Report

Open Session on Cell Cultivated Products

Advisory Committee on Novel Foods and Processes 170th Meeting: Open Session on Cell Cultivated Products held on the 5th February 2025.

Summary

Cell-cultivated products (CCPs) cover a variety of foods that can be made using a production process without slaughter or traditional farming and agricultural practices. Cells isolated from animals or plants, including cells from meat, seafood, fat and offal, or eggs, are grown in a controlled environment, and then harvested to make a final food product. A new ACNFP Subgroup for cell cultivated proteins and alternative proteins was established in September 2024. In line with the FSA's Regulatory Sandbox on CCPs, the Subgroup will have an initial 2-year focus on animal tissue cells grown in cell culture.

An ACNFP open session was held on 5th February 2025 to discuss the potential hazards associated with cell cultivated products (CCPs) of animal origin. This aimed to explore key topic areas relevant to the safety assessments of these novel foods. This session included observers from industry, allowing for greater transparency on the working of the ACNFP and FSA. This document is a record of the session held during the 170th meeting. Relevant background information is also provided below which provides context on the prior discussions held by ACNFP on CCPs.

Background on previous discussions held by ACNFP on Cell Cultivated Products (CCPs)

1. On 18th September 2024 in the 168th ACNFP meeting, the Committee reviewed and accepted a proposal by FSA and FSS to establish a Subgroup of the ACNFP for cell cultivated proteins and alternative proteins to support safety assessments of

these novel foods. The terms of reference for the Subgroup were discussed and the Secretariat agreed to further develop these for the next meeting review.

2. The discussion explored topics to be considered for these assessments. Emphasis was placed on exploring these topics further and gaining input in future from a range of stakeholder's views where possible.

3. On 20th November 2024 in the 169th ACNFP meeting, the Committee reviewed a revised version of the terms of reference for the new Subgroup and agreed on the scope of its role in supporting the FSA's new regulatory 2-year sandbox programme for cell cultivated products (CCPs). The Subgroup Members and Chair of the Subgroup were appointed.

4. The Committee agreed that the scope of the Subgroup for the first two 2-yearwould focus specifically on CCP novel foods rather than the broader scope on alternative proteins. This would align with the objectives of the FSA CCP regulatory sandbox programme.

5. The Committee discussed the structure and approach for an ACNFP open session to be held at the next 170th meeting in February 2025. The intention was to discuss potential hazards and risks associated with CCPs specifically and inform the 2-year work of the Subgroup.

Meeting session introduction

6. The FSA Secretariat provided the Committee with an overview of the launch of the FSA Cell Cultivated Products (CCP) Sandbox and its objectives. The Sandbox was set up by FSA to ensure that novel laboratory engineered cell-based foods would not pose food safety risks to consumers upon entering the market, whilst aiming to support industry innovating with CCP 'engineering biology' technology to navigate the regulatory landscape. Members were informed that the FSA CCP Sandbox is a 2-year programme that will facilitate dialogues between industry and regulators to inform four-nation regulatory decisions, under the novel foods regulation, for novel foods for the UK market.

7. The Committee was informed about the challenges the FSA faces and the need for additional guidance to support tailoring the assessment within the novel food framework for any risks CCPs may pose. The future role of the ACNFP Committee, and its newly established CCP Subgroup, in assessing associated hazards and conducting CCP risk assessments was explained. This will provide necessary advice for FSA and FSS in supporting the evaluating these novel and innovative

foods.

8. The Committee was provided with an overview of the scope, purpose and objectives of the open session. The Secretariat advised that industry (including potential applicants, biology engineering technology experts, independent scientists and stakeholders) had been openly invited to observe the session.

9. The open session would allow industry to observe the first full discussion of the ACNFP on potential hazards and risks associated with CCPs while providing greater transparency on the working of the ACNFP and FSA. It was noted by Members that the FSA Sandbox aims to develop guidance for future applicants seeking regulatory approval and that the session would be the first step in helping to inform guidance development.

ACNFP open session meeting

10. The Chair welcomed the Members of the ACNFP, representatives from the FSA, the observers from the devolved administrations, the Secretariat team and 25 external observers from industry. The Chair introduced the scope, purpose and objectives of the ACNFP open session and the key focus for the Committee’s discussion.

11. The Secretariat invited Members to provide views or raise key questions on hazards and uncertainties associated with cell cultivated products (CCPs) with a focus on seven assessment areas: cell line identity, production process, growth media composition, toxicological hazards, microbiological hazards, nutritional disadvantage and allergenicity. To reflect the scope of the Sandbox, the discussion was limited to animal tissue cells grown in cell culture. The Secretariat clarified that this excluded precision fermentation and culture of non-animal cells.

12. Members were presented with a list of potential hazards that had been identified for these areas, providing two publications as supporting references: the Food and Agriculture Organization of the United Nations (FAO & UN) 2023 report on food safety aspects of cell-based food and the FSA 2022 Hazard identification: identification of hazards in cultured animal cells.

13. The Secretariat informed Members of the key questions they sought to understand and develop from the discussion and sought to address the following (as summarised from the Committee discussion paper):

- Which hazards would have the greatest impact on, or barrier to, the assessment of safety of CCPs.
- Identification of the key hazards and a hazard ranking (greatest impact on risk and raising safety questions).
- Key uncertainties: which uncertainties could be reduced, or must be addressed, in order to improve the safety assessment of CCPs.

14. The Secretariat will send feedback forms to Committee Members and the 25 industry observers to gain further information on the ranking of hazards. This would inform the workplan to review these and help identify relevant expertise required to support the work of the FSA Sandbox.

Identity

15. With regards to identity, Members raised uncertainty regarding the need for product consistency across batches throughout the total lifetime of the production of the product. Members noted that any variation must not mislead the consumer. Monitoring of cell characteristics such as phenotype during the lifetime of the product would provide necessary information to further understand any impact on safety.

16. With regards to cell stability, the implications of genetic variation on safety were discussed. The genotypic and phenotypic changes that might occur in CCPs were discussed and the need for genetic analyses was highlighted. Natural epigenetic changes with culture duration and impact on safety was also raised.

17. Members discussed aspects of appropriate cell bank management. For products from cells where gene expression had been intentionally altered, it was agreed that the stability of this change needs to be monitored. Members discussed whether cells or tissues from certain animals are more predisposed to genetic drift and raised uncertainty over this. The effect of the scale of the production process on genetic drift would also need to be understood.

18. Demonstrable efficiency of the cell differentiation was raised. The impact efficiency may have on the end product (the proportion of differentiated cells and cell types) would need to be assessed and processes put in place to confirm consistency. However, the degree of variation that is acceptable for these assessments is not yet understood. Appropriate specifications or parameters with this regard would need further consideration.

Production process

19. The Committee explored hazards arising from the source animal such as viruses or chemical contamination from veterinary drugs. The need for information on the health of the source animal to understand these risks was raised. This included use of antibiotics in the source animal and potential wider implication for drug resistance. The cell sourcing and cell isolation processes and management of such hazards in process were discussed.

20. A new topic for the FSA to consider was the potential for use of precision bred animals as the source animal and how this would be managed through the associated assessment routes would need to be explored. It was also not clear what potential for new hazards this may have and the impact on risk.

21. Hazards arising from the potential contamination of cells with plastics, plasticisers and other contact materials used in culture vessels or other production steps were discussed. Members advised that information needed for the assessment on these aspects needed to be further explored.

22. Hazards arising from quality issues of raw materials used during product development were raised. This may include ingredients or reagents lacking food grade quality. An approach to assessing hazards based on multiple factors was discussed: quality criteria, purity, food or pharmaceutical grade with end product testing and further assessment of toxicity or allergenicity, where required.

23. The potential for unknown ways of obtaining starting cultures was highlighted which may pose new hazards. The standard methods currently used, such as, isolation from an animal, somatic cell lines, stem cells and immortalised cell cultures, were discussed. It was advised that alternative or new methods as they are developed and validated would therefore need further consideration on whether they pose new risks.

24. Potential hazards from materials used in the production were discussed, for example in scaffolds and impact on the cells from processing. Scaffold material may be retained in the cells giving rise to potential hazards including allergenicity risks. The Committee discussed implications in terms of detection. The effect of cell washing was explored, including hazards arising from cells under stress, such as the production of growth factors.

Growth media composition

25. Components in the culture media such as growth factors and hormones and novelty of these in foods were discussed. New constituents in the CCP that have not been fully removed, may pose additional hazards, the impact of which on risk should be explored. The Committee discussed whether non detection should always be demonstrated for certain constituents (e.g., growth factors) or evidence of levels that are too low to cause any concern.

Toxicological hazards

26. With regards to potential hazards arising from the culture media, an appropriate toxicological assessment approach was discussed which considered detection methods for residues (such as isotope analysis) and use of HBGV's (Health-Based Guidance Value) and other threshold levels.

27. It was noted by the Committee that 90-day studies or testing on the whole food should not be a strict requirement and moreover is unlikely to be helpful. The Committee advised that the first focus of an assessment would be testing for levels of chemical residues or contaminants.

Microbiological hazards

28. Considerations for the health of the source animal were discussed. Safety questions were also raised with regards to opportunities for viruses or prions to become part of the genetic machinery and propagate in cultures.

29. Microbial stability was explored, the need for pH analyses, storage and packaging considerations were raised. Additionally, as CCPs are likely to have a high-water content, members discussed the additional complexities for appropriate packaging and shelf-life testing. Additionally, exploration of whether current management strategies for similar products remain effective for these products was raised.

30. The potential for development of biofilms in process was discussed and would need to be explored further.

Nutritional disadvantage

31. Members discussed that compositional changes may occur depending on culture duration. Changes to the amino acid profile as well as protein digestibility for example would be a factor in review of nutritional disadvantage.

32. Members shared a range of views on the need for, or suitability of, an appropriate non-CCP comparator to assess potential nutritional disadvantage. In the context of the current novel foods guidance a comparator is not strictly a requirement. However, this could be a useful tool when considering nutrition. A comparator that is most similar to the food replaced by a CCP under the intended uses was considered appropriate in this context. Constituents typically found in the traditional meat may not be found in the CCP product and as such may lead to a nutritional disadvantage for the consumer.

33. Members raised the need for an understanding on how nutritional intakes are affected by replacing the comparator with a CCP under the intended uses. Due to differences in added or intrinsic components of the CCP, consideration of the levels, structure and bioavailability of the individual micronutrients could be required to assess potential nutritional disadvantage for the consumer.

34. Proteins present in the culture media that may contaminate the CCP was raised as a potential hazard. Additionally, these proteins might change during process manufacture. New proteins may also be formed in process.

Allergenicity

35. On allergenicity it was recognised that fish is already required to be managed and labelled under assimilated Regulation 1169/2011 EU. Allergenicity considerations might occur from cross contamination of the source sample reagents / media containing known foods allergens and scaffold use. Differences in the proteins produced by this method may need consideration in the context of whether the classical assessment strategies address these areas.

Other topics discussed

36. Members questioned the effect of cooking or curing on CCPs and how this may impact safety. It was advised that more information on this could be needed. Acrylamide formation would also need consideration in relation to residues or the scaffold.

37. It was noted that, consumer behaviour towards CCP products with regards to dietary preferences, was outside the scope of the Subgroup.

38. Regarding specifications and key parameters, it is not yet clear which of these can or cannot remain confidential for the authorisation.

General points and principles for the assessment

39. It was recognised that in line with the regulations, assessments would need to be on a case-by-case basis. Authorisations in the US and Singapore, while subject to different regulations, could be a source of information for reviewing these technologies.

40. Members also discussed guiding principles and aims of the Subgroup, including proportionality. They recognised that with new innovations there is a balance on getting the information needed to assure safety and not presenting regulatory barriers. Members advised that the FSA ensure these products fit appropriately into the current regulatory novel foods framework to allow efficient and proportionate review. Members discussed the need for a consideration of ethics. However, this would fall outside the scope of the Terms of Reference for the Subgroup. It was noted that the potential for conflicts of interest for experts could arise as part of the discussion. It was agreed to manage this in the usual way for the Committee. This is through a case-by-case review of any interest with the aim of supporting a range of opinions on the evidence to be elicited. Members highlighted that there may be factors to be considered by others including UK health and safety legislation and General Food Law.