

CODEX ALIMENTARIUS COMMISSION



Food and Agriculture
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World Health
Organization

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Fifty-Fifth Session

DISCUSSION PAPER FOR NEW WORK ON DEVELOPMENT OF GUIDELINES FOR FOOD SAFETY ASSESSMENT OF CELL CULTURE MEDIA COMPONENTS IN CELL-BASED FOOD PRODUCTION

(Prepared by Singapore and China)

Background

1 “Cell-based food¹ production” is a working term that has been used by the FAO and WHO to describe the growing of animal agricultural products directly from cell cultures instead of using livestock. Cell-based food utilises novel technologies that have not been used in food previously and has been explored as a potentially sustainable option to complement the conventional livestock agricultural system.

2 In 2022, the FAO and WHO conducted a comprehensive food safety hazard identification of cell-based food production². While some hazards are already well-known and exist in conventionally produced foods, there are additional hazards unique to the production of cell-based foods due to the nature of the materials, inputs, ingredients, and equipment used that may not have been used previously for food production. For instance, the use of unorthodox culture media components (e.g. growth factors, small drug-like molecules) during the production process poses difficulties in assessing food safety risks associated.

3 Cell-based food products are currently at various stages of development across the world. Whilst some companies are still at research and development stage, others have started commercial sale of products. Cell-based foods have been allowed for sale in countries like Singapore and the United States of America. More approvals are expected in the coming years as the safety of such food are assessed in Australia and New Zealand, as well as the European Union.

4 The industry's rapid growth trajectory suggests that the prevalence of cell-based foods is likely to increase globally. As more countries develop national requirements for assessing the safety of cell-based food, the diversity in approaches used may discourage further adoption of cell-based food production technologies and result in trade issues in the trade of cell-based food.

Discussions related to cell-based food at Codex

5 Cell-based food were first discussed at Codex as part of discussions on New Food Sources and Production Systems (NFPS)³ at CAC44(2021) in response to a FAO-WHO document seeking advice on addressing NFPS related issues. Subsequently, a Circular Letter (CL) was issued on the topic and further discussion held at CAC45(2022). As there were diverse views on whether existing Codex mechanisms were sufficient to address new work proposals on NFPS, a second CL was issued to identify specific topics for more discussion, including identification of topics that the current Codex mechanisms could not address.

6 NFPS was further discussed extensively at CAC46(2023), where there was a general recognition on the importance and relevance of NFPS among Members and Observers. CAC46 highlighted the importance of addressing challenges posed by NFPS and the important role Codex could play in this and noted that current

¹ In this document, the term “cell-based foods” is used as a working terminology to indicate food produced through the culturing of cells isolated from animals. This includes cells isolated from poultry, bovine, porcine, fish and crustacean sources.

² FAO & WHO. 2023. Food safety aspects of cell-based food. Rome. <https://doi.org/10.4060/cc4855en>

³ According to the definition in CAC44, new foods denote those that have not been widely consumed either because they have recently emerged into the global retail space thanks to technological innovations, or because their consumption has been historically restricted to specific regions in the world. Such foods are also considered ‘new’ within the framework of existing Codex standards. New food production systems reflect novel innovations or advancements in pre-existing food technologies that help to produce some of the new foods under discussion.

Codex working mechanisms were adequate to address new work proposals on NFPS. Additionally, CAC46 encouraged Members to submit discussion papers or new work proposals either to active Codex Committees or to the Executive Committee through the Codex Secretariat.

7 Leading up to the discussions at CCEXEC86(2024), Singapore engaged with Members across all Codex Regions, in meetings coordinated by the Regional Coordinators. During these meetings, there was general recognition from Members on the benefits and the need for Codex guidance to ensure food safety of cell-based foods. Members also generally expressed interest to have a better understanding of the importance of the work and how Codex could proceed to carrying out discussions on cell-based foods.

8 During CCEXEC86, Singapore highlighted the intention to submit two new work proposals on cell-based foods ([EXEC/86 CRD02](#)):

- Guideline for the conduct of food safety assessment of cell culture media components used in the production of cell-based foods.
- Code of hygienic practice for manufacture of cell-based foods.

CCEXEC86 recommended that the proposed guidelines on safety assessment may be submitted to CCFA, and the proposed code of hygienic practice be submitted to CCFH in response to the request for new work proposals.

9 The recent CAC47(2024) noted the intention by Singapore and China to submit new work proposals on cell-based foods and members countries generally expressed interest in this initiative. Singapore and Saudi Arabia also co-organised a [side event](#) during CAC47 to increase awareness of cell-based foods and how Codex can help to address food safety challenges of cell-based food.

Importance of establishing internationally harmonised guidelines

10 With the potential to contribute to a global sustainable food system, countries such as Australia, China, Singapore, and United States, are investing in research into future foods, including cell-based foods. As the cell-based food sector expands, food regulatory agencies worldwide face the dual challenge of addressing safety concerns whilst fostering innovation and facilitating trade. The industry's anticipated growth underscores the critical need for a global consensus on safety standards and regulations. Given Codex Alimentarius' mandate to protect consumer health and facilitate trade, there is a pressing need for the organisation to address these challenges proactively.

11 Although trade in cell-based foods is currently minimal, there has been interest from the World Customs organisation on explore development of Harmonised Commodity Description and Coding System to classify such products. This interest indicates an expectation of increased trade in this sector.

12 By developing harmonised guidelines and standards for cell-based foods, Codex can ensure consumer safety as the industry grows, facilitate international trade by aligning standards across countries, support innovation by providing clear regulatory pathways, and stay ahead of technological advancements in the food industry. While the cell-based food industry is still in its early stages, Codex has a significant opportunity to fulfil its mandate through timely and comprehensive guidelines. This proactive approach will help protect consumer health, promote fair and efficient international trade, and support responsible innovation in this rapidly evolving sector.

Addressing food safety challenges of cell culture media components at CCFA

13 Cell culture media is essential in the production of cell-based foods and comprises of a complex mixture of individual components including, salts, sugars (glucose), vitamins, amino acids, organic acids, growth factors, hormones and small molecules. The cell culture media components confer a range of functions in the culture media such as providing nutrients, encouraging cell proliferation, inducing differentiation. Some of these compounds are already present in conventional foods, while other compounds have no prior history of use in food. Although most of the cell culture media would be either utilised by cells or removed during the production process, some could remain in the cells as residues hence presenting potential food safety risks that will need to be managed. A non-exhaustive list of cell culture media components, and their technological function in culture media is shown in **Appendix 1**.

14 CCFA is a relevant committee address this work as it focuses on both food additives and processing aids. The cell culture media components could be considered as processing aids⁴ given the following reasons:

- Cell culture media components are intentionally added to serve technological functions during culturing of the cells.
- Cell culture media components are not intended to be consumed as food ingredients by themselves.
- Cell culture media is removed upon harvest of cells, but non-intentional and unavoidable residues of some cell culture media components may be present in the final product.

While some food additives are also used as cell culture media components, they serve technological functions in cell culture that are different from those listed in the *Class name and the international numbering system for food additives* ([CXG 36-1989](#)).

15 Currently, there is a lack of internationally harmonised guidelines for assessing cell culture media components when they are used for the production of cell-based foods. The development of a guideline for the conduct of food safety assessment of cell culture media components used in the production of cell-based foods would help to facilitate Codex members' assessment and management of food safety risks associated with these cell culture media components, which have not been previously used for food production. As such, Singapore and China are putting forth the development of guidelines to manage the conduct of food safety assessment of cell culture media components used in the production of cell-based foods as part of risk management measures (**Appendix 2**).

16 As the range of cell culture media components is diverse, the proposed guidelines could potentially include a categorisation framework to utilise a tiered approach to provide guidance on the level of evidence required to conduct safety assessments of cell culture media components, in relation to the level of potential food safety risk that these media components may pose if present in the final product.

17 Considering the rapid development of the cell-based food industry and given that Members may be developing new and potentially divergent approaches to assessing the safety of cell culture media components used in cell-based food production, it would be important for CCFA to consider all relevant information in making a future decision on development of a guideline to manage the conduct of food safety assessment of cell culture media components used in production of cell-based food.

Recommendations

18 CCFA55 is invited to consider the new work proposal for the development of the guideline for the conduct of food safety assessment of cell culture media components used in production of cell-based foods (**Appendix 2**).

⁴ Processing aid means any substance or material, not including apparatus or utensils, and not consumed as a food ingredient by itself, intentionally used in the processing of raw materials, foods or its ingredients, to fulfil a certain technological purpose during treatment or processing and which may result in the non-intentional but unavoidable presence of residues or derivatives in the final product. (Extracted from the Codex Alimentarius Commission Procedural Manual)

Appendix 1

TYPES OF CELL CULTURE MEDIA COMPONENTS

Please note that this is a non-exhaustive list that serves as an example of the types of cell culture media components and its technological purpose.

Category	Compounds	Technological Function in Culture Media
Amino Acids	Glycine	Nutrients
	L-Alanine	Nutrients
	L-Arginine hydrochloride	Nutrients
	L-Asparagine monohydrate	Nutrients
	L-Aspartic Acid	Nutrients
	L-Cysteine	Nutrients
	L-Glutamic Acid	Nutrients
	L-Glutamine	Nutrients
	L-Histidine hydrochloride monohydrate	Nutrients
	L-Isoleucine	Nutrients
	L-Leucine	Nutrients
	L-Lysine hydrochloride	Nutrients
	L-Methionine	Nutrients
	L-Phenylalanine	Nutrients
	L-Proline	Nutrients
	L-Serine	Nutrients
	L-Threonine	Nutrients
	L-Tryptophan	Nutrients
	L-Tyrosine sodium salt dihydrate	Nutrients
	L-Valine	Nutrients
Glucose	D-Glucose	Nutrients
Growth Factors	Transforming growth factor β	Cell proliferation, Cell differentiation
	Fibroblast growth factor	Cell proliferation
	Epidermal growth factor	Cell proliferation
Hormones	Hydrocortisone	Cell proliferation, Cell differentiation, Anti-inflammatory
	Insulin	Cell proliferation
Inorganic Salt	Sodium selenite	Nutrients
	Sodium bicarbonate	pH buffering
	Potassium chloride	Maintain osmolarity
Proteins	Transferrin	Regulate iron homeostasis,

Category	Compounds	Technological Function in Culture Media
		Antioxidant
	Albumin	Antioxidant, Fatty acid source
	Serum	Cell proliferation, Shear stress protectant, Antioxidant, Nutrients
Vitamins	Biotin (Vitamin B7)	Cell metabolism
	Folic acid (vitamin B9)	Cell metabolism
	Vitamin C (Ascorbic Acid)	Antioxidant, Cell differentiation
Others	Poloxamer 188	Shear stress protectant

PROJECT DOCUMENT:**NEW WORK PROPOSAL FOR DEVELOPMENT OF GUIDELINES FOR THE CONDUCT OF FOOD SAFETY ASSESSMENT OF CELL CULTURE MEDIA COMPONENTS USED IN PRODUCTION OF CELL-BASED FOODS****1. Introduction**

Cell culture media is a critical component in the production of cell-based foods⁵. During the production process of cell-based foods, animal cells are cultured in cell culture media which contains a complex mixture of salts, sugars (glucose), vitamins, amino acids, organic acids, growth factors, hormones and small molecules for the cells to grow. Some of these components are utilised as the cells proliferate, whilst others may remain in the cultivated cells as residues which have no further technological function and could be considered as processing aids. However, there are currently no internationally harmonized guidelines defining which cell culture media components are deemed acceptable for use in cell culture media.

2. Purposes and scope of the standard

The purpose of the proposed new work is to develop guidelines to manage the conduct of food safety assessment of cell culture media components used in the production of cell-based foods. The scope of the guideline would include a framework on the general considerations and the associated studies/ evidence required to assess the safety of different types of cell culture media components and a glossary of terms that would be used in this document.

3. Relevance and Timeliness

At CAC44, the FAO and WHO called for Codex to recognise food system innovations that seek to address challenges related to feeding a growing global population, and at the same time produce food more sustainably. CAC46 extensively discussed and underscored the importance of addressing the challenges related to new food sources and production systems (NFPS) and encouraged the submission of new work proposals pertaining to NFPS. These developments reflect the growing recognition of the need for Codex to establish international frameworks and guidelines to ensure the safety and regulation of NFPS on a global scale.

As a form of NPFS, cell-based foods offer a potential solution to global food challenges, addressing issues such as the limited availability of arable land and the unpredictable threats posed by climate change. Additionally, cell-based foods have the potential to complement the conventional livestock agricultural system by offering a more resource-efficient alternative. The feed conversion ratio for cell-based foods is lower compared to conventional farmed animals like beef, pork, and chicken, resulting in reduced resource usage⁶. The production of cell-based foods has the potential to significantly reduce the environmental impact of food production by reducing carbon emissions and minimizing water and land use⁷. Moreover, the sustainable production of cell-based foods aligns with the global shift towards environmentally friendly and ethical food sources, thereby contributing to a more sustainable and resilient food system for the future.

An increasing number of countries are granting approval for the commercial sale of cell-based foods with more approvals anticipated in the near future. As of early 2024, cell-based foods have been allowed for commercial sale in Singapore, the United States of America and Israel, while other Codex members such as Australia, New Zealand, Switzerland, the Republic of Korea, and the European Union are in the process of reviewing safety assessments or have made modifications to safety assessment criteria in order to ensure the safety of cell-based foods.

The safety assessment of cell culture media components is crucial as it would provide guidance on the evidence required for cell culture media components in relation to the food safety risk that it would pose if present in the final product. This provides assurance to consumers that cell culture media components that may be present in cell-based foods will not cause harm when consumed, especially when considering components that have not been previously used for food production. This assessment requires the gathering of various types of evidence to demonstrate that these components do not pose any unacceptable food safety risk. The guidelines will serve as

⁵ In this document, the term “cell-based foods” is used as a working terminology to indicate food produced through the culturing of cells isolated from animals.

⁶ Swartz, E. (2021). Anticipatory life cycle assessment and techno-economic assessment of commercial cultivated meat production. *The Good Food Institute*.

⁷ Tuomisto, H. L., & Teixeira de Mattos, M. J. (2011). Environmental impacts of cultured meat production. *Environmental science & technology*, 45(14), 6117-6123.

a foundational reference for establishing risk management measures to ensure the safety of cell-based foods. By promoting a consistent approach to safety assessment, these guidelines also pave the way for harmonization among regulators in their evaluation of the safety of cell-based foods. This harmonization, in turn, facilitates trade by ensuring a unified standard that can streamline international market access for such products.

To provide clarity, a glossary of terms that would be used would also be included to improve understanding and comprehension of the guideline.

4. Main aspects to be covered

The guidance document will encompass a framework outlining the necessary evidence for various types of culture media components. It will provide regulators and industry stakeholders with a reference for general considerations and the associated studies and evidence needed to assess the safety of these components. An outline of the draft guidelines is included in **Appendix 3**.

5. Assessment against Section 2: Criteria for establishment of work priorities

General Criterion

Consumer protection from the point of view of health, food safety, ensuring fair practices in the food trade and taking into account the identified needs of developing countries.

The proposed new work will significantly support food agencies in developing their framework for assessing cell-based foods by providing a reliable reference on the necessary information to assess the safety of cell culture media components with no consumption history. This is crucial in enhancing safety as it allows regulators to establish comprehensive safety assessments for components that have not been traditionally consumed in food products.

By having clear guidelines and reference points, regulators can effectively evaluate the potential risks associated with these novel components, thereby ensuring the safety of cell-based foods for consumers.

Criteria applicable to general subjects

a) Diversification of national legislations and apparent resultant or potential impediments to international trade.

The lack of international guidance on safety assessments for cell-based foods will not only lead to diverging approaches and confusion on the requirements but also impede trade by creating barriers due to differing regulations and standards across countries. The harmonization efforts by Codex can play a crucial role in assisting countries in the development of a unified framework for the regulation of cell-based foods, thereby facilitating smoother trade and market access for these products.

b) Scope of work and establishment of priorities between the various sections of the work.

Please refer to section two which includes the scope of work to be undertaken.

c) Work already undertaken by other international organizations in this field and/or suggested by the relevant international intergovernmental body(ies)

FAO/WHO published a document on the food safety aspects of cell-based food which includes a section on hazard identification of cell-based foods. Separately, FAO has been organising a few conferences on the topic of cell-based foods, such as an expert consultation to identify food safety hazard in cell-based foods in 2022 and the yearly stakeholder roundtable meeting on cell-based food production and precision fermentation.

d) Amenability of the subject of the proposal to standardization.

The subject of the proposal is amenable to standardization as the guideline would be developed using science-based risk assessment approach.

e) Consideration of the global magnitude of the problem or issue

The nascent field of cell-based food presents an exciting frontier in the food industry, with numerous companies actively developing innovative products in this space. However, before these cell-based foods can enter the market, they would require regulatory approval. This lack of regulatory clarity has the potential to impede the growth and development of the cell-based food industry. The Codex guidance would represent the first step towards international harmonisation of safety assessments for cell-based foods. It would also offer regulators a foundational reference upon which they can develop their own risk management measures to evaluate the safety of cell-based foods.

The Codex Procedural Manual also includes references to the volume of production, consumption, and trade, which help Codex determine its work priorities. Currently, over 160 cell-based food companies are keen to obtain approval to market their cell-based food products but are unable to do so due to differences in regulatory processes. The establishment of international standards would facilitate the approval process for companies across various countries, thereby driving industry growth and facilitating trade of the product. This advancement holds the potential to address global food challenges by contributing to the development of a sustainable and resilient food system through the production of meat.

6. Relevance to Codex Strategic Objectives

The proposed work directly relates to several Codex strategic goals from the Codex Strategic Plan: 2026-2031.

- Respond to Members' needs for protecting the health of consumers and ensuring fair practices in the food trade in an evolving global environment by developing science-based standards

The production of cell-based foods offers a more sustainable alternative to conventional meat production. Cell-based foods are a more sustainable option as it requires less land and water and have a lower global warming potential⁸. Prioritizing sustainably produced food is crucial for ensuring the long-term availability of food while minimizing adverse environmental impact. Sustainable food production plays a pivotal role in addressing food security challenges by ensuring stable and resilient food supplies. It also contributes to equitable access to affordable and nutritious food, thereby bolstering food security for future generations.

With cell-based food production being an emerging industry, the guidance will act as a base reference for member countries to establish their own risk management approaches for cell-based foods. Furthermore, it provides a unique opportunity to be proactive and address the food safety challenges in a timely manner. The guidance will also leverage on expertise from various FAO expert committees/meetings. This ensures that scientific advice is used consistently in line with Codex risk analysis principles.

- Maximize the impact of Codex by increasing the visibility and use of standards

As there is currently no international guidance for cell-based foods, member countries would refer to Codex standards for cell-based foods to develop cell-based foods regulations, which would increase awareness and utilisation of Codex standards.

7. Information on the relationship between the proposal and other existing Codex documents, as well as other ongoing work

The proposed work will consider the principles and guidelines on risk analysis as provided in the following Codex documents:

- *Guidelines on the application of risk assessment for feed* (CXG 80-2013),
- *Principles and guidelines for the conduct of microbiological risk assessment* (CXG 30-1999),
- *Working principles for risk analysis for food safety for application by governments* (CXG 62-2007),
- *Principles for the risk analysis of foods derived from modern biotechnology* (CXG 44-2003),
- *Guideline for the conduct of food safety assessment of foods produced using recombinant-dna microorganisms* (CXG 46-2003) and
- *General standard for food additives* (CXS 192-1995)

The proposed work will also consider the principles and methods for risk assessment of chemicals in food outlined in EHC 240.

8. Identification of any requirement for and availability of expert scientific advice

There might be a need to seek scientific advice from FAO/WHO's expert body (JECFA) for inputs on risk assessment required for cell culture media components.

9. Identification of any need for technical input to the standard from external bodies, for planning purposes

⁸ Sinke, P., Swartz, E., Sanctorem, H., van der Giesen, C., & Odegard, I. (2023). Ex-ante life cycle assessment of commercial scale cultivated meat production in 2030. *The International Journal of Life Cycle Assessment*, 28(3), 234-254.

None identified so far.

10. Proposed timeline for completion of new work, including the start date, proposed date for adoption at Step 5, proposed date for adoption by the Commission

Subject to the agreement of the Committee and Codex Alimentarius Commission's approval, it is anticipated that the proposed work can be completed in three sessions of Codex Committee on Food Additives.

Appendix 3**DRAFT GUIDELINES FOR THE CONDUCT OF FOOD SAFETY ASSESSMENT OF CELL CULTURE MEDIA COMPONENTS USED IN PRODUCTION OF CELL-BASED FOODS**

1. INTRODUCTION
2. SCOPE
3. DEFINITIONS
4. CATERGORISATION OF CELL CULTURE MEDIA COMPONENTS

A decision tree will be developed to categorise the cell culture media components, recognising that different categories of components have different considerations and will require varying levels of evidence to assess their safety. For instance, cell culture media components not conventionally added to food may necessitate additional scrutiny. In such cases, evidence might be required to demonstrate whether these components occur naturally in other foods and to address any potential safety concerns. This ensures that each component is evaluated appropriately based on its specific characteristics and potential impact on food safety.

5. GENERAL CONSIDERATIONS FOR EACH CATEGORY

This section will describe the different considerations for the abovementioned categories and the information required to assess the safety of the media components.