Supplemented food submission checklist – supplemental ingredient

Instructions

This checklist is divided into several main sections, each with a specific set of requirements:

Section 1: Administrative
Section 2: Description
Section 3: General information on health risk
Section 4: Toxicological considerations
Section 5: Allergenicity considerations
Section 6: Chemical considerations
Section 7: Nutritional considerations
Section 8: Microbiological and molecular biological considerations
Section 9: Additional considerations

As you work through each section, check off ☑ each completed item. If you have any questions concerning the items in this checklist, please contact the Submission Management and Information Unit (SMIU) via the following email address: smiu-ugdi@hc-sc.gc.ca. For information on how to prepare a submission to request a modification to the List of Permitted Supplemental Ingredients, please refer to Health Canada's Guidance Document: Pre-market Submission Process for Supplemented Foods. If further guidance is required, it is strongly recommended to request a pre-submission consultation with the Food Directorate.

How to submit

The submission should be sent electronically through the Online Application Form for Pre-Market Submissions to the Food Directorate. Please review the guidance document, titled How to Complete the Online Application and Transport Form for Pre-Market Submissions to the Food Directorate.

Note: Your submission must be organized following the order and titles of the main sections (Sections 1 to 9) set out above. Failure to do so will result in the closure of your submission.

If you cannot provide each piece of information required by the checklist (i.e., if you do not check off ☐ one of the boxes in the boxes in the checklist), you must provide a written explanation to justify why each piece of missing information is not provided to support the safety assessment of the supplemental ingredient. For example, if you are requesting that the conditions of use for an existing supplemental ingredient be modified such that it does not require the cautionary statement "Not recommended for those under 14 years old", you must submit data establishing safety for age groups 4 to 13, and explain why data are not being provided for populations ≥ 14 years old (e.g., because the substance has already been established to be safe for use in supplemented foods for those ≥ 14 years old under the same conditions of use).

Your explanation must be provided in the corresponding section of your submission, not in the checklist.

All fields are mandatory, unless otherwise indicated.

Section 1: Administrative	
1.1 Name of petitioner (manufacturer, company, consultant, importer, etc.):	
1.2 Name of proposed substance or supplemental ingredient:	

1.3 Cover letter The signed and dated cover letter must include the following information:	
☐	Title of submission[1]
☐	Submission type (i.e., supplemented foods)
☐	Submission sub-type (i.e., new supplemental ingredient OR modification to supplemental ingredient)
☐	Substance name, as it appears or is intended to appear in the List of Permitted Supplemental Ingredients
☐	Substance source, where applicable, as it appears or is proposed to appear in the List of Permitted Supplemental Ingredients
☐	Comment on eligibility of the substance for inclusion in the List of Permitted Supplemental Ingredients (i.e., is the substance included in the List of contaminants and other adulterating substances in foods; the List of maximum levels for various chemical contaminants in foods; Section 4.2.10.1, or Section 4.2.11.1 of the *Guidance Document: Supplemented Foods Regulations*; Schedule I to V of the *Controlled Drugs and Substances Act;* the Prescription Drug List; item 1 or 3 of Schedule 1 to the *Cannabis Act*?)
☐	Executive summary explaining the proposed conditions of use (including supplemented food categories to which the substance is proposed to be added; maximum amount per serving and per day; proposed cautionary statements required on the label and corresponding threshold levels; and any other proposed conditions of use)
☐	Reference to related submission number(s) (or titles if a submission number is not yet available), where applicable (e.g., pre-submission consultation, closed submission, cross-linked supplemented food category submission)

[1] Please follow the naming convention for the title: For new supplemental ingredients (SI), the naming convention is: [SI name] (from [source] when applicable) in [SF category [X] (subcategory if applicable)] OR [all SF categories] OR [name of proposed SF category]. E.g., L-theanine in SF category 9; Ashwagandha root extract in all SF categories; Creatine in SF category 5 (granola bars). For a modification to an SI, the naming convention is: Change to [condition of use] for [SI name] (from [source] when applicable) in [SF category (X) (subcategory if applicable)] OR [all SF categories] OR [proposed SF category]. E.g., Change to conditions of use for biotin in all SF categories; Change to maximum amount for caffeine in SF category 5 (protein-isolate- and cereal-based bars); Change to cautionary statements for L-Leucine in pudding.

1.4 Authorization forms **Note:** A signed DPA form need only be provided if the primary contact is a designated party (e.g., consultant) authorized to act on behalf of the petitioner. The primary contact serves as the individual to which all correspondence from the Food Directorate will be sent.	
☐	Signed Designated Party Authorization (DPA) Form

Section 2: Description	
☐	Identity of substance (Proper name and/or descriptive name; Chemical Abstract Service (CAS) Registry Number(s), where applicable)
☐	Source material (if applicable)
☐	Natural presence in diet and/or human body (if applicable)
☐	Detailed description of manufacturing process (including identification of all raw materials used[2] and a detailed explanation of each step[3])
☐	Composition (name and quantitative declaration of components; function of components)
☐	Specifications (i.e., active components or key constituents, impurities, stability, etc.)
☐	Analytical methods for specifications
☐	Specifications and standards of quality developed by other organizations (if available)
☐	Proposed maximum amount (per serving and per day)
☐	Food category(ies) of interest for addition of the substance
☐	Proposed cautionary statements and corresponding threshold levels
☐	Other proposed conditions of use

Section 3: General information on health risk (including non-food formats)[4]	
☐	Safety narrative (regarding the overall safety of the substance under the proposed conditions of use, based on the conclusions of Sections 3 to 9 of this checklist)

[2] Including CAS Registry number where applicable; technological purpose; level of use; identification of the step in the manufacturing process at which each raw material is used (See Appendix 1, Section 1.6 of the Guidance Document: Pre-market Submission Process for Supplemented Foods)
[3] Please ensure to highlight details about the control measures taken to ensure that the microbiological safety/quality parameters of the proposed substance are consistently met (See Appendix 1, Section 1.8 of Guidance Document: Pre-market Submission Process for Supplemented Foods)
[4] Note that this information is requested in order to assess the safety of the substance under proposed conditions of use; however, substances that require more extensive cautionary labelling (e.g., contraindications, duration of use statements) under the proposed conditions of use are not appropriate for supplemented foods

☐	Adverse effects (e.g., unintended response to the substance)
☐	Evidence of interactions (e.g., with Natural Health Products[5], other foods, drugs, clinical diagnostic tests)
☐	Sensitive sub-populations (e.g., children, pregnant or breastfeeding women, individuals with medical conditions)
☐	Other requirements or instructions for use (e.g., do not use longer than X duration)
☐	Scientific evaluation, approvals, and regulatory status in other jurisdictions

Section 4: Toxicology considerations

☐	Summary of toxicology studies[6] provided (including discussion of how the test results support the safety of the substance under the proposed conditions of use, and the relevance of the test material from the toxicology studies to the substance proposed for addition to the List)
☐	Pharmacokinetic/toxicokinetic studies
☐	Acute toxicity studies
☐	Short-term (sub-chronic) toxicity studies
☐	Long-term (chronic) toxicity and carcinogenicity studies
☐	Genotoxicity studies
☐	Developmental toxicity studies
☐	Reproductive toxicity studies
☐	Other specialized toxicity studies
☐	Human clinical studies
☐	Alternative methods

Section 5: Allergenicity considerations

☐	Detailed discussion of the allergenic safety of the substance under the proposed conditions of use, with reference to supporting data
☐	For each study provided, a discussion of how the results of the study support the allergenic safety of the substance under the proposed conditions of use

[5] As per the *Natural Health Products Regulations*.
[6] Studies submitted should be conducted using the oral route of exposure

☐	Comments on the presence of priority allergens in the substance

Section 6: Chemical considerations	
☐	Confirmation and supporting rationale that all raw materials used (identified in manufacturing process detailed in Section 2) are of food-grade quality
☐	Residual level of materials used during manufacture (e.g., carrier or extraction solvents) in the finished substance or detailed scientific rationale (chemistry-based) explaining the absence of residues
☐	Contaminants (Inorganic)
☐	Contaminants (Organic)
☐	Contaminants (Natural, including mycotoxins)

Section 7: Nutritional considerations	
☐	Nutritional safety summary (discussing the overall nutritional quality and safety, including direct and indirect impacts, of the requested substance and its metabolic products under the proposed conditions of use)
☐	Presence and composition of anti-nutritional factors (e.g., saponins, tannins, isoflavones)
☐	Potential or observed interactions with nutrients
☐	Exposure for Canadian population as a whole and/or for sensitive sub-populations
☐	Nutrient composition, and standardization or concentration of nutrient content
☐	Bioavailability and metabolic fate of the substance and/or its components
☐	Impacts on metabolic organs (e.g., liver, adipose tissue, gastrointestinal tract) and potential clinical outcomes (e.g., obesity, diabetes)

Section 8: Microbiological and molecular biological considerations	
☐	Microbiological specifications that capture the relevant foodborne pathogens and spoilage microorganisms that would impact the safety and quality of the proposed substance
☐	Results of certificates of analysis from 3 non-consecutive production lots demonstrating that the microbiological specifications of the proposed substance are consistently met, including the lack of antimicrobial resistance
☐	Internationally recognised, standardised methods used for microbiological analysis, with reference materials

☐	Control measures taken to ensure that the microbiological safety/quality parameters of the proposed substance are consistently met (as outlined in manufacturing process described in Section 2)
The following information is required for a substance consisting of, or derived from, a microorganism. Otherwise, please provide written confirmation, in the corresponding section of your submission, that the substance does not consist of, nor is it derived from, a microorganism.	
☐	An accurate identification of the strain with appropriate taxonomic designation (i.e., family, genus, species, and strain and/or culture collection number [e.g., deposition or accession number], based on the INCP International Code of Nomenclature of Prokaryotes or the International Code of Nomenclature for algae, fungi, and plants) along with a brief description of the type of tests used to identify the organism, with references
☐	Data on the potential of the microorganism for pathogenicity, virulence, or other hazards to human health, such as metabolites or allergens
☐	Demonstration that the microorganism does not express clinically relevant antibiotics
☐	Demonstration of the absence of the microorganism in the final product/substance, where applicable
☐	Data on the presence of antimicrobial resistance factors if the microorganism is present in the end product/substance
☐	The number of viable cells (colony-forming unit, CFU) in the final product/substance
☐	Data on the capacity of the microorganism to survive and/or colonize the gastrointestinal tract
The following information is required for a substance that is, or is sourced from, a genetically modified organism. Otherwise, please provide written confirmation, in the corresponding section of your submission, that the substance does not consist of, nor is it sourced from, a genetically modified organism.	
☐	Information on the method of genetic modification, including references
☐	Characterization of the inserted genetic material, or if no inserted material, a characterization of the modification made to the host genome
☐	Where the gene(s) of interest (e.g., coding sequence, signal sequence, codon optimization) differ(s) from its/their wildtype counterpart, information on the nature of those changes and safety implications
☐	Information indicating that the genetically modified microorganism is well-characterized morphologically and phenotypically
☐	Scientific data that establish the molecular characterization of the genetically modified microorganism, including but not limited to, insert intactness, expression cassettes copy number, orientation of tandem expression cassettes, integration sites, specificity of integration
☐	Information showing the genetic modification had no unintended effects

☐	Information on any genes and/or regulatory elements that were disrupted, deleted, silenced, modified, or affected by the insertion at the integration site(s), or are proximal to the insertion site(s)
☐	Scientific data that demonstrate the genetic stability of the integration event or plasmid across several generations
☐	Information on whether the integration event(s) is/are likely to affect expression of genes proximal to the insertion site(s)
☐	Bioinformatic analysis performed at the insertion site(s) and flanking sequences for any similarity hits against known toxins, allergens, and secondary metabolites
☐	Information on the characteristic/substance (protein, other molecule, etc.) that results from the modification

Section 9: Additional considerations	
☐	Additional information about food categories being considered, if applicable (e.g., clear description of the food category; special packaging considerations)
☐	Verification that the notification requirements have been met regarding environmental assessments for new ingredients under the New Substances Notification Regulations (NSNR)[7]
☐	Other (as applicable)

[7] The *New Substances Notification Regulations (Chemicals and Polymers)* and the *New Substances Notification Regulations (Organisms)* (collectively referred to as the NSNR) of the *Canadian Environmental Protection Act*, 1999. Guidance documents on current New Substances Notification requirements for all new substances are available on Environment and Climate Change Canada's New Substances program website. Questions concerning the NSNR for substances in products regulated under the *Food and Drugs Act* should be directed to the Environmental Assessment Unit of Health Canada (eau-uee@hc-sc.gc.ca).