BQ2. Botanical identity and quality

Botanical identity and quality must be assured throughout the growing, harvesting, post-harvest handling, and further processing of botanical materials. Improper or careless practices at any stage may result in material that is misidentified, adulterated, or that fails to meet the necessary specifications.

BQ2.1 General considerations

i. All steps in the production of a botanical material must be performed properly to ensure the quality of the resulting finished material. This includes everything from site location and cultivation, to harvest, to post-harvest steps such as washing, cutting, dehydrating, packaging, storing, and transporting.

ii. Written specifications. Appropriate written specifications should be established for botanical materials, either by the buyer, the seller, or both. Such specifications should address the various criteria set forth in the sections below with respect to identity, physical and chemical characteristics, and potential contaminants, to the extent applicable to the buyer’s or seller’s needs.

1. Specifications for raw materials and ingredients to be used in manufacturing should be developed taking into account the effect of the processing on the characteristic in question. For example, an extraction process may serve to either concentrate or remove a contaminant, and the allowed level of the contaminant in the crude botanical should be adjusted accordingly. Similarly, a manufacturing process may serve to destroy microorganisms in the botanical material, which may obviate the need to control for pathogens in the raw material.

2. Specifications for finished processed products should take into account the intended use of the product (e.g., whether it will be used for consumer products or rather will be used for agricultural or industrial purposes; whether it will be further processed by another company or whether it will be sold directly to consumers; etc.).

iii. Sources of information. Recommended specifications and test methods for many botanical materials are provided in pharmacopoeial monographs and other compendia. See also Appendix 5.

iv. Sampling. Tests and examinations for botanical materials must be performed on samples that are properly representative. Crude botanicals, in particular, must be sampled with close attention to their inherent heterogeneity. Many pharmacopoeia provide guidelines for proper sampling of botanical materials.[[1]](#footnote-1)

v. Botanical materials must meet all representations made in labels and labeling, specification documents, certificates of analysis, guarantees, written agreements, and other documentation, not only with respect to test results but also with respect to identity, grade (e.g., organic, Kosher, or USP[[2]](#footnote-2)), form (e.g., whole, powder, extract), locations of harvest and/or processing, dates of harvest and/or processing, and all other representations made regarding the material.

BQ2.2 Identity

i. Any material offered as a particular genus, species, subspecies, variety, cultivar, hybrid, or other lesser division of a species must in fact be that exact taxon.

ii. The botanical identity of each botanical material should be documented with as much specificity as appropriate.

1. In general, the scientific name (genus, species (if applicable and relevant), subspecies/variety (if applicable and relevant), and author (if necessary for clarity) of each plant material should be documented.[[3]](#footnote-3)

2. In some cases, identification to the genus level is sufficient. For example, geranium species used to make geranium oil are commonly used interchangeably and are often labeled in commerce as “geranium,” so the scientific name for such materials need only be documented as “*Pelargonium* spp.”[[4]](#footnote-4) Similarly, cinnamon species are often used interchangeably and are often labeled in commerce simply as “cinnamon,” in which case the scientific name need only be documented as “*Cinnamomum* spp.”[[5]](#footnote-5)

3. The local ethnic name and standard English common name (where available) may also be recorded.[[6]](#footnote-6)

4. Other information, such as the cultivar or hybrid name, ecotype, chemotype or phenotype, may be recorded if applicable and relevant.

5. In the case of materials represented as belonging to a landrace grown or collected in a specific region, records should be kept of the locally named line, including the source of the original seeds, plants or propagation materials if known.

iii. The highest standard for identification of botanical species is examination by an expert (e.g., botanist, pharmacognosist, or other person with appropriate training) of the plant’s morphologic characteristics.

1. Information regarding the morphologic features of various plant species is available in various pharmacopoeia, material medicas, floras, taxonomic keys, and other compendia and authoritative references.[[7]](#footnote-7) Authenticated reference or herbarium samples may also be used for comparison. In some cases, authenticated live plants may be found growing at universities and public gardens, and it may be possible to obtain specimens for comparison from such sources.

2. Morphologic identification may require examination of the flower or fruit morphology, in which case (if the flower or fruit is not the article of commerce) the plant should be properly identified by a person having access to the plant while in flower or fruit, either *in situ* at the harvest site or in the form of a voucher specimen or other reference specimen.

3. The identification should be documented with detailed descriptions of the organoleptic, macroscopic, and microscopic characteristics observed, along with drawings, photographs, and/or photomicrographs for future reference.

4. Where potential adulterating species are known, the presence or absence of features characteristic of the adulterant should be documented.

iv. Additional evidence of identity may be developed by a number of other means.

1. Chemical fingerprinting may be performed using various kinds of chromatography (e.g., TLC, HPTLC, HPLC, GC[[8]](#footnote-8)) to confirm the presence of peaks or bands that are diagnostic of the correct species and/or to confirm any diagnostic relative intensities or ratios between peaks. The fingerprint of an authentic specimen may also be compared to that of the test sample.[[9]](#footnote-9),[[10]](#footnote-10) Furthermore, fingerprints of the test sample may be used to demonstrate the absence of bands or peaks characteristic of an adulterant or substitute. A printout or photograph of the resulting fingerprint(s) should be maintained on file for future reference.

2. DNA analysis may be performed where applicable, such as DNA barcoding or other techniques.[[11]](#footnote-11) A photograph of the resulting DNA barcode or fingerprint should be maintained on file for future reference; alternately, results may be printed from software that reduces the data to a number that quantifies the degree of similarity or difference from the reference material or expected sequences.

3. Quantitative testing may be performed for the presence of one or more botanical constituents that are consistent with the target botanical, or for the absence of botanical constituents indicative of a potentially adulterating species.[[12]](#footnote-12) The results of the analysis should be maintained on file.

4. Infrared testing (e.g., FTIR or NIR[[13]](#footnote-13)) may be performed on the material.[[14]](#footnote-14) A printout of the resulting IR spectrum should be maintained on file; alternately, results may be printed from software that reduces the spectral data to a pass or fail result based on the degree of similarity or difference between the observed vs. the expected spectrum.

v. Voucher specimens of the plant or other archival samples (e.g., of viable seeds or of the crude botanical prior to processing) may also provide evidence of botanical identity.[[15]](#footnote-15)

1. Where voucher specimens are used, they should be prepared of the whole plant (if possible), preferably with flowers or fruit, collected from the harvest site, and should be assigned a unique identification code. Vouchers should be labeled with the botanical identity, date of preparation, person who prepared the voucher, and person who harvested the plant. Details such as the harvest/collection date, harvest/collection site (e.g., country and latitude/longitude), and general descriptions of the plant and habitat at the time of harvest should be annotated on the voucher or maintained in associated documentation. See Appendix 7 for additional details on the preparation of voucher specimens.

2. Where samples of viable seed are kept as evidence of identity, the samples may be prepared by growers from the lot of seed used for planting, or may be prepared by growers or wild collectors from the plant population once the seed is mature.

3. Archival samples of botanical raw materials for manufacturing should always be prepared prior to processing, especially before size reduction or extraction as these will destroy or remove important morphologic features.

vi. The identity of processed botanicals, such as those that have been powdered, extracted, and/or blended with other botanicals, often cannot be definitively proven by testing the finished processed material. Microscopy, chemical testing, and/or DNA testing may be used where adequate and scientifically valid methods exist, but these at best provide evidence of identity rather than proof of identity.

BQ2.3 Physical characteristics

i. A variety of physical characteristics may be relevant to the quality of a botanical material. These may include:

1. Moisture content. An appropriate specification should be set for the moisture content or loss on drying. Fresh materials will contain a much higher amount of water than dried. For dried materials, moisture content should be low enough to minimize microbial growth and prevent spoilage.

2. Particle size. For cut, chopped, or milled materials, specifications for the size of the pieces or particles should be established where relevant. The piece or particle size of manufacturing materials will affect operations such as steam sterilization, extraction, and encapsulation. In finished products, the particle size may affect mouthfeel, bioavailability, and stability.

3. Other relevant tests for powdered materials may include tapped density and bulk density.

4. Other relevant tests for liquid materials may include pH, density or specific gravity, viscosity, and total dissolved solids.

ii. For crude botanical materials, especially in whole form, additional tests may be relevant:

1. Soil content. It may be appropriate to set a quantitative limit for the amount of dirt and soil permitted in the material.

2. Foreign organic material. It may be appropriate to set a quantitative limit for the amount of non-target plant parts, foreign species, insects, etc. permitted in the material.

3. Unacceptable pieces. It may be appropriate to set a quantitative limit for the levels of discolored, damaged, broken, or moldy pieces permitted in the material.

BQ2.4 Chemical characteristics

i. A variety of chemical characteristics may be relevant to the quality of a botanical material. These may include:

1. Extractives. In many cases it is desirable to establish a specification for the content of extractable material (“extractives”) in the botanical; this provides a measure of the chemical richness of the material.[[16]](#footnote-16)

2. Marker content. Specifications may be established for the levels of one or more botanical constituents in the material. Such tests may provide an indication that the material has been handled and stored properly to maintain freshness; for process control; to monitor shelf life; to limit the presence of toxic constituents; or, in those cases where a particular constituent or class of constituents is linked to the physiologic effect of the botanical, to control the physiologic activity.[[17]](#footnote-17)

3. Other relevant tests may include the content of essential oils or fixed oils, total ash, acid-insoluble ash, water-soluble ash, crude fiber, etc. For finished formulated products, testing for preservative effectiveness and/or preservative content may also be appropriate.

BQ2.5 Contaminants

i. Limits should be established for impurities and contaminants that may adulterate the material or adversely affect its quality, as follows.

ii. Adulterating species. Specifications should be established to exclude the presence of known adulterants and substitutes. Depending on the form of the material and the nature of the adulterant, such testing may be performed using gross morphology or microscopy, or may involve chemical tests for constituents characteristic of the adulterant (e.g., pyrrolizidine alkaloids; see also Appendix 8).[[18]](#footnote-18)

iii. Microbiology. Specifications for the microbiological characteristics of the material (including indicator organisms, spoilage organisms, and/or potential pathogens) should be established where appropriate.[[19]](#footnote-19),[[20]](#footnote-20) Microbiological specifications may not be relevant to raw agricultural commodities, materials intended for further processing, and those intended for use other than as a food or drug. However, microbial limits are often important for processed botanicals and finished consumer products (especially food products that will not be thoroughly cooked by the end-user prior to consumption).

iv. Heavy metals. Specifications for the levels of heavy metals are often important in botanical materials intended for use as or in consumer products. If the material will eventually be sold as food in the State of California, due consideration should be given to the Proposition 65 safe-harbor levels for various metals.[[21]](#footnote-21)

v. Pesticides. Establishment of pesticide specifications may be appropriate depending on the nature (e.g., cultivated vs. wild harvested) and intended use (e.g., food use vs. other uses) of the botanical. Tolerable pesticide levels in botanical crops vary from country to country. In the US, no detectable level of any pesticide is permitted on a food crop (or in food materials derived from that crop) unless a tolerance has been established for that specific pesticide on that specific crop (or for a defined Crop Group that includes the crop). As a result, the *de facto* tolerance for most pesticides and their breakdown products in most food botanicals is zero (or more accurately, “not detected” using a highly sensitive analytical test). However, as a practical matter, it is not possible to test a material for residues of every known pesticide; there are simply too many pesticides in use. Therefore, where pesticide specifications are established, consideration must be given to the range of pesticides that will be tested. Depending on the circumstances, it may be appropriate to use a standard pesticide panel (e.g., as per USP) or to create a customized panel to include pesticides employed during the cultivation or collection of the crop, those previously applied to the cultivation site, and/or those applied to neighboring fields.

vi. Radioactivity. A specification for content of radioactivity may be important if the material is sourced from an area known to contaminated. For example, residues from the Chernobyl accident are still present in Eastern Europe.

vii. Other relevant tests may include sulfur dioxide, ethylene oxide residue, polycyclic aromatic hydrocarbons (PAHs), aflatoxins and other mycotoxins, presence of genetically modified DNA, solvent residues, etc.

1. As an example, the U.S. Pharmacopoeia (USP) has sampling instructions for articles of botanical origin; see Second Supplement to USO 38 – NF 33, Chemical Tests <561> Articles of Botanical Origin. [↑](#footnote-ref-1)
2. USP refers to the United States Pharmacopeia. [↑](#footnote-ref-2)
3. The correct scientific names for botanicals are available from sources such as GRIN Taxonomy (https://npgsweb.ars-grin.gov/gringlobal/taxon/taxonomyquery.aspx). In general, names should be provided in accordance with the current International Code of Nomenclature for algae, fungi, and plants (http://www.iapt-taxon.org/nomen/main.php), unless there is reason to use outdated nomenclature (e.g., where conformity to a pharmacopoeial monograph is claimed and the monograph used outdated nomenclature). [↑](#footnote-ref-3)
4. See 21 CFR § 582.10. [↑](#footnote-ref-4)
5. For example, the American Spice Trade Association’s (ASTA’s) Spice List describes cinnamon merely as “Cinnamomum spp.” See <http://www.astaspice.org/government-relations-advocacy/complying-with-u-s-policy-regulations/spice-list/>. [↑](#footnote-ref-5)
6. The standard English names for many botanicals are provided in AHPA’s *Herbs of Commerce* (McGuffin, M *et al.* 2000. *Herbs of Commerce*, 2nd ed. Silver Spring, MD: AHPA). [↑](#footnote-ref-6)
7. Several of these authoritative resources, such as the AHPA Botanical ID References Compendium, are listed in Appendix 5. [↑](#footnote-ref-7)
8. TLC = Thin Layer Chromatography

 HPTLC = High Performance Thin Layer Chromatography

 HPLC = High Performance Liquid Chromatography

 GC = Gas Chromatography [↑](#footnote-ref-8)
9. For materials purchased from another party, it may be preferable to look at a full fingerprint rather than just a few bands or peaks to avoid inadvertent purchase of a material to which exogenous plant constituents have been added but not disclosed. [↑](#footnote-ref-9)
10. It is to be noted that legitimate differences may occur between the fingerprint of an authentic crude botanical sample vs. a sample of the same species that has been processed (as by heating, extracting, etc.). In addition, fingerprints may vary due to the natural chemical variation that occurs due to weather, season, soil chemistry, external stressors such as insects, etc. Thus, if the fingerprints of test sample and the authentic sample do not match exactly, this does not necessarily mean the test sample is improperly identified. [↑](#footnote-ref-10)
11. Although the layperson might expect DNA to provide definitive identity results, in fact the use of DNA testing in botanical identification is not yet a fully developed science, and is known to produce false negatives and false positives. At the time of this writing it is often not sufficiently robust and reliable to provide definitive identification and is not generally accepted either by industry or by the scientific community as a replacement for morphologic examinations. Furthermore, usable DNA is not present in many botanical ingredients that have been processed as by heating, extraction, etc. [↑](#footnote-ref-11)
12. The constituents used for this purpose should be characteristic of, and preferably unique to, the botanical in question, or to the potential adulterating botanical whose presence is to be excluded. However, it must be kept in mind that testing for individual constituents can be easily fooled by spiking the botanical material with those constituents obtained from an exogenous source. [↑](#footnote-ref-12)
13. FTIR = Fourier Transform Infra-Red spectroscopy

 NIR = Near Infra-Red spectroscopy

 [↑](#footnote-ref-13)
14. Where infrared testing is used in conjunction with software that analyzes the spectrum to yield a “pass” or “fail” result, the software must be extensively trained with a sufficient number and diversity of authentic samples; otherwise, false negatives and false positives are likely to be obtained. [↑](#footnote-ref-14)
15. Any such voucher or other archival sample is only useful, however, if it is an accurate and positively identified sample of the species; therefore, such samples cannot replace direct examination and/or testing of the actual botanical material itself. [↑](#footnote-ref-15)
16. Measuring the content of extractives may be helpful in preventing the inadvertent purchase of material that has previously been extracted (i.e., spent extraction marc). In addition, use of materials containing a consistent level of extractives allows powdered extracts to be made with a reasonably consistent native extract ratio, and liquid extracts to be made with a reasonably consistent content of dissolved solids. [↑](#footnote-ref-16)
17. For more complete information about the use of marker compounds, refer to the American Herbal Product Association’s (AHPA’s) “Use of Marker Compounds in Manufacturing and Labeling Botanically Derived Dietary Supplements” and “Standardization of Botanical Products: White Paper,” available at www.ahpa.org. [↑](#footnote-ref-17)
18. DNA testing might also be used, but since DNA testing cannot provide quantitative results, there is no way to know whether the presence of adulterant DNA indicates significant levels of adulteration or only an insignificant trace, especially when highly sensitive DNA technologies are used (e.g., PCR). Due to its extreme sensitivity, such testing commonly detects “adulterants” consisting merely of airborne pollen, or other stray plant or animal cells that are widespread both in the fields and in processing and laboratory environments. [↑](#footnote-ref-18)
19. See AHPA’s “Guidance Policy on Microbiology and Mycotoxins” (2012); accessible at <http://www.ahpa.org/Portals/0/PDFs/Policies/Guidance-Policies/AHPA_Microbiology___Mycotoxin_Guidance.pdf?ver=2016-04-26-121351-030>. [↑](#footnote-ref-19)
20. It should be noted that microbiological testing of a botanical material cannot, by itself, ensure the microbiological safety of the material, because low levels of pathogenic microorganisms may be missed during sampling and testing. To ensure microbiological safety, it is necessary to either (a) grow the botanical under strict conditions (such as those prescribed in 21 CFR Part 112) to preclude pathogenic contamination, or (b) formulate and/or process the botanical in a manner that destroys pathogens, as by combining with acid, heating, extracting, steam sterilizing, etc. [↑](#footnote-ref-20)
21. See AHPA’s “Background on California Proposition 65: Issues Related to Heavy Metals and Herbal Products” (2008) and AHPA’s Guidance Policy on Heavy Metals (2012), accessible at <http://www.ahpa.org/Portals/0/PDFs/Policies/Guidance-Policies/AHPA_Heavy_Metals_Guidance.pdf?ver=2016-04-26-121351-157>. [↑](#footnote-ref-21)