (*e.g.,* corn meal) or that are single-ingredient foods (*e.g.,* wheat flour, wheat bran), molasses and treacle, oils, other fruit and vegetable products that do not contain food allergens (*e.g.,* snack chips made from potatoes or plantains), other grain products that do not contain food allergens (*e.g.,* popcorn), other herb and spice products (*e.g.,* chopped or ground dried herbs), peanut or tree nut products, (provided that they are single-ingredient, or are in forms in which the consumer can reasonably be expected to recognize the food allergen(s) without label declaration, or both (*e.g.,* roasted or seasoned whole nuts, single-ingredient peanut or tree nut flours)), processed seeds for direct consumption, soft drinks and carbonated water, sugar, syrups, trail mix and granola (other than those containing milk chocolate and provided that peanuts and/or tree nuts are in forms in which the consumer can reasonably be expected to recognize the food allergen(s) without label declaration), vinegar, and any other processed food that does not require time/temperature control for safety and that does not contain food allergens (*e.g.,* vitamins, minerals, and dietary ingredients (*e.g.,* bone meal) in powdered, granular, or other solid form);

(ix) Making baked goods from milled grain products (*e.g.,* breads and cookies);

(x) Making candy from peanuts and tree nuts (*e.g.,* nut brittles), sugar/syrups (*e.g.,* taffy, toffee), and saps (*e.g.,* maple candy, maple cream);

(xi) Making cocoa products from roasted cocoa beans;

(xii) Making dried pasta from grains;

(xiii) Making jams, jellies, and preserves from acid fruits and vegetables with a pH of 4.6 or below;

(xiv) Making molasses and treacle from sugar beets and sugarcane;

(xv) Making oat flakes from grains;

(xvi) Making popcorn from grains;

(xvii) Making snack chips from fruits and vegetables (*e.g.,* making plantain and potato chips);

(xviii) Making soft drinks and carbonated water from sugar, syrups, and water;

(xix) Making sugars and syrups from fruits and vegetables (*e.g.,* dates), grains (*e.g.,* rice, sorghum), other grain products (*e.g.,* malted grains such as barley), saps (*e.g.,* agave, birch, maple, palm), sugar beets, and sugarcane;

(xx) Making trail mix and granola from cocoa products (*e.g.,* chocolate), dried/dehydrated fruit and vegetable products (*e.g.,* raisins), other fruit and vegetable products (*e.g.,* chopped dried fruits), other grain products (*e.g.,* oat flakes), peanut and tree nut products, and processed seeds for direct consumption, provided that peanuts, tree nuts, and processed seeds are treated to significantly minimize pathogens;

(xxi) Making vinegar from fruits and vegetables, other fruit and vegetable products (*e.g.,* fruit wines, apple cider), and other grain products (*e.g.,* malt);

(xxii) Mixing baked goods (*e.g.,* types of cookies), candy (*e.g.,* varieties of taffy), cocoa beans (roasted), coffee beans (roasted), dried/dehydrated fruit and vegetable products (*e.g.,* dried blueberries, dried currants, and raisins), dried/dehydrated herb and spice products (*e.g.,* dried, intact basil and dried, intact oregano), honey (pasteurized), milled grain products (*e.g.,* flour, bran, and corn meal), other fruit and vegetable products (*e.g.,* dried, sliced apples and dried, sliced peaches), other grain products (*e.g.,* different types of dried pasta), other herb and spice products (*e.g.,* chopped or ground dried herbs, dried herb- or spice-infused honey, and dried herb- or spice-infused oils and/or vinegars), peanut and tree nut products, sugar, syrups, vinegar, and any other processed food that does not require time/temperature control for safety (*e.g.,* vitamins, minerals, and dietary ingredients (*e.g.,* bone meal) in powdered, granular, or other solid form);

(xxiii) Packaging baked goods (*e.g.,* bread and cookies), candy, cocoa beans (roasted), cocoa products, coffee beans (roasted), game meat jerky, gums/latexes/resins that are processed foods, honey (pasteurized), jams/jellies/preserves, milled grain products (*e.g.,* flour, bran, corn meal), molasses and treacle, oils, other fruit and vegetable products (*e.g.,* pitted, dried fruits; sliced, dried apples; snack chips), other grain products (*e.g.,* popcorn), other herb and spice products (*e.g.,* chopped or ground dried herbs), peanut and tree nut products, processed seeds for direct consumption, soft drinks and carbonated water, sugar, syrups, trail mix and granola, vinegar, and any other processed food that does not require time/temperature control for safety (*e.g.,* vitamins, minerals, and dietary ingredients (*e.g.,* bone meal) in powdered, granular, or other solid form);

(xxiv) Pasteurizing honey;

(xxv) Roasting and toasting baked goods (*e.g.,* toasting bread for croutons);

(xxvi) Salting other grain products (*e.g.,* soy nuts), peanut and tree nut products, and processed seeds for direct consumption; and

(xxvii) Sifting milled grain products (*e.g.,* flour, bran, corn meal), other fruit and vegetable products (*e.g.,* chickpea flour), and peanut and tree nut products (*e.g.,* peanut flour, almond flour).

(i)(1) Subparts C and G of this part do not apply with respect to alcoholic beverages at a facility that meets the following two conditions:

(i) Under the Federal Alcohol Administration Act (27 U.S.C. 201 *et seq.*) or chapter 51 of subtitle E of the Internal Revenue Code of 1986 (26 U.S.C. 5001 *et seq.*) the facility is required to obtain a permit from, register with, or obtain approval of a notice or application from the Secretary of the Treasury as a condition of doing business in the United States, or is a foreign facility of a type that would require such a permit, registration, or approval if it were a domestic facility; and

(ii) Under section 415 of the Federal Food, Drug, and Cosmetic Act the facility is required to register as a facility because it is engaged in manufacturing, processing, packing, or holding one or more alcoholic beverages.

(2) Subparts C and G of this part do not apply with respect to food that is not an alcoholic beverage at a facility described in paragraph (i)(1) of this section, provided such food:

(i) Is in prepackaged form that prevents any direct human contact with such food; and

(ii) Constitutes not more than 5 percent of the overall sales of the facility, as determined by the Secretary of the Treasury.

(j) Subparts C and G of this part do not apply to facilities that are solely engaged in the storage of raw agricultural commodities (other than fruits and vegetables) intended for further distribution or processing.

(k)(1) Except as provided by paragraph (k)(2) of this section, subpart B[40] of this part does not apply to any of the following:

(i) "Farms" (as defined in §1.227 of this chapter);

(ii) Fishing vessels that are not subject to the registration requirements of part 1, subpart H of this chapter in accordance with §1.226(f) of this chapter;

(iii) Establishments solely engaged in the holding and/or transportation of one or more raw agricultural commodities;

(iv) Activities of "farm mixed-type facilities" (as defined in §1.227 of this chapter) that fall within the definition of "farm"; or

(v) Establishments solely engaged in hulling, shelling, drying, packing, and/or holding nuts (without additional manufacturing/processing, such as roasting nuts).

(2) If a "farm" or "farm mixed-type facility" dries/dehydrates raw agricultural commodities that are produce[41] as defined in part 112 of this chapter to create a distinct commodity, subpart B of this part applies to the packaging, packing, and holding of the dried commodities. Compliance with this requirement may be achieved by complying with subpart B of this part or with the applicable requirements for packing and holding in part 112 of this chapter.

[40] Subpart B establishes basic requirements for food processing facilities, equipment, personnel, etc.

[41] Note that this establishes a requirement applicable to all produce, not just "covered produce" as defined in Part 112.

§117.7 Applicability of subparts C, D,[42] and G of this part to a facility solely engaged in the storage of unexposed packaged food.

(a) Applicability of subparts C and G. Subparts C and G of this part do not apply to a facility solely engaged in the storage of unexposed packaged food.

(b) Applicability of subpart D. A facility solely engaged in the storage of unexposed packaged food, including unexposed packaged food that requires time/temperature control to significantly minimize or prevent the growth of, or toxin production by, pathogens is subject to the modified requirements in §117.206 for any unexposed packaged food that requires time/temperature control to significantly minimize or prevent the growth of, or toxin production by, pathogens.

§117.8 Applicability of subpart B of this part to the off-farm packing and holding of raw agricultural commodities.

Except as provided by §117.5(k)(1), subpart B of this part applies to the off-farm packaging, packing, and holding of raw agricultural commodities. Compliance with this requirement for raw agricultural commodities that are produce as defined in part 112 of this chapter may be achieved by complying with subpart B of this part or with the applicable requirements for packing and holding in part 112 of this chapter.

[42] Subpart D sets forth simplified requirements for certain types of operations.

Appendix 5: Sources of specifications and test methods

Appropriate specifications and/or test methods for botanical materials are available from a variety of sources.

Compendia

American Herbal Pharmacopoeia

The American Herbal Pharmacopoeia® began developing qualitative and therapeutic monographs in 1994, and produces monographs on botanicals, including many of the Ayurvedic, Chinese and Western herbs most frequently used in the United States. These monographs represent the most comprehensive and critically reviewed body of information on herbal medicines in the English language, and serve as a primary reference for academicians, health care providers, manufacturers, and regulators.
http://www.herbal-ahp.org/

British Herbal Compendium

Published by the British Herbal Medicine Association (BHMA) Scientific Committee, the British Herbal Compendium is a two volume publication containing monographs which offer authoritative summaries of Constituents (with phytochemical structure diagrams) and Therapeutics, copiously referenced to worldwide scientific literature, together with a section on Regulatory Status and excerpts from French guidelines and German Commission E monographs.
More information about Vol. 1 (1992) is available at http://bhma.info/index.php/british-herbal-compendium-vol-1/.
More information about Vol. 2 (2006) is available at http://bhma.info/index.php/british-herbal-compendium-vol-2/.

British Herbal Pharmacopoeia (1996)

Published by the BHMA, the British Herbal Pharmacopoeia Monographs of the British Herbal Pharmacopoeia (BHP) provide quality standards for 169 herbal raw materials – basically those listed for the two volumes of the British Herbal Compendium plus six others.
Those herbs official in the European Pharmacopoeia or British Pharmacopoeia at the time of publication are covered by abbreviated monographs in this volume. Subsequent work by the European Pharmacopoeia Commission (Council of Europe) has led to the introduction of many more herbal monographs in the European Pharmacopoeia.

More information about the British Herbal Pharmacopoeia is available at
http://bhma.info/index.php/british-herbal-pharmacopoeia-1996/.

European Pharmacopoeia

The European Pharmacopoeia (Ph. Eur.) is Europe's legal and scientific benchmark for pharmacopoeial standards which contribute to delivering high quality medicines in Europe and beyond. The Ph. Eur. is applicable in 37 European countries and used in over 100 countries worldwide.

More information about the European Pharmacopoeia 10th edition (2019) is available at https://www.edqm.eu/en/european-pharmacopoeia-ph-eur-10th-edition

United States Pharmacopeia – National Formulary (USP-NF)

The United States Pharmacopeia and The National Formulary (USP–NF) is a book of public pharmacopeial standards for chemical and biological drug substances, dosage forms, compounded preparations, excipients, medical devices, and dietary supplements. USP–NF is a combination of two compendia, the United States Pharmacopeia (USP) and the National Formulary (NF). Monographs for drug substances, dosage forms, and compounded preparations are featured in the USP. Monographs for dietary supplements and ingredients appear in a separate section of the USP. Excipient monographs are in the NF.

More information about the USP-NF is available at http://www.usp.org/usp-nf.

Food Chemicals Codex

The Food Chemicals Codex (FCC) is a compendium of internationally recognized standards for the purity and identity of food ingredients published by the U.S. Pharmacopoeial Convention (USP). It features over 1,200 monographs, including food-grade chemicals, processing aids, foods (such as vegetable oils, fructose, whey, and amino acids), flavoring agents, vitamins, and functional food ingredients (such as lycopene, olestra, and short chain fructooligosaccharides).

More information about the FCC is available at https://www.foodchemicalscodex.org/.

Official Methods of Analysis of AOAC International

AOAC International is an independent, third-party, nongovernment association of international industry organizations, government agencies, research institutions, and individual scientists. AOAC's Official Methods of Analysis is an international source of methods, with many countries and organizations contributing their expertise to standards development and method validation. The Official Methods of Analysis is the most comprehensive and reliable collection of chemical and microbiological methods available in the world and are contained in many of the Codex food standards.

More information about AOAC International's Official Methods of Analysis is available at http://www.eoma.aoac.org/.

Pharmacopoeia of the People's Republic of China (2015)

Compiled by the Pharmacopoeia Commission of the Ministry of Public Health, the Chinese Pharmacopoeia (CP) covers 784 medicinal herbs, plant oils, and Chinese formulated medicines and 967 western medicines and preparations. The 2015 edition of CP was adopted at the plenary session of the Executive Committee of the Tenth Chinese Pharmacopoeia Commission. On June 5, 2015, China Food

and Drug Administration (CFDA) promulgated the 2015 edition of Chinese Pharmacopoeia, which went into effect on December 1, 2015.
English editions of the CP are available through on-line retailers.

Books

American Herbal Pharmacopeia, (2011). Microscopic Characterization of Botanical Medicines. BocaRaton. FL: CRC Press.

Reich, E. and Schibli, A. (2007) High-Performance Thin-Layer Chromatography for the Analysis of Medicinal Plants. New York, NY: Thieme Medical Publishers Inc.

Wagner, H. and Bladt, S. (1996) Plant Drug Analysis. Berlin, Germany: Springer-Verlag.

Wichl, M. (2004) Herbal Drugs and Phytopharmaceuticals. Boca Raton, FL: CRC Press.

Online resources

AHPA's Botanical ID References Compendium

The AHPA Botanical Identity References Compendium is maintained by AHPA and was developed by AHPA with the support of many individuals and organizations with a common interest in sharing knowledge and resources relevant to accurate identification of herbal materials.

The AHPA Compendium is a cooperative and centralized source of information on physical characteristics and test methods that can be used by qualified and experienced analysts to determine the identity of plant species and articles of trade obtained from these plants.
http://www.botanicalauthentication.org/index.php/Main_Page

Appendix 6: Other good agricultural practice guidelines

Other documents that have been valuable in the process of preparing and reviewing this work are referenced here.

European Herb Growers Association (EUROPAM)
Guidelines for Good Agricultural and Wild Collection Practices for Medicinal and Aromatic Plants (GACP-MAP), No. 7.3 (2019)
https://www.europam.net/documents/

European Medicines Agency's Working Party on Herbal Medicinal Products and the Committee on Herbal Medicinal Products
Guideline on Good Agricultural and Collection Practice for Starting Materials of Herbal Origin, (2006)
https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-agricultural-collection-practice-gacp-starting-materials-herbal-origin_en.pdf.

FairWild Foundation
International Standards for Sustainable Wild Collection of Medicinal and Aromatic Plants (ISSC-MAP) (2007)
https://www.wwf.de/fileadmin/fm-wwf/Publikationen-PDF/Standard_Version1_0.pdf

Global G.A.P.
General Regulations – Part 1, General Rules (2019)
https://www.globalgap.org/.content/.galleries/documents/190201_GG_GR_Part-I_V5_2_en.pdf

Tea and Herbal Infusions Europe (formerly the European Herbal Infusions Association)
Guidelines for Good Agricultural and Hygiene Practices for Raw Materials Used for Herbal and Fruit Infusions (*GAHP*) (2018)
https://thie-online.eu/files/thie/docs/2018-09_PU_GAHP_Version_9.pdf.

World Health Organization
WHO Guidelines on Good Agricultural and Collection Practices (GACP) for Medicinal Plants. (2003)
http://apps.who.int/iris/bitstream/10665/42783/1/9241546271.pdf.

Appendix 7: Preparation of voucher specimens

by Wendy Applequist, Ph.D., Missouri Botanical Garden

A "voucher" is a specimen that documents the identity of plant material observed or collected at a particular place, at a particular time. The ideal voucher specimen is composed of plant material which preserves an intact plant or portion of the plant, including leaves and any reproductive structures present at the time of collection. Preparation of a voucher specimen has four steps: collection of the material to be preserved; arranging the material in a plant press; drying it; and mounting it.

First, purchase or make a plant press. A homemade press may be made by assembling two lattices of narrow wooden lath about ¼" thick, with four parallel 18" strips overlaid by five parallel 12" strips and solidly attached at the intersections. An alternative is to use two pieces of solid plywood with a grid of large holes drilled to permit some airflow; these are much heavier and less desirable. The press should contain a small stack of 12" by 18" pieces of corrugated cardboard; folded single-page sheets of newspaper will also be needed, and if possible, some 12" by 18" blotters or pieces of felt. A pair of sturdy buckled straps are needed to hold the press together.

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1. ***Collection of material***

   For preparation of voucher specimens, the material to be preserved should fit on standard-sized voucher sheets (most frequently 16.5" by 11.5"). If the species to be collected is a small herbaceous plant, collect a whole plant for each sheet, or even multiple plants per sheet if they are tiny. Bend a tall single-stemmed plant into a V or N shape to allow it to fit on a sheet. If the plants are large, cut portions that adequately represent the aboveground parts present, including, for example, a stem portion with small leaves, a large leaf, and an inflorescence. If a variety of developmental stages are present, add a fragment with developing fruits to a flowering specimen or vice versa. For small herbs, include the root (with soil removed); for trees, it is desirable to include a piece of bark. Slice thick organs (e.g., large fruits or roots) before pressing; separately preserve large hard structures that cannot be sliced. For plants with large parts, e.g., palms, it may be necessary to collect only portions of a plant organ and to prepare more than one sheet's worth of material from each plant. Specific guidance on how to prepare specimens from difficult plants is available in the Missouri Botanical Garden's guide to field procedures: http://www.mobot.org/MOBOT/molib/fieldtechbook/welcome.shtml.

   Take field notes at the time of collection. These should include the collectors' names, the date, the exact locality (with altitude if known), and the habitat type (e.g., forest, cultivated field), together with any morphological data that will not be visible in the finished specimen (e.g., height of a large plant, whether a large herb is branched, flower color).

2. ***Pressing***

   For some species, a delay in pressing will lead to a deterioration of the material. Have a plant press handy and at least place the material in the press temporarily, after which final specimen arrangement may be delayed for hours. Place the material for each specimen in a sheet of

newspaper and mark the outside of the sheet with the collection number. Place the specimens between sheets of corrugated cardboard in the press, then put the straps on the press. Orient all sheets of newspaper in the same direction so that the press can be set on edge with all folded edges downwards (so that loose bits do not fall out of the open side).

After material has been in the press for a few hours, it will have relaxed somewhat and may be easier to arrange into the final shape desired for it. Numerous layers of overlapping branches, leaves, etc. are not desirable, as they impede drying and the lower layers are not visible. If the specimen is too big or has too much overlapping material, trim off some side branches, leaves, etc. Leave a small stub, if possible, to show where material was removed. Spread out remaining parts to display the material to best advantage. If necessary, material can be dried in two newspaper sheets and overlapped on a single voucher sheet later (e.g., a large leaf and a separate inflorescence). Ensure that both leaf surfaces are visible by twisting a branch or individual leaves, or folding over one edge of a single large leaf; multiple views of large flowers are also desirable. After the material has been finally arranged, sandwich each newspaper sheet between two pieces of blotter paper or felt (or, if blotters are not available, two sections of several sheets of newspaper) and then between pieces of cardboard. Close the press as tightly as possible; lean on the press or have someone stand on it to compress it while pulling on the straps.

3. Drying

To avoid molding, moisture needs to be removed as quickly as possible. A variety of means have been devised to speed drying of pressed samples by encouraging the flow of air, preferably warm, through the press. If an electric plant press dryer is not available, the press may be suspended over almost any source of warmth, such as a heat lamp; use caution, as material will be damaged by too-intense heat and even more so by catching on fire! Place the press on its side with the folded edge of the newspapers down and the open long edge up, so that air can flow through the corrugated cardboards in the press. Airflow through the press may be increased by placing it in front of a fan or even tying it to the roof of a field vehicle. Change blotters regularly (every day for very fleshy plants) and retighten the press straps, as material will shrink on drying. If no artificial means of drying is available, keep the press in a warm, low-humidity, well-ventilated place and change the blotters or extra pieces of newspaper frequently (if possible, twice per day). Continue drying until even the thickest portions of material are not at all flexible. Dry out damp blotters before stacking and storing them, or they may mold.

4. Mounting

Attach dried specimens to a sheet of heavy stock with dots of white glue or strips of mounting tape. Standard-size voucher sheets can be purchased; if material is to be preserved indefinitely, the use of acid-free paper is essential. Use glue or tape only as necessary to fix the specimen in place, preferentially on any stem portions in direct contact with the paper. It is not necessary to coat the whole specimen in glue; avoid gluing or taping flowers and leaves directly. Weight down glued specimens until the glue dries. Leave room on the sheet for a label providing the field data recorded at the time of collection; this is traditionally placed in the lower right corner and should be made

from archival-quality, acid-free paper. Place any small loose fragments such as detached fruits into a small paper envelope folded out of acid-free paper and glue it to a convenient empty spot on the sheet.

Appendix 8 Prevention and reduction of pyrrolizidine alkaloid (PA) contamination

Background

This Appendix provides information and resources to support specific actions that can be taken by crop growers, botanical material suppliers, and finished product manufacturers to prevent the inadvertent presence of pyrrolizidine alkaloids (PAs) in botanical crops intended for use in human food (including dietary supplements) or animal feed.

Pyrrolizidine alkaloids are a group of naturally-occurring compounds based on the pyrrolizidine ring structure. The occurrence of these compounds is common in several plant families, and more than 600 PA and PA oxide compounds have been identified in over 6000 plant species. The plant families most commonly containing PAs include Asteraceae, Fabaceae, and Boraginaceae, and PA containing species can also be found in the Orchidaceae, Convolvulaceae, and Lamiaceae families. Many of these plants are noxious, invasive weeds that are widespread in agricultural areas, pastures, and along roadsides, etc. [43]

PAs may be present in food or feed in the following ways:

- Incidental co-harvesting of PA-containing plants while harvesting a target botanical that results in PA contamination of the target botanical raw material, and the subsequent ingredients and products derived from it.
- Direct consumption of a botanical or part of a botanical in which PAs are naturally occurring, or of a product derived from such a botanical, in the absence of sufficient processing controls to reduce the level of PAs to an acceptable level; some examples of such plants include comfrey (*Symphytum officinale*) and borage (*Borago officinalis*).
- Uptake of PAs from soil contaminated by PA-containing plants and contact with pollen from PA-containing plants, [44] although the significance of these routes to contamination of botanical crops used for food and feed is not clear.

This guidance is intended to address the prevention and reduction of the inadvertent presence of PAs in food crops, and not the direct use or consumption of botanicals in which PAs are naturally occurring. Co-harvesting even a small number of PA-containing weeds with a botanical intended to be used for food or feed can be sufficient to contaminate the crop with PAs at levels of concern for chronic human exposure.

[43] Some of the most common species are listed in the Food Supplements Europe document *Guidelines and recommendations to reduce the presence of pyrrolizidine alkaloids in food supplements*.

[44] See Nowak M, Wittke C, Lederer I, Klier B, Kleinwächter M, Selmar D. Interspecific transfer of pyrrolizidine alkaloids: An unconsidered source of contaminations of phytopharmaceuticals and plant derived commodities. *Food Chem*. 2016 Dec 15;213:163-168 and Selmar D, Wittke C, Beck-von Wolffersdorff I, Klier B, Lewerenz L, Kleinwächter M, Nowak M. Transfer of pyrrolizidine alkaloids between living plants: A disregarded source of contaminations. *Environ Pollut*. 2019 May;248:456-461.

The primary concern for the presence of PA compounds in food and feed is the significant toxicity associated with many of these compounds, particularly those that are unsaturated in structure (having one or more double chemical bonds), which increases the chemical reactivity of the compound. Some PA compounds have been shown to be hepatotoxic, as well as genotoxic and carcinogenic.[45]

Regulation of pyrrolizidine alkaloids in botanicals

To date, several regulatory actions have been taken to help consumers avoid the ingestion of unsafe levels of PAs in articles of food or supplement products. Individual countries have taken the following actions.

In Germany, since 1992 the Federal Department of Health has restricted the use of botanical products containing PAs to 6 weeks at an intake of less than 1 µg/day; more prolonged usage should be at a limit of 0.1 µg/day.[46] In the United States, the US Food and Drug Administration (US FDA) issued an advisory in 2001 to the dietary supplement industry to remove products containing common comfrey (*Symphytum officinale), prickly* comfrey (*S*. *asperum*), and Russian comfrey (*S*. × *uplandicum*) from the market.[47] Both of these regulations address the direct consumption of PA-containing plants as dietary supplements or medicinal products.

In December 2020, the European Commission (EC) adopted a regulation containing specific maximum levels for the occurrence of PAs in a variety of botanical foodstuffs, including food supplements and teas.[48] This regulation is intended to address the inadvertent presence of PAs in botanical products through the co-harvesting of PA-containing weeds. Compliance will be based on analysis for 35 PAs specified in the regulation and the sum of detected levels as compared to the maximum level of PA content for the defined food category. The development of the regulation follows the release of the European Food Safety Authority (EFSA) scientific opinion on PAs in food and feed in 2011[49] and an assessment of dietary exposures to PAs in the European population released in 2016.[50]

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[45] Moreira R, Pereira DM, Valentão P, Andrade PB. Pyrrolizidine Alkaloids: Chemistry, Pharmacology, Toxicology and Food Safety. *Int J Mol Sci*. 2018;19(6):1668.

[46] German Federal Department of Health Bureau. Bundesanzeiger. Dtsch. Apoth. Ztg. 1992, 132, 1406–1408.

[47] Food and Drug Administration. FDA Advises Dietary Supplement Manufacturers to Remove Comfrey Products from the Market; FDA Office of Nutritional Products, Labeling, and Dietary Supplements; Center for Food Safety and Applied Nutrition: College Park, MD, USA, 2001.

[48] Details on the European Commission "Amending Regulation (EC) No 1881/2006 as regards maximum levels of pyrrolizidine alkaloids in certain foodstuffs" and the Annex of maximum levels for each foodstuff can be found here: https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32020R2040&rid=1.

[49] *Scientific opinion on Pyrrolizidine alkaloids in food and feed*. European Food Safety Authority, 2011. Accessed at https://efsa.onlinelibrary.wiley.com/doi/abs/10.2903/j.efsa.2011.2406.

[50] *Dietary exposure assessment to pyrrolizidine alkaloids in the European population*. European Food Safety Authority, 2016. Accessed at https://efsa.onlinelibrary.wiley.com/doi/10.2903/j.efsa.2016.4572.

The regulatory limits established by the EC are specific to several food product categories, for example:

- 400 µg/kg (ppb) for food/dietary supplements
- 150 µg/kg (ppb) for flavored tea and tea (*Camellia sinensis*)
- 200 µg/kg (ppb) for other herbal infusions
- 500 µg/kg (ppb) for pollen-based food supplements and other pollen-based foods

The implementation date for this regulation is July 1, 2022; product manufactured prior to this date may remain in the European market until December 31, 2023.

Some of the challenges to demonstrating compliance to these thresholds is the lack of validated analytical methods for all of the PAs listed in the regulation and the lack of formal recognition for analytical methods used for testing PAs, as well as the relatively high cost. USP[51] is working to develop resources such as an Informational General Chapter on pyrrolizidine alkaloids and a General Chapter on analysis of contaminant PAs that may assist marketers with analytical issues.

Botanical supply chain responsibility for prevention of PA contamination

The prevention of inadvertent PA contamination in botanical products is the collective responsibility of each entity in the botanical supply chain and requires cooperative action at each stage.

As previously stated, many of the PA-containing plants are noxious, invasive weeds that are commonly found in agricultural areas, pastures, and other areas where the soil has been disturbed. Effective measures taken to control PA-contamination of crops at the cultivation stage are critical, as it becomes much more difficult to control or remove PA contamination as the botanical material is harvested and processed into ingredients and finished products. The ultimate responsibility to comply with any regulatory limits for PA contamination in finished products belongs to the finished product marketer. As botanicals move from the field to manufacturing facilities, responsible entities in the supply chain should institute the use of risk assessments, specifications, process controls, and testing that serve to identify and minimize PA contamination.

Table 1 below provides an overview of general considerations and recommended practices that can be implemented at each stage of the botanical supply chain to prevent or reduce PA contamination of crops and finished products. Multiple guidance documents and codes of practice have been developed to provide additional detailed information about prevention of PA contamination in botanical materials and are listed here (links accurate as of the date of publication):

[51] US Pharmacopoeia is developing <1567> Informational General Chapter: Pyrrolizidine Alkaloids as Contaminants (see https://www.uspnf.com/notices/1567-gc-prospectus-20200731) and <567> General Chapter: Analysis of Contaminant Pyrrolizidine Alkaloids (PAs).

***Guidelines and recommendations to reduce the presence of pyrrolizidine alkaloids in food supplements*. Food Supplements Europe, 2020.**
https://foodsupplementseurope.org/wp-content/themes/fse-theme/documents/publications-and-guidelines/Pyrrolizidine_Guidelines-June2020.pdf

This detailed guidance provides recommendations for the responsibilities of both growers and processors with the intention of preparing for the European Commission regulations coming into force. It contains a useful Annex of common plants that contain PAs with descriptions and color images consisting of the following species:
Anchusa arvensis L.
Borago officinalis L.
Cynoglossum officinale L.
Echium vulgare L.
Eupatorium cannabinum L.
Heliotropium europaeum L.
Leucanthemum vulgare Lam.
Lithospermum arvense L.
Myosotis arvensis (L.) Hill.
Myosotis stricta Link ex Roem. & Schult.
Petasites hybridus (L.) G. Gaertn., B. Mey. & Scherb.
Pulmonaria officinalis L.
Senecio erucifolius L.
Senecio inaequidens DC.
Senecio jacobaea L.
Senecio nemorensis L.
Senecio viscosus L.
Senecio vulgaris L.
Symphytum asperum Lepech.
Symphytum officinale L.
Symphytum × *uplandicum* Nyman (hybrid between S.asperum and S.officinale)
Tussilago farfara L.

***Code of Practice zur Vermeidung und Verringerung der Kontamination pflanzlicher Nahrungsergänzungsmittel mit Pyrrolizidinalkaloiden.* AK NEM, 2019. [in German]**

(Code of Practice to Prevent and Reduce Contamination of Herbal Supplements with Pyrrolizidine Alkaloids)
https://www.lebensmittelverband.de/de/verband/organisation/arbeitskreis-nahrungsergaenzungsmittel-ak-nem/code-of-practice-cop-pyrrolizidinalkaloide-pa-nahrungsergaenzungsmittel-nem

This German Code of Practice is directed towards supplement manufacturers and provides recommended procedures for reducing PA contamination from the manufacturing perspective. It contains an Appendix for assessing risks throughout the botanical supply chain, and suggested practices for controlling those risks.

***Code of Practice to Prevent and Reduce Pyrrolizidine Alkaloid Contamination in Raw Materials for Tea and Herbal Infusions*. Tea and Herbal Infusions Europe, 2018.**
https://www.thie-online.eu/fileadmin/inhalte/Publications/THFI/2018-07-12_THIE_Code_of_Practice_PA_in_TEA-HFI_ISSUE_1.pdf

This detailed guidance is directed toward weed management practices for the reduction of PA contamination in raw materials used to produce teas and herbal effusion products, however, most of the recommended practices are applicable for reduction of PA contamination in other botanical products as well. It contains an Annex with detailed suggested practices to be implemented throughout the supply chain for tea and herbal infusion raw materials.

***Code of Practice for weed control to prevent and reduce pyrrolizidine alkaloid contamination in food and feed*. Codex Alimentarius, 2014.**
http://www.fao.org/home/search/en/?q=pyrrolizidine%20alkaloids

This Code of Practice provides general guidance for the avoidance of PA contamination in food and feed. It describes the general risk assessment process and recommended agricultural management practices for reducing PA contamination.

Table 1. Recommended practices to prevent or reduce pyrrolizidine alkaloid contamination in botanical materials

Process stage	Responsibility	Practice recommendations and considerations
Cultivation: planning	Grower	Conduct a risk characterization of the growing environment. Assess overall risk by the type of botanical being cultivated – e.g., leafy green botanicals and those that are low-growing and machine-harvested crops may be at highest risk of contamination with PA weeds during harvest. Assess risk by proximity to any known local areas of PA-containing weeds. Develop an integrated weed management system from this information to be used during cultivation. Consider soil testing for PAs to determine extent of prior contamination of the growing area.
Cultivation: seed procurement	Grower, seed supplier	Prevent or limit contamination of seed with PA containing weed seeds (level of risk depends on nature of the plant). Consider technological limits to seed cleaning that may impact effectiveness. Consider using certified seed sources.
Cultivation: cultivation process	Grower, local authorities, etc.	Education and training of growers is essential; dissemination of information on identification of PA containing weeds prevalent in local growing area. Determine level of risk based on the likelihood and proximity of any PA-containing weeds spreading to the cultivated land.
Cultivation: pre-harvest	Grower	Implementation of integrated weed management using agricultural, mechanical, and chemical methods to prevent and control PA-containing weeds. Use appropriate handling and disposal of any material contaminated with PA-containing weeds to prevent continued spread. Avoid contamination in the cultivation area by cleaning clothing, equipment, transport vehicles (tires), etc.
Harvest	Grower	Compliance with GACP harvest practices. Optimize machine harvesting techniques, such as adjusting cutting height to avoid inclusion of weeds.
Post-harvest: inspection and preparation of plant material	Grower, botanical supplier	Remove PA-containing weeds during cleaning and drying of harvested crops, although it is highly personnel intensive and difficult to eliminate all contamination at this stage. Handle and dispose of any material contaminated with PA-containing weeds in an appropriate fashion.
Cross-contamination with PA-containing botanical material during further processing stages	Raw material processor, extractor, manufacturer	Assess risks according to the botanical used and its source; risk of cross-contamination should be low and can be avoided by implementing GMP process controls and careful cleaning and maintenance of processing and manufacturing equipment.

Process stage	**Responsibility**	**Practice recommendations and considerations**
Extract production	Extractor, finished product manufacturer	Assess risk and establish specifications for possible PA contamination for incoming plant material intended for extraction. Perform inspections of incoming botanical raw material. Test finished extract for detectable levels of PAs and compliance with any applicable regulations for intended market.
Production of food/food supplement from botanical ingredient	Finished product manufacturer	Assess risk and establish specifications of possible PA contamination for incoming botanical ingredients. Test finished product for detectable levels of PAs and compliance with any applicable regulations for intended market.