Annex C. Organisms (Animals)

A consideration for the environmental risk/safety assessment of a transgenic plant is the evaluation of the potential for it to have adverse effects, relative to the comparator, on: (1) animals in the environment and on their role in ecological functions, including food webs; and/or (2) human/animal health due to non-dietary exposure.

Concepts and terms

Plants interact with many other organisms in the environment in a variety of ways. This consideration focuses on a subset of organisms – animals (invertebrates and vertebrates) – that a transgenic plant may interact with, particularly those that may have a role in ecological functions (including food webs), in managed ecosystems (i.e. beneficial organisms in agriculture) or in the wider environment (unmanaged ecosystems). The interactions generally considered include feeding on transgenic plant material by non-domesticated animals, but also encompass non-dietary exposure to animals (including humans). To avoid confusion, the humans are specifically indicated when they are the subject of consideration. Other types of interactions of transgenic plants with organisms are dealt with in other annexes: Annex A (Invasiveness and Weediness, e.g. plant competition); Annex B (Vertical Gene flow, i.e. to other plants); Annex D (Soil Functions, e.g. micro-organisms); Annex E (Plant Health, e.g. pests and pathogens); Annex F (Crop Management Practices, e.g. other organisms in crop fields); and Annex G (Biodiversity, e.g. protected species).

Ecological functions are those functions that an organism, population or community contributes to in the ecosystem in which it resides. Ecological functions include processes, such as pollination, decomposition and nutrient cycling, and the role of organisms as a food source in food webs. Ecological functions become ecosystem services when humans benefit from these functions (Sodhi and Erlich, 2010). Examples of ecosystem services for humankind are pest control by natural enemies (i.e. biological pest control), pollination (e.g. increased fruit set and yield from honeybee activity), soil fertility (e.g. supported by invertebrate detritivores such as springtails) and recreation (e.g. bird watching).

Feeding is the consumption or uptake: of growing or dead plant material by organisms (e.g. by herbivores, pollen consumers and decomposers); or of organisms that have directly fed on plant material (e.g. by parasitoids, scavengers or predators). Dietary considerations associated with the use of transgenic plants as food by humans or feed for domesticated animals, including livestock, are beyond the scope of this document. They are more appropriately addressed in the work programmes of the OECD Working Party for the Safety of Novel Foods and Feeds (WP-SNFF) and the Codex Alimentarius Commission. However, incidental feeding by animals, including non-domesticated animals, on plants or plant parts never intended for use as human food or feed for domesticated animals (e.g. potato meant for industrial starch production, plantation trees, ornamentals) would be relevant for this consideration.

Non-dietary exposure to animals (including humans) may result from any route other than direct feeding, such as dermal contact with the transgenic plant or plant parts or an inhalation exposure to pollen or plant dusts (e.g. from harvesting or processing). Non-dietary exposure also includes interactions via plant structures (e.g. trichomes of stinging nettles) or repellents that prevent herbivore attack (e.g. Agarwal and Rastogi, 2008). Non-dietary exposure may be relevant for human and animal health.

Problem formulation

For this consideration, below is a simple example that illustrates the approach for planning an environmental risk/safety assessment. It includes a discussion of assessment endpoints, potential adverse effects, and a linear pathway to harm with corresponding risk hypotheses and information elements to illustrate the approach. As previously indicated in the document (section 1.2.6), the process is often more complex.

(a) Determination of assessment endpoints

A transgenic plant may have impacts on individual organisms (animals) with which it interacts. These impacts may then affect populations of the species and subsequently ecological functions. Therefore, potential adverse effects at the level of individuals are usually addressed first via tiered testing (Romeis et al., 2011). Impacts at population level on ecological functions and the food web are only expected to arise if the abundance, reproductive biology or behaviour of an organism is affected.

Two examples of assessment endpoints for organisms (animals) are: (1) the quality of the ecological functions of non-domesticated animals (e.g. in pollination; as food source; as beneficial insects, such as ladybird beetles); and (2) human health (i.e. allergic/toxic responses) as a result of non-dietary exposure.

(b) Identification of potential adverse effects on the assessment endpoints

The identification of potential adverse effects of a transgenic plant to an animal considers characteristics of the transgenic plant linked to the genetic modification (e.g. trait, phenotype), and the potential receiving environments.

The potential adverse effects of a transgenic plant on an animal may derive directly from the trait in the transgenic plant. This may include novel proteins (e.g. Cry proteins from *Bacillus thuringiensis*) or double-stranded RNA (dsRNA) that are intended to control a target pest, as well as compounds that repel pest species. Such newly expressed gene products or compounds may also affect animals other than the target pests in terms of survival (i.e. lethal effect), growth, development, reproduction (i.e. sub-lethal effects), behaviour or health (e.g. Romeis et al., 2011).

Potential adverse effects of a transgenic plant on an animal may also derive from intentional or unintentional changes to the plant's composition (e.g. change in levels of endogenous toxicants[1]), morphology (e.g. trichomes) or other characteristics (e.g. changes to response mechanisms of the transgenic plant that are consequences of changes to metabolic pathways). If there is a plausible basis for such changes, then a compositional analysis and phenotypic characterisation can be useful in highlighting differences between the transgenic plant and the comparator, and analysis of differences may suggest a pathway to harm that warrants further consideration.

Consideration of the altered characteristics of the transgenic plant aids in identifying potential adverse effects on assessment endpoints associated with animals. Depending on the changed characteristics that warrant further consideration, potential adverse effects according to the assessment endpoints may include: (1) reduced quality of ecological functions of an animal (e.g. pollination); and (2) increased allergic/toxic responses in humans from non-dietary exposure.

(c) Identification of plausible pathways to harm, formulation of risk hypotheses, and identification of information elements relevant to evaluating the risk hypotheses

In this section, two plausible pathways to harm are postulated. For each step of the postulated pathways to harm, a corresponding risk hypothesis is formulated that will enable the risk assessor to determine whether the pathway is likely to occur. Once it is shown that any part of the pathway is highly unlikely, one does not need to continue evaluating the subsequent steps in the pathway and can conclude that the specific pathway to harm is unlikely to occur. In addition, examples of information elements that can be used to evaluate the risk hypotheses are given along with their rationales.

Postulated pathway leading to reduced quality of ecological function of an animal

Animals present in an agricultural field or in field margins and surroundings can interact with the transgenic plant through direct exposure (e.g. a herbivore feeds directly on the transgenic plant or an animal is affected by repellents produced by the transgenic plant) or indirect exposure (e.g. a parasitoid or predator feeds on herbivores that have fed on the transgenic plant). If the transgenic plant has a changed phenotype (see (b)) that could change the abundance of an animal (e.g. an insect pollinator) this could lead to reduced quality of ecological functions (e.g. reduced pollination of plants in the field and/or field margins that depend on pollination for reproduction).

One example of a postulated pathway to harm for this adverse effect is shown in the first column of Table A C.1. Risk hypotheses for each step of the pathway are formulated in the second column and the third column provides examples of information elements for evaluating the hypotheses.

Table A C.1. Postulated pathway leading to reduced quality of an ecological function, corresponding risk hypotheses, and relevant information elements

Pathway steps	Risk hypotheses	Examples of information elements
In relation to the comparator, the transgenic plant produces a novel gene product in pollen	In relation to the comparator, the transgenic plant does not produce a novel gene product in pollen	Expression of a novel gene in pollen
The pollinator ingests the novel gene product in pollen	The pollinator does not ingest the novel gene product in pollen	Level of expression of the novel gene product; Level of exposure of pollinator to the novel gene product during flowering
The novel gene product has toxic properties for the pollinator when ingested	The novel gene product has no toxic properties for the pollinator when ingested	Nature of the trait of the transgenic plant; Survival, behaviour and reproduction of the pollinator exposed to pollen and/or novel gene product of the transgenic plant
The abundance of the pollinator in the environment is adversely reduced	The abundance of the pollinator in the environment is not adversely reduced	Information on abundance of the pollinator; Other factors influencing the abundance of the pollinator
Pollination is adversely reduced	Pollination is not adversely reduced	Information on reduction in pollination (e.g. seed production, abundance of plants that depend on the pollinator)
Quality of the ecological function of pollination is reduced		

It is important to note that examples of information elements in this table are intended to illustrate the types of information that can be used in evaluating a risk hypothesis, i.e. to determine whether particular pathway steps are likely to occur. However, for any step there might be other information that would be relevant. Rationales for how such information elements may be used to evaluate the risk hypotheses include:

- Expression of the novel gene in the pollen of the transgenic plant as this provides information on whether there is a relevant pathway for exposure to a pollinator;
- The expression level of the novel gene product in pollen and the level of exposure of pollinator to the novel gene product as this provides information on the magnitude of exposure and on whether the pollinator is exposed to sufficient amounts of the protein to adversely affect it;
- The nature of the introduced trait and the phenotype of the transgenic plant informs identification of potential adverse effects (e.g. any insecticidal properties of the novel gene product that could result in direct toxicity to the pollinator). Survival, behaviour and reproduction of the pollinator exposed to the novel gene product as this provides information on the potential adverse effects of that novel gene product to the pollinator. Such data are typically generated using a tiered testing approach in the laboratory;
- Information on the abundance of the pollinator and other factors influencing its abundance (e.g. climatological conditions, current insecticide use and presence of food sources other than the transgenic plant) as this provides information on the impact of the transgenic plant on the pollinator;
- Reduction in pollination (e.g. seed production in plants that depend on the pollinator) as this provides information on whether and by how much pollination capacity is reduced.

Postulated pathway leading to increased allergic/toxic responses in humans from non-dietary exposure

Humans can come into contact with the transgenic plant through non-dietary exposure by way of inhalation of pollen, dermal exposure to plant material during cultivation, or dust during harvest and processing. Such interactions may result in allergic/toxic responses (e.g. allergic symptoms to grain dust exposure (Manfreda et al., 1986)). If the transgenic plant has a changed contact toxicity or allergenicity profile, respiratory or dermal contact may lead to an increased level of dermal and inhalation reactions relative to the comparator.

One example of a postulated pathway to harm for this adverse effect is shown in the first column of Table A C.2. Risk hypotheses for each step of the pathway are formulated in the second column and the third column provides examples of information elements for evaluating the hypotheses.

Table A C.2. Postulated pathway leading to increased allergic/toxic responses in humans from non-dietary exposure, corresponding risk hypotheses, and relevant information elements

Pathway steps	Risk hypotheses	Examples of information elements
In relation to the comparator, the transgenic plant produces a novel protein	The transgenic plant does not produce a novel protein	Production of novel protein
Humans are exposed to the novel protein via non-dietary means	Humans are not exposed to the novel protein via non-dietary means	Routes of non-dietary exposure; Level and pattern of expression of the novel protein in transgenic plant
The novel protein has a human toxicity or allergenicity potential	The novel protein does not have a human toxicity or allergenicity potential	Similarity of novel protein to known human allergens/toxins; Available results of toxicity studies
Toxicity or allergenicity is increased	Toxicity or allergenicity is not increased	Experience with handling the transgenic plant; Data on allergenicity
Toxic or allergic responses in humans are increased due to non-dietary exposure		

It is important to note that examples of information elements in this table are intended to illustrate the types of information that can be used in evaluating a risk hypothesis, i.e. to determine whether particular pathway steps are likely to occur. However, for any step there might be other information that could be relevant. Rationales for how such information elements may be used to evaluate the risk hypotheses include:

- Production of novel proteins in the transgenic plant (e.g. from expression of the introduced trait or from novel open reading frames created by insertion of the DNA sequences) as this provides information on whether there are novel proteins expressed in the transgenic plant compared to the comparator;
- Routes of non-dietary exposure of humans to the transgenic plant or plant parts as this provides information on the interaction between the transgenic plant and humans;
- Similarity of the novel protein(s) to known human allergens or toxins (e.g. via bioinformatic analysis) as this provides information on whether the transgenic plant has a human toxicity or allergenicity potential;
- Experience with the handling of the transgenic plant, including any reports of toxic or allergenic effects, and information from allergenicity assessment (e.g. sera screening) and toxicity laboratory studies with animals as this provides information on whether there are increased allergenic or toxic effects.

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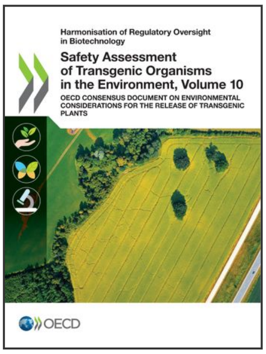
Note

[1] The Consensus documents on plant composition issued by the OECD WP-SNFF contain information on endogenous toxicants, allergens and anti-nutrients, https://www.oecd.org/chemicalsafety/biotrack/consensus-document-for-work-on-safety-novel-and-foods-feeds-plants.htm.



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