Meeting

Open Session of the ACNFP – Discussion of Hazards Associated with Cell Cultivated Products

Committee Paper for Discussion - ACNFP/170/07

Advisory Committee For Novel Foods and Processes

Open Session of the Advisory Committee on Novel Foods and Processes - Discussion of hazards associated with Cell Cultivated Products (CCP's).

Issue

Members are invited to provide views on the outlined hazards associated with cell cultivated products (CCPs), and how addressing key uncertainties associated with these hazards will impact the risk assessment. This discussion will inform the subsequent work of the FSA CCP sandbox, the ACNFP and the ACNFP CCP Subgroup in developing a framework with which the safety of CCPs can be effectively established.

Background

1. The culturing of animal cells is an established technology used for research and medical purposes, but is now becoming an emergent technology for the production of food. Though these new cell cultivated products (CCPs) are fundamentally novel foods, they raise challenging new and different questions around how to demonstrate and assess their safety.

2. To address these challenges the FSA has established the CCP sandbox programme, which will provide a collaborative space for regulators, industry stakeholders and independent scientists. Through the Sandbox the FSA will develop public guidance on the key hazards, and how the efficacy of the

mitigation of hazards will contribute to the assessment and reaching conclusions on the safety of CCPs as food. Crucially, this will seek to develop an overview of the FSA data requirements needed from applicants to support their safety narrative.

3. To support the scientific aims of the CCP sandbox and progress assessment of CCPs, the CCP Subgroup of the ACNFP has been established to provide expertise to the FSA. This will support the development of guidance for each of these key hazards, including what data applicants will need to provide to reduce uncertainties in the assessment and demonstrate that hazards have been effectively mitigated. This guidance will then be used to support the risk assessment of at least two of these products by the end of 2026. Further details of the sandbox work are outlined in Annex A.

Key hazards

4. Due to the novel nature of these products, and the rapidly developing technology, there is much to be understood about these new foods. To support placing the effort on the areas of the assessment that would have the greatest impact, the discussion is seeking to gain the Committees views on:

- Which of the hazards would you expect to have the greatest impact on the assessment of risk for these innovative novel foods,
- Where could reducing the uncertainties improve the assessment of CCP novel foods and;
- Which hazards represent the greatest barrier to concluding on the safety of CCP novel foods and what key uncertainties need to be addressed.

The views will support review of the hazards in more detail over the next two years, through the work of the CCP Sandbox and CCP Subgroup, to deliver at least two risk assessments of CCP products. The discussion will inform the prioritisation of the work to determine the data required to minimise the largest uncertainties that have the greatest potential to impact on the safety of the consumer.

Using the published FSA CCP hazard ID Annex B, FAO food safety of cell-based food Annex C and internal work within the FSA; the following is a list of the hazards have been identified.

Cell line identity

5. The source, modification, processing and long-term storage of the production cell line are each key factors to ensuring that the final product is consistent across production batches. As cells divide, they accumulate mutations and diverge from the starting cell line. Furthermore, many producers are developing their product with adapted cell lines designed to thrive under culture conditions outside of an animal, but it is not currently clear if these adaptations are likely to impact on the safety of the final product. An improved understanding of the implications of appropriate cell banking management to mitigate any risk identified, will be required to ensure the safety of the final product.

6. The cell banking process is intrinsically linked with the wider cell culture process, and to help address the uncertainties in this we are undertaking a scoping research project that will deliver a final report in April 2025.

Production process

7. Many working in the CCP industry do not have a background in the food sector, even fewer with regulated products. As such, when compared to the requirements for a novel food dossier, applicants may not provide comprehensive descriptions of their production process and how these relate to food safety risks to allow for it to be effectively assessed as a novel food. Moreover, most companies are currently working at a pilot scale of production, before these products reach the market in significant quantities these processes will need to undergo significant scale up. The potential safety implications of this scale up are not yet clear.

Growth media composition

8. For animal cells to grow under culture conditions, they require all the nutrients and chemical signals usually provided by the body of the animal. Though many of the chemicals in this complex cocktail may be found in the diet already, some are not, and others may be present in the media at vastly different concentrations. Though additional processing steps may mitigate these hazards, some applicants are expected to not choose to take this step, and even when further steps are taken it is not clear how media composition may affect the safety profile of the cells themselves.

Nutritional disadvantage and allergenicity

9. The replacement of protein in the diet poses a risk for nutritional disadvantage to the consumer, as such the nutritional profile of CCPs must be considered. Furthermore, CCPs may pose a different allergenic profile to ‘traditional meat’, for instance, the use of scaffolds for cell growth or ingredients in the media could introduce unexpected allergens.

Microbiological hazards

10. Due to the production methods used in CCP production, they are generally less likely to be contaminated with common food pathogens than mat produce by traditional agricultural practices. However, that does not rule out contamination with these pathogens, in addition to the potential for contamination with other microbiological hazards often found in molecular biology lab cell cultures such as viruses and mycoplasma.

11. To help address the uncertainties in this we are undertaking a scoping research project that will deliver a final report in April 2025.

Toxicological hazards

12. To grow and differentiate animal cell lines outside of the organism requires various growth promoters, hormones and processing chemicals to be used that are not usually found in the diet. Depending on the production process, these compounds may still be found in the final product. Toxicological testing of a whole food is not an explicit requirement of novel foods, where justified. It is currently unclear which compounds would require toxicological studies such as a 90-day study, or where alternative approaches such as residue testing may be sufficient to demonstrate the safety of the final product. It is worth noting that the nature of these hazards may evolve over time depending on the innovation and changes in production that are seen as part of iterative authorisations in this space.

13. In this discussion, the Committee is asked to focus on the following key questions:

- Which hazard(s) is likely to have the greatest impact on risk?
- What questions need to be asked relating to the hazards that are different from ‘standard’ novel foods?
- What knowledge, standards or expertise from other sectors could inform the approach to risk assessment?

- How could the existing guidance be amended, or the assessment tailored, to reflect the nature of CCPs?
- At the end of the discussion, Committee members will be asked to rank the hazards in order of the strength of their impact on the risk assessment.

14. To reduce the breadth of this discussion, the Committee is asked to consider the following scope.

In scope:

- The key broad hazards associated with CCPs, produced from the culturing of animal cells.
- The impact of reducing key uncertainties on the CCP risk assessment.
- How could existing international guidance be applied to these assessments – i.e. EFSA tox guidance on novel proteins.

Out of scope:

- Specific hazards i.e. specific chemical residues or genetic changes.
- The efficacy of specific testing methods or specific data requirements.
- Non-animal cell culture for food, i.e. plants, algae, bacteria, fungi.

Committee Actions Required

Members are asked whether the hazards identified reflect the key areas for review and key uncertainties associated with hazards from the CCP production process?

Members are asked does the current guidance for producing novel food need review and updates to support the assessment of CCPs?

Members are asked what order of importance would you rank these hazards impact on the ability for assessors to conclude on the safety of a CCP application?

ACNFP Secretariat

January 2025

Annexes

Annex A – Overview of the Sandbox.

Annex B - FSA hazard identification of cell cultivated meat.

Annex C – FAO hazard identification on CCPs.