

Quality of Botanical Preparations

Specific Recommendations for the Manufacturing of Botanical Preparations,
Including Extracts as Food Supplements

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QUALITY OF BOTANICAL PREPARATIONS

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INTRODUCTION

This guidance document reflects the views of Food Supplements Europe on quality of botanical preparations used in or as food supplements, including extracts. It is intended to complement the Food Supplements Europe Guide to Good Manufacturing Practice for Manufacturers of Food Supplements¹, specifically in relation to extracts. These recommendations are not legally binding but represent principles of best practice.

It falls under the responsibility of the manufacturer to ascertain that the final products are in accordance with applicable food/food supplement legislation for the intended European Union (EU) Member State or export market.

As described in the Food Supplements Europe Guide to Good Manufacturing Practice for Manufacturers of Food Supplements, all botanical preparations used in food supplements intended for sale in the EU must comply with all relevant requirements of EU food legislation with regard to composition, quality and safety. The quality of the preparation and consistency of production is particularly important where a quantitative or qualitative claim is made for a botanical, botanical preparation or for one or more of its constituents.

This guidance covers the requirements necessary to ensure that the production of botanical preparations complies with the compositional and quality requirements of EU food law, and food supplement manufacturers are encouraged to bring these guidelines to the attention of their suppliers of botanical preparations. Whilst it is recognised that some of the following guidance will be more directly applicable to the suppliers of botanicals and botanical preparations, it is important that the manufacturers of food supplement finished products understand the key issues relating to the quality of botanical preparations, to enable them to select the highest quality ingredients for their products.

The general safety requirements of EU food law also apply. To assess the safety of a botanical food supplement, both the inherent safety risks of the plant concerned and its manufacturing process must be considered. A questionnaire has been developed to accompany this guidance to assist food supplement manufacturers with assessing the quality of botanical preparations when selecting their raw materials and to highlight areas where further information may need to be requested from the supplier.

¹ See www.foodsupplementseurope.org

1. Definitions

1.1 Botanical

Botanical materials, including whole, fragmented or cut plants, plant parts, plant products (such as exudates), algae, fungi and lichens.

1.2 Botanical Preparation

All preparations obtained from botanicals by various processes (e.g. pressing, squeezing, extraction, fractionation, distillation, concentration, drying up and fermentation). These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates.

1.3 Botanical Extract

A **Botanical Extract** is the complex, multi-component mixture obtained after extracting a botanical raw material (consisting of one or more botanicals) with a solvent. The extraction process may be such as to select for, or remove, components of the botanical material. Extracts may be in dry, liquid or semi-solid form.

A **Native Extract** is the material consisting only of extracted components present in the original botanical or formed during the extraction process and excludes any technological additives or any other added substances.

This term may refer to liquid extracts or semi-solid extracts from which the added solvent has been removed or to a dry extract or that portion of a finished extract that is comprised solely of botanical components.

Note:

When determining whether two extracts are comparable, the native extracts should be used for comparison.

A **Commercial Extract** is a native extract to which one or more technological additives (for example, inert carriers, anti-caking agents) or other food ingredients (for example maltodextrin, dextrose, vegetable oil) may have been added to facilitate inclusion in the final supplement product. It should be noted that the added substances can, in some cases, comprise a very large proportion of the commercial extract.

A. SELECTION OF RAW MATERIAL

1. Origin of Botanical Sources and Compliance with Good Agricultural and Collection Practices

1.1 Origin of Botanical Source

The growth, development and chemical profile of a botanical is influenced by a number of external factors such as soil quality and water (mineral content, pH etc.), temperature, sunlight, the season of cultivation and time of harvesting. All these factors influence and often determine the composition of the botanical matter.

As a consequence, the presence and concentration of physiologically active substances in a botanical species can vary considerably depending on where, when and how the botanical was grown.

It is important that the batches of the botanical raw material undergo appropriate testing before acceptance for further processing to ensure that the concentrations of substances with known physiological effects fall within predetermined limits and allow for the natural variability of the botanical material. Testing should include identification, purity tests and assay of physiologically active constituents or other, relative quality markers. This is particularly important when the sourcing of the botanical is changed or when there are other considerations known to affect the quality of the source material, e.g. environmental or climatic conditions.

1.2 Good Agricultural and Collection Practices

It is important that the botanical raw material source follows the basic principles of good agricultural and collection practices, to ensure identification and traceability. The supplier of the botanical raw material should provide sufficient information regarding how the botanical has been cultivated/collected, harvested, stored and, where relevant, processed.

Botanical identification at the harvesting stage is imperative, particularly with botanicals harvested in the wild. At least the following information should be available:

- a. Scientific name (See part 2.1)
- b. Common name (See part 2.1)
- c. Whether cultivated and/or collected
- d. Plant part or plant product
- e. Geographical origin (where relevant, country and province/state)
- f. Period/season of harvest
- g. Appropriate information to enable traceability as required by EU law (e.g. information on source, lot number)
- h. Signed certification/declaration

For both cultivated botanicals and those harvested in the wild, particular areas of concern at the harvesting/primary processing stage are cross contamination or adulteration, foreign matter contamination (from harvesting and from pest infestation), pesticide residues, contamination with mycotoxins (toxic excretory by-products of fungal/mould growth) and contamination with polycyclic aromatic hydrocarbons (PAHs).

The botanical should be inspected and sorted prior to primary processing. This should include visual and physical inspections for cross-contamination by other botanical species and/or plant parts, foreign matter and fungal/mould growth. Any plant parts showing signs of fungal/mould growth should be discarded.

The basic principles of good agricultural and collection practices are described in the Codex Alimentarius Code Of Hygienic Practice For Spices And Dried Aromatic Herbs (CAC/RCP 42-1995), which applies to the dried aril, bark, berries, buds, bulbs, leaves, rhizomes, seeds, stigmas, pods, resins, fruits or plant tops. It should be read in conjunction with the Codex Code of Hygienic Practice for Fresh Fruits and Vegetables (CAC/RCP 53-2003) and the General Standard for Contaminants and Toxins in Food and Feed (CODEX STAN 193-1995).

1.3 CITES

All botanical species used for the production of botanical extracts must comply with the requirements of the Convention on International Trades in Endangered Species of Wild Flora and Fauna (CITES).

The objective of the CITES international agreement is to ensure that trade in wild plants does not threaten the survival of the species. The endangered species and the degree of protection assigned to them are given in three Appendices to the CITES agreement. The status of a botanical should be checked before it is sourced from the wild.

2. Botanical Identification and Characterisation

2.1 Identity of Source Material

It is critical that there is an accurate identification of all botanical source material selected for further processing.

As the accurate identification of some botanical sources can be complicated, it is recommended that the nomenclature of the European Pharmacopoeia is followed where appropriate. Other authoritative sources such as the 'World Checklist of Selected Plant Families' (Royal Botanic Gardens, Kew, UK) or 'The International Plant names Index', theplantlist.org may also be used.

Care should be exercised with the identification, as there are many cases where botanicals have been renamed or reclassified. Care must also be taken with the use of common names as these can vary from region to region and in some instances can be used for a different species. For example, due to difficulties in translation, the common name given to some Chinese botanicals can relate to more than one species and identification must be made on the basis of the Scientific (Latin) classification.

The following scheme should be used for the identification of a botanical.

Scientific (Latin) name:	<i>full systematic species name incl. botanical family, genus, species, variety, subspecies, author's name, and chemotype if applicable</i>
Synonyms:	<i>botanical name(s) that may be or have been used interchangeably with the preferred scientific name</i>
Common names:	<i>vernacular name(s)</i>
Part used:	<i>e.g. root, leaf, seed, etc.</i>
Geographical origin:	<i>continent, country, region</i>
Growth and harvesting conditions:	<i>wild or cultivated, cultivation practices, time of harvest in relation to both season and stage of the plant growth</i>

2.2 Confirmation of Identity

Identification of the botanical material should be confirmed by the following, as appropriate:

- a. Macroscopic examination;
- b. Microscopic examination;

and, where necessary:

- c. Chromatographic/spectroscopic examination: e.g. thin layer chromatography (TLC); high-performance liquid chromatography (HPLC); high performance thin layer chromatography (HPTLC); (in most cases, TLC will be sufficient);
- d. Other characteristic assay.

Details of the identity specifications for most of the commonly used botanicals can be found in the scientific literature (e.g. Bisset's Herbal Drugs and Phytopharmaceuticals, British Herbal Pharmacopoeia, Eur. Ph. 'Plant Drug Analysis' – Wagner, etc.).

In some cases other chemical and physical tests can support the identification. Where applicable, these are provided in the monographs relating to the botanical in the Pharmacopoeia.

Examples of such tests are:-

- Total ash
- Insoluble ash
- Water soluble extractive
- Foreign organic matter
- Loss on drying

3. Traceability

All botanicals intended for use in food supplements and foods must comply with the traceability requirements as given in the EU Regulation on General Food Law.

All business operators involved in the supply chain for botanicals must be able to identify any entity from whom they have been supplied with a botanical intended to be incorporated into a food supplement or food and also to identify the business to which the botanical or products containing the botanical have been supplied.

All information on traceability must be kept for a relevant period, such as the shelf-life of the extract and/or product plus one year. Information on traceability must be made available to the Competent Authority on demand. Botanical products placed on the market in the European Union (EU) must be adequately labelled and identified so as to facilitate traceability.

4. Treatments of the Source Material

4.1 Irradiation

All botanicals and botanical products intended to be marketed as foods must comply with the EU legislation relating to the irradiation of foods and ingredients. This legislation covers the categories of foods and ingredients that are permitted to be irradiated, the maximum levels of irradiation, EU approved irradiation facilities and labelling requirements.

Irradiated botanicals or products can only be placed on the market in any country of the EU if they comply with the following conditions.

- the botanical is on the permitted list of foods and ingredients that can be irradiated
- the irradiation is carried out at an EU approved facility
- the dosage of irradiation is below the maximum given in law for the product category
- the documentation that accompanies the consignment complies with the requirement of the law
- the consignment and the labels of the products derived from it, contain the statement that the botanical has been irradiated

In practice, very few botanicals used in supplements are permitted to be irradiated.

Most Member State enforcement authorities across the EU are equipped for the rapid detection of irradiated materials.

4.2 Genetic Modification

The botanical source must comply with all current EU legislation concerning the use of genetically modified organisms (GMO).

There is a considerable amount of food legislation relating to the approval and use of botanicals derived from genetic modification (GM) using any GM technique defined in the legislation.

No botanical or its derivatives can be placed on the market in the EU if it is produced from a GMO, unless that GMO has been authorised in accordance with the requirements of the legislation. This ban includes food additives which are derived from GM animal and plant sources. For example, cellulose powders can be derived from GM cotton.

The use of an approved GMO or an ingredient derived thereof in a product must be labelled accordingly.

5. Integrity of Botanical Material

5.1 Foreign Matter

The harvested botanical material must be screened for extraneous foreign matter. This includes stones, soil, insects and insect parts, rodent droppings etc.

Procedures for both visual and physical examinations for the presence of foreign matter should be in place and should be applied to all batches.

Any botanical batches showing signs of fungal/mould growth must be discarded.

5.2 Cross-contamination and Adulteration of Botanical Source

Care must be taken to prevent cross-contamination or adulteration of the botanical source by other species, particularly where the extraction of another species may present a hazard to human health. For example, the contamination of *Plantago* sp. with *Digitalis* sp. There are certain botanicals that co-exist in the same environment as other species and can be co-harvested.

Appropriate controls should be in place to ensure co-harvesting is avoided, and that only one species of botanical is present in the harvested material.

5.3 Integrity of Botanical Source

For most botanicals only specific parts of the plant are intended to be used (e.g. leaf, root/rhizome, fruit, flower etc.).

There should be limits for the presence of other parts of the plant where a specific part is required. For example, if only the leaves are to be extracted, there should be a limit, based on percentage, for the inclusion of the stem.

Some parts of plants may contain toxic substances whilst other parts can be consumed. Recognised textbooks, national positive/negative lists and the EFSA 'Compendium of Botanicals' are useful references to be consulted. For parts of the plant intended for extraction identified as being of concern, appropriate production/extraction processes and subsequent quality control measures should be applied to ensure the safe use of the botanical.

6. Contaminants and Residues

Botanicals can be susceptible to a wide range of contaminants and residues. Whilst most have environmental origins, some result from agricultural treatments during cultivation.

Many of the contaminants and residues that can potentially be found in botanicals can be the subject of legal limits. Food operators should be aware of the legislation in the countries in which the bulk supplies or final products are intended to be marketed.

As the following contaminants and residues appear in European Union food legislation and in the food legislation of a number of economic areas/countries, it is advisable that appropriate testing relevant to the botanical preparation is carried out and specification limits agreed between customer and supplier.

Food operators should be aware of the specific risk of contamination and residues linked to specific botanicals. In such cases a safety-based approach should be applied, including the use of specific limits where no legal limits exist.

- a. Heavy metals, particularly:
 - cadmium
 - lead
 - mercury
 - arsenic (not currently in EU legislation, but in the national legislation of some Member States)
- b. Mycotoxins:
 - These are excreted by-products produced during the growth of certain fungi (moulds).
 - Mycotoxins already limited by legislation in the EU include the aflatoxins and ochratoxin A.
 - Certain species of botanicals are specifically covered by the EU legislation on mycotoxins.
- c. Environmental contaminants:
 - These are organic contaminants found in the environment and which can be found on botanical matter.
 - The main ones are:
 - Dioxins, furans and dioxin-like Polychlorinated biphenyls (PCBs) which can be found in botanical oils and fats
 - Polycyclic aromatic hydrocarbons (PAHs), regulated in the EU for botanical oils and botanical food supplements
 - Radioactivity: where cultivation/harvesting is in proximity to nuclear disasters (for example, Chernobyl and Fukushima)

d. Plant metabolites

Certain metabolites produced by plants within specific plant families have been recognised as being harmful to humans when ingested in quantity.

- Examples include:
 - Pyrrolizidine alkaloids (PAs), produced by a wide variety of plants from the plant families of Asteraceae (tribes of Senecio, Eupatorium), Boraginaceae (most genera) and Fabaceae (Crotalaria genus).
 - Tropane alkaloids (TAs), produced by plants from numerous plant families such as Erythroxylaceae (including coca) and Solanaceae (including mandrake, henbane, deadly nightshade, datura, potato, tomato), Proteaceae, Euphorbiaceae, Rhizophoraceae, Convolvulaceae and Cruciferae.
 - Limits for botanicals and/or botanicals food supplements are under discussion within the EU and may be set in the future.

e. Residues

- Pesticide, herbicide and fungicide residues
- Ethylene oxide, the use of which is not permitted in EU food law.
- Other fumigants (e.g. phosphine or methyl bromide)

As contaminants or pesticides may be concentrated during the extraction process, this must be taken into consideration when adopting and agreeing with the raw material supplier the maximum levels in the botanical raw material. Where applicable, concentration factors may be taken into consideration as described in the EU Regulations on pesticide residues and contaminants in foods.

Appropriate sampling and analysis of product for chemical contamination should be applied in conformity with the requirements laid down in EU legislation. Where no specific requirements have been laid down in legislation, other references can be used, e.g. sampling frequency applied or recommended by enforcement authorities or specified in pharmacopeia for botanicals.

The frequency of testing for chemical contaminants is dependent on the potential risk of contamination. Heavy metals are normally associated with the soil content in the area of cultivation. Mycotoxins can be related to climatic conditions and more importantly to post-harvest storage.

Dioxins and PAHs are normally the result of combustion processes (industrial combustion, vehicle emissions and fires) and in certain regions a high frequency of testing may be required.

Under EU food legislation, any product in which the level of contaminants exceeds those permitted in the law cannot be traded in the EU for human consumption and cannot be exported. It is also illegal to mix batches with high contaminant levels with ones of lower levels to bring the mixed batches below the limits.

7. Microbiological Contamination

Microbiological contamination with potentially pathogenic organisms can be a serious risk, particularly in situations where animal waste (faeces) is used as a fertiliser during cultivation or where surface water is used for irrigation. In addition, during harvesting, post-harvesting, drying and subsequent processing stages, contamination with microbial pathogens relevant to human safety may occur. Routine testing should therefore be established for microbiological quality.

Since no specific provisions exist in EU law for food supplements or botanicals in terms of methodology and microbial limits, the specifications set out in the European Pharmacopoeia under 5.1.8 (Microbiological quality of herbal medicinal products for oral use) may serve as a guide to maximum acceptable levels.

The following microbiological tests should be carried out on the botanical source:

- Total Plate Count (Total Viable Count)
- Escherichia coli
- Salmonella spp.
- Enterobacteriaceae
- Moulds/Yeasts (total combined)

The frequency of testing is dependent on the form of cultivation and growing conditions.

8. Precedence of Food Law

For all botanicals sold as food supplements or foods, the requirements of food law take precedence over medicines law and Pharmacopoeial monographs. For example, if medicines law sets an upper level for a specific contaminant, and EU food law lays down an upper level for the same contaminant that is below that set in medicines law, then the lower level laid down by food law takes precedence and is the one with which the botanical must comply.

In the case of chemical contaminants, the limits under EU food law are often more stringent than those given in the Pharmacopoeial monographs.

QUALITY OF BOTANICAL PREPARATIONS

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B. EXTRACT PREPARATION

A botanical extract is a complex product, the composition/substance profile of which is mainly determined by the quality/natural variability of the raw material and the extraction process applied. To ensure consistency in quality, it is necessary to determine the specifications both of the production process and the final extract. For changes in raw materials or processing parameters, the verification of the conformity with the specifications must be reassessed and where appropriate the necessary modifications applied. Key parameters necessary to support equivalence between two extracts are the solvent and extraction conditions, as well as the ratio of the starting plant material to the final extract, which is considered as a range related to the natural variability of the plant material. This is of importance to the supplement manufacturer, who may have to make significant changes to a product formula to accommodate an alternative source of extract (see also Section C2).

1. Definitions and Legal Aspects of Different Forms of Extract

1.1 Standardised Extract

Standardised botanical extracts are adjusted within an acceptable tolerance to a given content of specific and relevant physiologically active constituents.

Standardisation is achieved by adding additives or other food ingredients (such as maltodextrin) for adjustment to the botanical extract or by blending batches of the botanical extract.

For standardised botanical extracts, the name and content of the constituent(s) with known physiological activity, together with details and quantities of all additives (including carriers) and other food ingredients (such as maltodextrin) should be given in documents accompanying the batch of standardised extract.

1.2 Quantified Extract

Quantified botanical extracts are adjusted to a defined range of those constituents considered to contribute to the physiological activity. Adjustments are made by blending batches with differing constituent levels to achieve the desired range. Additives (including carriers) and other food ingredients can be used but in fixed quantities.

For quantified extracts the names of the active markers on which the adjustments are made should be given, together with their quantity or range. The details, together with information on the types and quantities of any additives should be given in documents accompanying the batch of quantified extract.

1.3 Other Botanical Extracts

For botanical extracts where there are no known constituents with defined physiological activity or active markers, the extracts can only be defined by their production process and by appropriate specifications. Such extracts can be produced from one botanical or mixtures of botanicals.

For such extracts the quantity of the native (genuine) botanical extract and details and quantities of any additives (including carriers) and other food ingredients should be given in documents accompanying the batch of extract. Additives (including carriers) and other food ingredients can be used but in fixed quantities.

1.4 Legal Aspects of Specific Extract Forms

For extracts destined to be used in food supplements or foods within the EU, it is essential that the extracts are fully compliant with all relevant EU food law. General guidance can be found in the Food Supplements Europe Guide to Good Manufacturing Practice for Manufacturers of Food Supplements.

This includes the requirement that full traceability back to the source of the botanical for each batch supplied must be ensured, with each business in the food chain keeping, as a minimum, a record of their supplier(s) and of their onward customer(s).

In each case, the Novel Food Regulation should be considered with respect to composition or processing.

The process of standardisation and quantification should not include the addition of substances, whether synthetic or derived from botanical matter, other than permitted technological additives and carriers.

All technological additives and carriers must conform to the requirements of EU food law. Only additives approved for the particular category of food (e.g. food supplements) can be used and the levels of use must comply with the legislation.

The levels of all chemical contaminants that have legal limits under food law must be controlled. The law strictly prohibits the mixing of contaminated extract with non-contaminated extract to reduce the contaminant levels.

All extracts must be in compliance with EU legislation on irradiation and radioactivity.

Solvent usage and residue levels for botanical extracts are also controlled by food law. This control applies to all uses of solvents, including as eluents.

For all forms of extracts, full specifications should be supplied to the purchaser.

Under the European food supplement Directive, the amounts of the active substances shall be declared on the label. Therefore, it is important that sufficient information be provided with the botanical extract, including the levels of any non-active ingredients (additives, carriers & substances used like carrier), to enable the food supplement manufacturer to correctly label the finished product.

2. Marker Determination

A marker is a chemically defined characteristic constituent, or group of constituents, present in a specified botanical material.

Markers can be classified into two categories. The first is termed the **'active marker(s)'**, which is a constituent or group of constituents that are generally accepted as contributing to a physiological effect in the body.

The second category is known as **'analytical marker(s)'**, which is a constituent or group of constituents that are known to be characteristic of the botanical material and for which there are established analytical methods. Analytical markers can be used to assure identity and consistency of a botanical preparation.

The ideal marker is one or more constituent(s) for which there is an established and validated assay method and for which the assay is not subject to interference from other constituents in the botanical source or from processing.

In cases where constituents with a physiological effect are known, or where suitable analytical markers can be determined, markers can be used for quality control purposes.

Markers do not have to have any physiological activity, as their function is to assist in the determination of the composition and quantification of the final extract

3. Botanical : Extract Ratio

In practice, the extract ratio can be expressed either in relation to the native extract or the commercial extract. It is important that the reference is clearly indicated (either 'native extract' or 'commercial extract'). For the purpose of this document, whenever botanical : extract ratios are mentioned, they refer to native extracts, unless otherwise specified.

A botanical : extract ratio is the ratio of the dry mass of the botanical material entering the extraction process, to the mass of the resulting native extract.

The ratio is normally given in the form:

Botanical mass (dry material) : native extract mass

Due to the natural variability of botanical raw materials botanical : extract ratios will normally vary within an empirical range specific for the botanical/solvent combination. For example, a 3-5 : 1 ratio means that 3-5kg botanical material has to be extracted to give 1kg of native extract.

In the case of liquid extracts, a ratio of e.g. 1 : 6 means that from one kg of botanical material, a yield of 6 kg of liquid extract is obtained. Because of the fixed botanical : solvent ratio (see below) botanical : extract ratios are fixed in liquid extracts. The term "native" extract is not applied in liquid extracts.

It is important that the extraction process selected will give a realistic extract ratio in terms of the chemistry of the original botanical.

The extraction ratio is linked to the weight fraction that is extracted from the starting plant material. It mainly depends on the starting plant material itself, its natural variability (range), extraction solvents/conditions and eventual purification phases.

The extraction ratio should be expressed with the intention of providing the user with the number and quantity of the constituents of the extract on which the usage has been based. This is particularly important if the final product is to be marketed on the basis of traditional use of the botanical.

If no explicit reference is made on the label to specific constituents, it is important that the selected extract ratio is capable of representing the composition of the original botanical.

4. Selection of Extraction Solvent

Solvent ratios are normally defined in terms of the ratio of the solvents (e.g. aqueous/ethanol 60 : 40). In some cases the percentage of the major solvent can be given (e.g. ethanol 40% v/v).

The selection of the appropriate solvents and solvent ratios is an important aspect of the extraction process.

The type, concentration and quality of each extraction solvent will affect the spectrum of components obtained from a given amount of botanical material and can have an impact on the safety of the preparation. For example, certain solvents may lead to a concentration of unwanted constituents in the final preparation, thus it is important that the most appropriate solvent be selected for each botanical.

A detailed knowledge of the chemistry of the botanical material is required before the solvent(s) can be selected. The chemistry of the material has to be reviewed in the context of its aqueous (water) extractable components and its alcohol/organic solvent extractable components. Frequently, both forms of solvent and the ratio of the solvents will need to be adjusted to the proportions of the relevant extractables.

Once the solvents and solvent ratios have been theoretically selected, they should be tested in practice, to verify that the selected solvents and solvent ratio are appropriate for the intended extract. An appropriate solvent will result in a substance profile of native extract that is similar to the phytochemical profile of the starting material

Once a solvent system is selected and verified, it should be ensured that the extract composition and quality remain comparable in the event of necessary modifications of the extraction process, including the solvent system.

Once the solvent ratio/concentration has been established, the acceptable tolerances for the variation in the ratio should be defined. The tolerance is the variation either side of the target quantity. For example, a $\pm 5\%$ tolerance on a 60 : 40 ratio would be from 65 : 35 to 55 : 45.

It cannot be assumed that a single tolerance is applicable for all botanicals. A justification for the tolerance applied should be available.

All solvents used for the preparation of botanical extracts, regardless of the actual method of extraction, must comply with the EU legislation on extraction solvents used in the production of foodstuffs and food ingredients.

This legislation lists the permitted solvents, and for a number, conditions of use and maximum residue levels.

5. Composition of Extract as Marketed (Commercial Extract)

5.1 Technological Additives, Carriers, and Other Food Ingredients

Under EU food law the user of the extract (product manufacturer) must be provided with full details of the composition of the extract.

As a large proportion of commercial extracts contain technological additives, carriers and other food ingredients for good technical reasons, the identity and quantity of each of the additives and other food ingredients must be provided by the extract supplier to the next business operator in the supply chain. This is a legal requirement in the EU under the food labelling regulations, to allow for the calculation of actives and the full ingredient listing.

5.2 Declaration of Additives

All additives must be declared by the names or 'E numbers' assigned to them in the Regulation on Food Additives (EC) No 1333/2008 as amended. Each additive must comply with the specifications given in the purity criteria.

5.3 Declaration of Native Extract Content

For extracts containing additives or other food ingredients, the native extract content must be declared as such, together with the calculation of the basis for the botanical equivalency and extract ratio.

The quantity of native extract should be given in all specifications and marketing literature relating to the commercial extract.

When determining whether two similar extracts are, in fact, equivalent, the native extracts should be the basis for comparison.

6. Product Stability and Shelf-Life

6.1 Product Shelf-Life

EU food law requires that all products, including those based on botanicals, must contain a date of minimum durability (expiry date) on the label.

The manufacturer of the product is responsible for determining the expiry date and this should be based on knowledge of the shelf-life of the supplement product in the final packaging as marketed to the ultimate consumer.

The information required to determine the shelf-life can either be obtained by the performance of shelf-life studies on the final product in the packaging in which it is to be marketed, or from accumulated data obtained from previous studies on similar products, data on the stability of the active components, and data on the packaging.

In order to assess the stability of the final product, the manufacturer should consider stability information available from the extract manufacturer/supplier.

The stability of the complex chemical composition of many botanicals can be influenced by a number of physical and chemical factors and also by the production process.

Knowledge of the chemistry of the major components of the botanical, or extensive experience of the stability of botanical products, is necessary before the potential stability can be assessed.

6.2 Stability Testing

If stability studies are determined to be necessary to estimate the shelf-life of a botanical food supplement product, (for example, in cases where there is no appropriate accumulated data as described in the section above), tests should be carried out on the final supplement product as sold to the ultimate consumer.

As the product stability is dependent on the barrier properties and seal integrity of the packaging, all stability studies should be carried out in the selected packs. Any change in packaging can require a re-evaluation of stability.

The stability studies on the extract should be designed in such a way that changes to the chemical composition of the botanical(s) can be detected.

In particular, it is recommended that the following factors are checked under normal conditions of transportation and storage, both in sealed containers and after opening and during usage, to replicate the typical storage and manufacturing conditions of the extract user.

The following checks should help to ensure that the expiry date of the extract is valid. They should also provide important data on the stability of the extract, which is required for the determination of the minimum durability of the final supplement product.

- a. Organoleptic properties (taste, smell, presentation/appearance, colour) and notably:
 - colour and flavour stability.

- b. Chemico-physical and microbiological properties, and notably:
 - that the extract does not permit microbiological growth;
 - oil stability (oxidation/rancidity in oils);
 - physical changes on storage (appearance, caking, agglomeration);
 - there are no interactions between components (to confirm theoretical checks based on the chemistry of the components);
 - levels of any relevant active constituents and extract composition profile are maintained within justified limits throughout the shelf-life;
 - where relevant, the stability in use of the extract i.e. the stability of the extract after opening the pack and during the expected usage period.
 - chromatographic fingerprinting to support the composition stability.

7. Specifications

A comprehensive specification must be developed for all botanical extracts traded between the extract producers and the product manufacturers.

The specification should cover details of the botanical source, the extraction process and all relevant chemical, microbiological and physical parameters. Where measurable parameters are given, they should include the target value and acceptable range. Physical, chemical and microbiological parameters should also be accompanied by the test methods from which the values were determined.

As a minimum, the following should be available in all specifications for botanical extracts used as ingredients in food supplements:

- a. The accepted scientific name (Latin name) of the species used.
- b. The precise part(s) or products of the plant used in the process.
- c. Confirmation of compliance with the basic principles of good agricultural and collection practices for the plant source (see Part A section 1.2).
- d. A description of the post-harvesting process, the form of extraction (e.g. maceration, percolation) with solvents specified and any post-extraction processing to obtain the commercial extract.
- e. Details of the extract ratio (native and commercial extract).
- f. A full quantitative declaration of all additives, (including carriers), other food ingredients and processing aids used in the commercial extract.
- g. Confirmation that all solvents used are legally permitted in foods, together with levels of solvent residues where relevant.
- h. The name and quantity of the constituent(s) with known physiological activity or the name and quantity of the analytical marker(s), as appropriate.
- i. Details of relevant parameters, ranges and limits to confirm identification of the extract. This should include positive identification such as chromatography and/or quantification of a marker substance.
- j. Confirmation of compliance with all relevant contaminants and residues controlled by legislation in the EU (including pesticide and solvent residues). The relevance of a contaminant should be discussed with the food supplement manufacturer.
- k. Specification of micro-biological criteria.
- l. Ranges of levels of relevant safety-related constituents.
- m. A statement on the Genetically Modified Organism and irradiation status of the botanical source and confirmation of compliance with the radioactivity legislation of the EU.

QUALITY OF BOTANICAL PREPARATIONS

Specific Recommendations for the Manufacturing of Botanical Preparations, Including Extracts as Food Supplements

C. QUALITY CONTROL OF EXTRACTS

1. Requirements

1.1 General Requirements

Product documentation should be produced and maintained. This documentation should cover in detail all aspects of the product, from the agreed specifications for the raw botanical material through to the release for sale of the extract. This documentation should include a specification sheet and a flow chart.

The documentation should contain all the agreed specification parameters. The following should also be provided, as appropriate, when requested by the food supplement manufacturer:

- acceptance of raw materials including additives
- verification of solvent concentration/ratios
- in-process controls
- acceptance of native extract quality
- acceptance criteria for standardised/quantified extracts, where appropriate
- acceptance criteria for commercial extract

All raw material specifications and test procedures should be agreed with the suppliers of the materials. Details of the acceptance criteria for the commercial extract and information on the relevant analytical procedures should be made available to each customer.

Information to support the analytical methods reliability should be provided.

The documentation should be reviewed at periodic intervals and any amendments made should be recorded, with the date of amendment.

1.2 Confirmation of Active Content

Each batch of commercial extract should be analysed to confirm that specified marker substance levels are within the required range and that the chemical composition/component spectrum (for example, chromatogram) is also within acceptable limits.

1.3 Confirmation of Compliance with Contaminants Legislation

Botanical products sold under food law in the EU must comply with the EU legislation on chemical contaminants. To ensure compliance, the raw materials specifications for the botanical sources must contain upper limits, based on dry weight, for all relevant chemical contaminants, including pesticides. Appropriate sampling and analytical procedures need to be applied.

1.4 Certificate of Analysis

Each batch of commercial extract must be accompanied by a Certificate of Analysis (CoA) that provides the results of the tests carried out on that batch. Where the stated results are not given per batch, but are the result of, for example, skip-lot testing, these should be appropriately indicated and supporting statements provided. The decision to undertake skip-lot testing for certain contaminants should be made via a risk-based approach, following the accumulation of substantial data over a sufficiently long period that demonstrates a low risk of variation in the contaminant levels at all periods of growth, harvesting and processing of the botanical.

As a minimum, the CoA should include:

- specific identification of the batch, including date of manufacturing
 - confirmation of the identity of the botanical extract
 - confirmation that the extract complies with the specification with regard to the physical and chemical composition of the extract
- confirmation that the extract complies with the legal and otherwise agreed requirements for contaminants with full details provided either on the CoA itself or in an accompanying document

Confirmation of the irradiation status of the commercial extract (including the botanical source) and other relevant compliance declarations can be reported on CoA or on separate statements.

For extracts intended for use in food supplements, it is essential that the CoA and any accompanying documents contain sufficient analytical data on extract composition and contaminant levels to allow the manufacturer of the supplement to ensure compliance of the final supplement product with all relevant food legislation. Where contaminant legal upper levels are based on the finished food supplement product, the food supplement manufacturer is required to calculate the cumulative input of the contaminant using the CoA from each individual ingredient. The CoA should describe the parameter tested, the specification value and range, the test result and a reference to the analytical method.

2. Verification of Process

Consistency of the production should be supported by appropriate use of master batch records and change control procedures.

In the framework of the HACCP system in place, manufacturers should take the necessary measures to ensure that all stages of the process will consistently achieve the expected results. Manufacturing and quality assurance should be conducted in accordance with defined procedures. At each step the results and conclusions should be documented.

New processes or formulas should be designed to meet consistently the defined parameters of quality.

Any changes to the manufacturing process or to the raw material source, including any change in equipment, should be addressed by necessary modifications to the quality system. The safety profile of the preparation should also be re-verified.

A trend analysis should be carried out by the extract manufacturer on all analytical results at periodic intervals to ensure consistency of production.

3. Confirmatory Batches

Once a process has been verified, a sufficient number of production batches should be produced (where possible using different batches of raw material) and assayed to confirm consistency of production.

4. Questionnaire to assist Manufacturers with the assessment of Botanical Preparations

Accompanying this guidance is a Self-Assessment Questionnaire that has been developed to assist food supplement manufacturers with assessing the quality of botanical preparations when selecting their raw materials and to highlight areas where further information may need to be requested from the supplier; and also to help suppliers ensure that they provide adequate information to their customer.

It is recommended that companies apply this questionnaire and justify any omission of data.

The questionnaire should be duly completed, dated and signed by the responsible person in the company or by the supplier.

The Self-Assessment Questionnaire can be found at www.foodsupplementseurope.org

The European food supplement sector brings together many of the most innovative and dynamic companies in the food area, making a substantial contribution to Europe's public health goals.

Food Supplements Europe combines the unique expertise of associations and companies committed to building partnership with regulatory, scientific and consumer bodies to help shape the future regulatory and policy framework in this area and to ensure that consumers can benefit from safe and high quality products.



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