Guidance Document #06
Feed Ingredients Environmental Risk Assessment Approach
June 2023
At Step 7: Steering Committee Endorsement

FEED INGREDIENTS ENVIRONMENTAL RISK ASSESSMENT APPROACH

Endorsed by the Steering Committee
June 2023

It is recommended for the companies planning to submit applications/dossiers for pre-market authorization, to contact the jurisdictions of the countries to confirm their acceptance of the current guidance document.

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).

TABLE OF CONTENT

TABLE OF FIGURES

TABLE OF TABLES

FEED INGREDIENTS ENVIRONMENTAL RISK APPROACH

1. INTRODUCTION

1.1. Objective of the guidance

This document provides guidance on the approach to be considered when preparing an application for pre-market approval or authorization of feed ingredients, with regard to environmental impact.

This guidance document has been developed with an international team of experts and is considered the best practice for the provision of meaningful data and information relative to environmental impact.

While the guidance document provides recommendations for 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 for a new use of an authorized ingredient. This will ensure that the information provided is acceptable or needed for a specific pre-market approval or authorization.

1.2. Definitions

The following definitions apply:

Active substance[1]: Any substance in a feed ingredient that contributes to the intended effect[2].

Contaminant[3]: Any substance not intentionally added to feed, which is present in such feed as a result of the production, manufacture, processing, preparation, treatment, packaging, transport or holding of such feed, or as a result of environmental contamination.

Constituent entity: Any chemical moiety present in the feed ingredient, including active substance(s).

[1] Active substance includes microorganisms that contribute to the intended effect.
[2] The intended effect refers to the conditions of use of the feed ingredient and not to the potential hazardous effect of the substance.
[3] Adapted from the CODEX Alimentarius General Standard for contaminants and toxins in food and feed (CXS 193-1995), considering CAC/GL 80-2013. This term does not include insect fragments, rodent hairs, and other extraneous matter.

Environmental compartment: A spatially distinct and homogeneous part of the physical environment, for instance soil, water, or air.

Feed (Feedingstuff)[4]: Any single or multiple materials, whether processed, semi-processed or raw, which is intended to be fed directly to animals.

Feed Ingredient[4]: 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.

Flow rate: The water flow through an aquaculture system, aiming at ensuring a sufficient aeration of the system (oxygen concentration in water), biological and solid filtration, and water exchange.

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.

Predicted Environmental Concentration (PEC): The estimation of the concentration of a constituent entity of the feed ingredient that reaches the relevant environmental compartment.

Predicted no effect concentration (PNEC): The estimation of the maximum concentration of a constituent entity of the feed ingredient that, when present in an environmental compartment, is not expected to cause adverse effects in non-target species.

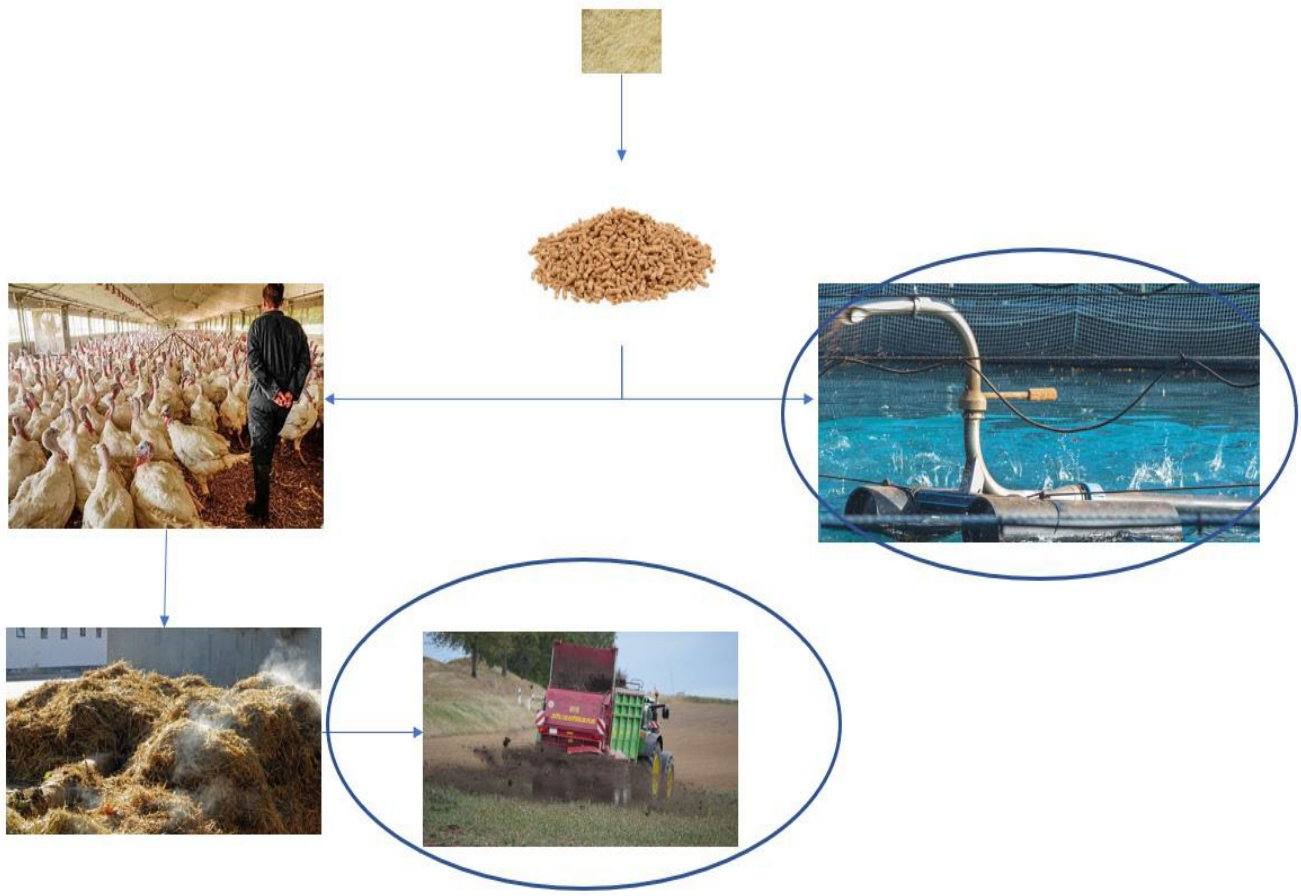
Target species: The animal species or class(es) for which a feed ingredient is intended in the application.

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 intended to be marketed. In general, the feed ingredients considered are the ones containing chemically defined constituent entities, although, under certain circumstances (e.g., potentially invasive species), other types of feed ingredients may be considered (e.g., plants or microorganisms).

[4] Adapted from Codex Alimentarius, Code of Practice on good animal feeding (CAC/RCP 54-2004)

This guidance document provides an approach for the assessment of the environmental risk of feed ingredients, as fed to the target species for the soil and water compartments (Figure 1). In the case of use in aquaculture, the potential risk of the feed ingredient to the aquatic environment through direct exposure should be assessed. In certain jurisdictions, the risk of feed ingredients for the air compartment could be evaluated on a case-by-case basis. This guidance document does not consider the air compartment. This guidance document is aimed to define when a further environmental risk assessment is required and its level of detail and complexity.



The circles represent the scope of this Guidance Document

Figure 1 – Approach taken for environmental risk assessment of feed ingredients

This guidance document is not applicable for feed ingredients intended to be used **only** for non-food producing animals (e.g., dogs, cats, zoo animals).

Regulations and definitions of Genetically Modified Organisms (GMO) differ between jurisdictions. Due to these differences, this guidance document does not cover the evaluation of the genetic modification, nor the environmental risk assessment of GMO, when released into the environment (e.g., cultivation of Genetically Modified Plants or rearing of Genetically Modified Animals). However, this guidance document covers feed ingredients (e.g., starch extracted from Genetically Modified wheat, active substances obtained from fermentation of Genetically Modified Microorganisms), when fed to the target species. In situations where the feed ingredient contains remnants of concern (e.g., presence of DNA coding for antimicrobial resistance, production of antimicrobials, toxins, or of virulence factors), the applicant should contact the relevant jurisdictions, to ascertain if any additional information is needed.

2. GENERAL PRINCIPLES

The environmental risk assessment aims at evaluating the potential impacts on the environment from the use of the feed ingredient[5]. The risk assessment estimates the risks to exposed ecosystems (usually, soil and water) by characterising and integrating information on estimated environmental concentrations and ecological effects obtained using established approaches and test methodologies. It is a stepwise assessment, where:

- The potential exemption of the feed ingredient to undergo an environmental risk assessment is evaluated based on a set of criteria (see Annex I).
- For a feed ingredient not being exempted from the environmental risk assessment (See Annex I), the concentration of feed ingredient in the environmental compartments is estimated and compared with threshold values (Phase 1 - see Section 3).
- If the concentration of feed ingredient in at least one environmental compartment exceeds the threshold values, the environmental risk assessment includes the refinement of the estimated concentration of feed ingredient in the relevant compartment, the determination

[5] The evaluation of a feed ingredient encompasses the active substance(s), the metabolite(s) originating from the active substance and all contaminants, as described in accordance with the Guidance Document on 'Identification and Characterization'.

of the potential effects of the feed ingredient on non-target species, and their comparison using the risk quotient method (a deterministic approach) (Phase 2 - see Section 4).

This guidance document aims to protect plant and non-target animal species at the population level for the relevant environmental compartments. It also aims at protecting microorganisms at the biological functional group level[6].

The evaluation should consider the active substance(s) and contaminant(s) of concern present in the feed ingredient, or the ingredient market formulation used in feed. When no active substance is defined (e.g., a plant extract), the risk assessment will aim at defining the types of constituent entity(ies) (e.g., protein, carbohydrates, polyphenols, relevant botanical compounds) present in the feed ingredient under assessment and evaluate them individually. If a mixture of feed ingredients is submitted for assessment, each feed ingredient of the mixture shall be evaluated individually, using the flow chart described in Annex I. Some complex mixtures may contain unidentified constituent entities. The environmental risk of these unidentified constituent entities requires a case-by-case evaluation, considering the origin of the complex mixtures and its potential associated risks. In such a case, the applicant should contact the relevant regulatory jurisdiction, where the feed ingredient is intended to be marketed.

3. PHASE 1 – SCREENING PHASE

Phase 1 is designed to determine if the use of a feed ingredient may result in an environmental concentration harmful to the environment, and if further evaluation in a Phase 2 assessment is necessary.

For Phase 1, the following environmental compartments are considered:

1. The soil compartment, with the focus of Phase 1 on the manure application on agricultural land, including the consideration of run-off[7].
2. The water compartment either from manure application on agricultural land or direct application (in the case of aquaculture), with the focus on surface water and sediment.

[6] A biological functional group is a collection of organisms with similar functional trait attributes that are likely to be similar in their response to environmental changes and effects on ecosystem functioning.
[7] Depending on the jurisdictions, the estimation of the concentration of feed ingredient in pore water and groundwater may be required.

Phase 1 screens the feed ingredients based on a series of criteria. The focus of the assessment is on the feed ingredient, when fed to the target species or introduced directly into water, in the case of aquaculture. The criteria have been organized in the form of a flow chart (see Annex I) and are described below:

1. Target species: the environmental risk assessment is focused on food producing animals, including those kept for breeding purposes.
2. Feed ingredients may contain one or more constituent entities. Each constituent entity in the feed ingredient[8] should be evaluated against the following criteria to decide whether or not it can be exempted from the estimation of environmental concentration:
    a. Constituent entities naturally present in the environment, and their metabolites, should be considered of low concern, if the use of the feed ingredient under assessment does not lead to a substantial increase (evaluated on a case-by-case basis) of its concentration and distribution in the receiving environmental compartment.
    b. Constituent entities extensively metabolized in animals or rapidly and completely degraded in manure during storage will not reach the environment and are considered of low concern (e.g., proteins).
3. Constituent entities
    a. which may potentially increase in concentration in the environment after multi-year use of the feed ingredient and /or
    b. presenting a specific mode of toxic action of concern, showing specific toxicological properties (e.g., reproductive toxicity, growth inhibition) in studies conducted with terrestrial and/or aquatic non-target organisms, or having the potential to present a toxic effect of concern on environmental biota,

should proceed to a Phase 2 assessment (see Section 4).

4. In some jurisdictions[9], certain feed ingredients may require a specific assessment of the capacity of the constituent entities to potentially persist, bioaccumulate in, and/or be toxic for the environment (assessment of the potential of the constituent entities to be

[8] Note that, if it is determined that a risk assessment should be conducted for the ingredient market formulation (e.g., due to a modification of the environmental fate of the feed ingredient in the environment), the evaluation should follow the recommendations of Section 4.
[9] It is recommended to consult the appropriate regulatory authority to determine the need for such evaluation.

Persistent, Bioaccumulative, and Toxic (PBT) or very Persistent and very Bioaccumulative (vPvB)). To assess whether a constituent entity of the feed ingredient requires a specific evaluation, a second set of criteria can be used, as described in Annex II. PBT or vPvB constituent entities are considered unsafe for the environment.

If the feed ingredient or any constituent entity(ies) it contains is not exempted from an environmental assessment in the screening Phase 1, it will be necessary to calculate the Predicted Environmental Concentration (PEC) in the different environmental compartments (for example, PEC_{soil} and PEC_{water}).

3.1. Calculation of the Predicted Environmental Concentration in soil

The PEC, calculated under a Phase 1 assessment, considers a conservative approach for the relevant environmental compartments (3). Some jurisdictions provide calculations for PEC, while others do not. Hence, the calculation of PEC_{soil} and PEC_{water} described below is recommended if calculations are not prescribed in the relevant jurisdiction. Alternative methods may be used if scientifically supported and properly justified. The calculations of PEC for additional environmental compartments (e.g., $PEC_{groundwater}$ and $PEC_{sediment}$) may be required depending on the jurisdiction.

The use of the feed ingredient, i.e., its concentration in feed and the duration of the exposure should be considered when calculating the PEC for the soil compartment in Phase 1.

3.1.1. Calculating total intake

The total intake of the feed ingredient is thus calculated as follows:

Equation 1 – Calculation of the target species total intake of the feed ingredient

$$E = C \times FI$$

Where:

- E = the total intake of the feed ingredient by the target species for a defined period (mg)[10]
- C = the concentration of the feed ingredient in the feed (mg/kg)
- FI = is the total feed intake during the defined period of the feed ingredient (kg)

[10] The PEC calculation is based on the total amount of the constituent entity(ies) of concern in the environment for a defined period (e.g., per year, per animal place, conditions of use of the feed ingredient)

The total feed intake depends on the target species, the animal management practices, and the duration of use of the feed ingredient. As the target species characteristics and the management practices differ by jurisdiction, this guidance document does not provide PEC calculation default values for these parameters. When available, it is recommended to use the default values relevant to the jurisdiction, where the feed ingredient will be evaluated.

3.1.1. Calculating total excretion and concentration in manure

As a conservative approach, the total quantity of feed ingredient ingested is considered excreted, i.e., it is assumed in Phase 1 that the constituent entity(ies) of the feed ingredient is(are) neither metabolized, nor retained by the animals. Hence the total excretion of the feed ingredient is equal to the exposure of the animals.

Equation 2- Calculation of the quantity of feed ingredient excreted by the animals

$$F = E$$

Where:

- F = the quantity of feed ingredient excreted (mg)
- E = the total intake of the feed ingredient by the target species for a defined period (mg)

The Predicted Concentration (PC) in manure, does not consider the degradation of the constituent entity(ies) present in the feed ingredient during manure storage. The concentration of the feed ingredient in manure is based either on the target species nitrogen excretion, the phosphorus excretion, or the total mass of excreta, based on default values related to the quantity of nitrogen or phosphorus excreted, or mass of excreta produced by the different animal species (and/or animal categories), during the period of exposure.

Equation 3 – Calculation of the concentration of feed ingredient in the manure

$$PC_m = \frac{F}{NE}$$

Or

$$PC_m = \frac{F}{PE}$$

Or

$$PC_m = \frac{F}{TE}$$

Where:

- PC_m = the Predicted Concentration of the feed ingredient in the manure (mg/kg N, mg/kg P, mg/kg excreta)
- F = the quantity of feed ingredient excreted (mg)
- NE = the quantity of nitrogen excreted by the animals during the defined period (kg)
- PE = the quantity of phosphorus excreted by the animals during the defined period (kg)
- TE = the mass of excreta produced by the animals during the defined period (kg)

Because the quantity of nitrogen (NE) and phosphorus excreted (PE), and the total mass of excreta (TE) varies by target species, and the usual composition of the feed and the farm management systems differ by jurisdiction, it is recommended to contact the regulatory authority for appropriate default values. In addition, the reference to nitrogen excreted (NE), phosphorus excreted (PE), or total mass of excreta (TE) depends on the jurisdiction. For example, for the European Union and Canada, the preferred reference nutrient to use in the calculation is nitrogen, while the nutrient used for calculations in the United States is typically phosphorus and may be total excretion on a case-by-case basis.

3.1.2. Calculating Predicted Environmental Concentration in the soil

The manure management is based on the current practices of the different jurisdictions. The manure management system considers the soil depth related to the system of manure application on soil (e.g., no tilling systems) or in soil (e.g., injection), and the maximum quantity of manure applied on the soil (either based on a maximum annual nitrogen emission standard[11], the nitrogen or phosphorus content of the manure or the total amount of manure used as fertilizer).

Equation 4 – Calculation of PEC soil

$$PEC_{soil} = \frac{PC_m \text{ x Maximum N load}}{\text{Mass of soil}}$$

or

$$PEC_{soil} = \frac{PC_m \text{ x Maximum P load}}{\text{Mass of soil}}$$

or

$$PEC_{soil} = \frac{PC_m \text{ x Maximum manure load}}{\text{Mass of soil}}$$

Where:

- PEC_{soil} = the Predicted Environmental Concentration of the feed ingredient in soil (mg/kg)
- PC_m = the Predicted Concentration of the feed ingredient in the manure (mg/kg N or mg/kg P or mg/kg excreta)
- Maximum N load = the maximum nitrogen amount to be spread/injected on a hectare of soil during the defined period (kg N/ha)
- Maximum P load = the maximum phosphorus amount to be spread/injected on a hectare of soil during the defined period (kg P/ha)

[11] As an example, in the European Union, the maximum nitrogen load is based on the maximum amount of nitrogen allowed to be used in nitrogen vulnerable zones, according to Directive No 91/676/EC

- Maximum Manure load = the maximum mass of excreta used as fertilizer on a hectare of soil during the defined period (kg/ha)
- Mass of soil = the quantity of soil in which the manure is mixed and is calculated as described in Equation 5 (kg)

Equation 5 – Mass of dry soil

$$Mass\ of\ soil = Soil\ density\ x\ 10000\ x\ depth\ of\ soil$$

Where:

- Soil density = the bulk density of the dried soil (kg/m^3)
- 10000 = the number of m^2 in a ha
- Depth of soil = the depth of soil to which the manure is mixed (0.05 m for manure spreading system with no till and/or 0.15 m for manure injection systems)

The maximum P load, N load, excreta load, the depth of soil and the number of applications depend on the manure management systems, the crops considered and the potential regulatory limits. They are variable depending on the jurisdictions and it is recommended to consider the default value for the jurisdiction, where the feed ingredient will be evaluated.

3.2. Calculation of Predicted Environmental Concentration in water

For land-based aquaculture systems, the PEC_{water} represents the concentration of the constituent entity(ies) of the feed ingredient in the water compartment from its use in aquaculture systems. For the purposes of this guidance document, the PEC_{water} does not account for dilution in the water body receiving the effluent discharge from the aquaculture system, and therefore, is considered the highest initial concentration of the constituent entity(ies) in surface water[12].

A simplified method for calculating PEC_{water} from the use of a feed ingredient in a flow through aquaculture facility is provided below. Depending on the jurisdiction, more complex calculations may be required. Applicants are advised to consult the appropriate regulatory authority and their guidelines during the development of a new aquaculture feed ingredient or for a new use of an authorized feed ingredient for aquaculture systems (e.g., flow through, raceway, ponds, marine net pens).

[12] Some jurisdictions refer to this as an environmental introductory concentration (EIC). The EIC represents the concentration of the feed ingredient in the effluent discharge of an aquaculture facility (e.g., end of pipe), and does not consider dilution in the receiving waterbody.

3.2.1. Calculating total intake

The total feed intake is calculated as follows.

Equation 6 – Calculation of the target species total intake of the feed ingredient

$$E_{fish} = C \times FR$$

Where:

- E_{fish} = the daily intake of the feed ingredient (mg/kg fish/day)
- C = the concentration of the feed ingredient in the feed (mg/kg)
- FR = the daily feed ration (kg feed/kg fish/day)

3.2.2. Calculating Predicted Environmental Concentration in water

The Predicted Environmental Concentration in water is calculated as follows.

Equation 7 – Calculation of PEC_{water}

$$PEC_{water} = \frac{E_{fish}}{Flow\ rate \times Dilution\ factor}$$

Where:

- PEC_{water} = Highest initial concentration of the constituent entity(ies) in surface water (mg/L)
- E_{fish} = the exposure of the fish to the feed ingredient for a defined period (mg/kg fish/day)
- Flow rate[13] = Water flow rate through the system (L/kg fish/day)
- Dilution Factor = certain jurisdictions allow for the use of a dilution factor (e.g., 10 (8))

3.3. Comparison with threshold values

The PEC is then compared to threshold values to determine the need for further environmental risk assessment of the feed ingredient in Phase 2. If the PEC is less than the threshold value, the risk assessment is complete. If the PEC exceeds or equals the threshold value, further assessment is required under Phase 2 (See Section 4). The threshold values depend on the specific jurisdiction and their specific objectives with regard to the potential environmental concentration. It is therefore

[13] Applicant should use the relevant default values, defined in the guidelines of the jurisdictions, when available, or provide justification of the flow rate chosen, relevant to the aquaculture system(s) and the country/region, where it is applied.

advised to consult the jurisdiction, where the feed ingredient will be marketed (see Table 1 for examples).

Jurisdiction	Threshold values		References
	Terrestrial (µg/kg)	Aquatic (µg/L)	
United States	100	1	CVM GFI #89 (7)
European Union	10	0.1	EFSA Guidance Document (8)

Table 1 – Threshold values adopted by different jurisdictions and used to determine the need for a Phase 2 assessment

4. PHASE 2 – RISK QUOTIENT METHOD

When Phase 1 indicates a potential concern for the environment or the concentration (PEC) in at least one environmental compartment is above the respective threshold values, Phase 2 provides an approach to further evaluate the potential risk posed by the feed ingredient. Phase 2 of the environmental risk assessment is further developed in an additional Guidance Document.

It includes three recommendations for:

1. further refining the PEC of the feed ingredient in the environmental compartments of concern,
2. establishing Predicted No Effect Concentrations (PNECs) of the feed ingredient that result in no adverse effects in non-target organisms, and
3. characterizing environmental risk by comparing the PEC to the PNEC in the environmental compartments.

Additional information regarding these recommendations is provided below.

For constituent entities having a log K_{ow} (n-octanol-water partition coefficient) above a certain threshold ($\geq$ 3 or $\geq$ 4, depending on the jurisdiction considered), the risk for secondary poisoning (food web transfer) should be evaluated (4).

4.1. Refinement of the estimated environmental concentration

The refinement of the estimated environmental concentration is developed in different tiers, including:

- Consideration of
  - the physico-chemical characteristics of the feed ingredient,
  - its environmental fate.
- Evaluation of existing information
  - on the actual composition of the substance excreted by the animals, including results of Absorption, Distribution, Metabolism and Excretion studies, and
  - on the potential degradation of the excreted feed ingredient during manure storage and application to agricultural land, including the yearly number of applications.

4.2. Determination of the potential adverse effects on non-target species

The adverse effect(s) of the feed ingredient on the environmental compartments should be evaluated in non-target species. As it is impractical to test all non-target organisms, studies are performed on pre-established surrogate organisms (e.g., particular species of earthworms, invertebrates, plants, fish, algae) representing a diversity of biota and various trophic levels in the environment. Potential adverse effects are evaluated using pre-defined population-level biological endpoints (e.g., mortality, growth, reproduction) measured in ecotoxicity studies. The PNEC is determined by an appropriate assessment factor to the lowest toxicity value (i.e., most sensitive endpoint) of the relevant toxicity data available for a feed ingredient.

4.3. Characterization of environmental risk

To characterize the environmental risk of using the feed ingredient, the PEC is divided by the PNEC to calculate a risk quotient (RQ). When the RQ value is < 1, no further testing is recommended. A RQ ≥ 1 indicates the potential for environmental risk because the concentration of the feed ingredient expected in the environment from the proposed conditions of use is greater or equal to the concentration that elicits an effect in a non-target organism. In this case, additional studies, PEC refinements, and/or computer modeling may be required.

5. ABBREVIATIONS

ADME	Absorption, Distribution, Metabolism and Excretion
GMO	Genetically Modified Organism(s)
K_{ow}	n-Octanol-water partition coefficient
PBT	Persistent, Bioaccumulating and Toxic
PEC	Predicted Environmental Concentration
PNEC	Predicted No-Effect Concentration
RQ	Risk Quotient
vPvB	very Persistent and very Bioaccumulating

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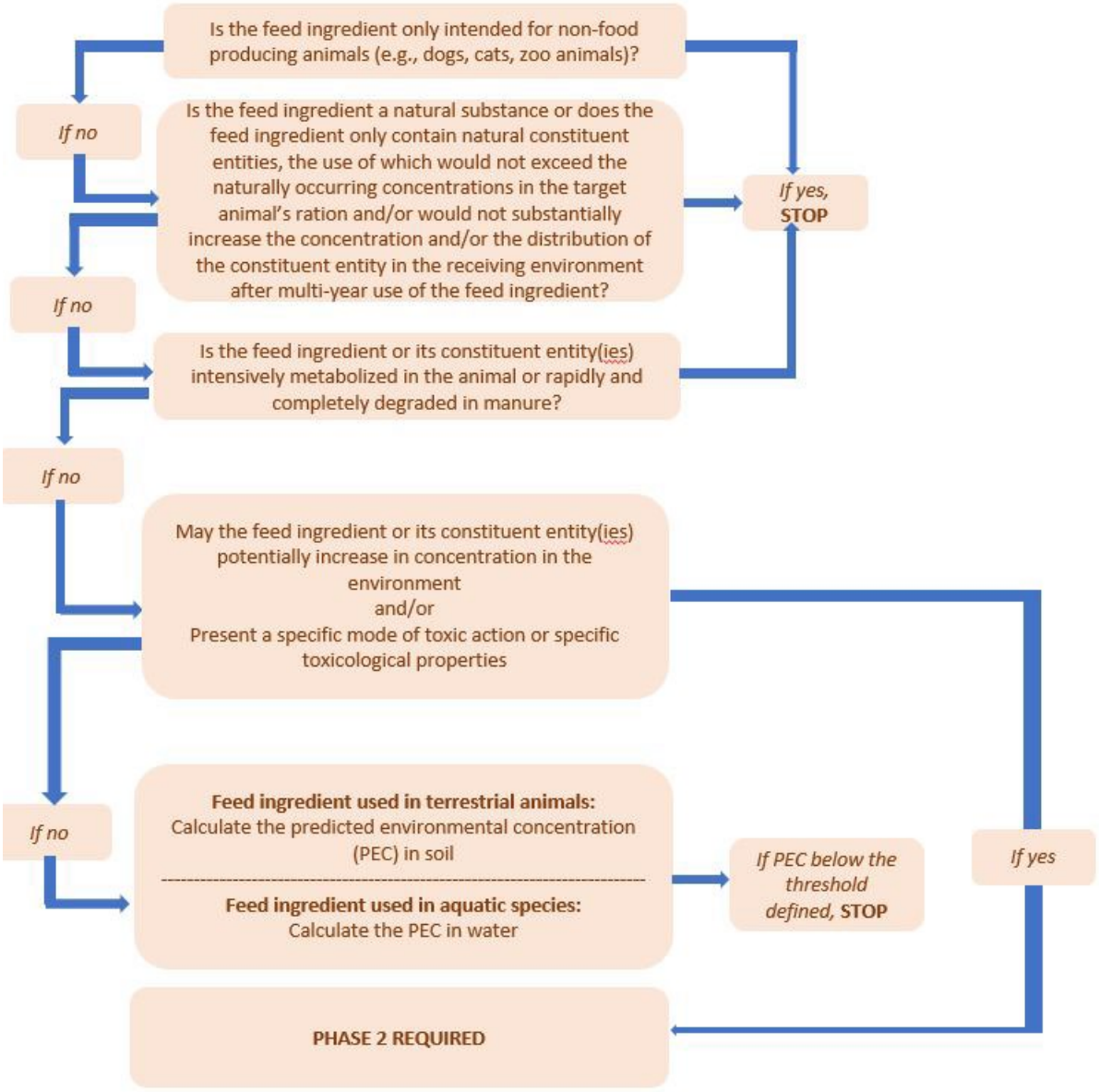
ANNEX I – DECISION TREE FOR EVALUATING THE NEED FOR FURTHER ASSESSMENT



ANNEX II – ADDITIONAL DECISION TREE FOR ASSESSMENT OF THE RISK OF BIOACCUMULATION OR PERSISTENCE