Guidance Document #04
Manufacturing Process and Specifications
December 2020
At Step 4: Public Consultation

MANUFACTURING PROCESS AND SPECIFICATIONS

December 2020
adopted by the ICCF Steering Committee

The International Cooperation for Convergence of Technical Requirements for the Assessment of Feed Ingredients (ICCF) was launched in 2017 and aims to develop and establish common guidance documents to provide technical recommendations for the assessment of feed ingredients, including new uses of existing feed ingredients.

This guidance document has been developed by the appropriate ICCF Experts Working Group and was subject to consultation by the Parties, in accordance with the ICCF Process.

The founding members of the ICCF include the Canadian Food Inspection Agency (CFIA), the European Commission (DG SANTE), the U.S. Food and Drug Administration (FDA), as well as the American Feed Industry Association (AFIA), the Animal Nutrition Association of Canada (ANAC), the EU Association of Specialty Feed Ingredients and their Mixtures (FEFANA) and the International Feed Industry Federation (IFIF).

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1. INTRODUCTION

1.1. Objective of the Guidance

This document provides guidance regarding the requirements to be included in application for pre-market approval or authorization for feed ingredients with regards to their manufacturing process and specifications.

The required information is an important part of assessing safety during a feed ingredient's pre-market approval or authorization process. It also supports the identification of the feed ingredient. This guidance document has been developed with an international team of experts and considers the best practices for the provision of meaningful data and information.

While the guidance document supports the acceptability of the types of data and information to be provided, applicants are advised to consult the appropriate regulatory authorities and their guidelines during the development phase of new feed ingredients or a new use of an authorized ingredient. This will help to determine whether the information provided is acceptable or needed for a specific pre-market approval or authorization.

1.2. Definitions

The following definitions apply solely in the context of this guidance document:

Active substance[1]: Any substance in a feed ingredient that contributes to its intended effect.

Batch: An identified quantity of a feed ingredient having uniform characteristics, with specified limits and is produced from the same cycle of manufacturing production.

Microbial Biomass: The result of a fermentative process. It may include the total product of the fermentative step or the by-product of fermentative steps, where the active substance has been removed for further steps or to produce the ingredient market formulation(s).

Carrier: A feed ingredient or water used to facilitate the handling of the feed ingredient under assessment and its incorporation into ingredient market formulations, premixtures, feeds or water. The use of a carrier does not alter the feed ingredient's intended effect and purpose.

[1] Active substance includes microorganisms that contribute to the intended effect.

Contaminant[2]: Any substance not intentionally added to feed , which is present in such feed as a result of the production, manufacture, processing, preparation, treatment, packing, packaging, transport or holding of such feed, or as a result of environmental contamination.

Feed (Feedingstuff)[3]: Any single or multiple materials, whether processed, semi-processed or raw, which is intended to be fed directly to animals.

Feed ingredient[3]: A component part or constituent of any combination or mixture making up a feed, whether or not it has nutritional value in the animal's diet. Ingredients are of plant, animal, microbial or aquatic origin, or other organic or inorganic substances.

Hazard Analysis and Critical Control Points (HACCP) Programme[3]: A system which identifies, evaluates, and controls hazards which are significant for feed safety.

Ingredient market formulation: The feed ingredient under assessment formulated with carrier(s) and/or other feed ingredient(s). It is the commercial product used to incorporate the feed ingredient under assessment into premixtures, feeds or water.

Materials[4]: Substances, including raw materials and other inputs (excluding processing aids and carriers) used for the manufacturing process. (see flow chart).

Purity: Concentration or other quantitative measurement of the active substance in the feed ingredient.

Processing Aid[5]: Any substance, not including apparatus or utensils, and not consumed as a feed ingredient by itself, intentionally used in the processing of materials, feed or feed ingredient, to fulfil a certain technological purpose during treatment or processing and which may result in the non-intentional but unavoidable presence of residues or derivatives in the feed ingredient or its ingredient market formulation, provided that these residues and derivatives do not have an adverse effect on animal health, human health or the environment[6].

Specification[3]: A list of tests results, referenced to analytical procedures, and appropriate acceptance criteria that are numerical limits, ranges, or other criteria for the test described. It establishes the set of criteria to which a feed ingredient and materials must conform to be considered acceptable for its intended use.

[2] Adapted from the CODEX Alimentarius General Standard for contaminants and toxins in food and feed (CXS 193-1995), considering CAC/GL 80-2013. This definition covers the impurities linked to the process or carried over from the materials. This term does not include insect fragments, rodent hairs, and other extraneous matter.
[3] Note adapted from Code of Practice on good animal feeding (CAC/RCP 54-2004).
[4] Note that processing aids are not considered as materials.
[5] Adapted from the CODEX Alimentarius general Standard for the labeling of food additives when sold as such and from the definitions in the Regulation 1831/2003/EC on additives in animal nutrition.
[6] Note that some processing aids may also be used as functional feed ingredients.

1.3. Scope of the Guidance

The types of feed ingredients covered by this guidance document are determined by the relevant regulations and statutes of each regulatory jurisdiction, where the feed ingredient is to be marketed.

This guidance document also provides support for the development of the specifications of the feed ingredient.

Note that the aspects related to the actual genetic modification of an organism that produces/is the feed ingredient are out of the scope of this document.

2. GENERAL PRINCIPLES

There can be significant variability in manufacturing processes given the broad range of feed ingredients used. This guidance document captures this variation. The information to be provided in an application may depend on the process and/or the feed ingredient under assessment. However, in the development of the application, it is necessary for the applicant to consider all data required for a complete assessment of the feed ingredient and its specification, in relation to its manufacturing process.

The description of the manufacturing process of the feed ingredient is an important complement to its identification and characterization. The manufacturing process should be completely described and include all process steps from the materials to the packaging of the feed ingredient and/or its ingredient market formulation. The establishment of specification linked to the manufacturing process is also an essential part of the identification and characterization of the feed ingredient.

One of the main principles of this guidance document should be the verifiable justification that the process is sufficiently controlled to produce a safe feed ingredient of consistent quality (purity criteria, physico-chemical characteristics, contaminants, and other undesirable substances).

When the manufacturing process is based on a series of different steps (e.g., a fermentation step followed by a chemical step), each of the different steps and their sequence should be clearly described.

The flow chart in ANNEX I illustrates the different steps of the manufacturing process for a feed ingredient and its ingredient market formulation. It may be used as a template for the description of the feed ingredients' manufacturing processes.

While the information regarding the manufacturing process of feed ingredients may be protected by Intellectual Property Rights, its disclosure during the pre-market assessment may be covered by confidentiality rules. It is advisable to contact the authority of the country/region, where the documentation is to be submitted, to be informed on the confidentiality rules existing in that country/region.

3. DESCRIPTION OF THE MANUFACTURING PROCESS

The description of the manufacturing process provides important information for the safety assessment of the feed ingredient. It allows for the verification that potential contamination of the feed ingredient or its ingredient market formulation, as appropriate, is sufficiently controlled by the applicant to produce a safe feed ingredient in a consistent manner. The description of the critical control points of the process provides confidence that the presence of contaminants and the introduction of potential hazards are monitored and controlled.

Feed ingredients can be manufactured using various processes. It is neither realistic nor achievable to provide detailed guidance for all possible processes. Rather, this guidance document can help applicants to identify what relevant information should be provided in their application. For example, the following information could be included:

- The materials and/or processing aids used in the manufacturing process,
- The manufacturing process steps,
- The ingredient market formulation process, including carrier(s) and/or other feed ingredient(s) used,
- The packaging step, including description of the packaging used.

3.1. Materials

All the materials used in the manufacturing process of the feed ingredient under assessment should be listed and identified using international naming standards, when available. Their quality and safety should be documented by the compilation of safety and/or product datasheets. A quantitative approach may be required when the safety profile of the feed ingredient or one of its contaminants justifies it.

3.1.1. CHEMICAL MATERIALS

The following information may be provided for chemical materials, as applicable:

- Chemical name (IUPAC), scientific name, common name, and/or other internationally accepted names/synonyms,
- CAS and/or EINECS number,
- Molecular and/or structural formula,
- Specification,
- Consideration of potential contaminants,
- Representative analysis to verify its identity and specification.

3.1.2. BIOLOGICAL MATERIALS

3.1.2.1. MATERIALS OF PLANT ORIGIN

The following information may be provided for material of plant origin, as applicable:

- Identification and description of the plant derived material,
- Name, source, and taxonomic classification of the plant from which the material is derived,
- Part of the plants used (e.g., seeds, meal, grain, leaves and other parts/co-products),
- Specification
- Consideration of potential contaminants and toxins,
- Representative analysis to verify its identity and specification.

3.1.2.2. MATERIALS OF MICROBIOLOGICAL ORIGIN

For microorganisms marketed as such, used as a source of a feed ingredient (production strains), or used to produce a feed ingredient (e.g., microbial biomass) the following information may be provided, as applicable:

- Identification and description of the microbiologically derived material,
- Taxonomic identification of the microorganism according to the most recent taxonomic nomenclature. The information should include genus, species, and/or strain (when applicable),
- The microorganism's name and its code, identifier, or deposition number (when applicable),
- Specification
- Consideration of potential contaminants and toxins,
- Representative analysis to verify its identity and specification.

3.1.2.3. MATERIALS OF ANIMAL ORIGIN

The following information may be provided for materials of animal origin, as applicable:

- Identification and description of the animal derived material,
- Name, source (including country of origin of the material) and taxonomic classification of the animal,
- Part of the animals used (e.g., blood, tissue, gland, bone, feather),
- Specification,
- Consideration of potential contaminants, including disease vectors,
- Representative analysis to verify its identity and specification.

3.1.3. MINERAL MATERIALS

The following information may be provided for mineral materials, as applicable:

- Identification and description of the mineral derived material,
- Name and source of the material (including country of origin),
- Specification,
- Consideration of potential contaminants,
- Representative analysis to verify its identity and specification.

3.2. Manufacturing Process steps

A feed ingredient manufacturing process is usually composed of multiple successive steps. The data required for the assessment of the feed ingredient shall cover the whole manufacturing process and each step should be described as below.

The description of the manufacturing process steps will help in assessing the safety and quality of the feed ingredient. With regards to safety, the applicant should provide information according to the principles of Hazard Analysis and Critical Control Points (HACCP) or an equivalent system. With regards to quality, the applicant should provide evidence that the manufacturing process ensures the production of a feed ingredient with consistent quality to meet the established specification.

The sequence of addition of the materials and/or processing aids during each of the manufacturing process steps should be described to allow the evaluation of the potential carry-over of unreacted materials and/or their by-products remaining in the feed ingredient or ingredient market formulation.

The description of manufacturing process steps should be provided in the form of a narrative along with a flowchart, describing the critical control points and process conditions.

Different types of manufacturing process steps can be envisaged, such as:

- Chemical steps, involving one or more chemical reactions,
- Fermentation/biological steps, involving the use of microorganisms or enzymes,
- Mechanical steps, involving the use of machinery (e.g., grinding),
- Thermo-physical steps, such as those involving the use of high temperature or pressure.

Specific details for each of these types of manufacturing process steps are given below.

3.2.1. CHEMICAL STEPS

The following information may be required for the description of chemical steps used in the manufacturing process of a feed ingredient:

- Measures applied to monitor chemical step performance within appropriate limits,
- List of material(s) and/or processing aid(s), (see Section 3.1.1),
- Key elements of the manufacturing process step such as:
  - The sequence of addition of the different material(s) and/or processing aid(s),
  - The subsequent chemical reactions, preferably with the chemical equation,
  - Indication of typical process conditions (e.g., times, temperatures, pH conditions, etc.),
- Controls considered for the identification of potential reaction by-products, carry over of unreacted materials, residual solvents, and contaminants (Note that contaminants may be carried over from the material(s) and/or processing aid(s) or may be generated during the chemical step).

Based on this description, the applicant should identify the potential reaction by-products, carry-over of unreacted materials, and processing aids. This will support the identification of potential contaminants, likely to be found in the resulting material or feed ingredient.

3.2.2. FERMENTATION/BIOLOGICAL STEPS

The following information may be required for the description of fermentation/biological steps used in the manufacturing process of a feed ingredient:

- Measures applied to monitor fermentation/biological step performance within appropriate limits:
  - The microorganism maintenance from batch to batch (e.g., master cell, working cell bank),
  - The sterilization and cleaning techniques applied,
  - The methods used to monitor the fermentative conditions,

- List of material(s) and/or processing aid(s) (see Section 3.1.2),
- Key elements of the manufacturing process step such as:
  - The sequence of addition of the different material(s) and/or processing aid(s),
  - The use of antimicrobials,
  - The indication of typical fermentation or growth conditions, for example temperature,
- Controls considered for the identification of potential contaminants.

Based on this description, the applicant should identify any potential substances of concern likely to be found in the resulting material or feed ingredient at the end of the fermentation/biological step, (such as viable cells, presence of fermentation by-products, carry-over of substrate, and microbiological contaminants).

3.2.3. MECHANICAL STEPS

The following elements may be required for the description of a mechanical step used in the manufacturing process of a feed ingredient:

- Measures applied to monitor mechanical step performance within appropriate limits and hygienic conditions of the equipment,
- List of material(s) and/or processing aid(s) (See Sections 3.1.2 and 3.1.3),
- Key elements of the manufacturing process step such as:
  - The type of mechanical step used (e.g., grinding, mixing),
  - The indication of typical mechanical step (e.g., duration, pressure)
- Controls considered for the identification of potential contaminants.

Based on this description, the applicant should identify the potential carry-over of material(s) and the contaminants, linked to the manufacturing process step, relevant to the feed ingredient.

3.2.4. THERMO-PHYSICAL STEPS

The following elements may be required for the description of a thermo-physical step used in the manufacturing process of a feed ingredient:

- Measures applied to monitor the thermo-physical step performance within appropriate limits and hygienic conditions of the equipment,
- List of material(s) and/or processing aid(s) (See Sections 3.1.1, 3.1.2, and 3.1.3),
- Key elements of the manufacturing process step such as:
  - The type of thermo-physical steps used,

- The source of energy used for the creation of heat and potential contacts with vapor or other emanation during the thermo-physical step used (e.g., combustion, boilers),
- The indication of the typical thermo-physical step conditions (e.g., time, temperature, pressure,
- Controls considered for the identification of potential contaminants.

Based on this description, the applicant should identify the potential carry-over of material(s) and the contaminants linked to the production method for the feed ingredient.

3.3. Ingredient market formulation process

Where an ingredient market formulation is required for the feed ingredient, the following information may be required:

- Description of the carrier(s) and/or other feed ingredient(s) included to produce the ingredient market formulation,
- Concentration of the feed ingredient under assessment or its active substance(s) in the ingredient market formulation,
- Typical composition of the ingredient market formulation,
- Process steps to obtain the ingredient market formulation.

3.4. Additional information

In addition to the description of the manufacturing process step(s), it may be required to provide additional information related to the packaging and the further use of the feed ingredient, such as:

- Description of the packaging material,
- Recommended storage conditions (e.g., temperature, specific handling),
- Shelf-life,
- Intended product labelling, including directions for use.

4. FEED INGREDIENT SPECIFICATIONS

This section provides guidance on how to describe the feed ingredient regarding its purity criteria and other relevant quality parameters. Contaminants likely to be inherent to the materials and/or processing aids used or introduced during the manufacturing process steps should be included in the specification. In the case of an ingredient market formulation, specification should consider the carrier(s) and/or other feed ingredient(s) used to produce it.

The purity of the feed ingredient and/or its active substance should be established based on the analysis of multiple batches (typically 3 to 5) of production[7], using validated or internationally recognized methods of analysis. It should be consistent with label indications.

A description of typical relevant contaminants based on the different manufacturing process step(s) and materials used is provided in ANNEX II of this guidance document for information.

The specification, necessary for the control of the compliance of the feed ingredient, should be proposed by the applicant, based on proper justification. They should reflect the identity, safety, quality (including the purity) and intended effect of the feed ingredient.

The description of the specification should also include the acceptable limits, units of measurement, and analytical methods used.

5. SPECIAL CONSIDERATIONS

There are cases where one or more of the manufacturing process step(s) of a specific feed ingredient may not fall under one of the process steps types described above (Sections 3.2.1, 3.2.2, 3.2.3, and 3.2.4). In these cases, the manufacturing process step(s) should be described in such a way that the relevant information is provided with the same level of detail as described in this guidance document for other types of manufacturing process steps.

6. BIBLIOGRAPHY

6.1. CODEX Alimentarius

1. General Standard for Contaminants and Toxins in Food and Feed (CXS 193-1995) – adopted in 1995, revised in 1997, 2006, 2008, 2009 and amended in 2010, 2012, 2013, 2014, 2015, 2016, 2017, 2018, 2019 - http://www.fao.org/fao-who-codexalimentarius/sh-proxy/en/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FStandards%252FCXS%2B193-1995%252FCXS_193e.pdf
2. The CODEX Code of Practice on Good Animal Feeding (CAC/RCP 54-2004) – 61 pages - http://www.fao.org/3/i1379e/i1379e06.pdf
3. Codex Standard (STAN 107-1981) - General Standard for the labelling of food additives when sold as such – 4 pages - http://www.fao.org/input/download/standards/2/CXS_107e.pdf
4. Hazards associated with animal feed – Joint FAO/WHO expert meeting, 2015 - 286 pages - http://www.fao.org/3/ca6825en/ca6825en.pdf

[7] In the case the number of batches is defined by the jurisdiction, where the feed ingredient is to be marketed, the applicant should use the number of batches as defined.

6.2. United States of America

5. CVM GFI #221 – Recommendations for Preparation and Submission of Animal Food Additive Petition - June 2015 – Section 2 https://www.fda.gov/regulatory-information/search-fda-guidance-documents/cvm-gfi-221-recommendations-preparation-and-submission-animal-food-additive-petitions

6.3. European Union

6. Regulation No 1831/2003 of the European Parliament and of the Council of 22 September 2003 on additives for use in animal nutrition, last amended by Regulation (EU) 2019/1243 of the European Parliament and of the Council of 20 June 2019 – EUR Lex Consolidated version pf 26.07.2019
7. EFSA FEEDAP Panel (EFSA Panel on additives and products or substances used in animal feed), Rychen G, Aquilina G, Azimonti G, Bampidis V, Bastos ML, Bories G, Chesson A, Cocconcelli PS, Flachowsky G, Gropp J, Kolar B, Kouba M, Lopez-Alonso M, Lopez Puente S, Mantovani A, Mayo B, Ramos F, Saarela M, Villa RE, Wallace RJ, Wester P, Anguita M, Galobart J and Innocenti ML, 2017; Guidance on the identity, characterization, and conditions of use of feed additives, EFSA Journal 2017; 15(10):5023 12 pp https://doi.org/10.2903/j.efsa.2017.5023
8. EU Regulation (EC) No 183/2005 of the European Parliament and of the Council of 12 January 2005 laying down requirements for feed hygiene, last amended by Commission Regulation (EU) 2015/1905 of 22 October 2015 – EUR-Lex Consolidated version of 23.04.2016

6.4. Others

9. FAMI-qs Code of Practice (Version6/Rev.4) 2018-10-02- 35 pages

ANNEX I – Flow Charts

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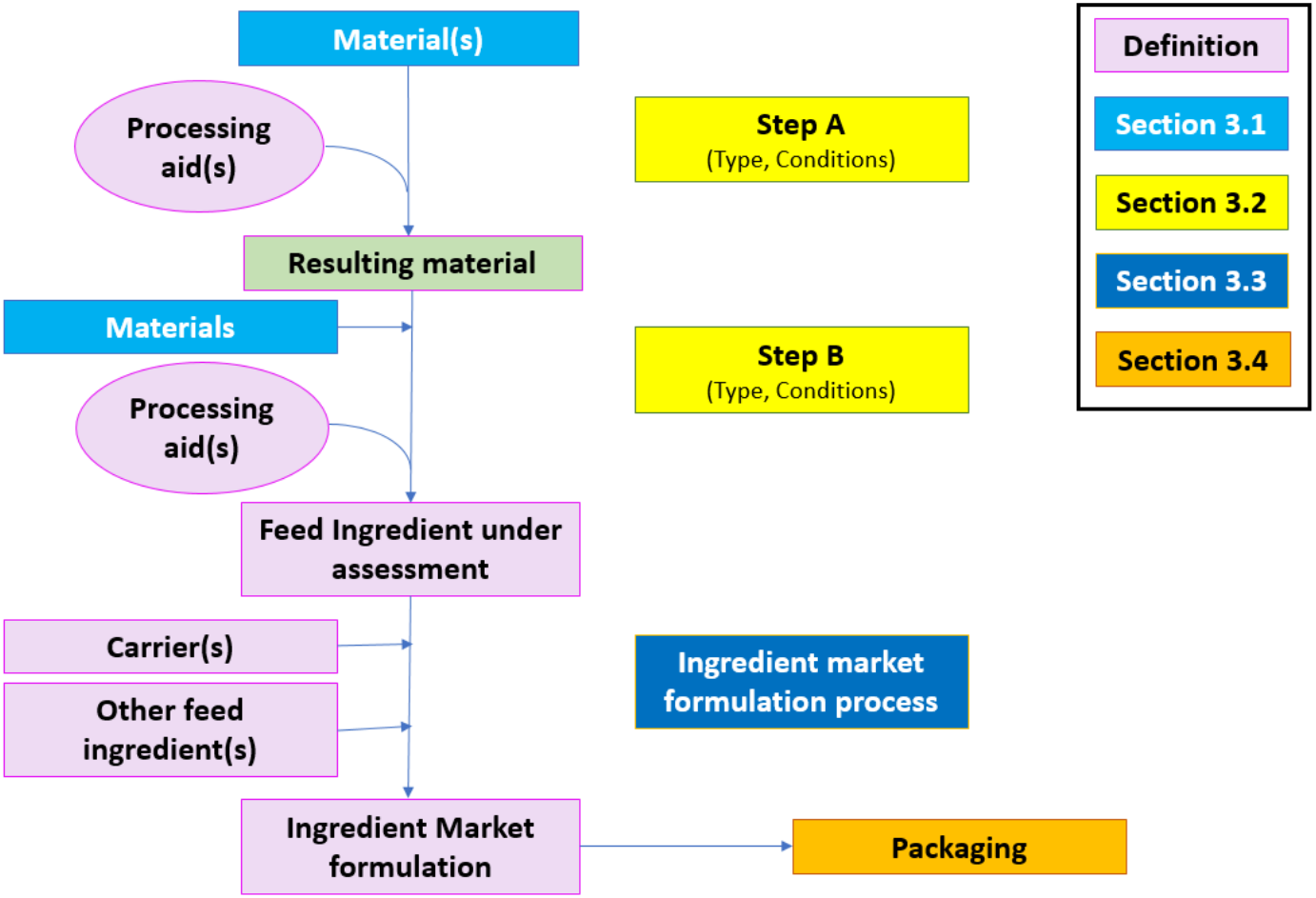
ANNEX I–1 Generic Flow Chart



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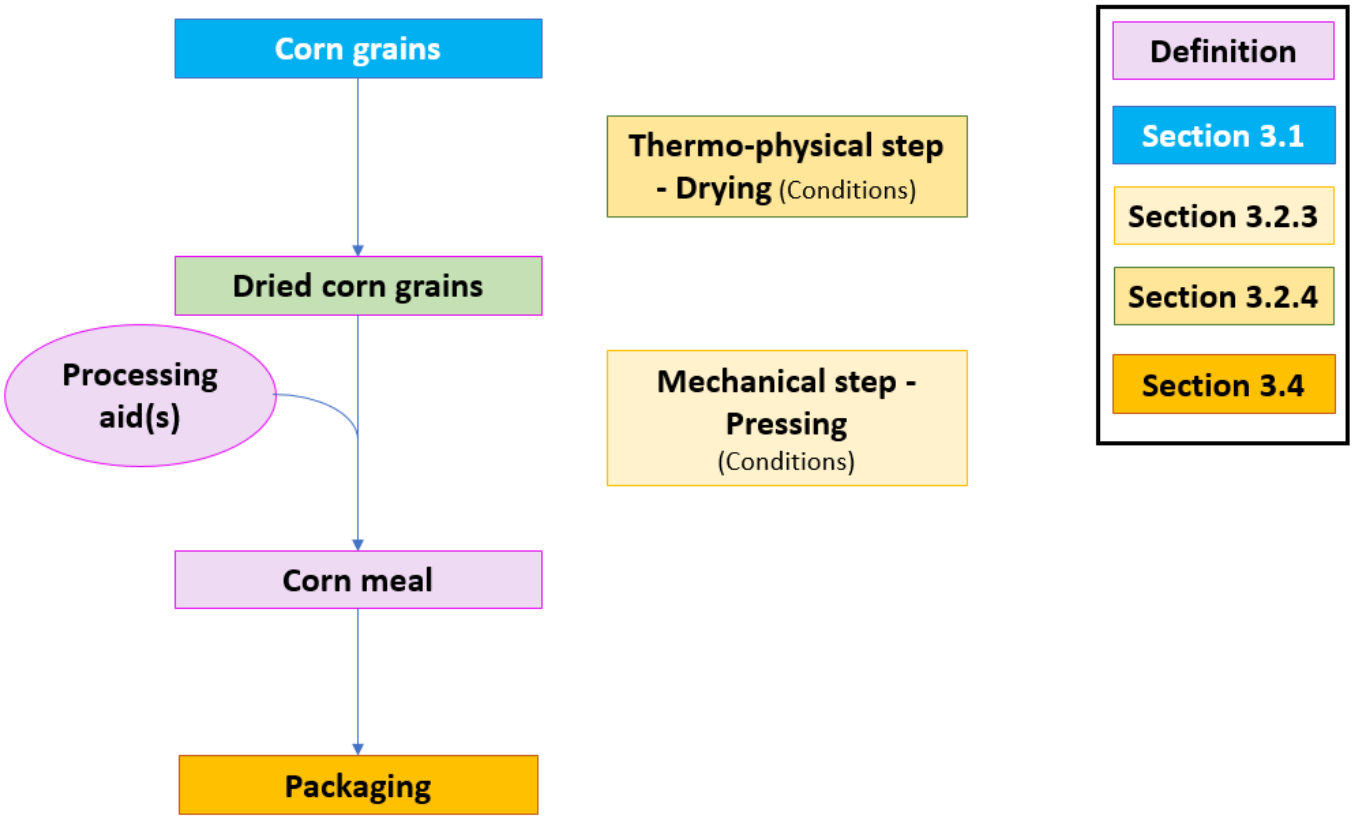
Annex I–2 Manufacturing process of a meal of agricultural product (e.g., corn grain)



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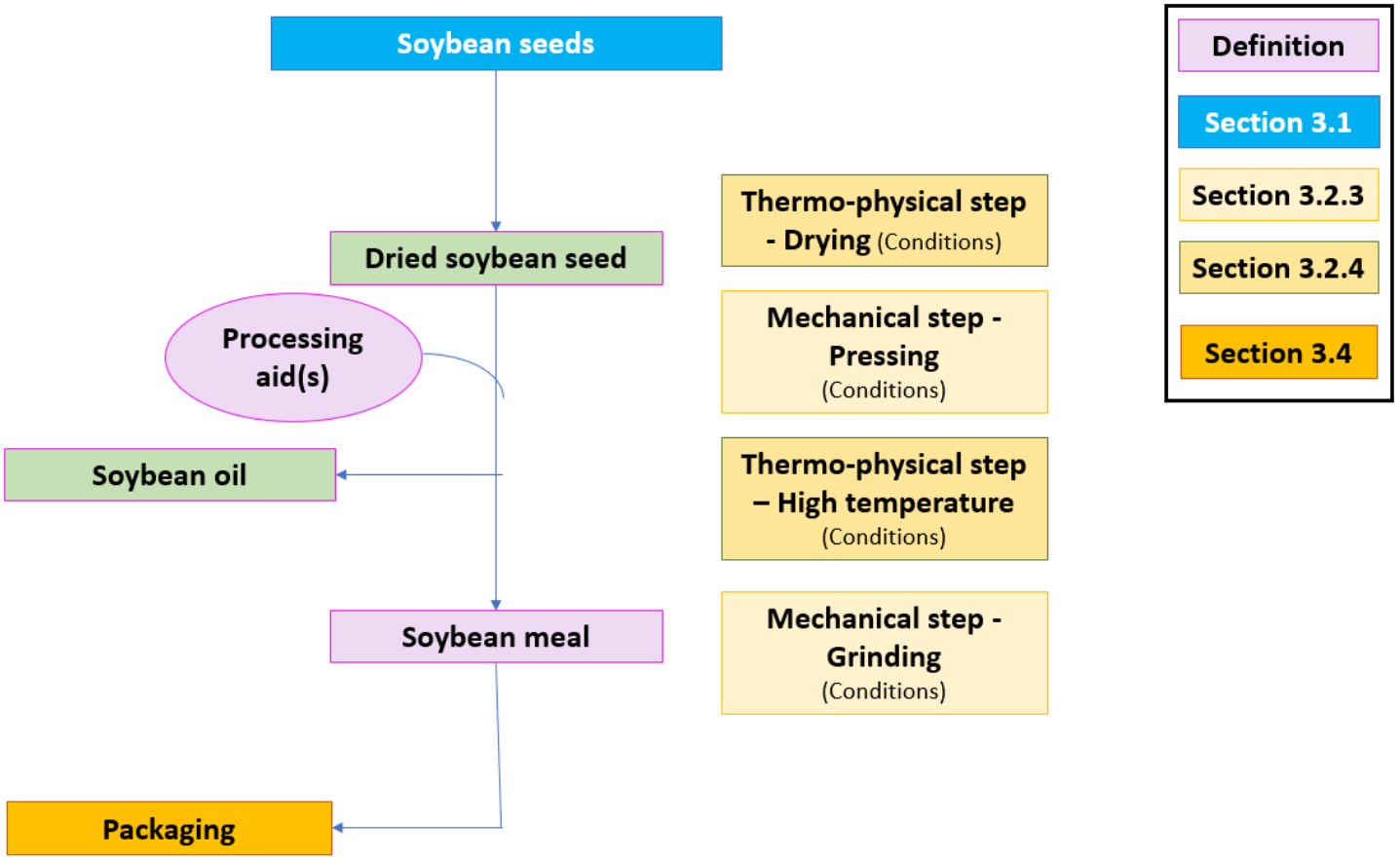
Annex I-3 – Manufacturing Process of a co-product of oil production (e.g., soybean oil)



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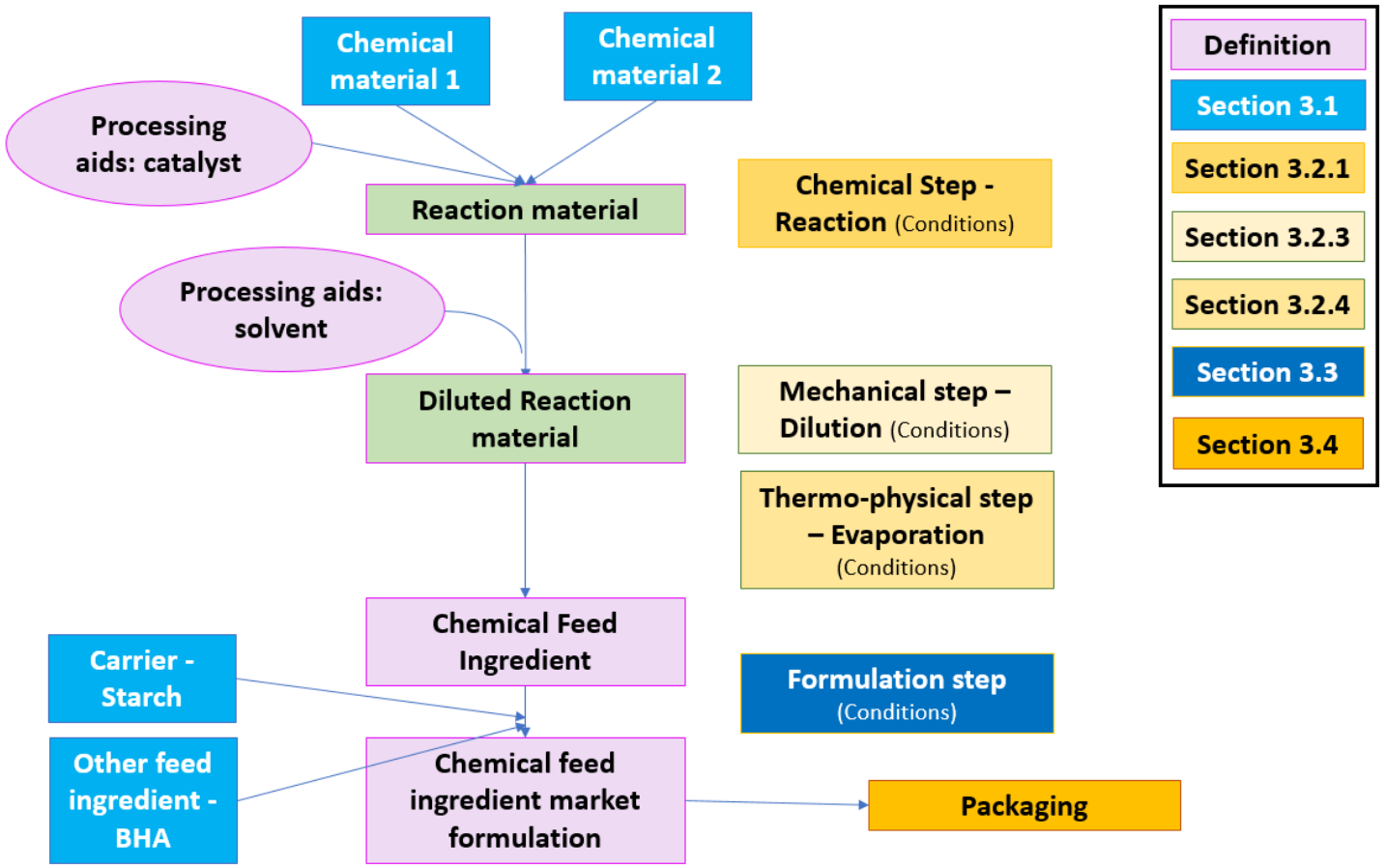
Annex I-4 – Manufacturing Process of a feed ingredient produced with a chemical step, placed on the market in a specific formulation



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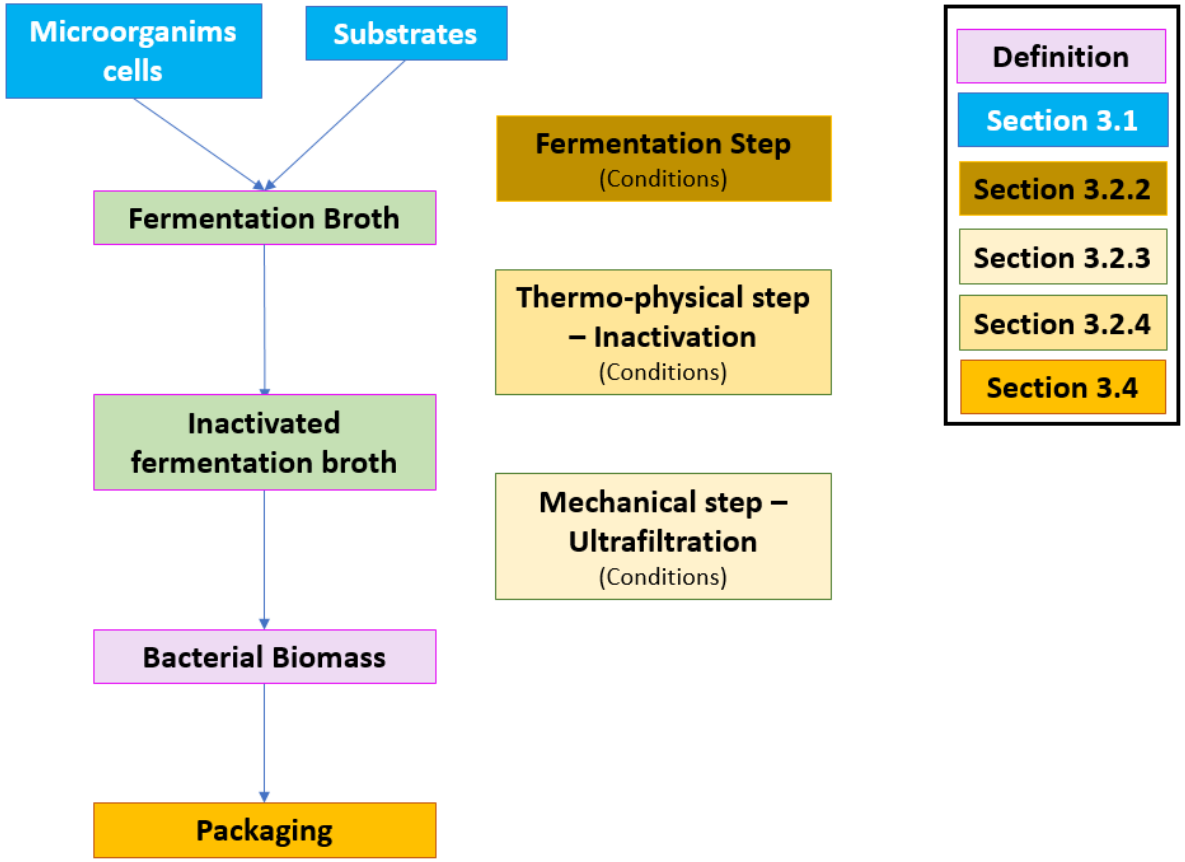
Annex I-5 – Manufacturing Process of a microbial biomass



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ANNEX II – Contaminants likely to be linked to the materials used in the manufacturing process of a feed ingredient

This table provides some examples of potential contaminants to be envisaged from different materials and manufacturing process steps used to produce a feed ingredient. This list is indicative and should be used as a guide for the assessment of the feed ingredient under assessment.

Source	PCBs and Dioxins	Heavy metals	Pesticides	Chemical residues	Micro-organisms	Drugs and antibiotics	Biotoxins (incl. mycotoxins)	Animal disease vectors
Materials								
Chemical material	X	X		X		X		
Plant material	X		X		X		X	
Microbiological material					X	X	X	
Animal material[8]	X				X	X		X
Mineral material	X	X		X				
Steps								
Chemical step	X	X		X				
Fermentation Step					X	X	X	
Mechanical Step								
Thermo-physical step	X				X			

In blue in the table, the potential contaminants in relation with the origin of the materials used in the process / In yellow in the table, the potential contaminants in relation with the manufacturing process steps used.re likely in the case of plant materials rich if fats and oils

[8] Animal material encompasses insects