STATEMENT

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Animal dietary exposure in the risk assessment of feed derived from genetically modified plants

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Abstract

EFSA carries out the risk assessment of genetically modified plants for food and feed uses under Regulation (EU) No 503/2013. Exposure assessment – anticipated intake/extend of use shall be an essential element of the risk assessment of genetically modified feeds, as required by Regulation (EU) No 503/2013. Estimates of animal dietary exposure to newly expressed proteins should be determined to cover average consumption across all the different species, age, physiological and productive phases of farmed and companion animals, and identify and consider particular consumer groups with expected higher exposure. This statement is aimed at facilitating the reporting of the information that applicants need to provide on expected animal dietary exposure to newly expressed proteins and to increase harmonisation of the application dossiers to be assessed by the EFSA GMO Panel. Advice is provided on the selection of proper feed consumption and feed concentration data, and on the reporting of exposure's estimates. An overview of the different uncertainties that may be linked to the estimations is provided. This statement also explains how to access an Excel calculator which should be used in future applications as basis to provide a more consistent presentation of estimates of expected animal dietary exposure.

Keywords: GM feed, animal dietary exposure, newly expressed proteins, concentration data, consumption data

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1. Introduction

The Panel on genetically modified organisms of the European Food Safety Authority (EFSA GMO Panel) carries out the risk assessment of genetically modified plants (GMP) for food and feed uses under Regulation (EC) No 1829/2003[1], giving its scientific advice on the food and feed safety for humans and animals.

The EFSA GMO Panel assesses the information submitted by applicants in GMPs dossiers, in line with the principles of Regulation (EU) No 503/2013[2], Directive 2001/18/EC[3] and the guidance for risk assessment of food and feed from GMP (EFSA GMO Panel, 2011).

According to Regulation (EU) No 503/2013, Section 2 of part II in Annex II, 'exposure assessment – anticipated intake/extend of use', an 'estimate of the expected intake' shall be an essential element in the risk assessment of genetically modified food and feed. In particular, the concentrations of the newly expressed proteins, in those parts of the genetically modified plant intended for food or feed use shall be determined, and the expected intake of these constituents shall be estimated. For the sake of consistency with previous EFSA scientific opinions and to fulfil specific EU regulatory requirements, the 'estimate of the expected intake[4]' of NEPs is hereafter referred as 'estimate of expected animal dietary exposure (ADE)'.

Therefore, estimates of expected ADE are required for the risk assessment of GM feed (i.e. feed containing, consisting of or derived from a GMP) for the safety of farmed (both food-producing and non-food-producing species) and companion animals, and apply to submission of all applications for authorisation of GM plants.

Dietary exposure of GM feed is the quantitative and/or qualitative evaluation of the likely or expected exposure to or intake of new constituents resulting from the genetic modification (e.g. newly expressed proteins), or endogenous constituents with levels altered as a result of a genetic modification (e.g. due to changes in metabolic pathways) in those parts of the GMP intended for feed uses (adapted from EFSA, 2019a).

Since the entry into force of Regulation (EU) No 503/2013, numerous applications have been submitted to EFSA for the import and processing authorisation of GMPs for food and feed use.[5]

The EFSA GMO Panel noted that the EU regulatory framework and the related guidelines applicable to the risk assessment of GMPs provide general principles (e.g. Regulation 503/2013, Annex II), but no detailed recommendations on the way of estimating and presenting expected ADE for GM feed. Applicants have therefore developed diverse and inconsistent approaches to estimate and present expected ADE. The EFSA GMO Panel has produced this document to facilitate data generation and presentation which should lead to a greater consistency in estimates of expected ADE presented in dossiers.

2. Aim of the statement

The EFSA GMO Panel aims to provide advice for applicants, and also for the risk analysis community,[6] on how to report information and to improve consistency on estimates of expected ADE in applications for authorisation of GMPs under Regulation (EC) No 1829/2003. This expands on information available in Regulation (EU) 503/2013, in the guidance document on risk assessment of food and feed from GM plants (EFSA GMO Panel, 2011), in the EFSA scientific report on animal dietary exposure (EFSA, 2019b), and EFSA (e.g. EFSA FEEDAP Panel, 2017) or other international

[1] Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed. OJ L 268, 18.10.2003, pp. 1–23.

[2] Commission Regulation (EU) No 503/2013 of 3 April 2013 on application for authorisation of genetically modified food and feed in accordance with Regulation (EC) No 1829/2003 of the European Parliament and of the Council and amending Commission Regulations (EC) No 604/2004 and (EC) No 1981/2006.

[3] Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC - Commission Declaration. OJ L 106, 17.4.2001, pp. 1–39.

[4] Dietary intake generally refers to the ingestion of constituents which have nutrition or health purposes. While, dietary exposure mainly refers to the ingestion of substances unintentionally present in feed or added for a technological purpose. It is noted that some constituents could be considered both nutrients and compounds that have been incorporated to food/feed crops without nutritional or health purposes (adapted from EFSA, 2019a). It is further noted that the expected intake of the constituent is linked to the extent of use of the GM feed materials through daily dietary intake of feed material.

[5] At the date of adoption of this document: 26 already adopted and 20 ongoing.

[6] All potential users of this EFSA output (e.g. risk managers and other risk assessment bodies in Member countries and authorities, national governments, authorities, international organisations, industry, academia).

(OECD, 2009a, 2013) guidelines for animal dietary exposure in other risk assessment contexts (e.g. feed contaminants and pesticides), and facilitates the provision of such information.

Regulation (EU) 503/2013 requires that in the risk assessment of a GMP for feed uses, information on the levels and an estimation of the expected exposure to newly expressed proteins (NEPs) is provided. The EFSA GMO Panel considers that to address this requirement, in the absence of agreed methodologies (e.g. lack of a harmonised feed classification system and comprehensive database of EU feed consumption), it is adequate to provide exposure estimates based on agreed default values. Advice is provided in the subsequent sections of this document.

The GMO Panel is aware that refined exposure estimates might be required on a case-by-case basis (e.g. if specific hazards are identified) for further risk characterisation; this scenario is not covered by the present document.

Furthermore, the EFSA GMO Panel is aware that a comparative animal dietary exposure may be performed when the purpose of the assessment is to compare qualitative and quantitative exposures between a constituent in GM feed with the same or a homologous constituent in conventional feeds, to establish safe use levels. Also in this case, the advice given in this document may be adapted on a case-by-case basis, but it will not be covered specifically by the present document.

3. Transition period

Since applicants regularly provide estimates of expected ADE as part of GMO application dossiers submitted under Regulation (EU) 503/2013 making use of the data (consumption and concentration data) described and addressed in this statement, a general 6-month transition period is granted for the application of the advice described in this document after its publication. The advice outlined in this document will be applicable for GM plant applications submitted after this transition period.

4. Estimation of expected animal dietary exposure in the risk assessment of GM plants: current approaches

Estimation of expected ADE to NEPs combines feed consumption data (type and amount of feed materials fed on a daily basis to farmed and companion animals) with concentration data (amount of NEPs in feed materials and feed commodities).

The EFSA GMO Panel is aware that the EU regulatory framework applicable to the risk assessment of GMP introduced general principles for estimation of expected ADE through the consumption of GM feed, albeit giving no detailed recommendations on how to perform it. This has resulted in the development of inconsistent approaches. Examples of the variability of these approaches across dossiers, related to the use of feed consumption and concentration data, are described below, in Sections 4.1 and 4.2.

4.1. Feed consumption data

The lack of a harmonised feed classification system and of a comprehensive database of EU feed consumption (EFSA, 2019b) has resulted in expected ADE estimates to NEPs based on different and customised approaches, characterised by: (i) heterogeneous selection of animal species and categories, (ii) heterogeneous selection of feed materials entering the final diet or ration used to estimate overall exposure to the target substance and (iii) the use of a variety of predefined default values publicly available for the total daily amount of feed consumed, feed inclusion rate in standard diets, animal body weight and the type of productivity (e.g. milk production) and the physiological status, to predict feed intake in animals.

4.1.1. Animal species selection

The EU GMO regulatory framework introduced the principles underlying the selection of particular groups of the European populations of farmed and companion animals with an expected higher exposure to be considered within the risk assessment, although no specific advices for applicants are given with regard to the species, the different age and the physiological and productive phases. In the applications reviewed, livestock and poultry are always selected, albeit not always the same species or life stage, while companion animals and fish have been selected only in a few cases (see Table 1). Horses have never been selected.

Table 1: Examples of animal species currently selected as relevant across different dossiers

Maize dossiers
– cattle for fattening, dairy cow; chicken for fattening, laying hen, turkey for fattening; sheep/goat; pig for fattening, sow lactating; dog, cat; salmon
– cattle (beef, dairy); poultry (broiler, layer, turkey); sheep (ram/ewe, lamb); swine (breading, finishing)
– lactating dairy cow; finishing pig, broiler
Soybean dossiers
– cattle for fattening, dairy cow; chicken for fattening, laying hen, turkey for fattening; sheep/goat; pig for fattening, sow lactating; dog, cat; salmon
– cattle (beef, dairy); poultry (broiler, layer, turkey); sheep (ram/ewe, lamb); swine (breading, finishing)
– lactating dairy cow; finishing pig, broiler
Oilseed rape dossiers
– cattle (beef, dairy); poultry (broiler, layer, turkey); sheep (ram/ewe, lamb); swine (breading, finishing)
Cotton dossiers
– cattle for fattening, dairy cow; chicken for fattening, laying hen, turkey for fattening; sheep/goat; pig for fattening, sow lactating; dog, cat;
– cattle (beef, dairy); poultry (broiler, layer, turkey); sheep (ram/ewe, lamb); swine (breading, finishing)

4.1.2. Feed materials selection

The EU GMO regulatory framework introduced the principle of selecting those parts of the GMPs intended for feed use in the estimation of expected ADE; however, there is no further specific advice for identifying the appropriate raw and processed feed materials entering the final diet and rations fed to farmed and companion animals. In the applications reviewed, there is considerable variability in the feed materials considered between applicants, and in some cases across different applications from the same applicant (see Table 2).

Table 2: Examples of feed materials currently selected as relevant across different dossiers

Maize
– grain
– grain; forage
– grain; gluten feed; gluten meal
– grain; gluten feed; gluten meal; silage
– grain; gluten meal; gluten feed; milled by-products; hominy feed
Soybean
– meal
– meal; forage
– forage, hay, silage, seed, meal, hulls, and aspirated grain
Oilseed rape
– meal
– meal; forage
Cotton
– undelinted (fuzzy) seeds; meal
– undelinted (fuzzy) seeds; meal; hulls; gin by-products

With regard to raw materials, although maize and soybean forage is commonly fed to animals (EFSA, 2018a), it is not always selected by some applicants, based on the argumentation that the

scope of the application does not include cultivation of the crop in Member States of the European Union. In these cases, on the assumption that forage might be imported into the EU, to complete the assessment of GM maize and soybean crops, the EFSA GMO Panel has estimated the dietary exposure to NEPs based on data available for the consumption of forage.

4.1.3. Predefined default values selection

Unlike for human dietary consumption, there is no systematic collection of data on animal feed consumption. The lack of a comprehensive feed consumption database results in estimations of feed consumption and dietary exposure based on predefined default values for daily feed intake (FI), inclusion rate (IR) of GM feed materials in diets, body weight (BW) and the physiological status (e.g. milk production). In the EU GMO regulatory framework, there is no specific advice for selecting these default values. The main sources used are the OECD guidance documents (OECD, 2009a, 2013) and the recommendations given in the FEEDAP Guidance (e.g. EFSA FEEDAP Panel, 2017), as recently described (EFSA, 2019b). In a limited number of cases, applicants have used ad hoc references from the literature, which were considered on a case-by-case basis by the EFSA GMO Panel (see Table 3).

Table 3: List of sources currently selected for predefined default values across different dossiers

Maize
– OECD, 2009a for daily FI and BW and IR% in livestock
– OECD, 2013 for daily FI and BW and IR% in livestock
– EFSA FEEDAP Panel, 2017 for daily FI and BW in all species with: – OECD, 2013 for IR% in livestock – FAO (2017) for IR% in salmon – Communication by the applicant for IR% in dogs and cats
Soybean
– OECD, 2009a livestock for daily FI and BW and IR%
– OECD, 2013 livestock for daily FI and BW and IR%
– EFSA FEEDAP Panel, 2017 for daily FI and BW in all species with: – OECD, 2013 for IR% in livestock – FAO (2017) for IR% in salmon – Communication by the applicant for IR% in dogs and cats
Oilseed rape
– OECD, 2013 livestock for daily FI and BW and IR%
Cotton
– OECD, 2013 livestock for daily FI and BW and IR%
– EFSA FEEDAP Panel, 2017 for daily FI and BW in all species with: – OECD, 2013 for IR% in livestock – O'Keefe (2003) salmon IR% – Communication by the applicant for IR% in dogs and cats

FI: feed intake; BW: body weight; IR%: inclusion rate of feed materials in standard diet or ration.

4.2. Feed concentration data

Although the EU GMO regulatory framework introduced the principle of selecting the concentrations of the NEPs in those parts of the genetically modified plant intended for feed use, it lacks specific recommendations for the selection of appropriate concentration data in raw and processed commodities intended for feed uses. This has resulted in the estimation of expected ADE being approached in different ways by applicants.

In particular, the EFSA GMO Panel has noted differences among applicants, with regard to:

- selection of concentration data in raw and derived or processed commodities;
- use of concentration data measured on dry or fresh weights;

— use of mean or highest concentration data;
— use of the limit of quantification or detection (LOQ or LOD) levels, when necessary.

5. Estimation of animal dietary exposure in the risk assessment of GM plants: updated advice on how to assess and report information

The EFSA GMO Panel has noted that the EU regulatory framework and the related guidelines applicable to the risk assessment of GMPs provide no detailed recommendations on the way estimations of expected ADE for GM feed should be conducted, and proposes advice in Sections 5.1, 5.2 and 5.3 below, to improve consistency on expected ADE estimation for GM feed among applicants, facilitating the provision of such information.

5.1. Advice on feed consumption data

While data on food consumption of the European human population are systematically collected through surveys, and made available in the EFSA Comprehensive European Food Consumption Database[7] (EFSA, 2011) for the estimates of human dietary exposure, nothing similar exists for the population of farmed and companion animals.

The absence of a harmonised feed classification system and of a comprehensive database of EU feed consumption results in different and customised approaches for expected ADE estimates to NEPs, based on publicly available sources of default values for the animal body weight, the total amount of feed consumed daily and the inclusion rate of feed materials in standard diets and rations (EFSA, 2019b).

The EFSA GMO Panel provides below advice to select appropriate default values with the aim to harmonise estimation of expected ADE across applicants.

5.1.1. Selection of animal species and categories for the prediction of feed consumption

Provisions of Regulation 1829/2003 are set in order to protect animal health when fed feed consisting of, containing or produced from genetically modified organisms[8] and should apply to farmed and companion animals (from recital 8 of Regulation 1829/2003). Furthermore, Regulation 503/2013 requires that the applicant identifies and considers particular groups of the European populations of farmed and companion animals with an expected higher exposure and shall consider this higher exposure within the risk assessment.

To ensure a well-defined selection of the appropriate population of farmed and companion animals, the EFSA GMO panel proposes a list of animal species (see Table 4) adapted from the relevant animal species for ADE in EFSA (2019b).[9,10]

Table 4: EU populations of farmed and companion animals for which estimation of expected ADE might be applicable

Farmed animals
Food-producing animals
ruminants (e.g. dairy and beef cattle)
small ruminants (e.g. sheep and goats)
other herbivorous (e.g. rabbits)
monogastrics (e.g. swine)
poultry (e.g. broilers, laying hens, turkeys, ducks)
farmed fish (e.g. salmon and carp)

[7] https://www.efsa.europa.eu/en/data/food-consumption-data
[8] From article 1 of Regulation 1829/2003, and then repeated in different parts of the regulation.
[9] The interest on mink farming is decreasing in EU because of the tendency to phase out their husbandry for fur production but the EFSA GMO Panel considers they remain relevant for consideration; however, at this stage, they need not be selected for estimation of expected ADE, unless specific aspects identify them as being of particular concern.
[10] There is an important interest on ornamental birds and fish, and non-conventional companion animals, but at this stage, they need not be selected for estimation of expected ADE, unless specific aspects identify them as being of particular concern.

Non-food-producing animals
minks
Companion animals (pets)
cats
dogs
horses
birds and fishes
non-conventional companion animals (e.g. gerbils, hamsters)[10]

- The EFSA GMO Panel recommends limiting the estimation of expected ADE to NEPs to some animal species only, as described below inSection 5.3, Table 5.

5.1.2. Selection of predefined default values to predict feed consumption in animals

There are no comprehensive databases that provide homogeneous data on feed consumption for farmed and companion animals with relevance for the EU population, and that are suitable for the determination of exposure to NEPs in feed commodities.

An EFSA procurement[11] is ongoing to explore the feasibility of implementing a harmonised feed classification system and developing an EU feed consumption database, to support a more accurate estimation of expected ADE, by approaching the standards in place for human dietary exposure (EFSA, 2019b). Until this procurement is completed, the EFSA GMO panel is not in the position to propose specific feed consumption data and therefore suggest to continue using an approach based on predefined default values publicly available for body weights, total daily intakes and inclusion rate of feed materials in standard diets or rations, to predict feed consumption in animals.

- The EFSA GMO Panel recommends for the estimation of expected ADE to NEPs to continue using an approach based on predefined default values for body weights, total daily intakes and inclusion rate of feed materials in standard diets or rations, as described below in Section 5.3, Table 5.

5.1.3. Selection of feed materials incorporated in a standard diet or ration

Considering the large number of feed materials of plant origin available for incorporation in standard diet or rations for farmed and companion animals and the current lack of a harmonised feed classification across several databases in place at international and national levels (EFSA, 2019b), the EFSA GMO Panel proposes a list of crop-related feed materials based on the classification proposed in the EU catalogue of feed materials and in the Harmonised OECD tables of feedstuffs derived from field crops. These are two international databases that are officially part of the EU regulatory framework (EFSA, 2019b, Appendix 1A and 1B).[12]

- The EFSA GMO Panel recommends for the estimation of expected ADE to NEPs the use of selected feed materials, as described below in Section 5.3, Table 5.

5.2. Advice on feed concentration data

The EU regulatory framework for GMPs requires that the concentration data of NEPs are analytically determined in different plant tissues, including those intended for feed uses. For the estimation of expected ADE to NEPs, essential aspects are the analytical data determined at specific growth stages in those parts of the plant destined to become feed; these represent raw commodities (e.g. grains, seeds, beans and forage) entering the feed production chain.

Information on the source of concentration data in raw commodities used in the exposure estimations should include the number of samples analysed, the analytical data expressed on a dry weight basis, the part of the plant, the growth stage and the number of field sites used.

[11] https://etendering.ted.europa.eu/cft/cft-documents.html?cftId=9124

[12] efs25896-sup-0001-Appendix_1A-1B.xlsx. Mapping of the EU Catalogue of feed materials (Regulation (EU) 2017/1017) to the EFSA FoodEx2 system, and Mapping of the OECD GD on residues in livestock (OECD, 2013) to the EFSA FoodEx2 system.

- The EFSA GMO Panel recommends that if concentration data for the NEPs are available for more than one growth stage entering the feed chain (e.g. maize grains R6 and senescent, maize forage R4 and R6), expected ADE should be estimated using the growth stage with the highest mean expression levels.

5.2.1. Concentration data in raw and derived or processed commodities

Concentration levels of the NEPs in raw feed materials (e.g. grains, seeds, beans and forage) obtained from GMPs should be used both as occurrence data and to estimate concentration data in derived or processed commodities intended for feed uses (e.g. meal).

5.2.1.1. Conversion factors

The concentration of NEPs in derived or processed commodities intended for feed uses (e.g. by-products, co-products, processed products, dried or silage products) should be normalised to the respective raw materials by using ad hoc conversion factors. The use of concentration data analytically determined in derived or processed materials (e.g. toasted meal) is not recommended as the results might be influenced by specific conditions of preparation and not be generally applicable at this first step.

Ad hoc conversion factors should be derived as the ratio between the mean concentration of total protein (dry weight basis) in the conventional derived or processed commodity and its concentration in the related conventional raw commodity (e.g. conventional maize gluten meal vs. conventional maize grain), assuming that no losses of newly expressed proteins occur during processing of the raw commodity to the processed commodity/fraction. The concentration of the NEPs in the processed commodity is then calculated as the concentration in the raw material multiplied by this ratio.

- The EFSA GMO Panel recommends using the conversion factors for estimation of expected ADE to NEPs in GMPs through the consumption of derived or processed commodities, as described below in Section 5.3, Table 6.

5.2.1.2. Dry vs. fresh weight

Concentration data of the NEPs in feed materials expressed in dry weight are the most appropriate to estimate expected ADE because this way of expression is unique in animal nutrition and facilitates comparisons between feed materials with different content of moisture. The GMO Panel recommends to use concentrations of NEPs on a dry weight basis, as analytically determined, whenever available, instead of referring to conversion from fresh weight based on standard default values for dry matter.

- The EFSA GMO Panel recommends for the estimation of expected ADE to NEPs in GMPs the use of concentration data expressed in dry weight, analytically determined in raw materials (e.g. grain, forage) or in derived or processed feed commodities (e.g. meal, silage) by calculation using the conversion factors in Table 6.
- In line with the principles of the explanatory note on the determination of NEP levels in the context of GMP applications for EU market authorisation (EFSA, 2018b), a description of the method followed to obtain the dry weight-based concentration data should be provided.

5.2.1.3. Mean vs. high concentrations

When dealing with dietary exposure assessment, it is important to distinguish between acute exposure and chronic exposure. In animals, acute and chronic exposure estimates mainly depends on the concentration of the chemical of interest in the feed material, considering that within a given production system, feed intake (per kg body weight) remains relatively stable from day to day, and under controlled conditions (EFSA, 2019b). The GMO Panel considers that, due to the extensive mixing which will normally occur in the production of animal feeds and controlled conditions of feed supply to farmed and companion animals, the estimation of expected ADE based on the average content (mean levels) of an NEP in feed is adequate for animals fed by humans.

- The EFSA GMO Panel recommends for the estimation of expected ADE to NEPs the use of mean concentration data, analytically determined in raw materials obtained from sampling GMP among different field sites, or calculated in derived or processed feed commodities by using conversion factors (Table 6).

- Ad hoc scenarios might be needed when the concentration of an NEP differs significantly among the field sites; this could be indicative of certain environmental conditions affecting the concentration of the NEP. Under this specific scenario, the average concentration of the site where the highest concentration is reported should be used to cover a hypothetical worst-case scenario where processed feeds are produced from GM crops cultivated in that site (adapted from EFSA, 2019a), and the applicant should clearly justify and explain the choice of this approach.

5.2.1.4. Limit of quantification/limit of detection (LOQ/LOD)

The mean concentration of an NEP should be derived by using all available samples.

When individual analytical results for constituents are reported as below the limit of detection (LOD) or the limit of quantification (LOQ) in raw commodities, these left-censoring limits should be used to obtain the mean values to be used for dietary exposure estimations, in raw and processed commodities. This approach is also applicable when all available samples have mean concentration of NEPs below LOD or LOQ. The values falling below the LOD are replaced by the value reported as LOD and those below the LOQ by the value reported as LOQ; this is an upper bound scenario (conservative) which relies on the substitution method commonly used in EFSA for the treatment of left-censored data and recommended in the 'Principles and Methods for the Risk Assessment of Chemicals in Food' (adapted from EFSA, 2019a).

- The upper bound value is obtained by assigning the numerical value of LOD to values reported as less than the LOD or by assigning the numerical value of LOQ to values reported as < LOQ, depending on whether LOD or LOQ is being reported.
- The EFSA GMO panel recommends that the values of the LOQ/LOD are used in the calculation of means when measured values are below the LOQ/LOD, respectively.

5.2.2. Concentration data in GMP stacked event

Concentration data of the NEPs in feed materials obtained from the GMP stacked event are the most appropriate to estimate expected ADE. The dietary exposure to NEPs in a GMP stacked event may differ from the exposure in the context of the respective GMP single events previously assessed, as a consequence of potential differences in either consumption data (e.g. new feed materials enter the market) or concentration data (e.g. expression levels in the stack are the combined/additional result of two or more events of the GMP stack).

- The EFSA GMO Panel recommends for the estimation of expected ADE to NEPs in GMP stacked event the use of concentration data determined in feed materials obtained from the GMP stacked event itself.

5.2.3. Concentration data in herbicide-tolerant GMPs

Concentration data of the NEPs in feed materials obtained from GMPs treated with the intended herbicide(s) are the most appropriate to estimate expected ADE. These data are the most representative of the growing conditions of the GM crop entering the feed chain once authorised.

- The EFSA GMO Panel recommends for the estimation of expected ADE to NEPs in GMPs expressing traits for herbicide tolerance the use of concentration data determined in feed materials obtained from the GMP treated with the intended herbicide(s).

5.3. Advice on the reporting of estimates of expected animal dietary exposure

When reporting estimates of expected ADE to NEPs according to the principles addressed in this document, the EFSA GMO Panel recommends how the information should be reflected in the dossier.

5.3.1. Declaration of the purpose of the ADE study

Based on the outcome of the hazard identification, the applicant should clarify the purpose of the estimation of the anticipated exposure to NEPs in farmed and companion animals, through consumption of selected feed materials derived from the GM crop, considering that:

- If a hazard is not identified, there is no need to provide a further risk characterisation, and estimation of expected ADE on selected animal species, as required by Regulation 503/2013 and as described in this statement, complies with regulatory requirements.
- If a hazard is identified, the assessment of NEPs requires further risk characterisation, and an ad hoc assessment should be provided by the applicant, but this scenario is not covered by the present document.

5.3.2. Description of current uses of feed materials from a conventional crop in farmed and companion animals

The aim of this section is to describe the dietary role and the existing production processes of conventional feed obtained from the crop under assessment for farmed and companion animals (see Table 4), according to the current uses in the EU.

- Current uses of feed commodities in standard diet or rations should be discussed here, including raw commodities (e.g. grains, seeds, root, forage and top) and co-products or by-products (e.g. meal, soybean protein concentrates).
- Emerging uses of feed commodities (e.g. canola protein isolates and their whey fractions) should also be discussed here.

5.3.3. Description of expected uses of feed materials from the GM crop in farmed and companion animals

The aim of this section is to describe the dietary role and the existing production processes of the GM feed obtained from the crop under assessment for farmed and companion animals, highlighting similarities or differences compared to the conventional feed, e.g.:

- The dietary role of the GM feed materials and the existing production processes are the same as for the conventional feed materials from the crop of interest, and no different uses of feed materials from the GM crop are expected in farmed and companion animals.
- The dietary role of the GM feed materials and the existing production processes are different from the conventional feed materials from the crop of interest, and different uses of feed materials from the GM crop are expected in farmed and companion animals. Explanation of the differences and impact on the risk assessment should be provided.

5.3.4. Advice on ADE reporting

Expected ADE to NEPs in GM crops (e.g. maize, soybean, rapeseed, cotton and sugar beet) should be estimated across selected animal species, assuming the consumption of selected crop's products is representative of those most commonly entering the feed supply chain.

A conservative scenario with 100% replacement of conventional crop's products by the GM crop's products should be considered for all crops and feed materials.

Feed consumption data for estimation of expected ADE to NEPs should be based on the use of predefined default values for animal body weight, daily feed intake and inclusion rates (percentage) of feed materials in diets or rations, as recommended in Table 5. The consumption of maize forage and soybean forage and sugar beet tops should always be considered when estimating expected ADE to NEPs, in line with EFSA (2018a).

Concentration levels of the NEPs analytically determined in feed raw materials such as grain, seed and bean from GMPs should be used either as occurrence data, and to estimate levels in derived or processed commodities intended for feed uses of (e.g. meal), based on conversion factors. The conversion factors take into account the ratio between the total protein content in common crop's feed products relative to grain, seed, bean and forage, assuming that no NEP is lost during their production or processing, as recommended in Table 6.

Estimates of an NEP in feed materials should be based on concentration data in dry weights, and the average content (mean levels) should be used.

The LOQ or LOD values should be used as the assumed mean amount of protein in the sample, whenever the NEPs concentration data analysed in raw commodities (e.g. grain or forage), samples of the GM crop across different field sites are below the limit of detection or the limit of quantification (LOD/LOQ).

In GMP stacked event, the concentration data of the NEPs determined in feed materials obtained from the GMP stacked event itself should be used.

For trait-specific herbicide tolerance, the concentration data of the NEPs determined in feed materials obtained from the GMP treated with the intended herbicide(s) itself should be used.

5.3.5. Recommended default values for feed consumption

Animal species and predefined default values for animal body weight, daily feed intake and inclusion rates (percentage) of feed materials in diets or rations recommended to estimate feed consumption for expected ADE are summarised in the below Tables 5a–e. The values presented are considered by the EFSA GMO panel to be the most appropriate ones available in the published literature, and references are provided.

Table 5a: Maize feed consumption

Animal species and category	Body Weight (kg)	Total daily intake (kg/animal)	Inclusion rates (%)				
			Forage/ silage	Grain	Gluten feed	Gluten meal	Milled by-products[(c)]
Dairy cow	650[1]	25[1]	60[1]	30[1]	30[1]	20[1]	30[1]
Beef cattle	500[1]	12[1]	80[1]	80[1]	30[1]	15[1]	30[1]
Dairy Sheep	80[2]	2.8[2]	80[6]	25[7]	10[8]	10[8]	NA
Dairy Goat	60[2]	3.4[2]	36[9]	67[10]	20[11]	14[12]	NA
Rabbit	2[2]	0.15[2]	NA	30[13]	11[14]	NA	NA
Fattening pig[(a)]	100[1]	3[1]	NA	70[1]	20[1]	10[1]	75[1]
Lactating sow[(b)]	200[1]	6[1]	20[1]	70[1]	20[1]	10[1]	75[1]
Piglet	20[2]	1[2]	NA	24[15]	NA	2.5[16]	NA
Broiler	2[3]	0.158[3]	NA	70[1]	10[1]	10[1]	60[1]
Laying hens	1.9[1]	0.13[1]	10[1]	70[1]	NA	10[1]	50[1]
Turkey	7[1]	0.5[1]	NA	50[1]	NA	10[1]	50[1]
Salmon	5[4]	0.03[5]	NA	NA	10[17]	10[17]	NA
Carp	1[2]	0.02[2]	NA	6[18]	NA	NA	NA
Cat	4[2]	0.06[2]	NA	50[19]	15[20]	35[19]	NA
Dog	25[2]	0.36[2]	NA	50[21]	30[22]	32[23]	NA
Horse	450[2]	9[2]	45[24]	30[25]	NA	NA	NA

NA: the GMO Panel is not able to recommend specific data. No data is expected.
(a): BW, TDI and IR% data, as available in OECD, 2013 for finishing pig.
(b): BW, TDI and IR% data, as available in OECD, 2013 for breeding pig.
(c): although inclusion rates are available, the GMO Panel is not able to recommend specific data for the appropriate conversion factors (see Table 6a). No data is expected.
1: OECD, 2013
2: EFSA, 2019b, Table 3 – as per EFSA CONTAM Panel, 2011.
3: EFSA, 2019b, Table 3 – as per EFSA FEEDAP Panel, 2017.
4: https://mowi.com/it/wp-content/uploads/sites/16/2020/06/Mowi-Salmon-Farming-Industry-Handbook-2020.pdf - *Mowi Salmon Farming Industry Handbook 2020*.
5: Calculation based on feed intake as percentage of body weight based on Aas et al., 2020.
6: Aksu et al., 2006.
7: Bianchi et al., 2014.
8: Milis et al., 2005.
9: Baldin et al., 2014.
10: Sun et al., 2018.
11: Sampelayo et al., 1998.
12: Laudadio and Tufarelli, 2010.
13: Lebas and Duperray, 2017.
14: De Blas et al., 1995.
15: Agazzi et al., 2020.
16: Ahasan et al., 2019.
17: Berntssen et al., 2018.
18: https://www.iaffd.com - *the International Aquaculture Feed Formulation Database*.
19: Funaba et al., 2005.
20: Hill, 2004.

21: Félix et al., 2012.
22: Kawauchi et al., 2011.
23: Yamka et al., 2004.
24: Gatta et al., 2007.
25: Peiretti et al., 2011.

Table 5b: Soybean feed consumption

Animal species and category	Body Weight (kg)	Total daily intake (kg/animal)	Inclusion rates (%)				
			Forage/ silage	Full fat seed	Meal	Hulls	Protein concentrate
Dairy cow	650[1]	25[1]	20[6]	10[1]	25[1]	10[1]*	NA
Beef cattle	500[1]	12[1]	NA	10[1]	20[1]	10[1]	NA
Dairy Sheep	80[2]	2.8[2]	NA	14[7]	20[8]	45[9]	NA
Dairy Goat	60[2]	3.4[2]	NA	11[10]	25[11]	61[12]	NA
Rabbit	2[2]	0.15[2]	NA	20[13]	24[14]	32.5[15]	NA
Fattening pig[(a)]	100[1]	3[1]	NA	20[1]	30[1]	10[1]	NA
Lactating sow[(b)]	200[1]	6[1]	NA	10[1]	30[1]	10[1]	NA
Piglet	20[2]	1[2]	NA	30[16]	22[17]	3[18]	9[19]
Broiler	2[3]	0.158[3]	NA	20[1]	40[1]	10[1]*	NA
Laying hens	1.9[1]	0.13[1]	10[1]	15[1]	25[1]	5[1]	NA
Turkey	7[1]	0.5[1]	NA	15[1]	45[1]	NA	NA
Salmon	5[4]	0.03[5]	NA	NA	NA	NA	10[20]
Carp	1[2]	0.02[2]	NA	NA	42[21]	NA	NA
Cat	4[2]	0.06[2]	NA	NA	29.5[22]	14[23]	25[24]
Dog	25[2]	0.36[2]	NA	30[25]	30[26]	7.5[27]	18.7[28]
Horse	450[2]	9 [2]	NA	NA	NA	75[29]	NA

NA: the GMO Panel is not able to recommend specific data. No data is expected.
(a): BW, TDI and IR% data, as available in OECD, 2013 for finishing pig.
(b): BW, TDI and IR% data, as available in OECD, 2013 for breeding pig.
1: OECD, 2013 (* value from OECD, 2009a was selected, since more conservative).
2: EFSA, 2019b, Table 3 – as per EFSA CONTAM Panel, 2011.
3: EFSA, 2019b, Table 3 – as per EFSA FEEDAP Panel, 2017.
4: https://mowi.com/it/wp-content/uploads/sites/16/2020/06/Mowi-Salmon-Farming-Industry-Handbook-2020.pdf - *Mowi Salmon Farming Industry Handbook 2020*.
5: Calculation based on feed intake as percentage of body weight based on Aas et al., 2020.
6: OECD consensus document, 2002.
7: Ferreira et al., 2018
8: Bianchi et al., 2014
9: Miccoli et al., 2022.
10: Schmidely and Andrade, 2011.
11: Baldin et al., 2014.
12: López et al., 2014.
13: Lebas, 2004.
14: Lebas and Duperray, 2017.
15: De Blas et al., 1999.
16: Zarkadas and Wiseman, 2005.
17: Agazzi et al., 2020.
18: Pascoal et al., 2012.
19: Perricone et al., 2020.
20: Berntssen et al., 2018.
21: https://www.iaffd.com - *the International Aquaculture Feed Formulation Database*.
22: Carciofi et al., 2009.
23: Detweiler et al., 2019.
24: Kim et al., 1995.
25: Félix et al., 2020.
26: Vanelli et al., 2021.
27: Cole et al., 1999.
28: Venturini et al., 2018.
29: Booth et al., 2004.

Table 5c: Rapeseed feed consumption

Animal species and category	Body Weight (kg)	Total daily intake (kg/animal)	Inclusion rates (%)	
			Full fat seed	Meal
Dairy cow	650[1]	25[1]	NA	10[1] (canola and rape meal)
Beef cattle	500[1]	12[1]	NA	20[1] (rape meal)
Dairy Sheep	80[2]	2.8[2]	NA	20[6]
Dairy Goat	60[2]	3.4[2]	8[7]	4.2[8]
Rabbit	2[2]	0.15[2]	NA	20[9]
Fattening pig[(a)]	100[1]	3[1]	NA	20[1] (canola and rape meal)
Lactating sow[(b)]	200[1]	6[1]	NA	20[1] (canola meal)
Piglet	20[2]	1[2]	NA	20[10]
Broiler	2[3]	0.158[3]	NA	18[1] (canola meal)
Laying hens	1.9[1]	0.13[1]	NA	10[1] (canola and rape meal)
Turkey	7[1]	0.5[1]	NA	20[1] (canola and rape meal)
Salmon	5[4]	0.03[5]	NA	NA
Carp	1[2]	0.02[2]	NA	13[11]
Cat	4[2]	0.06[2]	5[12]	5[12]
Dog	25[2]	0.36[2]	5[12]	30[13]
Horse	450[2]	9[2]	NA	8[14]

NA: the GMO Panel is not able to recommend specific data. No data is expected.
(a): BW, TDI and IR% data, as available in OECD, 2013 for finishing pig.
(b): BW, TDI and IR% data, as available in OECD, 2013 for breeding pig.
1: OECD, 2013.
2: EFSA, 2019b, Table 3 – as per EFSA CONTAM Panel, 2011.
3: EFSA, 2019b, Table 3 – as per EFSA FEEDAP Panel, 2017.
4: https://mowi.com/it/wp-content/uploads/sites/16/2020/06/Mowi-Salmon-Farming-Industry-Handbook-2020.pdf - *Mowi Salmon Farming Industry Handbook 2020*.
5: Calculation based on feed intake as percentage of body weight based on Aas et al., 2020.
6: Pascual et al., 2019.
7: Schmidely and Andrade, 2011.
8: Shi et al., 2015.
9: Lebas, 2004.
10: Hong et al., 2020.
11: https://www.iaffd.com - *the International Aquaculture Feed Formulation Database*.
12: Hill, 2004.
13: Brown et al., 1976.
14: Saastamoinen et al., 2021.

Table 5d: Cotton feed consumption

Animal species and category	Body Weight (kg)	Total daily intake (kg/animal)	Inclusion rates (%)	
			Undelinted seed	Meal
Dairy cow	650[1]	25[1]	10[1]	5[1]
Beef cattle	500[1]	12[1]	NA	5[1]
Dairy Sheep	80[2]	2.8[2]	25[6]	20[7]
Dairy Goat	60[2]	3.4[2]	20[8]	15.5[9]
Rabbit	2[2]	0.15[2]	NA	43[10]
Fattening pig[(a)]	100[1]	3[1]	NA	5[1]
Lactating sow[(b)]	200[1]	6[1]	NA	10[1]
Piglet	20[2]	1[2]	NA	NA
Broiler	2[3]	0.158[3]	NA	5[1]
Laying hens	1.9[1]	0.13[1]	NA	5[1]
Turkey	7[1]	0.5[1]	NA	10[1]
Salmon	5[4]	0.03[5]	NA	NA
Carp	1[2]	0.02[2]	NA	NA

Animal species and category	Body Weight (kg)	Total daily intake (kg/animal)	Inclusion rates (%)	
			Undelinted seed	Meal
Cat	4[2]	0.06[2]	NA	NA
Dog	25[2]	0.36[2]	NA	NA
Horse	450[2]	9[2]	NA	10[11]

NA: the GMO Panel is not able to recommend specific data. No data is expected.
(a): BW, TDI and IR% data, as available in OECD, 2013 for finishing pig.
(b): BW, TDI and IR% data, as available in OECD, 2013 for breeding pig.
1: OECD, 2013.
2: EFSA, 2019b, Table 3 – as per EFSA CONTAM Panel, 2011.
3: EFSA, 2019b, Table 3 – as per EFSA FEEDAP Panel, 2017.
4: https://mowi.com/it/wp-content/uploads/sites/16/2020/06/Mowi-Salmon-Farming-Industry-Handbook-2020.pdf - *Mowi Salmon Farming Industry Handbook 2020*.
5: Calculation based on feed intake as percentage of body weight based on Aas et al., 2020.
6: Arieli, 1992.
7: Aksu et al., 2006.
8: Sampelayo et al., 1998.
9: Alves et al., 2013.
10: Lebas, 2004.
11: Moise and Wysocki, 1981.

Table 5e: Sugar beet feed consumption

Animal species and category	Body Weight (kg)	Total daily intake (kg/animal)	Inclusion rates (%)	
			Beet, sugar tops	Beet, sugar dried pulp
Dairy cow	650[1]	25[1]	30[1]	20[1]
Beef cattle	500[1]	12[1]	20[1]	20[1]
Dairy Sheep	80[2]	2.8[2]	NA	36[6]
Dairy Goat	60[2]	3.4[2]	NA	40[7]
Rabbit	2[2]	0.15[2]	NA	15[8]
Fattening pig[(a)]	100[1]	3[1]	NA	20[1]
Lactating sow[(b)]	200[1]	6[1]	10[1]	20[1]
Piglet	20[2]	1[2]	NA	3[9]
Broiler	2[3]	0.158[3]	NA	NA
Laying hens	1.9[1]	0.13[1]	5[1]	NA
Turkey	7[1]	0.5[1]	NA	NA
Salmon	5[4]	0.03[5]	NA	NA
Carp	1[2]	0.02[2]	NA	NA
Cat	4[2]	0.06[2]	NA	16[10]
Dog	25[2]	0.36[2]	NA	9[11]
Horse	450[2]	9[2]	NA	30[12]

NA: the GMO Panel is not able to recommend specific data. No data is expected.
(a): BW, TDI and IR% data, as available in OECD, 2013 for finishing pig.
(b): BW, TDI and IR% data, as available in OECD, 2013 for breeding pig.
1: OECD, 2013.
2: EFSA, 2019b, Table 3 - as per EFSA CONTAM Panel, 2011.
3: EFSA, 2019b, Table 3 - as per EFSA FEEDAP Panel, 2017.
4: https://mowi.com/it/wp-content/uploads/sites/16/2020/06/Mowi-Salmon-Farming-Industry-Handbook-2020.pdf - *Mowi Salmon Farming Industry Handbook 2020*.
5: Calculation based on feed intake as percentage of body weight based on Aas et al., 2020.
6: Carta et al., 2022.
7: Schmidely and Bahloul, 2022.
8: Lebas, 2004.
9: Badaras et al., 2022.
10: Loureiro et al., 2017.
11: Cole et al., 1999.
12: Murray et al., 2008.

5.3.6. Recommended conversion factors for selected feed materials

Conversion factors recommended to obtain concentration data of the NEPs in feed materials from concentrations analytically determined in the raw commodities are summarised in Tables 6a–d. These factors take into account the total protein content in common crop's feed products, relative to the grains, seeds, beans, assuming that no NEP is lost during their production or processing.

Table 6a: Conversion factors for maize's feed products

MAIZE	Total protein (dw %)	Conversion factors
Field maize kernel	9.35[1]	–
Maize gluten meal	66.95[1]	× 7.16
Maize gluten feed	24.19[1]	× 2.59
Maize milled by-products	NA	NA

NA: the GMO Panel is not able to recommend specific data. No data is expected.
1: OECD consensus document 2002.

Table 6b: Conversion factors for soybean's feed products

SOYBEAN	Total protein (dw %)	Conversion factors
Soybean seed	40.6[1]	–
Soybean meal (49%)	53.81[1]	× 1.32
Soybean hull	13.9[1]	× 0.34
Soybean protein concentrate (70–90%)	84.4[2]	× 2.07

1: OECD consensus document, 2012.
2: https://www.feedtables.com - *INRAE-CIRAD-AFZ Feed tables*.

Table 6c: Conversion factors for canola's feed products

CANOLA	Total protein (dw %)	Conversion factors
Canola seed	24.7[1]	–
Canola meal	39.9[1]	× 1.6

1: OECD consensus document, 2011.

Table 6d: Conversion factors for cotton's feed products

COTTON	Total protein (dw %)	Conversion factors
Cotton seed	25.88[1]	–
Meal solvent extraction	45.3[1]	× 1.75

1: OECD consensus document, 2009b.

5.3.7. The GM feed ADE calculator

To facilitate the consistent reporting of expected ADE estimations in the frame of the advice proposed in this document, for the NEPs, the EFSA GMO Panel proposes the use of an Excel calculator, based on the structure below:

Animal species	BW	TDI	IR feed material	DDI	NEP level	DDE	
category	kg	kg^{DM}/animal	%	g^{DM}/kg^{BW}	$\mu g^{NEP}/g^{DM}$	$\mu g^{NEP}/kg^{BW}$	mg^{NEP}/kg^{BW}
Dairy cow	650	25	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000
Beef cattle	500	12	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000
Dairy Sheep	80	2.8	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000

Animal species	BW	TDI	IR feed material	DDI	NEP level	DDE	
category	kg	kg^{DM}/animal	%	g^{DM}/kg^{BW}	$\mu g^{NEP}/g^{DM}$	$\mu g^{NEP}/kg^{BW}$	mg^{NEP}/kg^{BW}
Dairy Goat	60	3.4	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000
Rabbit	2	0.15	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000
Fattening pig	100	3	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000
Lactating sow	200	6	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000
Piglet	20	1	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000
Broiler	2	0.158	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000
Laying hens	1.9	0.13	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000
Turkey	7	0.5	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000
Salmon	5	0.03	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000
Carp	1	0.02	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000
Cat	4	0.06	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000
Dog	25	0.36	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000
Horse	450	9	See Table 5	[(TDI × IR%)/BW] × 1,000	To be selected	DDI × NEP	(DDI × NEP)/1,000

BW: body weight.
TDI: total daily intake; the total amount of feed given to animal on a daily basis, calculated as dry matter (a.k.a. feed intake).
IR%: inclusion rate; the percentage of a feed material incorporated in a standard diet or ration.
NEP level: the amount of a newly expressed protein analytically determined in raw feed materials, or determined by conversion factor in derived or processed feed materials.
DDI: daily dietary intake; the total amount of a feed material given to animal on a daily basis, calculated as dry matter.
DDE (daily dietary exposure): the total amount of a newly expressed protein given to animal on a daily basis.

A template based on this approach is presented at the end of this section for use in applications.

The use of the ADE calculator and the reporting of the results should follow the principles below:

a) Targeted selection of:

- relevant animal species and category
- related BW and TDI
- IR% for each selected feed materials
- NEP values analytically determined for raw feed materials
- NEP concentration data adjusted for the processed feed materials

b) Calculation of:

- DDI for each selected feed material: DDI = [(TDI × IR%)/BW] × 1,000
- DDE to NEP protein for each selected feed materials: DDE = DDI × NEP

c) Report in a table the results, with proper comments:

- Listing the DDE for each feed material, for all animal species

d) Provide calculations in an Excel file, as workable raw data

- An Excel template for each crop (i.e. maize, soybean, rapeseed, cotton and sugar beet) which should be used in future applications as basis to provide a more consistent presentation of expected ADE estimates is available under the Supporting Information Section of the online version of this output.

6. Uncertainties in dietary exposure estimations

The identification of the sources of uncertainties associated with dietary exposure estimations is pivotal for a reliable estimation of the overall risk and, at the same time, informs on the strengths and limitations of the assessment.

One of the main uncertainties identified by the GMO Panel is the lack of a comprehensive database with reliable data on feed consumption suitable for estimating dietary exposure to NEPs in farmed and companion animals, leading to the use of default values for BW, TDI and IR of selected feed materials.

The GMO Panel is aware that the default values for BW TDI and IR of selected feed materials (see Tables 5a–e) and for conversion factors (see Tables 6a–d) proposed to estimate dietary exposure to the NEPs might lead to c (Table 7). However, the GMO Panel considers this uncertainty acceptable for the purpose of this document.

These default values have been selected across data already consolidated also in other areas of the feed risk assessment (e.g. OECD, 2009a, 2013; EFSA, 2019b), or based on literature with the indication of the related bibliographic reference. In principle, when different default values were reported, the highest value was selected among those that showed no negative impact on the health and performance of the animals. Appendix A reports the full list of papers assessed for this purpose.

The main uncertainties are listed in Table 7 indicating the direction of their contribution on the outcome of the dietary exposure assessment.

Table 7: Main sources of uncertainty (qualitative evaluation) and their likely impact on the dietary exposure estimations to newly expressed proteins

Sources of uncertainty	Direction
Use of 100% replacement scenario due to the lack of consumption data on GM feeds	+
Concentration data (representativity of the samples, measurement uncertainty of analytical results, use of LOQ for values below LOQ)	+
Conversion model used to make use of the measured concentrations in raw primary commodities to estimate dietary exposure (conversion factors, total protein concentration, stability of the constituents, etc.)	+
Absence of a feed consumption database (EFSA, 2019b)	+(−)
Use of default values for animal body weight, total amount of feed consumed daily and the inclusion rate of feed materials in standard diets and rations (EFSA, 2019b)	+(−)

+ = Uncertainty with potential to cause overestimation of exposure.
+(−) = Uncertainty with potential to cause primarily overestimation, but cases of underestimation might occur.

Overall, the impact of the uncertainties from all the above-mentioned sources would be expected to lead to an overestimation of the dietary exposure to GM feed constituents, thus providing conservative estimates.

7. Conclusions

The EFSA GMO Panel is continuously working to improve harmonisation and clarity for the fulfilment of regulatory requirements.

Dietary exposure assessment is one of the essential elements of the risk assessment on GM feeds, as required by Regulation 503/2013.

Estimates of expected ADE to NEPs should be determined to cover average consumption across all the different species, age, physiological and productive phases of farmed and companion animals, and identify and consider particular consumer groups with expected higher exposure.

This statement is aimed at facilitating the reporting of the information that applicants need to provide on animal dietary exposure and to increase harmonisation of the application dossiers. Advice is provided on the selection of proper feed consumption and feed concentration data, and on the

reporting of exposure's estimates. An Excel calculator is provided, which should be used in future applications as basis to provide a more consistent presentation of estimates of expected animal dietary exposure.

As occurs in each of the steps of the risk assessment, estimation of expected ADE includes different sources of uncertainty that should be considered when interpreting the results and concluding on the risk assessment.

Dietary exposure estimates based on the advice given in this document are sufficiently conservative, and the different assumptions taken (e.g. replacement scenario for the consumption data) result, overall, in additional conservatism.

The GMO Panel is aware that refined exposure estimates might be required on a case-by-case basis (e.g. if specific hazards are identified) for further risk characterisation; however, this scenario is not covered by the present document.

Further revisions and updates of this statement will be provided in the future, as appropriate, after considering new scientific and regulatory developments in the risk assessment of GMP.

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Appendix A – List of bibliographical references assessed for the selection of feed material's inclusion rates

When different papers referred to different default values for inclusion rate of feed materials in standard diets or rations, the highest values among those that proved to have no negative impact on the health and performance of the animals was selected.

Table A.1: References for maize

	Paper referenced in Table 5a	Other papers assessed
Dairy goat		
Forage/silage	Baldin et al., 2014	Shi et al., 2015 Ravari et al., 2022
Grain	Sun et al., 2018	Baldin et al., 2014 Shi et al., 2015 Ravari et al., 2022 Laudadio and Tufarelli, 2010
Cat		
Gluten meal	Funaba et al., 2005	Hill, 2004
Dog		
Gluten feed	Kawauchi et al., 2011	Hill, 2004
Gluten meal	Yamka et al., 2004	Hill, 2004

Table A.2: References for soybean

	Paper referenced in Table 5a	Other papers assessed
Dairy goat		
Meal	Baldin et al., 2014	Ferreira et al., 2018 Shi et al., 2015 Schmidely and Bahloul, 2022 Ravari et al., 2022 Milis et al., 2005; Laudadio and Tufarelli, 2010
Hulls	López et al., 2014	Carta et al., 2022
Piglet		
Hulls	Pascoal et al., 2012	Slama et al., 2020
Protein concentrate	Perricone et al., 2020	Agazzi et al., 2020
Dog		
Meal	Vanelli et al., 2021	Félix et al., 2012

Table A.3: References for canola

	Paper referenced in Table 5a	Other papers assessed
Dairy Goat		
Canola meal	Shi et al., 2015	Schmidely and Bahloul, 2022
Dog		
Canola meal	Brown et al., 1976	Hill, 2004

Table A.4: References for cotton

	Paper referenced in Table 5a	Other papers assessed
Dairy Goat		
Undelinted seed	Sampelayo et al., 1998	Alves et al., 2013
Meal	Alves et al., 2013	Baldin et al., 2014

Table A.5: References for sugar beet

Dairy Sheep		
Beet, sugar dried pulp	Carta et al., 2022	Kohestani et al., 2011
Dairy Goat		
Beet, sugar dried pulp	Schmidely and Bahloul, 2022	Schmidely and Andrade, 2011 Laudadio and Tufarelli, 2010
Dog		
Beet, sugar dried pulp	Cole et al., 1999	Guevara et al., 2008
Horse		
Beet, sugar dried pulp	Murray et al., 2008	Olsman et al., 2004