Minutes

Advisory Committee on Novel Foods and Process (ACNFP). Subcommittee on Products of Genetic Technologies (PGT). Minutes of the 2nd Meeting held on the 8th of August 2022

These minutes are subject to confirmation by the Subcommittee.

Members are required to declare any personal interest in matters under discussion; where Members have a particularly close association with any item, the Chairman will limit their involvement in the discussion. In cases where an item is to be discussed in their absence, a Member may make a statement before leaving.

Minutes of the 2nd meeting of the Products of Genetic Technologies (PGT) Subcommittee of the Advisory Committee on Novel Foods and Processes (ACNFP), held on 8th of August 2022, hybrid face to face and online using Microsoft Teams.

Attendance

Committee Chair

Dr Andy Greenfield

Committee Members

Professor Paul Fraser

Professor Wendy Harwood

Professor Huw Jones

Dr Ray Kemp

Dr Elizabeth Lund

Professor Clare Mills

Professor Hans Verhagen

Professor Bruce Whitelaw

Observers (FSA)

Mr Chris Stockdale, Head Genetic Technology Policy

Mrs Alison Asquith, Senior GT Policy Advisor

Mrs Justine Gallie, GT Policy Advisor

Mrs Kate Shield, Senior Strategy Advisor

Observers (External)

Professor Pete Lund, ACRE Member

Dr Michael Ellis Defra, ACRE Secretariat

Observers (Devolved Administration)

Dr Karen Pearson, Food Standards Scotland

Ms Tamara Satmarean, Food Standards Scotland

Mr Ciaran Weir, FSA Northern Ireland

Secretariat

Mrs Ruth Willis, Head Regulated Products Risk

Assessment; Technical Secretary ACNFP.

Mr Donal Griffin, Team Leader, Regulated Products

Risk Assessment (Feed and GT)

Dr Rachael Oakenfull, Senior Secretariat

Dr Rhys Williams, Senior Secretariat

Dr Andrew Hartley, Science Secretariat

Dr Karin Heurlier, Science Secretariat

Dr Annalisa Leone, Science Secretariat

Miss Victoria Balch, Administrative Secretariat

1 . Apologies and Announcements

The Chair welcomed the Members, the representatives from the FSA, the observers from the devolved administrations, external observers and the Secretariat team. Professor Pete Lund represented the Advisory Committee on Release to the Environment (ACRE, Defra) as an observer, while his appointment as an ex officio Member is pending. Dr Martin Cannell (Defra Observer) and Ms Siobhan Watt (FSS Observer) sent their apologies.

This was a hybrid meeting and the first opportunity for the Subcommittee members to meet face-to-face in London.

Professor Bruce Whitelaw declared financially benefiting from a University of Edinburgh Commercialisation Licence with Genus plc regarding PRRSV-resistant pigs; this was noted and it was agreed that when discussing this particular case study, Professor Whitelaw would be present but only to answer questions on the case.

2. Minutes of the ACNFP/PGT1 meeting

ACNFP/PGT/1/Min

Minutes of the ACNFP/PGT1 meeting have been collated and will be circulated to Members for comments shortly. Once these are agreed, they will be used to report to ACNFP and ACNFP Chair. The expectation is that they will be published in the longer term, once a publication strategy is developed.

3. Matters Arising

ACNFP/PGT/2/MA

- The Secretariat began developing a statement from the discussions held in the PGT1 workshop. Discussion from the PGT2 workshop will be used to develop a final statement, as a basis for discussion with the full ACNFP at their September meeting.

- The Committee reviewed for the first time three applications for the renewal of Genetically Modified Soybean A5547-127 (RP188), Genetically Modified Soybean 40-3-2 (RP212) and Genetically Modified Maize MIR162 (RP652). The Secretariat is drafting positive opinions for these renewals, which will return to the Subcommittee for approval at the next opportunity, prior to being presented to ACNFP.

4. Precision Breeding Framework workshop

ACNFP/PGT/2/01

The Chair summarised the previous workshop for the benefit of Members who joined for the first time.

Members explored some previously identified sources of uncertainty that might suggest further review may be required. Examples included the introduction of multiple cisgenes, and no history of use of the progenitor or of the cisgene donor. The Subcommittee agreed that the challenge of developing approaches and criteria would be to ensure that unanticipated risks in products developed would not be allowed to escape scrutiny if they could negatively impact safety.

Substantial increases in the level of known allergens, toxins or antinutritional factors were also initially identified as potential hazards; it was noted that these might pose a greater risk if not identified. A specific example was given concerning changes in allergenic potential between different varieties of a crop. The concern over levels of compounds that might exceed typical levels was explored, but there was a question on the challenge of how best to define and analyse this.

The Subcommittee further explored the cross-cutting issues identified in the first workshop, including whether the speed of development of PBOs (as opposed to that associated with traditional processes) represents a heightened source of uncertainty for some products that could come to market. Observers present were invited to contribute and they flagged that the existing regulatory

framework in place ensures good checks and balances and prevents new TBO varieties from being placed on the market without appropriate testing (DUS, National Seed List).

Members noted the previous discussion on whether the Novel Food Regulation framework would provide a basis for the assessment of PBOs. Members were reminded that the Novel Food Regulation at present would not allow the review of feed uses of PBOs. It would also not be applicable to crops that do not meet the definition of a novel food. In conclusion, Members acknowledged that beyond the assessment of PBOs by scientific experts, the purpose of the framework was also to reassure consumers about a plant breeding process perceived as new. The regulatory approach developed would need to be transparent and robust, generating public confidence that the consideration of factors to take into account for development of the risk assessment framework was thorough.

Part 1 - In a first part of the workshop, Members investigated the risks that could be presented by a range of case studies expected to meet the definition of a PBO.

Members explored the likely limits of organisms that would meet the definition of a PBO, but where the probability of them arising through traditional processes would be low, potentially due to the time required to generate the relevant genome by traditional breeding. This discussion was aimed at understanding the full range of products that could be subject to any food and feed framework. Where new scenarios were identified, they were shared with ACRE to support their thinking on this topic.

The Subcommittee discussed the following:

- Toxic compounds are frequently known to be produced as part of the immune response to pathogens and this production is likely to vary if the immune response is the target of the change. The substantial increase in known toxic or allergenic compounds in a crop was identified as a possible cause of concern. In some cases, these hazards may require a different risk management strategy.

- High levels of processing can inactivate allergens or toxins, reducing concern over their presence. This is an addition to the complexity of considering the impact of changes in allergen or toxin levels and the impacts on related

biochemical pathways.

- The importance of consumers being informed of the enhanced levels of a metabolite in the food (for example, Vitamin D or Oleic Acid), when the targeted change was an increase in its concentration, to allow an appropriate use of the product as part of a wider diet.

- Differing impacts can exist for different parts of the population, based on the consequences that the level of a compound can cause.

- Introduction of a cisgene was not considered a scenario of concern by itself, but rather, the nature of the protein sequences encoded by the cisgene and whether these might be associated with a hazard, were felt to be relevant to risk. Knowledge of the cisgene donor species – particularly in the context of consumed food – would be critical in considering the level of uncertainty and the potential to alter risk.

- In the case of gene expression upregulated through a targeted deletion of intervening sequences to bring the promoter from one gene into close proximity with another, the function of the deleted sequences, if genic, and more precisely the phenotype resulting from the deletion, could also be a source of uncertainty that would hamper understanding of the full impact of a genetic change.

- Anticipated effects on relevant metabolic pathways and the nutritional profile associated with such pathways, potentially impacting known hazards, might justify greater scrutiny.

- Factoring in the number of edits to anticipate the risks: while a single edit could have a major phenotypic consequence, a combination of multiple edits could have little effect on phenotype. Therefore, the number of edits was not necessarily critical as a potential basis for identifying regulatory assessment criteria.

- Alterations to composition that impact on risk can occur in the context of traditional breeding too, and such concerns are not restricted to the

consumption of food/feed derived from PBOs.

Part 2 - In a second part of the workshop, Members reflected on the criteria that could define Tier 1 and Tier 2 in a two-tiered approach.

The Subcommittee noted the following:

- The case studies presented did not raise significant concerns about risk because they represented genomic features that could be readily generated by traditional processes, such as a simple deletion of a DNA sequence; they did not involve new compounds or associated predictable impacts on diet that raised more concerns than equivalent TBOs. The Subcommittee considered it likely that the majority of PBOs produced, at least initially, would be of this kind. These would not present risk profiles that differed significantly from counterpart TBOs, and as such they would belong in a first tier (Tier 1) in which assessment requirements would be comparable to those for existing TBOs.

- There is the possibility that some types of PBO could lead to much greater uncertainty (about composition) and raise associated concerns. A second tier, Tier 2, was viewed as a form of regulatory safety net that would allow capture of such (rarer) cases, potentially for further assessment and scrutiny.

- Theoretical examples were explored to anticipate situations that might represent a wider range of possible outcomes using the techniques available. The aim of the discussion was to consider types of PBO that were sufficiently different from the progenitor species, perhaps due to multiple changes, such that the degree of uncertainty that resulted could warrant further (Tier 2) assessment.

An initial proposal for the tiers was presented and the Subcommittee used this to have a discussion on what considerations might form the basis for developing Tier assignment criteria. Features of PBOs that were considered relevant included:

- The presence of compounds not normally of concern but for which higher levels in the diet could represent a risk, or alter nutrition, with potential consequences for all consumers or for a key consumer group;

- The presence of compounds of concern (toxins and allergens) in the specific food. This might be mitigated by testing during development before variety trial. Members sought to understand how likely it is that an issue of this type would be identified during rapid PBO development. Tests for these compounds currently happen (for TBOs) as part of due diligence, with no legal limits imposed by UK regulation except for substances representing a high risk for consumers (e.g. erucic acid, mycotoxins);

- The presence of compounds not known to be normally present in the specific food; this should take into account that stacked effects on the diet could result from consumption of several PBOs developed for the same nutritional benefit;

- The presence of compounds not known to be normally present in the diet. Unintended changes in unidentified compounds were also discussed, although it was noted this source of uncertainty would also exist for TBOs.

In conclusion, it was suggested that known hazards could be subject to an update in the accepted risk assessment with little additional data. Major changes to a pathway – when resulting in the production of a new compound of concern – were considered more significant, potentially requiring a deeper review to understand any implications for food safety risks.

Members discussed other cases that might require a deeper review, including introduction of cisgenes from sexually compatible varieties with little knowledge or experience related to their consumption. This scenario, and the potential for de novo domestication of wild species that would not normally be consumed, were recognised as representing different risks, since less would be understood about the gene source in the former or the progenitor species in the latter and how these factors might impact phenotypic traits and, in turn, risk. De novo domestication, in particular, might require extensive editing to improve both crop yield and to make products more edible/attractive. Few examples of such an application are currently available and so development of theoretical products to

test thinking is being explored. Members noted that opportunities for unicellular algae and protists, as well as insects, could challenge the thinking of the subcommittee to date. It was recommended that these be considered further in future discussions for the development of the framework.

Actions – The Secretariat to update the statement initiated after the first Subcommittee workshop

Members to develop credible, theoretical PBO case studies to support further discussion and challenge the framework as it is developed

ACRE to clarify whether data would be sought from applicants on the insertion site of any randomly inserted cisgene, to clarify whether any functional sequences had been disrupted.

5. Item for information

There was no significant development on GM or PB to be reported since the last meeting two weeks prior.

6. Any other business

The Subcommittee Members were informed of the creation of a Teams Channel for ACNFP-PGT to support the distribution of papers to those working with the Subcommittee.

The possibility of running another PGT workshop to support further development of the work ahead of the next ACNFP was explored. Members were invited to email their preference to the Secretariat.

7. Date of next meeting

The next meeting is an ACNFP plenary session scheduled for 7th September 2022, which will be held as a hybrid meeting. The Subcommittee is next due to meet virtually on 11th October 2022.