

# **Technical guidance to applicants for the authorisation of Precision Bred Organisms for food and feed - Annex A**

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To ensure this technical guidance remains current and supports informed decision-making from applicants, it will be regularly updated to reflect the regulator's experience and the development of technologies, tools and databases. Applicants must ensure they are using the latest version of the technical guidance found on the [FSA webpage](#).

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# Annex A – Quick reference guide to the data requirement for all applications

This document is a **quick reference guide to the data required to support** applications seeking authorisation for Precision Bred Organisms (PBOs) for food and feed use; it does not replace the main technical guidance described in Parts 2, 4 and 5 of [FSA Technical Guidance to applicants for the authorisation of Precision Bred Organisms for food and feed](#), which provides the full detail of the requirement. Sections referred to in this document are Sections of the main technical guidance document.

Applicants should first identify whether the phenotype introduces any changes in composition relevant to food or feed (Tables 1, 2, 3) before determining whether they are relevant for the quality or safety of food and feed and whether they are significant (Tables 5, 6, 7); this determines the information to be provided in an application.

When substances of interest are identified in Section 8, the questions in Tables 5, 6 and 7 must be answered and evidence provided for each relevant substance.

**The sub-questions in each criterion represent the ‘key considerations’ applicants should take into account and evidence to demonstrate how they reached their conclusions in relation to the criteria set out in paragraphs (1) (b) and (c) of regulation 20 (which are referenced in Schedule 4 (1) (5) of the [Genetic Technology \(Precision Breeding\) Regulations 2025](#)).**

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## 1. Identity

See Section 6 of the Technical Guidance document.

**Table 1. Information to be entered into the text box for “Identity, description of change and safety assessment hypothesis”, as relevant.** Information already required in the Marketing Notice to the Defra Secretary of State (Defra Marketing Notice, DMN) may be submitted to the FSA where requirements overlap.

Main guidance detailed section	FSA Requirements for all applications
<b>(Section 6.1)</b> Name of the PBO #	Defra unique reference number (URN, Defra registry for authorised PBOs).  <b>For a batch application:</b> individual identifiers and how many PBOs are included.
<b>(Section 6.2)</b> Taxonomic information *  Already required in DMN, Schedule 3 (1)	Scientific (Latin) name including genus, species, according to the international codes of nomenclature.

Main guidance detailed section	FSA Requirements for all applications
<p><b>(Section 6.2)</b> Taxonomic information #</p> <p>Additional information required by FSA</p>	<p><b>Where the genetic background may interact with the introduced trait:</b></p> <ul style="list-style-type: none"> <li>Subspecies or variety; <b>for a batch application</b>, subspecies or variety for each included PBO.</li> </ul> <p>[or confirmation that the subspecies is not relevant]</p>
<p><b>(Section 6.3)</b> Purpose of the change *</p> <p>Already required in DMN, Schedule 3 (2)</p>	<p>Brief description of the PBO and the purpose of the altered/introduced trait.</p>
<p><b>(Section 6.3)</b> Purpose of the change #</p> <p>Additional information required by FSA</p>	<p><b>Where relevant</b> - Further detail on the purpose of the change related to food or feed.</p> <p>[or confirmation that this has no effect on food/feed use]</p>
<p><b>(Section 6.4)</b> Intended use in food and feed *</p> <p>Already required in DMN, Schedule 2 (4)</p>	<p>Brief description of the achieved trait, including: any new intended use likely to be adopted as a result of the organism’s altered characteristic(s).</p>
<p><b>(Section 6.4)</b> Intended use in food and feed #</p> <p>Additional information required by FSA</p>	<p>Whether the PBO is intended to replace another source of food or feed.</p> <p><b>Where only specific parts of the organism are used for food</b> - Part(s) intended for food use, and whether they are affected by the change introduced by PB.</p> <p><b>Where the PBO is used for feed</b> - Part(s) intended for feed use or that may enter the feed chain, and whether they are affected by the change introduced by PB, specifying when intended use is exclusively in feed.</p> <p><b>Where conditions of use that are new to the species are identified for a PBO for food or feed use</b> - Brief description of new condition(s) of use; brief description of any intended labelling.</p> <p>[or confirmation that there are (as relevant): no intended use in food; no intended use in feed; no new conditions of use]</p>
<p><b>(Section 6.5)</b> Intended phenotype and rational</p>	<ul style="list-style-type: none"> <li>Effect of the introduced change at the molecular level: for example, partial or complete loss of function of the gene, alteration of the properties of the encoded gene product,</li> </ul>

Main guidance detailed section	FSA Requirements for all applications
for targeting the specific genomic region * Already required in DMN, Schedule 2 (5) (e)	<p>altered level of expression of the gene, gain of biological function, etc;</p> <ul style="list-style-type: none"> <li>• Intended trait and intended impact of the genetic change on the characteristics (phenotype, including general effects on the physiology) of the organism;</li> <li>• Why the trait was obtained in this particular way, including reasoning for the choice of the target.</li> </ul>

\* Information already required in the Marketing Notice to the Defra Secretary of State (Defra Marketing Notice, DMN) as described in Schedule 2 (3), (4) and (5) of the Genetic Technology (Precision Breeding) Regulations 2025; the DMN must be submitted to the FSA with a food and feed marketing authorisation application.

# **Additional information specifically relevant to food/feed use** must always be provided for the application to the FSA for a food and feed marketing authorisation.

## 2. Description of change

See Section 7 of the Technical Guidance document.

**Table 2. Information to be entered into the text box for “Identity, description of change and safety assessment hypothesis”, as relevant.** Information already required in the Marketing Notice to the Defra Secretary of State (Defra Marketing Notice, DMN) may be submitted to the FSA where requirements overlap.

Main guidance detailed section	FSA Requirements for all applications
<b>(Section 7.1)</b> Targeted sequence changes * Already required in DMN, Schedule 2 (5)	<ul style="list-style-type: none"> <li>• Gene(s) name(s) and alternative name(s) (if in coding sequence).</li> <li>• Primary function or hypothetical function of the coding sequence targeted, or primary function or hypothetical function (if any) of the non-transcribed sequence targeted.</li> <li>• Gene type, for example, whether it encodes a protein or is transcribed into non-coding RNA.</li> </ul>
<b>(Section 7.1)</b> Targeted sequence changes # Additional information required by FSA	<b>Where multiple copies of the target sequence exist in the genome - whether all copies were altered.</b>

<p><b>Main guidance detailed section</b></p>	<p><b>FSA Requirements for all applications</b></p>
	<p><b>Where level or activity of any substance(s) with potential to impact nutrition, toxicity or allergenicity is expected to be changed as a result:</b> these must be identified and further examined in (Section 8).   <span style="color: red;">[or confirmation that the genetic change instead consists of cisgenesis or intragenesis]</span></p>
<p><b>(Section 7.2) Cisgenesis and intragenesis *</b>                   Already required in DMN, Schedule 2 (5)</p>	<p><b>For cisgenesis</b> – detail of the genetic components introduced; how many copies were introduced; donor organism species and/or subspecies.   <b>For intragenesis</b> – for each genetic component inserted: description of the elements within the inserted DNA fragment; relevant information about the rationale for selecting the specific combination; how many copies were introduced; donor organism species and/or subspecies.</p>
<p><b>(Section 7.2) Cisgenesis and intragenesis #</b>                   Additional information required by FSA</p>	<ul style="list-style-type: none"> <li>• Clear identification of any metabolic function new to the plant, and the phenotype they result in.</li> </ul> <p>Where reasonably <b>anticipated:</b> clear identification of gene(s) normally silent in the plant which are now expressed; clear identification of gene(s) normally expressed in the plant which are now silent or have reduced expression.</p> <p><b>Where level or activity of any substance(s) with potential to impact nutrition, toxicity or allergenicity is expected to change as a result:</b> these must be identified and further examined in (Section 8).   <span style="color: red;">[or confirmation that no cisgenesis or intragenesis was involved]</span></p>
<p><b>(Section 7.3) Location(s) and size(s) of the change(s) / insertion(s) *</b>                   Already required in DMN, Schedule 2 (5)</p>	<ul style="list-style-type: none"> <li>• Whether it is in the nuclear genome OR in non-nuclear genomes; size of the alteration.</li> </ul>
<p><b>(Section 7.3) Location(s) and size(s) of the change(s) / insertion(s) #</b>                   Additional information required by FSA</p>	<p><b>For changes in transcribed regions</b> – identification of the specific exon or intron targeted, how this affects the amino acid sequence where relevant.   <b>For changes not in transcribed regions</b> – identification of the closest coding sequences and their functions on both sides, where they are within 1kb of the genetic change.</p>

Main guidance detailed section	FSA Requirements for all applications
	<p><b>Where non-random insertion is used:</b> relevant information about the rationale for selecting the specific site; direction of the insertion relative to the 5' end to 3' end of the DNA strand; description of any identified undesired on-target event resulting from precision breeding and its reasonably anticipated consequences on the compositional phenotype.</p> <p><b>Where level or activity of any substance(s) with potential to impact nutrition, toxicity or allergenicity is expected to change as a result:</b> these must be identified and further examined in (Section 8).</p> <p>[or confirmation that no unintended on-target event was identified]</p>
<p><b>(Section 7.4)</b> Unintended genetic change(s) attributable to the application of modern biotechnologies #</p>	<p><b>On identified unintended editing events resulting from precision breeding described in DMN</b> – information as per Sections 7.1, 7.2, 7.3 and 7.5.</p> <p><b>Where level or activity of any substance(s) with potential to impact nutrition, toxicity or allergenicity is expected to change as a result:</b> these must be identified and further examined in (Section 8).</p> <p>[or confirmation that no unintended off-target event was identified]</p>
<p><b>(Section 7.5)</b> Additional anticipated effects from connection to biological pathway #</p>	<ul style="list-style-type: none"> <li>• Identification of any related substance(s) whose levels are indirectly significantly affected by the genetic change; brief description of the mechanisms leading to the changes in levels.</li> </ul> <p><b>Where level or activity of any substance(s) with potential to impact nutrition, toxicity or allergenicity is expected to change as a result:</b> these must be identified and further examined in (Section 8).</p> <p>[or statement with rationale as to why no effects on composition are anticipated]</p>

\* Information already required in the Marketing Notice to the Defra Secretary of State (Defra Marketing Notice, DMN) as described in Schedule 2 (3), (4) and (5) of the Genetic Technology (Precision Breeding) Regulations 2025; the DMN must be submitted to the FSA with a food and feed marketing authorisation application.

# **Additional information specifically relevant to food/feed use** must always be provided for the application to the FSA for a food and feed marketing authorisation.

### 3. Substances of interest in edible parts

See Section 8 of the Technical Guidance document. Substances of interest are those substances which levels or activity are predicted to be changed as a result

of the genetic change(s). They must be present in the edible parts of the plant to be relevant to food and feed assessment.

**Table 3. Information to be entered into the text box for “Identity, description of change and safety assessment hypothesis”, as relevant.**

Main guidance detailed section	FSA Requirements for all applications
(Section 8) Distribution of substance(s) of interest in the edible parts	<p><b>For each substance of interest identified in Section (7):</b></p> <ul style="list-style-type: none"> <li>Description of the edible parts of the organism where the levels or activity of the substance(s) are expected to be changed, taking into account any well-established moonlighting and relevant transportation mechanisms.</li> </ul> <p><b>Where level or activity of substance(s) of interest are changed in the edible parts</b> – these must be assessed in Tier 1 for nutrition, toxicity and allergenicity.</p> <p>[or, in the Tier 1 safety assessment submission text box, confirmation of the absence of relevant substances of interest]</p>

## 4. Novelty

See Section 18 of the Technical Guidance document.

**Table 4. Information to be entered into the text box for “Novelty”, as relevant, to answer the question whether “the relevant precision bred organism belongs to a species that has a history of safe food use”.**

Step of Novelty Tier 1 assessment (Section 11)	FSA Applications requirements (for further detail, follow the cross-reference links)
<p><b>Novelty Step (1)</b></p> <p>Is the PBO from a species with <b>no</b> History of Safe Food Use (HSFU) in the EU or UK prior to 1997?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>Statement concluding on the presence of HSFU, relating to how the PBO is intended to be used as a source of food.</li> <li>Brief description of the extent of the experience of continued use, including details of the population for which the progenitor organism is part of the customary diet, its role(s) in their diet, and the country this applies to.</li> </ul>

<p><b>Step of Novelty Tier 1 assessment (Section 11)</b></p>	<p><b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)</p>
	<p><b>No further information needs providing on Novelty Tier 1 assessment – Complete Tier 1 assessment for Nutrition, Toxicity, Allergenicity and Other Safety Concern.</b></p> <p><b>If the answer is Yes:</b></p> <ul style="list-style-type: none"> <li>Statement concluding on the absence of HSFU, relating to how the PBO is intended to be used as a source of food.</li> </ul> <p><b>Proceed to Step (2)</b></p> <p><b>Also, complete Tier 1 assessment for: Other Safety Concern for food use; Nutrition, Toxicity, Allergenicity and Other Safety Concern for feed use.</b></p>
<p><b>Novelty Step (2)</b></p> <p>Does the species have a history of safe food use for at least 25 years in at least one third country?</p>	<p><b>If the answer is No:</b></p> <p><b>The PBO should be subject to further Tier 2 FSA-led safety assessment.</b></p> <p>Information to support the Tier 2 assessment by FSA for <b>PBOs from an organism with traditional use for food in a third country</b> (PB-OTUs) will need providing, as described in Sections 25.1, 25.2, 25.3, 25.4 (including additional information for PB-OTUs), 25.5, 25.7, 25.12.</p> <p><b>If the answer is Yes:</b></p> <p><b>The PBO should be subject to further Tier 2 FSA-led safety assessment.</b></p> <p>Information to support the Tier 2 assessment by FSA for <b>PBOs from a novel organism for food use</b> (PB-NvOs) will need providing, as described in Sections 25.1, 25.2, 25.3, 25.4 (including additional information for PB-NvOs), 25.6, 25.7, 25.8, 25.9, 25.10, 25.11, 25.12.</p>

## 5. Nutrition

See Section 19 of the Technical Guidance document.

**Table 5. Information to be entered into the text box for “Nutrition”, as relevant, to answer the question whether the introduced genetic changes are “expected to significantly alter the nutritional quality of the organism as it is being consumed**

**as food or feed at the date of the application in a way that is likely to be disadvantageous to the consumer.”**

<b>Step of Nutrition Tier 1 assessment (Section 12)</b>	<b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)
<p><b>Nutrition Step (1)</b></p> <p>Did you identify any substance of interest?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>Statement of confirmation that no substance of interest was identified (as per Section 8), and that there is no nutrition concern for the PBO</li> </ul> <p>No further information needs providing on Nutrition Tier 1 safety assessment – proceed to the Nutrition Step (<b>Conclusion</b>)</p> <p><b>If the answer is Yes:</b></p> <p>Proceed to Step (2)</p>
<p><b>Instructions for Steps (2) to (8)</b></p>	<p>Step (2), and following Step(s) as relevant, <b>need completing for each individual substance of interest identified in Section 8.</b></p> <p>Once all substances of interest have been assessed through the relevant steps, proceed to the <b>Nutrition Step (Conclusion)</b></p>
<p><b>Nutrition Step (2)</b></p> <p>Is the substance a nutrient?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>Statement of confirmation that the substance is not a nutrient.</li> </ul> <p>Proceed to Step (5)</p> <p><b>If the answer is Yes:</b></p> <ul style="list-style-type: none"> <li>Statement of confirmation that the substance is a nutrient, and brief description of its role in nutrition (Section 19.2)</li> </ul> <p>Proceed to Step (3)</p>
<p><b>Nutrition Step (3)</b></p> <p>Are levels significantly altered in the consumed parts compared to a benchmark reference?</p>	<p><b>If the answer is No:</b></p> <p>Summary of compositional data must support the conclusions on significance (Section 17.2)</p> <ul style="list-style-type: none"> <li>Statement of confirmation that levels are not significantly different from an appropriate and adequately justified benchmark reference, supported by a summary of the analysis of the compositional data (Sections 17.2, 17.3, 19.3)</li> </ul> <p>Proceed to Step (5)</p>

<p><b>Step of Nutrition Tier 1 assessment (Section 12)</b></p>	<p><b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)</p>
	<p><b>If the answer is Yes:</b></p> <p>Summary of compositional data must support the conclusions on significance (Section 17.2)</p> <ul style="list-style-type: none"> <li>• Summary of the analysis and conclusion on the significance of the change in levels compared to an appropriate and adequately justified benchmark reference, and identification of the parts of the plant for food or feed use containing increased levels (Sections 17.2, 17.3, 19.3)</li> <li>• Whether the nutrient is decreased or increased (Section 19.3)</li> </ul> <p>Proceed to Step (4)</p>
<p><b>Nutrition Step (4)</b></p> <p>Would consumption of the PBO adversely affect the diet of any population when compared to consumption of a benchmark reference?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>• Brief description of the relevant food or feed characteristics</li> <li>• Role of the food and feed produced from the PBO in the diet, including: identification of either human or animal population groups that typically consume food or feed from the PBO, referencing the consumption databases used to conduct the analysis</li> <li>• Brief description of any associated health risks, according to the literature</li> </ul> <p>Proceed to Step (5)</p> <p><b>If the answer is Yes:</b></p> <p>This is a substance of concern which must be subject to <b>further Tier 2 FSA-led safety assessment.</b></p> <p><b>Where substance levels are increased:</b></p> <ul style="list-style-type: none"> <li>• Brief description of the results of a literature search of any health risks associated with increased and/or very high levels.</li> <li>• Details of any population that may be adversely affected, if any, along with brief description of the analysis leading to this conclusion</li> </ul> <p><b>Where substance levels are decreased:</b></p>

<p><b>Step of Nutrition Tier 1 assessment (Section 12)</b></p>	<p><b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)</p>
	<ul style="list-style-type: none"> <li>• Details of any population that may be adversely affected, if any, along with brief description of the analysis leading to this conclusion</li> </ul> <p>Proceed to Step (5)</p>
<p><b>Nutrition Step (5)</b> Does the substance significantly alter bioaccessibility?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>• Identification of the substance of interest (Section 17.1)</li> <li>• Statement of confirmation that there is no evidence in the scientific literature that this substance alters bioaccessibility, including justification of benchmark reference as relevant (Sections 17.2, 17.3)</li> </ul> <p>Proceed to step (6)</p> <p><b>If the answer is Yes:</b></p> <p>This is a substance of concern which must be subject to <b>further Tier 2 FSA-led safety assessment.</b></p> <ul style="list-style-type: none"> <li>• Identification of the substance of interest (Section 17.1)</li> <li>• Brief referenced description of how bioaccessibility is altered, including details on: the affected biological pathways; any effects relevant to bioavailability (Section 19.5)</li> </ul> <p>Proceed to Step (6)</p>
<p><b>Nutrition Step (6)</b> Is the substance an antinutrient or an adjuvant?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>• Statement of confirmation that the substance is not a known antinutrient or adjuvant.</li> </ul> <p>This is the end of Tier 1 assessment for this substance - no further information needs providing on Nutrition Tier 1 assessment for this substance</p> <p><b>If the answer is Yes:</b></p> <ul style="list-style-type: none"> <li>• Statement of confirmation whether the substance is an antinutrient or an adjuvant, and brief description of the antinutrient or adjuvant and its classification.</li> </ul> <p>Proceed to step (7)</p>

<b>Step of Nutrition Tier 1 assessment (Section 12)</b>	<b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)
<p><b>Nutrition Step (7)</b></p> <p>Are levels or activity of the substance significantly reduced compared to a benchmark reference?</p>	<p><b>If the answer is No:</b></p> <p>Summary of compositional data must support the conclusions on significance (Section 17.2)</p> <ul style="list-style-type: none"> <li>• Summary of the analysis comparing the levels of the substance in each part from the PBO destined for food or feed use with those found in an appropriate and adequately justified benchmark reference from a species with HSFU, including statistical analysis using compositional information on the substance of interest (Sections 17.2, 17.3, 19.7)</li> </ul> <p>Proceed to step (8)</p> <p><b>If the answer is Yes:</b></p> <p>Summary of compositional data must support the conclusions on significance (Section 17.2)</p> <ul style="list-style-type: none"> <li>• Statement of confirmation that levels are below or not significantly different from an appropriate and adequately justified benchmark reference (Sections 17.2, 17.3, 19.7)</li> </ul> <p>This is the end of Tier 1 assessment for this substance - no further information needs providing on Nutrition Tier 1 assessment for this substance</p>
<p><b>Nutrition Step (8)</b></p> <p>Are levels expected to be above acceptable levels in food/feed from the PBO after anticipated processing?</p>	<p><b>‘Acceptable levels’ refers to levels/activity equivalent to or below those found in food/feed from a reference variety, after the same anticipated processing.</b></p> <p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>• Brief description of how antinutrients are removed by typical industrial or domestic processing, together with an identification of the processing step involved in the removal (Section 19.8)</li> </ul> <p>This is the end of Tier 1 assessment for this substance - no further information needs providing on Nutrition Tier 1 assessment for this substance</p> <p><b>If the answer is Yes:</b></p>

<p><b>Step of Nutrition Tier 1 assessment (Section 12)</b></p>	<p><b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)</p>
	<p>This is a substance of concern which must be subject to <b>further Tier 2 FSA-led safety assessment.</b></p> <ul style="list-style-type: none"> <li>Brief description of the evaluation of any anticipated industrial or domestic processing showing levels will be above acceptable levels after processing.</li> </ul> <p>This is the end of Tier 1 assessment for this substance - no further information needs providing on Nutrition Tier 1 assessment for this substance</p>
<p><b>Nutrition Step (Conclusion)</b></p> <p>Does any substance require Tier 2 safety assessment?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>Statement of confirmation that there is no nutrition concern over the PBO.</li> </ul> <p>No further information needs providing on Nutrition Tier 1 safety assessment</p> <p><b>If the answer is Yes:</b></p> <p>Any substance which results in concern in steps (2), (5) or (8) must be subject to further Tier 2 FSA-led safety assessment</p> <ul style="list-style-type: none"> <li>Conclusion that a Tier 2 assessment is needed to review the nutrition of the PBO, identifying the substance(s) of interest resulting in a concern.</li> </ul> <p>Further information will need providing for Tier 2 nutrition safety assessment of the substance(s) of concern, as identified in Section 26:</p> <p><b>Where nutrient content is of concern:</b></p> <ul style="list-style-type: none"> <li>The raw data used for the analysis in Step (3)</li> <li>Specify whether the PBO contains a nutrient that is new to the organism.</li> <li>Proximate analysis (quantification of protein, carbohydrate, fat, vitamin and mineral content)</li> <li>Any Nutrient-linked phenotypic data</li> </ul> <p><b>Where bioaccessibility or antinutrient content is of concern:</b></p> <ul style="list-style-type: none"> <li>The raw data used for the analysis in Step (7)</li> </ul>

<b>Step of Nutrition Tier 1 assessment (Section 12)</b>	<b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)
	<ul style="list-style-type: none"> <li>Any additional data relating to any known antinutritional hazards that may be impacted by the genetic change.</li> </ul> Digestibility data

## 6. Toxicity

See Section 20 of the Technical Guidance document.

**Table 6. Information to be entered into free text box for “Toxicity”, as relevant, to answer the question whether the introduced genetic changes are “expected to significantly elevate the toxicity of any food or feed produced from the precision bred organism”.**

<b>Step of Toxicity Tier 1 assessment (Section 13)</b>	<b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)
<b>Toxicity Step (1)</b> Did you identify any substance of interest?	<b>If the answer is No:</b> <ul style="list-style-type: none"> <li>Statement of confirmation that no substance of interest was identified (as per Section 8), and that there is no toxicity concern for the PBO</li> </ul> No further information needs providing on Toxicity Tier 1 assessment – proceed to the Toxicity Step ( <b>Conclusion</b> )
	<b>If the answer is Yes:</b> Proceed to Step (2)
<b>Instructions for Steps (2) to (9)</b>	Step (2), and following Step(s) as relevant, <b>need completing for each individual substance of interest identified in Section 8.</b> Once all substances of interest have been assessed through the relevant steps, proceed to the <b>Toxicity Step (Conclusion)</b>
<b>Toxicity Step (2)</b> Is the substance new to food/feed use?	<b>If the answer is No:</b> <ul style="list-style-type: none"> <li>Identification of the substance of interest (Section 17.1)</li> <li>Statement of confirmation that the substance is commonly found in the diet.</li> </ul> Proceed to Step (3)

<p><b>Step of Toxicity Tier 1 assessment (Section 13)</b></p>	<p><b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)</p>
	<p><b>If the answer is Yes:</b></p> <p>This is a substance of concern which must be subject to <b>further Tier 2 FSA-led safety assessment</b></p> <ul style="list-style-type: none"> <li>• Identification of the substance of interest (Section 17.1), clearly stating it is new to the diet</li> <li>• Processing method used for the production of food or feed from the benchmark reference; evaluation of the efficacy of the methods for removal and/or inhibition; anticipated levels in the food/feed product or range of intended food/feed products (Section 20.2)</li> <li>• Role of the food and feed produced from the PBO in the diet, including: identification of either human or animal population groups that typically consume food or feed from the PBO and identification of the main nutrient they provide, referencing the consumption databases used to conduct the analysis (Section 20.2)</li> <li>• Summary of the compositional data on the substance for each part intended for food and feed (Section 17.2).</li> </ul> <p>This is the end of Tier 1 toxicity assessment for this substance.</p>
<p><b>Toxicity Step (3)</b></p> <p>Does the substance have established toxicity, including toxicity by threshold?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>• Statement of confirmation that there is no evidence of established toxicity of this substance in the scientific literature (Section 20.3)</li> </ul> <p>This is the end of Tier 1 assessment for this substance - no further information needs providing on Toxicity Tier 1 assessment for this substance.</p> <p><b>If the answer is Yes:</b></p> <p>Summary of the compositional data on the substance for each part intended for food and feed use must be used as evidence in the following steps.</p> <p>Proceed to Step (4)</p>
<p><b>Toxicity Step (4)</b></p>	<p><b>If the answer is No:</b></p>

<b>Step of Toxicity Tier 1 assessment (Section 13)</b>	<b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)
<p>For protein toxins: is the structure changed in a way anticipated to significantly increase its toxicity?</p>	<p>Where the substance is not a protein whose encoding sequence has been altered by the genetic change - <b>Proceed to Step (5)</b></p> <p>OR</p> <ul style="list-style-type: none"> <li>Statement of confirmation that the changes in structure are presumed safe, supported by a summary of the functional sequence analysis of the structural changes (Section 20.4)</li> </ul> <p><b>Proceed to Step (5)</b></p> <p><b>If the answer is Yes:</b></p> <ul style="list-style-type: none"> <li>Brief description of the intended benefits, where relevant</li> <li>Summary of the functional sequence analysis of the structural changes and conclusions on the impact on the toxicity of the protein (Section 20.4)</li> <li>Identification of the parts of the plant for food or feed use containing the altered protein</li> </ul> <p><b>Proceed to Step (8)</b></p>
<p><b>Toxicity Step (5)</b></p> <p>Is the substance present at biologically relevant ranges?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>Statement of confirmation that the levels are not expected to be biologically relevant, supported by a summary of the scientific rationale (Section 20.5)</li> </ul> <p><b>This is the end of Tier 1 assessment for this substance - no further information needs providing on Toxicity Tier 1 assessment for this substance.</b></p> <p><b>If the answer is Yes:</b></p> <ul style="list-style-type: none"> <li>Brief description of the ranges for which the substance is expected to be biologically relevant (Section 20.5)</li> </ul> <p><b>Proceed to Step (6)</b></p>
<p><b>Toxicity Step (6)</b></p> <p>Is the PBO a new dietary source for the substance?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>Statement of confirmation that the substance is produced in the parent of the PBO (Section 20.6)</li> </ul> <p><b>Proceed to Step (7)</b></p>

<p><b>Step of Toxicity Tier 1 assessment (Section 13)</b></p>	<p><b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)</p>
	<p><b>If the answer is Yes:</b></p> <ul style="list-style-type: none"> <li>Brief description of the mechanism allowing the expression of the substance in the PBO.</li> </ul> <p>Proceed to Step (8)</p>
<p><b>Toxicity Step (7)</b> Are levels significantly increased in the consumed parts compared to a benchmark reference?</p>	<p><b>If the answer is No:</b> Summary of compositional data must support the conclusions on significance (Section 17.2)</p> <p><b>When legal limits exist</b> - Statement of confirmation that levels have been monitored and comply with existing legal limits</p> <p>OR</p> <ul style="list-style-type: none"> <li>Statement of confirmation that levels are presumed safe according to HSFU/PFC, supported by a summary of the analysis of the compositional data and a justification of benchmark reference (Sections 17.2, 17.3, 20.7)</li> </ul> <p>This is the end of Tier 1 assessment for this substance - no further information needs providing on Toxicity Tier 1 assessment for this substance.</p> <p><b>If the answer is Yes:</b> Summary of compositional data must support the conclusions on significance (Section 17.2)</p> <ul style="list-style-type: none"> <li>Summary of the analysis and conclusion on the significance of the change in levels compared to an appropriate and adequately justified benchmark reference, and identification of the parts of the plant for food or feed use containing increased levels (Sections 17.2, 17.3, 20.7)</li> </ul> <p>Proceed to Step (8)</p>
<p><b>Toxicity Step (8)</b> Are levels expected to be above acceptable levels in food/feed from the PBO</p>	<p><b>‘Acceptable levels’ refers to levels/activity equivalent to or below those found in food/feed from a reference variety, after the same anticipated processing.</b></p> <p><b>If the answer is No:</b></p>

<b>Step of Toxicity Tier 1 assessment (Section 13)</b>	<b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)
<p>after anticipated processing?</p>	<ul style="list-style-type: none"> <li>• Statement of confirmation that levels will be reduced to acceptable levels through current standard practices of food safety management, supported by a summary of the scientific rationale taking into account the processing method used to control the levels / activity of the substance(s) and its efficacy for removal and/or inhibition (Section 20.8)</li> <li>• Range of levels at which the substance is expected to be biologically active, and where possible, anticipated levels in the food/feed product or range of intended food/feed products.</li> </ul> <p style="color: red;">This is the end of Tier 1 assessment for this substance - no further information needs providing on Toxicity Tier 1 assessment for this substance.</p> <p><b>If the answer is Yes:</b></p> <ul style="list-style-type: none"> <li>• Processing method used to control the levels / activity of the substance(s) (Section 20.8)</li> <li>• Evaluation of the efficacy of the methods for removal and/or inhibition (Section 20.8)</li> <li>• Range of levels at which the substance is expected to be biologically active, and where possible, anticipated levels in the food/feed product or range of intended food/feed products.</li> </ul> <p style="color: red;">Proceed to Step (9)</p>
<p><b>Toxicity Step (9)</b></p> <p>Could the dietary exposure result in adverse consequences for the consumer?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>• Role of the food and feed produced from the PBO in the diet, including: identification of either human or animal population groups that typically consume food or feed from the PBO and identification of the main nutrient they provide, referencing the consumption databases used to conduct the analysis (Section 20.9)</li> <li>• Brief evidence of HSFU/PFC for UK or EU populations (Section 20.9)</li> <li>• Statement of confirmation that dietary exposure will not result in adverse consequences for the consumer, supported by a summary of the scientific rationale and conclusions on</li> </ul>

<p><b>Step of Toxicity Tier 1 assessment (Section 13)</b></p>	<p><b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)</p>
	<p>anticipated exposure, including justification of benchmark reference (Sections 17.2, 17.3, 20.9)</p> <p><b>This is the end of Tier 1 assessment for this substance - no further information needs providing on Toxicity Tier 1 assessment for this substance.</b></p> <p><b>If the answer is Yes:</b></p> <p><b>This is a substance of concern which must be subject to further Tier 2 FSA-led safety assessment.</b></p> <ul style="list-style-type: none"> <li>• Brief referenced summary of any health risk associated with increased levels, including details of any populations that may be adversely affected upon exposure (Section 20.9)</li> <li>• Role of the food and feed produced from the PBO in the diet, including: identification of either human or animal population groups that typically consume food or feed from the PBO and identification of the main nutrient they provide, referencing the consumption databases used to conduct the analysis (Section 20.9)</li> </ul> <p><b>This is the end of Tier 1 assessment for this substance - no further information needs providing on Toxicity Tier 1 assessment for this substance.</b></p>
<p><b>Toxicity Step (Conclusion)</b></p> <p>Does any substance require Tier 2 safety assessment?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>• Statement of confirmation that there is no toxicity concern over the PBO.</li> </ul> <p><b>No further information needs providing on Toxicity Tier 1 assessment</b></p> <p><b>If the answer is Yes:</b></p> <p><b>Any substance which results in concern in steps (2) and (9) must be subject to further Tier 2 FSA-led safety assessment.</b></p> <ul style="list-style-type: none"> <li>• Conclusion that a Tier 2 assessment is needed to review the toxicity of the PBO, identifying the substance(s) of interest resulting in a concern.</li> </ul> <p><b>Further information will need providing for Tier 2 toxicity assessment, as identified in Section 27:</b></p>

<b>Step of Toxicity Tier 1 assessment (Section 13)</b>	<b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)
	<ul style="list-style-type: none"> <li>• Qualitative and raw quantitative data used for the analysis in Steps (2) and (7)</li> <li>• Brief description and justification of toxicological testing strategy, including justifying when toxicological studies are not needed.</li> </ul> <p><b>Where the levels of the substance(s)/proteins of concern are not within the same range as in other varieties/species with a HSFU/PFC in the diet:</b></p> <ul style="list-style-type: none"> <li>• Brief description of absorption and breakdown as reported in the literature, and of chemical and physicochemical data.</li> <li>• Brief description of <i>in vitro</i> absorption data and <i>in vitro</i> comparative gastrointestinal metabolism data</li> </ul>

## 7. Allergenicity

See Section 21 of the Technical Guidance document.

**Table 7. Information to be entered into the text box for “Allergenicity”, as relevant, to answer the question whether the introduced genetic changes are “expected to alter the allergenicity of any food or feed produced from the precision bred organism”.**

<b>Step of Allergenicity Tier 1 assessment (Section 14)</b>	<b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)
<p><b>Allergenicity Step (1)</b></p> <p>Is the host plant or cisgene donor a clinically relevant allergenic organism?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>• Statement of confirmation that the host organism/cisgene donor species is not an allergenic organism, and that there is no reason to believe that the allergenicity of the PBO may be changed.</li> </ul> <p style="color: red;">This is the end of Tier 1 Allergenicity safety assessment - no further information needs providing on Allergenicity Tier 1 safety assessment</p> <p><b>If the answer is Yes:</b></p>

<p><b>Step of Allergenicity Tier 1 assessment (Section 14)</b></p>	<p><b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)</p>
	<ul style="list-style-type: none"> <li>Statement of confirmation that the host organism and/or cisgene donor has a significant history of inducing allergic responses.</li> </ul> <p>Proceed to Step (2)</p>
<p><b>Allergenicity Step (2)</b> Is there a clinically-relevant allergen amongst the identified substances of interest?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>Statement of confirmation that there is no evidence in the scientific literature of clinically relevant allergenicity for any of the substances of interest identified in Section 8</li> </ul> <p>This is the end of Tier 1 Allergenicity safety assessment - no further information needs providing on Allergenicity Tier 1 safety assessment.</p> <p><b>If the answer is Yes:</b> Proceed to Step (3)</p>
<p><b>Instructions for Steps (3) to (7)</b></p>	<p>Step (3), and following Step(s) as relevant, <b>need completing for each individual clinically-relevant allergen of interest identified in Step (2).</b></p> <p>Once all allergens of interest have been assessed through the relevant steps, proceed to the <b>Allergenicity Step (Conclusion)</b></p>
<p><b>Allergenicity Step (3)</b> Is the purpose of the change to <b>reduce the allergenicity</b> of the PBO to promote consumption (including by an allergic population)?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>Identification of the allergen (Sections 17.1, 21.3)</li> <li>Statement of confirmation that there is no intention to market the PBO with a claim of reduced allergenicity to promote consumption (including by an allergic population) (Section 21.3)</li> </ul> <p>Proceed to Step (4)</p> <p><b>If the answer is Yes:</b></p> <ul style="list-style-type: none"> <li>Identification of the allergen (Sections 17.1, 21.3)</li> <li>Clear identification of the parts of the plant for food or feed use which are expected to have reduced allergenicity.</li> </ul> <p><b>Where the decrease in allergenicity in the PBO results form a decrease in levels of the allergen:</b></p>

<p><b>Step of Allergenicity Tier 1 assessment (Section 14)</b></p>	<p><b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)</p>
	<ul style="list-style-type: none"> <li>• Summary of compositional data (Section 17.2)</li> <li>• Summary of the analysis and conclusion on the significance of the change in levels compared to an appropriate and adequately justified benchmark reference, and identification of the parts of the plant for food use containing decreased levels (Sections 17.2, 17.3, 21.3)</li> <li>• Scientific reasoning for conclusions on the expected effect on the allergenicity of food or feed produced from the PBO.</li> </ul> <p><b>Where the decrease in allergenicity in the PBO results form a change in structure of the allergen:</b></p> <ul style="list-style-type: none"> <li>• Identification of the parts of the plant for food or feed use containing the altered protein</li> <li>• Summary of the functional sequence analysis of the structural changes and conclusions on the impact on the allergenicity of the protein (Section 21.3)</li> <li>• Scientific reasoning for conclusions on the expected effect on the allergenicity of food or feed produced from the PBO</li> </ul> <p>This is trait of concern which is subject to <b>further Tier 2 FSA-led safety assessment</b>. Information will need providing for Tier 2 allergenicity safety assessment of this allergen.</p>
<p><b>Allergenicity Step (4)</b> Is the allergen structure changed in a way anticipated to significantly alter its allergenic properties?</p>	<p><b>If the answer is No:</b> Where the allergen encoding sequence has not been altered by the genetic change - <b>Proceed to Step (5)</b> OR</p> <ul style="list-style-type: none"> <li>• Statement of confirmation that the changes in structure are presumed safe, supported by a summary of the functional sequence analysis of the structural changes (Section 21.4)</li> </ul> <p><b>Proceed to Step (5)</b></p> <p><b>If the answer is Yes:</b></p> <ul style="list-style-type: none"> <li>• Identification of the parts of the plant for food use containing the altered protein</li> </ul>

<p><b>Step of Allergenicity Tier 1 assessment (Section 14)</b></p>	<p><b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)</p>
	<ul style="list-style-type: none"> <li>• Summary of the functional sequence analysis of the structural changes and conclusions on the impact on the allergenicity of the protein (Section 21.4)</li> </ul> <p>Proceed to Step (6)</p>
<p><b>Allergenicity Step (5)</b> Are levels significantly altered in the consumed parts compared to a benchmark reference?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>• Summary of compositional data must support the conclusions on significance (Section 17.2)</li> <li>• Brief rationale, with referenced evidence, that levels are presumed safe according to HSFU/PFC, supported by a summary of the analysis of the compositional data and a justification of benchmark reference (Sections 17.2, 17.3, 21.5)</li> </ul> <p>This is the end of Tier 1 Allergenicity safety assessment for this allergen - no further information needs providing on Allergenicity Tier 1 safety assessment for this allergen.</p> <p><b>If the answer is Yes:</b></p> <ul style="list-style-type: none"> <li>• Identification of the parts of the plant for food use containing the altered levels</li> <li>• Summary of compositional data must support the conclusions on significance (Section 17.2)</li> <li>• Summary of the analysis and conclusion on the significance of the change in levels compared to an appropriate and adequately justified benchmark reference, and identification of the parts of the plant for food use containing increased or decreased levels (Sections 17.2, 17.3, 21.5)</li> </ul> <p>Proceed to Step (6)</p>
<p><b>Allergenicity Step (6)</b> Have published clinical studies for the same trait in this species demonstrated unchanged allergenicity?</p>	<p><b>If the answer is No:</b></p> <p>Proceed to Step (7)</p> <p><b>If the answer is Yes:</b></p> <ul style="list-style-type: none"> <li>• Brief description of the published study, including reference; number of participants; form of the food consumed during the oral challenge; conclusions on allergenic safety.</li> </ul>

<p><b>Step of Allergenicity Tier 1 assessment (Section 14)</b></p>	<p><b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)</p>
	<ul style="list-style-type: none"> <li>Scientific reasoning for conclusions on the safety outcome of the PBO based on it exhibiting the same trait as the variety in the study</li> </ul> <p>This is the end of Tier 1 Allergenicity safety assessment for this allergen - no further information needs providing on Allergenicity Tier 1 safety assessment for this allergen.</p>
<p><b>Allergenicity Step (7)</b></p> <p>Does a benchmark reference for the same trait belonging to the same species have a history of consumption in the UK or the EU?</p>	<p><b>If the answer is No:</b></p> <p>This is an allergen of concern which is subject to <b>further Tier 2 FSA-led safety assessment</b>. Information will need providing for Tier 2 allergenicity safety assessment of this allergen.</p> <p><b>If the answer is Yes:</b></p> <ul style="list-style-type: none"> <li>Justification for the choice of the benchmark reference (Section 17.3)</li> <li>Scientific reasoning for conclusions on the safety outcome of the PBO based on it exhibiting the same trait resulting from a comparable genetic change.</li> </ul> <p>This is the end of Tier 1 Allergenicity safety assessment for this allergen - no further information needs providing on Allergenicity Tier 1 safety assessment for this allergen.</p>
<p><b>Allergenicity Step (Conclusion)</b></p> <p>Does any substance require Tier 2 safety assessment?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>Statement of confirmation that there is no altered allergenicity concern over the PBO.</li> </ul> <p>No further information needs providing on Allergenicity Tier 1 safety assessment</p> <p><b>If the answer is Yes:</b></p> <p>Any allergen or trait which results in concern must be subject to <b>further Tier 2 FSA-led safety assessment</b>.</p> <ul style="list-style-type: none"> <li>Conclusion that a Tier 2 assessment is needed to review the allergenicity of the PBO, identifying the substance(s) of interest resulting in a concern.</li> </ul> <p>Further information will need providing for Tier 2 allergenicity assessment, as identified in Section 28:</p>

<b>Step of Allergenicity Tier 1 assessment (Section 14)</b>	<b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)
	<p><b>For each substance of interest resulting in an allergenic concern:</b></p> <ul style="list-style-type: none"> <li>• Identification of the target population</li> <li>• Description of the intended use of the final product</li> <li>• Description of the final product</li> <li>• Raw data used for the analysis in Step (4)</li> </ul> <p><b>Where the genetic change(s) alters the levels of an allergenic protein:</b></p> <ul style="list-style-type: none"> <li>• Anticipated daily intake.</li> </ul> <p><b>Where the genetic change(s) alters the sequence encoding an allergenic protein:</b></p> <ul style="list-style-type: none"> <li>• Identification of the target allergen</li> <li>• Description of the structural change, supported by an amino acid sequence alignment of the protein targeted by the genetic change for the PBO and the progenitor, analysed using Protein-families, domains- and signatures-related databases.</li> <li>• Scientifically reasoned conclusion on the resulting change in the allergenicity of the protein</li> </ul> <p><b>Where the PBO is intended to have reduced allergenicity to allow consumption by allergic populations:</b></p> <ul style="list-style-type: none"> <li>• Raw data used for the analysis in Step (3)</li> <li>• Anticipated daily intake.</li> <li>• Brief description of any published clinical study, of the same trait evaluating its potential to elicit a reaction in sensitive people including reference; number of participants; form of the food consumed during the oral challenge; conclusions on allergenic safety.</li> </ul>

## 8. Other safety concerns

See Section 22 of the Technical Guidance document.

**Table 8. Information to be entered into the text box for “Other Safety Concern”, as relevant, to answer the question whether the introduced genetic changes are**

**“expected to introduce any additional features that may affect the safety of any food or feed produced from the PBO”.**

<p><b>Step of Other Safety Concern Tier 1 assessment (Section 15)</b></p>	<p><b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)</p>
<p><b>Other Safety Concern Step (1)</b></p> <p>Does the intended use of the PBO require a market authorisation to be subject to any conditions or limitations?</p>	<p><b>If the answer is No:</b></p> <p>Proceed to Step (2)</p> <p><b>If the answer is Yes:</b></p> <p>A Tier 2 safety assessment is required, the following information will need providing, as relevant:</p> <p><b>Where a restriction of use should apply to the PBO:</b></p> <ul style="list-style-type: none"> <li>• Description of the new condition of use</li> <li>• Recommended new risk management measure, if applicable</li> <li>• Description, with scientific rationale, of any population that should limit or avoid consumption of the PBO, if applicable</li> <li>• Description of any historic conditions of use associated with the organism, if applicable</li> <li>• Description of HSFU and PFC</li> </ul> <p><b>Where new parts of the plant are used in food:</b></p> <ul style="list-style-type: none"> <li>• Information for a novelty assessment for the new part use in food (Section 25)</li> </ul> <p><b>Where the PBO is for feed use only</b></p> <ul style="list-style-type: none"> <li>• Description of any HSFU, and any other relevant information to support the determination of appropriate management measures</li> </ul> <p><b>Where a restriction of use should apply to the PBO:</b></p> <ul style="list-style-type: none"> <li>• Brief description of how the increased concentration in the biofortified ingredient is intended to be communicated.</li> <li>• Recommended risk management measure, if applicable</li> <li>• Description, with scientific rationale, of any population that should avoid limit or avoid consumption of the PBO, if applicable</li> </ul> <p>Proceed to Step (2)</p>

<p><b>Step of Other Safety Concern Tier 1 assessment (Section 15)</b></p>	<p><b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)</p>
<p><b>Other Safety Concern Step (2)</b></p> <p>Are there any other safety concerns arising from significantly altered post-harvest handling and processing?</p>	<p><b>If the answer is No:</b></p> <p>Proceed to Step (3)</p> <hr/> <p><b>If the answer is Yes:</b></p> <p>A Tier 2 safety assessment is required, the following information will need providing, as relevant:</p> <p><b>Where alteration in processing or handling is intended:</b></p> <ul style="list-style-type: none"> <li>Detailed description of the process, including clear identification of the altered processing step(s); comparison to existing industry methods; evaluation of the impact on food safety and nutritional quality.</li> <li>Detailed description of the altered handling step(s), including: evaluation of the impact on food safety and nutritional quality.</li> </ul> <p><b>Where alteration in processing or handling is reasonably anticipated:</b></p> <ul style="list-style-type: none"> <li>Brief description of the changes to processing or handling resulting from a similar trait, and of any consequences this had on post-harvest management of food safety.</li> <li>Evaluation of the impact on food safety and nutritional quality.</li> </ul> <p><b>Where a novel process is intended to be used in conjugation with the genetic change to produce an intended compositional or structural trait with a food:</b></p> <ul style="list-style-type: none"> <li>Description of the intended trait and the novel process used to obtain it.</li> <li>Details of food safety management systems that will be used, identifying: critical control points; verification procedure; analytical methods.</li> <li>Evaluation of the impact on food/feed safety and nutritional quality.</li> </ul> <p>Proceed to Step (3)</p>
<p><b>Other Safety Concern Step (3)</b></p>	<p><b>If the answer is No:</b></p> <p>Proceed to Step (4)</p>

<p><b>Step of Other Safety Concern Tier 1 assessment (Section 15)</b></p>	<p><b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)</p>
<p>Is the phenotype reasonably anticipated to significantly alter how food or feed products from the PBO will be consumed?</p>	<p><b>If the answer is Yes:</b></p> <p>A Tier 2 safety assessment is required, the following information will need providing, as relevant:</p> <p><b>Where the change in consumption is intended:</b></p> <ul style="list-style-type: none"> <li>• Description of the intended change in consumption, including target population and any intended/beneficial use cases.</li> <li>• Estimation of the anticipated change in consumption by reference to appropriate consumption databases.</li> <li>• Description of any potential health concerns associated with high levels of consumption considering upper tolerable limits and dietary recommendations.</li> </ul> <p><b>Where a change in consumption is reasonably anticipated:</b></p> <ul style="list-style-type: none"> <li>• Brief description of the changes to consumption resulting from a similar trait, and of any consequences this had on post-harvest management of food safety.</li> <li>• Evaluation of the impact on exposure to substances of concern and on food safety.</li> </ul> <p>Proceed to Step (4)</p>
<p><b>Other Safety Concern Step (4)</b></p> <p>Are there any other safety concerns arising from traits that are new to the species?</p>	<p><b>If the answer is No:</b></p> <p>Proceed to Step (5)</p> <p><b>If the answer is Yes:</b></p> <p>A Tier 2 safety assessment is required, the following information will need providing, as relevant:</p> <p><b>Where there are changes in the physical morphology that may pose mechanical hazard:</b></p> <ul style="list-style-type: none"> <li>• Description of the change in morphology and the way in which the consumer could be harmed, and of any risk management measures that may be necessary.</li> </ul> <p><b>Where similar combinations of traits in related species are known to be harmful:</b></p>

<p><b>Step of Other Safety Concern Tier 1 assessment (Section 15)</b></p>	<p><b>FSA Applications requirements</b> (for further detail, follow the cross-reference links)</p>
	<ul style="list-style-type: none"> <li>• Identification of the relevant traits, description of their known hazards, and of any risk management that may be necessary.</li> </ul> <p>Proceed to Step (5)</p>
<p><b>Other Safety Concern Step (5)</b></p> <p>Are there any other areas of potential safety concern of which the FSA must be made aware?</p>	<p><b>If the answer is No:</b></p> <p>Proceed to Other Safety Concern Step (<b>Conclusion</b>)</p> <p><b>If the answer is Yes:</b></p> <p>A Tier 2 safety assessment is required, the following information will need providing, as relevant:</p> <p><b>Where there are significant gaps in knowledge or methodological uncertainties:</b></p> <ul style="list-style-type: none"> <li>• Description of the gaps in knowledge or methodological uncertainties that hindered the safety assessment.</li> <li>• Identification of which parts of the Tier 1 safety assessment were impacted.</li> </ul> <p><b>Where there are other well established scientific reasons to believe there may be safety concerns:</b></p> <ul style="list-style-type: none"> <li>• Description of the scientific rationale, clearly identifying the potential safety concerns</li> </ul> <p>Proceed to Other Safety Concern Step (<b>Conclusion</b>)</p>
<p><b>Other Safety Concern Step (Conclusion)</b></p> <p>Did you answer ‘Yes’ in any of the steps?</p>	<p><b>If the answer is No:</b></p> <ul style="list-style-type: none"> <li>• Statement of confirmation that, to the best of the applicant’s knowledge, there is no other safety concern over the PBO.</li> </ul> <p>No further information needs providing on other safety concern Tier 1 safety assessment</p> <p><b>If the answer is Yes:</b></p> <p>The information provided on the other safety concerns identified will be reviewed as part of a Tier 2 FSA-led safety assessment.</p>

## Abbreviations

Acronym	Definition
Defra	Department for Environment, Food and Rural Affairs
DNA	Deoxyribo Nucleic Acid
EU	European Union
FSA	Food Standards Agency
HSFU	History of Safe Food Use
PB	Precision Breeding
PB-NvO	Precision Bred from a Novel Organism for food use
PB-OTU	Precision Bred from an Organism with Traditional Use for food
PBO	Precision Bred Organism
PFC	Prior feed consumption
RNA	Ribo Nucleic Acid
UK	United Kingdom
URN	Unique Reference Number

## Definitions

Key words	Definitions
<b>Adverse health effects</b>	‘Change in the morphology, physiology, growth, development, reproduction or life span of an organism, system or (sub)population that results in an impairment of functional capacity to compensate for additional stress or an increase in susceptibility to other influences’ (EFSA Scientific Committee et al., 2017).
<b>Allergen</b>	<p>A protein molecule which leads to an allergic response due to recognition by serum IgE from an allergic individual (Aalberse, 2000), or recognition of gluten proteins due to celiac disease.</p> <p><b>Clinically relevant allergen:</b> An allergen from an organism with a significant severity, potency, and prevalence causing an allergic response in allergic individuals within the UK.</p>
<b>Anticipated Effect</b>	Any effect (desirable or non-desirable) on traits/phenotypes that can be predicted as potentially occurring as a consequence of the intended change. Anticipated effects from the initial submitted data will be considered by the safety assessment process being developed, whereas unanticipated effects cannot be safety assessed unless evidence emerges.
<b>Benchmark reference</b>	<p>Benchmark references are used as a comparison point to conclude on significance or safety outcome of a change.</p> <p>They can be used to compare composition, for example compositional data on suitable reference varieties that are proprietary, or from suitable published food composition datasets, or from suitable peer-reviewed scientific literature.</p> <p>They can be used to compare traits. For example, a closely related species (with HSFU and PFC) with the same trait (resulting from a comparable genetic change) and with a similar role in the diet can inform conclusions on the safety of food and feed from the PBO.</p>
<b>Bioaccessibility</b>	Bioaccessibility is the proportion of nutrients that are available for absorption.

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<b>Biofortification</b>	Biofortification for the purpose of this guidance is the intentional and significant increase in a nutrient in a PBO, as a result of the genetic change rather than by simply adding the nutrient in the way that fortification is typically understood.
<b>Cisgenesis</b>	DNA from the same or a cross-compatible donor species is inserted.
<b>Composition</b>	The combination of substances produced by the organism that individually and collectively comprise the nutritional, toxicological and allergenic properties of the organism intended for food or feed use.
<b>Conditions of use</b>	Specific restrictions or limitations under which food or feed produced from an authorised PBO may be placed on the market in England.
<b>Donor organism</b>	Organism from which an inserted DNA sequence (by cisgenesis or intragenesis) originates.
<b>Edible parts (of the PBO)</b>	Parts of the organism intended for food use, and parts intended for feed use or that may enter the feed chain. The parts intended for feed use may be different from the parts intended for food use. In some instance, the whole organism may be used as feed (silage).
<b>Feed and feedstuff</b>	Products from plant origin, 'in their natural state, fresh or preserved, and products produced from the industrial processing thereof, and organic or inorganic substances, used singly or in mixtures, whether or not containing additives intended for use in oral animal feeding either directly as such, or after processing, in the preparation of compound feedstuff or as substrates for premixtures'. As set in the assimilated Directive 2002/32/EC on animal feed.
<b>Food safety management system</b>	A set of procedures used by food business operators to prevent consumer illness caused by food hazards.

<b>Key words</b>	<b>Definitions</b>
<b>Genetic change</b>	A specific alteration of the genetic material of an organism. There can be multiple genetic changes introduced by precision breeding in the genome of an organism.
<b>Host organism</b>	Organism in which a genetic change is introduced.
<b>Intended trait</b>	The intended trait is the characteristic resulting from the genetic change which the precision breeding specifically aimed to develop.
<b>Intragenesis</b>	DNA from the same or a cross-compatible donor species is rearranged before being inserted into the genome of an organism.
<b><i>In vitro</i></b>	Performed outside living organisms in a controlled environment, such as in a test tube.
<b>Marketing Notice</b>	Information provided to the Defra Secretary of State when seeking a precision bred confirmation, as described in Schedules 2 and 3 of the Genetic Technology (Precision Breeding) Regulations 2025.
<b>Moonlighting</b>	Moonlighting is a phenomenon by which a gene may encode a different physiological function depending on where in the organism it is expressed.
<b>“On-target” (genetic) change</b>	An unintended genetic alteration that occurs at the targeted genomic location. When it can be reasonably attributed to the genetic technology/methodology used, the impact on food nutritional quality/safety of any unintended on-target alteration must be assessed in the same manner as intended alteration.
<b>Phenotype</b>	The phenotype is the physical or observable expression of traits.  The phenotype to assess for PBOs includes the intended trait and any additional associated characteristics reasonably anticipated to result from the genetic change.

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<b>Precision Bred Organism (PBO)</b>	As set out in the Genetic Technology (Precision Breeding) Act 2023: Briefly, an organism that is the product of modern biotechnology where the genetic change introduced is one that could have resulted from traditional processes.
<b>Prior feed consumption (PFC)</b>	Prior use of a feed as part of the diet of a target animal can inform on the safety of the feed; any materials that have already be used for animal feeds in the UK are listed on the <a href="#">Catalogue of Feed Materials</a> .
<b>Progenitor</b>	Organism from which the PBO is derived – a PBO is obtained by introducing a genetic change into the genome of its progenitor.  A progenitor may be used as a benchmark reference.
<b>Reasonably anticipated</b>	Predicted or inferred based on well-established current scientific knowledge (for example based on what is known about the function of the gene affected and its product according to published experimental data) or based on existing proprietary data (for example phenotypic observations).  Reasonably anticipated effects contribute to the hypothesis-driven identification of concerns.
<b>Regulation 20 application</b>	The application route to be used for a PBO where the criteria in Regulation 20 (1) (a) (b) and (c) of the Genetic Technology (Precision Breeding) Regulations 2025 have been met.
<b>Substance of interest</b>	Chemical components, nutrients, toxins or toxicants that are elements, compounds, or proteins, and are individual constituent components in a food stuff.  A substance can be one single chemical entity or can be composed of multiple components.  Substances of interest are those substances which levels or activity are predicted to be changed as a result of the genetic change(s), and which are known to have the potential to impact nutrition, toxicity or allergenicity. They must be

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	present in the edible parts of the plant to be relevant to food and feed assessment.
<b>Targeted (genetic) change</b>	Genetic alteration that occurs at the targeted genomic site and is the intended product of the methodology used for precision breeding.
<b>Tier 2 FSA safety assessment</b>	<p>An additional safety assessment process performed by the FSA after a Regulation 22 application has been received, where Regulation 20 criteria (Genetic Technology (Precision Breeding) Regulations 2025) have not been met.</p> <p>To note, a separate and unrelated tiered hierarchy is also used in the approach to the assessment of toxicity and allergenicity, as part of the assessment of the Tier 2 safety assessment of PBOs following international procedures.</p>