USP Guideline for Submission of New Food Ingredient Monographs to the Food Chemicals Codex

1. INTRODUCTION AND PURPOSE

The *Food Chemicals Codex* (*FCC*) is constantly updated and modernized through an open and transparent process. Many proposed updates to the *FCC*, including new monograph submissions, are submitted to FCC scientific staff by a Sponsor (i.e., contacts from industry, academia, regulatory bodies or any other interested party). A USP Scientific Liaison (Liaison) serves as a link between new monograph Sponsors and the Food Ingredient Expert Committee (–"FIEC"), the body of volunteers responsible for developing and approving *FCC* standards.) Sponsors proposing new food ingredient monographs to the *FCC* should understand that the public standard developed from any proposal may incorporate comments from other stakeholders and in all cases the text of the final standard will ultimately be decided by the FIEC.

This document provides basic guidance to Sponsors on how to submit information to support creation of a new food ingredient monograph in the *FCC*. All such requests shall be handled in accordance with Section 8.01(a) – (e) and other provisions of the 2015-2020 Rules and Procedures of the Council of Experts (CoE Rules), which govern all aspects of FCC's standards-setting processes. This Guideline is intended to promote optimal submissions from Sponsors to facilitate development and finalization of a public *FCC* standard in accordance with the processes outlined in the CoE Rules.

2. NEW MONOGRAPHS

The *FCC's* standards-setting process is an open and transparent process and public participation is encouraged. All requests to include a new food ingredient monograph in the *FCC* are assigned to a USP Liaison for the *FCC*. The Liaison works with the Sponsor of the new monograph to ensure that the submission contains the appropriate information and background materials required to initiate the standards-setting process. The Liaison also oversees the Sponsor's submission through completion of USP's standards-setting process. New food ingredient monographs submitted to the *FCC* are published as proposals in the *FCC Forum*, which publishes twice annually on the USP website (https://fccforum.usp.org).

The *FCC Forum* is free and open to the public and is the platform USP uses for proposing new and revised content to the *FCC*. The *Forum* opens on the last day of June and the last day of December. Once the *Forum* opens, interested parties may review proposed new food ingredient monographs and changes to existing *FCC* monographs and comment on the proposals. The comment period is 90 days from the opening of the *Forum* and all comments are routed to the Liaison responsible for the new food ingredient monograph. Comments received from the public may be used to alter the text of a proposed new monograph and

are always considered by the FIEC before voting on whether to adopt, modify, or reject a proposal.

To ensure that a new food ingredient monograph submission appears in the *FCC Forum* in a timely manner, it must include all relevant information and data r to support the submission (see below for necessary information). All requests to develop a new food ingredient monograph must be made to *FCC* staff via email or standard mail. The contact information for *FCC* staff is listed online at: www.usp.org/fcc/forum/staffDirectory.html.

For more complete information on the *FCC* Monograph Revision Process, please refer to the Guidelines for Revisions document available at: http://www.usp.org/food-ingredients/development-process/submit-monographs-revisions#guidelines

3. SUBMISSION OF A NEW FOOD INGREDIENT MONOGRAPH PROPOSAL

3.1 Overview

All proposals to add a new food ingredient monograph to the *FCC* should be accompanied by the following information and documentation, including but not limited to, the items listed below:

1. Documentation of the regulatory status (domestic or international) of the food ingredient and, if possible, a copy of any application or dossier previously submitted to a regulatory agency for the purposes of regulatory approval/assessment;
2. Technical details for the food ingredient (voluntary);
3. Proposed information for each appropriate monograph section;
4. Supporting data for all proposed specifications; and,
5. Method validation(s) for all proposed test procedures including all relevant test parameters.

3.2 Regulatory Documentation

Food ingredients appearing in the *FCC* must be permitted for use in foods or in food processing either in the United States or internationally. New food ingredient monograph proposals must include documentation regarding the regulatory status of the ingredient pertaining to its use in foods. This documentation may be provided to the *FCC* Liaison in several formats, including, but not limited to:

- *Code of Federal Regulations (CFR)* citations for approved food or color additives in the United States;
- Generally Recognized as Safe (GRAS) documentation, whether in the form of a formal Petition or Notification sent to the FDA, or the report created by a GRAS panel for a self-determined GRAS food ingredient;
- FDA responses to GRAS Petitions or Notifications;
- Color Additive Petitions;
- Food Additive Petitions; or,
- Documentation of regulatory approval for use in other countries (or sanction by an international regulatory body).

In all cases, it should be noted if the substance has been evaluated by the FAO/WHO Joint Expert committee on Food Additives (JECFA), which provides scientific advice to the Codex Alimentarius Commission and whether full specifications exist.

3.3 Technical Details

To aid USP Liaison and the FIEC in the evaluation of proposed specifications, relevant information on the method of manufacture and chemical composition of the food ingredient should be submitted if available. Method of manufacture information should include the principle(s) reagents used in the manufacturing process and a description of the manufacturing process including any reaction intermediates and solvents used. Chemical composition information should provide a characterization of the food ingredient sufficient to distinguish it from other similar food ingredients, including all available information on potential impurities and degradation products usually occurring in or arising from the method of manufacture employed.

While submission of these technical details is voluntary, it will aid the Liaison and FIEC in deciding whether or not the proposed monograph is comprehensive and merits inclusion in the *FCC*.

3.4 Draft Monograph Elements

3.4.1 Title and Chemical Information

A proposed title for the new monograph should be non-proprietary, preferably established by national legislation or used by international bodies. In the absence of these, the title may be chosen from existing common or trivial names and should be distinctive enough to enable the substance to be clearly distinguished from other food ingredients. Synonyms for the ingredient should be listed under the title and should account for all alternative names used in commerce and by regulatory authorities. The nomenclature used for flavoring agents may not be consistent with other authoritative sources.

Chemical information should be included directly under the title and synonyms list. This information includes the following elements when applicable: molecular structures, chemical formulas, formula weights, and applicable registry numbers such as those determined by CAS[1], FEMA[2], and INS[3]. If multiple registry numbers are relevant, please include all of them.

3.4.2 Description

Characteristics described and statements made in the *DESCRIPTION* section of a food ingredient monograph are not requirements, but are provided as additional information to *FCC* users. It often includes information on the origin of the substance and a brief description of the method of manufacture. The physical characteristics of the food ingredient, such as color and form of the specified substance are also described and information on the ingredient's stability under certain conditions of exposure to air and light may also be presented. Statements in this section also commonly indicate approximate physical properties of the ingredient such as solubility in various solvents, pH, melting point, and boiling point, with numerical values modified by "about," "approximately," "usually," "~," and other comparable nonspecific terms. The presence of other substances intentionally added in commercial preparations should also be indicated, as appropriate.

[1] CAS: Chemical Abstract Service
[2] FEMA: Flavor and Extract Manufacturers' Association of the United States
[3] INS: Codex International Numbering System for Food Additives (Codex Alimentarius Commission CAC/GL 36-1989)

3.4.2.1 Function

This section is also given for information only and not intended to limit in any way the use of the ingredient or to indicate that it has no other utility, nor should the *FCC* be seen as endorsing any specific use of the ingredient. A statement of function is provided to indicate the principal technical effect(s) of the ingredient in foods or in food processing (e.g., emulsifier) or a principal application such as "Nutrient". The terms used should be harmonized with those used in the most recent revision of the Codex Alimentarius *Class Names and International Numbering System for Food Additives* (CAC/GL 36-1989), or with those listed in the U.S. *Code of Federal Regulations* (21 *CFR* § 170.3(o)) or with existing *FCC* monographs of similar food ingredients if they exist.

3.4.2.2 Packaging and Storage

This section is advisory only and should provide statements describing the appropriate care for packaging and storage and emphasize instances where deterioration could be accelerated under adverse packaging and storage conditions, such as exposure to air, light, or temperature extremes, or where safety hazards are involved. Additional discussion is provided in the *General Provisions and Requirements Applying to Specifications, Tests, and Assays of the Food Chemicals Codex.*

3.4.2.3 Identification

The tests described under this heading are designed for application to substances taken from labeled containers and are provided as an aid to substantiate identification of a labeled food ingredient. These qualitative or quantitative tests may not be sufficient to establish proof of identity, but failure of a substance taken from a labeled container to meet the requirements of a prescribed identification test indicates that the ingredient does not conform to the requirements of the *FCC* monograph.

Proposed new *FCC* monographs should contain as many identification tests as necessary to differentiate the ingredient from similar components and, whenever possible, detect the presence of

relevant potential adulterants. Chromatographic and spectroscopic (infrared and ultraviolet) tests are common identification methods, and the use of a reference material may be indicated. The *General Tests and Assays* section of the *FCC* contains test procedures that may be applicable for a proposed new monograph.

3.4.3 Assay

Tests in this section provide a means of assessing the amount of the principal functional component(s) present in the food ingredient. This test (or tests) shall be quantitative and accompanied by a proposed minimum acceptable content or acceptable content range of the component. Typical *FCC* methods are titrimetric and chromatographic methods. Any required treatment of the sample should be clearly outlined and all calculations should contain adequately defined terms and variables with relevant units included. The *General Tests and Assays* section of the *FCC* contains test procedures that could be applicable for a proposed new food ingredient monograph.

3.4.4 Impurities

Test procedures and acceptance criteria for inherent impurities are provided to limit such substances to levels that are consistent with good manufacturing practices (GMPs) and that are safe and otherwise unobjectionable under conditions in which the food ingredient is customarily used. Sponsors should include impurity methods and limits based on their knowledge of all known manufacturing processes by which the food ingredient is produced and the raw materials used in that process. The *FCC* distinguishes impurities as either **Inorganic Impurities** or **Organic Impurities.** In most cases the FIEC expects any new monograph submission to include a limit for lead because of the prevalence of this impurity in food ingredients and the associated health risks.

3.4.5 Specific Tests

This section contains tests that do not clearly fall under any of the other sections of a monograph. They are included to provide a better description of the food ingredient, to ensure that the ingredient can be clearly distinguished from another, similar ingredient, and to minimize the opportunity for adulteration of the ingredient. In addition to any proposed tests unique to the food ingredient, the appendices in the *FCC* contain a number of general analytical procedures that may be appropriate as “specific tests”, such as Loss

on Drying, Residue on Ignition (Sulfated Ash), Acid Value, Iodine Value, and Viscosity. The Sponsor may choose to reference these existing procedures if they are relevant to the food ingredient.

3.4.6 Other Requirements

In some instances, a new FCC monograph will need to include a requirement that is clearly inappropriate for any of the other sections of the monograph. Where a labeling requirement is needed, it should be included under *Other Requirements.* Instances where a labeling requirement is appropriate include *FCC* monographs that specify more than one type of material, for instance solutions which may be sold in multiple concentrations.

4. DATA REQUIRED FOR NEW MONOGRAPH SUBMISSIONS TO *FCC*

4.1 Supporting Data

For all proposed acceptance criteria in a new monograph, supporting data should be presented from at least three independent and representative production batches. Such data can often be obtained from certificate of analysis documentation.

4.2 Method Validation

A new food ingredient monograph proposal including test procedures not currently contained in the *FCC* should be accompanied by the appropriate method validation package. A typical method validation package addresses some or all of the following parameters: specificity, linearity, range, limit of detection, limit of quantitation, ruggedness, robustness, accuracy, and precision. The data and information included in this package can vary depending on the type of test method involved. The section on *Validation of Food Chemicals Codex Methods* in the *FCC* provides a detailed discussion to assist in identifying necessary validation parameters.

If you have more questions, please contact the USP Food Ingredients Group at fcc@usp.org or 301-881-0666.

5. REFERENCE MATERIALS

When submitting a proposal to include a new food ingredient to the *FCC*, a Sponsor may be asked to provide all appropriate information and background materials, including suitable bulk reference materials, in accordance with the requirements set forth in USP's Guideline for Donors of USP Reference Standard Candidate Materials (http://www.usp.org/sites/default/files/usp_pdf/EN/referenceStandards/usp_reference_materi

al_information_form.pdf). If a Sponsor is unwilling to provide such reference materials or for any reason such reference materials prove inadequate for compendial use, USP may source such materials elsewhere or develop appropriate reference materials in its own laboratories, and use any such materials and resulting Reference Standard (RS) as a component in *FCC* monographs and as a part of USP's public *FCC* standards. Also note that USP RS are not reserved for use with any particular USP compendium or standard. It is USP policy that any reference materials likely to be required for use with an *FCC* standard (approved by the FIEC as suitable for use as comparison standards in *FCC* tests and assays) either accompany a Sponsor's submission, or be part of an overall monograph development commitment.

6. CONFIDENTIALITY, DOCUMENT DISCLOSURE AND INTELLECTUAL PROPERTY POLICIES

USP has established policies and rules that provide the highest safeguards to confidential information submitted by Sponsors during the course of the standards-setting process. USP's confidentiality policies and the CoE Rules require both USP expert volunteers and staff involved in USP's standards-setting process to maintain the confidentiality of information submitted to USP by a third party. Below is a brief summary and link that provides additional information on each of the specific policies, provisions of the CoE Rules, and procedures concerning confidentiality.

6.1 USP Code of Ethics Confidentiality Policy

The USP Code of Ethics (http://www.usp.org/ethics) applies to USP employees, expert volunteers and representatives. The Confidentiality Policy in the USP Code of Ethics obligates everyone at USP to protect confidential information and proprietary information, whether generated by USP or by third parties, unless disclosure is authorized or legally mandated. All information about USP and our compendial activities is considered confidential unless it is made publicly available by USP or it is known to be publicly available outside of USP.

Confidential information consists of information that is not available to or intended for the public to view and can fall within, but is not limited to, the following categories:

- financial, scientific or medical information; customer information;
- supply and service information; marketing information;
- correspondence between and among USP staff and members of its Board of Trustees, Council of Experts, and Expert Committees;

- personnel or consultant files;
- trade secrets; and,
- confidential information relating to manufacturing processes and other information which USP or a third party may deem confidential.

USP's confidentiality policy does not apply when a third party's information is required to be disclosed by law, regulation, rule, act or order of any governmental authority or agency, such as identifying country of origin on USP reference materials.

6.2 USP CoE Rules and Confidentiality

The CoE Rules (http://www.usp.org/about-usp/leadership/policies-rules/rules-procedures-council-experts) reinforce the obligation of USP expert volunteers to maintain confidentiality during their standards-setting activities. Under Rule 2.06, CoE and EC members must maintain the confidentiality of all information they receive during the standards-setting process and are prohibited from disclosing any information for any purpose unless the information is already publicly available. **In cases of doubt as to the confidentiality of information, the information in question must be treated as confidential unless otherwise shown.** Under Rule 6.02, government liaisons to such Expert Committees and Expert Panels also have access to such information and are permitted to use it only for USP standards-setting purposes. USP expert volunteers and government liaisons sign a confidentiality agreement with USP reflecting these obligations.

6.3 USP Document Disclosure Policy

Under USP's Document Disclosure Policy, which is a part of the Code of Ethics, USP provides disclosure of information and records regarding USP standards-setting activities to third parties upon request consistent with:

- The rights of individuals to privacy
- USP's need to protect the confidentiality of trade secrets and other proprietary commercial or financial information
- USP's need to promote frank internal deliberations and to pursue standards-setting activities without disruption

USP will not disclose any document containing trade secrets or confidential commercial secrets, "if such documents have been specifically designated as such

when submitted to USP . . . ."[4] Accordingly, sponsors should indicate in their Request for Revision whether any of the submitted documents or other information should be treated as confidential. Any submitted documents not clearly marked confidential will be subject to disclosure under the Document Disclosure Policy. As a general policy, USP undertakes to keep sponsor names confidential when providing documents under the Document Disclosure Policy, but USP reserves the right to disclose the identity of a sponsor at its discretion if circumstances warrant.

6.4 Intellectual Property

At times, issues of intellectual property arise regarding a monograph. Under USP's Intellectual Property Policy, available on USP's Website, USP respects intellectual property rights and uses its best efforts to adhere to all applicable laws regarding USP protection of intellectual property. USP is not, however, responsible for the protection or enforcement of intellectual property rights in the U.S. and elsewhere, and because USP's standards are intended to be public standards available for the use and benefit of all parties, USP requests that sponsors disclose in their Requests for Revision whether any portion of the methods or procedures submitted is subject to patent or other sponsor-held intellectual property rights. In cases where patented methods, procedures or materials required for compendial tests and assays (such as RS or photomicrographs) are proposed, USP may seek assistance from the sponsor in obtaining clearance or license for use by any persons seeking to use or apply a USP public standard incorporating such method, procedure or material, and may consider other approaches including the solicitation of other Requests for Revision that use alternative methods or procedures. USP reserves the right to indicate in a resulting monograph or general chapter whether methods or procedures are subject to such intellectual property rights.

This *Guideline* supersedes any previous guideline issued by USP on Submission of New Food Ingredient Monographs to the Food Chemicals Codex.

[4] However, the policy does allow documents submitted to USP by a third party containing trade secrets or confidential commercial secrets that ordinarily would be contained in a New Drug Application or Supplement thereto to be disclosed to the U.S. Food and Drug Administration upon its request in its review of any revision or proposed revision of the United States Pharmacopeia, National Formulary, or other USP compendium.