Minutes

Advisory Committee on Novel Foods and Process (ACNFP). Subcommittee on Products of Genetic Technologies (PGT). Minutes of the 3rd Meeting held on the 11th of October 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 3rd meeting of the Products of Genetic Technologies (PGT) Subcommittee of the Advisory Committee on Novel Foods and Processes (ACNFP), held on 11th of October 2022, 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

Professor Pete Lund - Co-opted

Observers (FSA)

Mr Chris Stockdale, Head Genetic Technology Policy

Mrs Alison Asquith, Senior GT Policy Advisor

Mrs Gemma Jones, Senior GT Policy Advisor

Mr Hoa Chang, GT Policy Advisor

Mrs Justine Gallie, GT Policy Advisor

Mrs Caragh Evans, Senior Strategy Advisor

Mrs Louise Carey, Comms

Observers (External)

Dr Mike Ellis, Defra, ACRE Secretariat

Professor Peter Gregory, Science Council

Observers (Devolved Administration)

Mr Andrew Dodd, Policy FSA Wales

Dr Karen Pearson, Food Standards Scotland

Ms Tamara Satmarean, Food Standards Scotland

Ms Siobhan Watt, FSA Northern Ireland

Mr Ciaran Weir, FSA Northern Ireland

Secretariat

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. Apologies were received from Ruth Willis, ACNFP Technical Secretariat.

Following the completion of the formalities of his appointment, Professor Pete Lund was welcomed as an ex officio Member and representative of the Advisory Committee on Release to the Environment (ACRE).

Professor Peter Gregory was introduced as an observer representing the Science Council; his experience in managing politically sensitive issues, as a former chair of the ACNFP committee, and his link to strategic thinking on innovation through Science Council were welcomed.

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.

The Chair noted that there is the potential for two types of interest to be declared, both related to commercialisation of PBOs: i) for several members who work on academic projects using these techniques, there is the potential to derive a benefit from future commercialisation of a PBO through their contribution to its

development, depending on the final regulatory model adopted; ii) similarly, for those members who act as consultants, there is also the potential to derive a benefit from advising on PBO regulation, depending on the final regulatory model adopted. The potential for future interest for experts in the technology was noted, it was agreed that the ACNFP website would be kept updated on this, and only conflicts of interest would be reported in future minutes. Further action was not considered necessary, since a range of perspectives has been included in the subcommittee's composition and that of the wider ACNFP and such potential conflicts could not be entirely eliminated.

2. Matters Arising

ACNFP/PGT/3/MA

The key points from the PGT discussions to date were used to inform the wider ACNFP workshop, as part of the 154th ACNFP meeting in September. The Secretariat developed an output of the workshop held at the ACNFP 154th plenary session, currently being circulated to Members for comments, with the intention to publish this once agreed by the Committee. This will provide transparency to the work of the Committee and inform the FSA board when making decisions on the approach to regulating PBOs in England.

The Secretariat thanked all Members for continuing to accommodate shorter than usual times for looking at papers ahead of meetings.

3. Minutes of the ACNFP/PGT1 and ACNFP/PGT2 meetings

ACNFP/PGT/1/Min and ACNFP/PGT/2/Min

Minutes from the previous two subcommittee meetings were reviewed for the first time by the subcommittee.

The discussion focussed on the level of detail in the minutes. Members agreed that this was a complex matter; on the one hand, the minutes must be comprehensive and accurately summarise the complex discussions occurring during the meetings, whilst on the other, they must be accessible and meaningful to a wide-ranging audience. The draft reviewed was seen as overly technical in parts and not sufficiently concise. Given the level of interest in, and the range of perspectives on the issues at hand, the minutes should focus on the overall

direction of discussion and identify where consensus was identified to build confidence in the process.

Members commented that delayed circulation of formal minutes after a meeting made it difficult to prepare for subsequent meetings and requested a ‘key points’ summary (including actions), for internal use only, to be circulated within a week or two of the meeting.

It was agreed minutes would be open for comments on the technical content by correspondence, following an updating of the drafts, taking into account the points raised in the discussion. In this instance, while undesirable, an agreement on a final version will be sought by correspondence; however, agreement on subsequent minutes should remain an item on the agenda in future meetings.

No comments were received on the draft executive summaries.

Actions – Members to provide written comments on the minutes of PGT 1 and 2 by 14th October 2022

The Secretariat to circulate updated versions of the draft minutes for PGT1 and PGT2, open to comments, to reach agreed final versions

The Secretariat to produce key notes with action points on ACNFP PGT3 within a week or two of the meeting

4. Precision Breeding Framework workshop

ACNFP/PGT/3/01

Session 1: Further discussion on potential risks identified from case studies

Building on the previous discussion of both the Subcommittee and the ACNFP, this session explored further the potential hazards identified from the case studies to date, to contribute to thinking on how a regulatory approach could be suitably robust. Considerations of proportionality were intentionally deferred to subsequent sessions to allow a focus on the nature and impact of any risks identified. The workshop focussed on clarifying the resulting risk(s) for each identified risk factor, and when possible, to determine which part of the population would be at risk and how significant the effects would be.

Subject to confirmation by ACRE, Members agreed as follows:

- An organism generated by effective reconstruction of a transgene, using multiple rounds of editing of an endogenous gene to create the desired sequence, was unlikely to be classed as a PBO. Similarly, products obtained through intragenesis, containing a genomic feature comprising a novel combination of sequences from distinct genes, derived from the same or related species, were also considered to be very unlikely to be classed as PBOs.

- The potential for using editing to recreate transgenes was discussed: given transgenics, however derived, are unlikely to satisfy the definition of a PBO and would therefore remain as a GMO, further consideration or screening of databases would not be required.

- For some techniques, such as random insertion of a cisgene, where genes of unrelated function could be interrupted with possible impact on additional phenotypes, there was a potential for unintended effects, where it would be desirable for applicants to understand any resulting changes in composition that were relevant for consumer safety.

- Elevated levels of gene expression were explored, and Members recognised that these are not necessarily correlated with any changes in levels of resulting proteins or metabolites. Because compositional changes in respect of nutrients cannot directly be linked to potential risk, Members suggested considering changes in nutritional components on the basis of the concept of “nutritional disadvantage”.

- Concerning the knowledge of progenitor strains and species, the potential use of cisgenes from less well known species was considered: the cisgene’s function and the resulting impact on composition, could be important for understanding any potential risk.

- Case studies in which a targeted, significant change in nutritional profile was introduced raised the question of when such a change would be considered significant and how this could be defined scientifically and statistically. It was proposed that only deliberate changes that could be anticipated (e.g., changes in a pathway that could lead to a change in composition) be

considered. There was no suggestion of a need to check for unintended changes in composition through proteomics, metabolomics, etc. given that such monitoring is not done as part of TBO production and such changes are no more likely to take place in PBOs compared to TBOs.

- When a cisgene derived from a donor organism that is not in the food chain, but is related to the target organism, is used to produce a PBO, there would be a greater level of uncertainty compared to donors with known risk profiles. As such, this represented a scenario where greater scrutiny may be required to understand the impact on composition. Conversely, the deletion of a sequence may not itself be considered a source of increased uncertainty.

- De novo domestication of a wild species not commonly consumed could raise potential concerns because of uncertainty about composition, and the nature of any hazards. Additionally, de novo domesticated species could change their adaptation to a certain climate/environment leading to, for example, toxin production. Moreover, de novo domestication would inevitably require multiple genome edits to a wild species, in order to obtain the desirable domesticated traits; the phenotypic differences between the derived PBO and the wild progenitor would be significant in this scenario, further increasing uncertainty about composition and potentially requiring the need for further scrutiny.

- An increased uptake of contaminants, for example, concomitant with an increased uptake of nutrients from soil, was identified as a possibility (e.g., genome editing of transporters also involved in metal uptake could represent a risk of causing higher concentrations of metals). It was recognised that this could be managed under existing frameworks for contaminants.

- Allergenicity is a potential risk with any plant breeding process, and can be influenced by many factors, including abiotic stress and food chain production processes - for example, the presence and potency of an allergen can change in some fruits during storage, maturation and post-harvest. Members explored whether the timescale for changes could influence the level of allergenicity and whether that should be reflected in assessments.

In conclusion, Members agreed that deliberate, significant changes that affect composition, nutrient profile and allergenicity were identified as those that may translate into changes in risk.

5. Precision Breeding Framework Workshop

ACNFP/PGT/3/02

Session 2: Models

Members were provided with three high-level models for assessing PBOs:

1. An approach with an acceptance of a level of uncertainty for the risks of PBOs is such as it is for TBOs and managed primarily through a due diligence approach, and where a trait-based assessment is developed only for PBOs where new hazards arise.

2. An approach where the greater uncertainty for risks in PBOs is viewed as an unacceptable risk, and a robust trait-based assessment for all PBOs is developed, similar to that used for Novel Foods.

3. An approach where any risks from PBOs are largely managed by due diligence. Where there is greater uncertainty over risks in PBOs, these could be compensated for by increased scrutiny (this is likely to be in cases where there are known hazards that may have been changed as a result of use of the technology), while a trait-based assessment is developed for PBOs where new hazards arise.

Members agreed that a robust trait-based system for all PBOs (option 2) is not consistent with the overall intention of the PB Bill, which implies that because PBOs have genomic features that could have arisen by traditional processes, PBOs and TBOs have similar risk profiles – and the subcommittee has seen no evidence that precision breeding techniques are inherently unsafe. If it is accepted that the current framework for TBO assessment is safe, works and does not require reform, further justification would be needed in order to consider additional aspects and respect proportionality.

The option of exploring an approach consistent with relying on due diligence, such as used for TBOs (option 1), and a second option where there was greater scrutiny of certain cases as considered above in the earlier workshop (option 3), where there could be heightened risks, were deemed appropriate options to

consider further. Both were considered to be consistent with a tiered approach.

Option 1 was recognised as placing greater emphasis on post-market surveillance, and Members explored whether the systems in place would support review and would provide sufficient benefits in comparison to the effort required to administer the system.

Option 3 was considered an appropriate and manageable approach to the assessment and control of risks; however, it implies a difference in risk profile between PBOs and TBOs. Members agreed that if taken forward, option 3 should focus on cases where the nature of the risks identified suggested a potential new hazard in a PBO, or where additional scrutiny can be justified.

Discussions touched on the need to be aware of consumer interests, and that a purely scientific approach to policy in this area is not appropriate. Whilst outside the scope of the Subcommittee's work, it was recognised that the acceptability of risk provides context to the Subcommittees work. The possibility of introducing temporary risk assessment measures, which could be adapted after a history of safe introduction of PBOs has been achieved, was discussed. Any description of criteria and approach must be carefully chosen to make it clear that potential hazards have been considered and deemed "acceptable", and "unacceptable" risks are not anticipated.

6. Precision Breeding Framework Workshop

ACNFP/PGT/3/03

Session 3: Criteria development

The purpose of this workshop session was for ACNFP PGT to identify scenarios and case studies that could underpin a tiered approach and would form the basis of an assessment for PBOs. Based on the discussions in Sessions 1 and 2, and on the potential risks identified to date, the Subcommittee considered what cases, situations or criteria would influence which tier of review should be applied. At this time, questions of proportionality, and how these might constrain the criteria, were again re-introduced.

Members discussed compositional questions that might be put to the applicant and potential consequences anticipated. In particular, Members examined options for considering compositional data – for example, in the standard way required of all new varieties produced by traditional processes, or as an additional request

made by the Committee at a later stage.

As part of defining the criteria for the assignment to tiers, possible decision trees were discussed. Members discussed at what point in the development process PBO status was decided by ACRE and how that may impact the data available to support a decision about assignment to a tier.

Actions – Members were asked to identify criteria for Tier 2 assignment and email them to the Secretariat before the next meeting.

Members were asked to develop possible decision trees for assignment to Tiers.

Members volunteered to develop an example of PBO assessment, considering how current regulations could manage the risks identified.

The Secretariat was asked to list regulations that manage different risks through General Food Law.

7. Genetically modified soybean A5547-127 RP188

ACNFP/PGT/3/04

Genetically modified soybean 40-3-2 RP212

ACNFP/PGT/3/05

Genetically modified maize MIR162 RP652

ACNFP/PGT/3/06

Three draft opinions were presented to the subcommittee concerning the three renewal applications considered in the July meeting (PGT1). RP188, RP212, and RP652 are renewal applications for food and feed use of three GM products: soybean A5547-127, soybean 40-3-2, and MIR162 maize, respectively. No comments were made on either format or content.

Action – Secretariat to ensure file access to all members to gather any outstanding comments

8. Any other business

A public letter questioning the definition of PBOs in the bill, previously received by the Secretariat, was shared with Members asking them to note it and refer any questions to the Secretariat. This letter, and Members responses to it, were discussed. It was agreed the Secretariat would handle any questions on the definition and coordinate with Defra leads on this matter.

The Secretariat sought views of Members on the most efficient approach to updating the main ACNFP Members ahead of the next plenary work on PBOs in November. It was decided that it would be most beneficial to do this as part of the main meeting, rather than through an interim session.

9. Date of next meeting

The next ACNFP meeting is scheduled for 16th November 2022 and will be held as a hybrid meeting. The next ACNFP-PGT meeting is scheduled for 21st of November 2022 and will be held virtually on Teams.