



JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEx COMMITTEE ON FOOD ADDITIVES

Fifty-sixth Session

REPORT OF THE WORKING GROUP ON 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

(Prepared by the Electronic Working Group chaired by Singapore, and co-chaired by China, Republic of Korea and Saudi Arabia)

Background

At CCFA55, Singapore and China submitted a new work proposal on development of guidelines to assess the safety of cell culture media components used in the production of cell-based foods. Discussions at CCFA55 noted support on the need to consider establishing Codex guidance on cell-based foods to ensure consumer safety and facilitate fair practices. CCFA55 also noted the need to review the document and established an electronic working group (EWG) chaired by Singapore and co-chaired by China, Republic of Korea and Saudi Arabia to improve the project document. The Term of References of the EWG agreed in CCFA55 are to:

- Revise the draft project document on the development of a guideline for the conduct of food safety assessment of cell culture media components used in production of cell-based food for consideration on the agenda of CCFA56.
- Develop a categorisation framework for cell culture media components and the corresponding evidence needed for safety assessment in each category.
- Determine specific areas requiring FAO and WHO scientific advice for the purpose of developing risk assessment frameworks for cell culture media components.

Members

A total of 32 Member Countries, 1 Member Organization and 6 Observer Organizations participated in the EWG¹.

Summary of Discussion

Two rounds of consultation were conducted in the EWG and all the suggestions and comments received were considered by the Chair and co-Chairs when revising the discussion paper (**Appendix 1**), project document (**Appendix 2**), draft guideline and categorisation framework (**Appendix 3**), and list of questions to seek scientific advice from FAO and WHO (**Appendix 4**).

Discussion on the discussion paper and new work proposal

Editorial suggestions made by members were incorporated. Substantive discussions on the new work proposal focused on scope, antimicrobial resistance, trade volume, and sustainability, and have been summarised below.

1. Scope of the proposal

There were two areas of discussion regarding the scope of the proposal: the expansion beyond animal cells and the inclusion of scaffolds.

¹ Australia, Austria, Belgium, Brunei Darussalam, Canada, Chile, China, Colombia, Egypt, European Union, France, Ghana, Greece, Hungary, India, Indonesia, Ireland, Italy, Japan, Mexico, New Zealand, North Macedonia, Norway, Qatar, Republic of Korea, Russian Federation, Saudi Arabia, Spain, Switzerland, Türkiye, United Kingdom, United States of America, Uruguay, FoodDrinkEurope, Food Industry Asia (FIA), Good Food Institute (GFI), International Council on Amino Acid Science (ICAAS), International Meat Secretariat (IMS) and Safe Supply of Affordable Food Everywhere (SSAFE).

Regarding the expansion beyond animal cells, some members suggested broadening the scope beyond animal cells, citing examples such as the culturing of mammary cells to produce milk and the culturing of cocoa cells. Whilst this suggestion warrants consideration, the use of non-animal cells remains largely at the research and development stage. Given this, the scope of the proposal was not expanded. However, a footnote was added in the discussion paper to acknowledge the potential future applicability of the guidelines beyond animal cells, noting that future expansion could be considered based on Codex needs and international developments.

Regarding the inclusion of scaffolds into the scope of the proposal, some members suggested that the guideline should apply to scaffolds as they might be used during the production of cell-based foods, although these scaffolds are not culture media components. Currently most commercial cell-based food companies are producing non-structured products that do not involve the growth of cells onto scaffold ingredients. In addition, it is also expected that most companies would utilise conventional food ingredients such as textured vegetable proteins or alginates as scaffolding materials.

In view of this, it is recommended that CCFA56 consider excluding scaffolds from the scope of the new work at this time, but acknowledge the possibility for future discussions on the inclusion of scaffolds into the scope of the guidelines as the industry matures and use of scaffolds becomes more common.

2. Use of antimicrobials and concerns of antimicrobial resistance (AMR)

Some members commented on the possibility that the use of antimicrobials could contribute to AMR, while other members noted that the issue of AMR has been considered in separate Codex texts. A member of the EWG noted that antimicrobials are generally confined to early cell-line development and are not used in final production. To balance these perspectives, the document was revised to include an acknowledgement of the importance of managing antimicrobial use and the potential for AMR and mentions of the relevant Codex texts on AMR have also been added to Section 7 of the project document.

3. Concerns on trade volume

Some members suggested including trade data and expressed concerns over initiating work on a product with low trade volume. Codex takes a proactive approach to supporting innovation and has a history of developing guidance for new technologies. In particular, CCFA has a long-standing approach of addressing the safety of food additives and processing aids regardless of existing trade volume. In addition, trade volume is mainly referenced in the criteria applicable to commodities in the Codex Procedural Manual. As the current work focuses on components used in cell-based food production rather than final cell-based food products, discussions on trade volume may not be directly relevant. In order to accurately reflect the discussions and present a balanced perspective, the revised document acknowledges the low trade volume of cell-based foods but frames it as not directly relevant to the safety assessment of media components.

4. Sustainability of the production technology

Some members expressed doubts on claims of environmental sustainability, pointing to the energy-intensive nature of cell-based food production over the sustainability of the production technology. In response, the project document was adjusted to adopt a neutral tone, with references to sustainability removed until more empirical evidence becomes available. This reflects the balance between recognizing Codex's strategic commitment to resilient food systems and acknowledging current uncertainties.

Other discussions in the EWG

In addition to discussions on the project document, the EWG also developed a draft guideline and categorisation framework (**Appendix 3**) and a list of questions to seek scientific advice from FAO and WHO (**Appendix 4**). While these elements are not part of the project document, they were developed as part of the Term of References for this EWG.

Many members provided technical comments to enhance the guideline and categorisation framework, including comments on the flow and format of the categorisation framework, use of Threshold of Toxicological Concern (TTC), and data requirements for the cell culture media components in each tier. Members also emphasized the need for tiered evidence requirements without presupposing the safety outcome and alignment with Codex risk analysis principles.

To focus efforts on improving the project document, technical information was removed from the guidelines. The technical guidelines can be discussed further once the new work is supported. While the framework remains preliminary, it provides a structured basis for further work should the new work be accepted.

The members also provided questions that may require scientific advice from FAO and WHO to further develop the guidelines. The comments provided for these two areas can act as a preliminary base for further discussion once the new work enters the step process.

Recommendations

CCFA56 is invited to consider the discussion paper (**Appendix 1**) and the project document on new work proposal for development of a guideline for the conduct of food safety assessment of cell culture media components used in the production of cell-based foods (**Appendix 2**).

For reference, and as required by CCFA55, the EWG has also developed a draft guideline for the conduct of food safety assessments of cell culture media components used in the production of cell-based foods (**Appendix 3**), as well as proposed questions to seek inputs from FAO/WHO (**Appendix 4**). These two documents are shared for information at this stage and may serve as a starting point should this new work proposal be approved.

Appendix 1

DISCUSSION PAPER FOR NEW WORK ON DEVELOPMENT OF A GUIDELINE FOR FOOD SAFETY ASSESSMENT OF CELL CULTURE MEDIA COMPONENTS IN CELL-BASED FOOD PRODUCTION**Background**

1 “Cell-based food² production” is a working term that has been used by the FAO and WHO to describe the growing of animal agricultural products directly from *in vitro* cell cultures rather than traditional farming methods. Cell-based food utilises novel technologies that have not been used in food production previously and has been explored as an option to complement the conventional livestock agricultural system. Cell-based food will be offered in addition to products made through traditional means of animal agriculture.

2 In 2022, the FAO and WHO conducted a comprehensive food safety hazard identification of cell-based food production³. While some hazards are already 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 material inputs and equipment used that may not have been used previously for food production. For instance, the use of novel culture media components (e.g. certain growth factors, small molecules) during the production process introduces a need to appropriately assess their potential food safety risks⁴.

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. As of mid-2025, cell-based foods have either received regulatory approval or completed regulatory evaluation in Australia, Israel, New Zealand, Singapore, and the United States of America. More approvals are also expected in the coming years as the safety of such food is assessed in other jurisdictions including Republic of Korea, Thailand, United Kingdom, Switzerland as well as the European Union.

4 As more countries develop national requirements for assessing the safety of cell-based food, if there is significant diversity in regulatory approaches, this may discourage further adoption of cell-based food production technologies and result in barriers to the trade of these foods.

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)⁵ at CAC44 in response to a FAO-WHO document seeking advice on addressing NFPS related issues. Subsequently, a Circular Letter ([CL 2023/31/OCS-CAC](https://doi.org/10.4060/cc4855en)) was issued on the topic and further discussion held at CAC45. 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, where there was a general recognition on the importance and relevance of NFPS among Members and Observers. CAC46 highlighted the importance of addressing new challenges posed by NFPS and the important role Codex could play in this and noted that current 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, Singapore engaged with Members across all Codex Regions, in meetings coordinated by the Regional Coordinators. During these meetings, there was 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.

² In this document, the term “cell-based foods” is used as a working terminology to indicate food and/or food ingredients produced through the culturing of cells isolated from animals. This includes, but is not limited to, cells isolated from poultry, bovine, porcine, caprine, ovine, game meat, fish and crustacean sources.

³ FAO & WHO. 2023. Food safety aspects of cell-based food. Rome. <https://doi.org/10.4060/cc4855en>

⁴ While this document focuses on cell culture media components used in the production of foods derived from animal tissue cells or fat cells, it is acknowledged that similar technologies may be applied to other types of cells in the future, such as the culturing of mammary cells to produce milk, cocoa cells to produce chocolate ingredients, or other cell types (e.g. plant cells). Consideration of these applications may be addressed in subsequent work, subject to Codex needs and international developments

⁵ 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.

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.

9. 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.

10 CAC47 noted the intention by Singapore and China to submit new work proposals on cell-based foods and member 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.

11 At CCFA55, Singapore and China submitted a new work proposal on development of guidelines to assess the safety of cell culture media components used in the production of cell-based foods. Discussions at CCFA55 noted support on the need to consider establishing Codex guidance on cell-based foods to ensure consumer safety and facilitate fair practices. CCFA55 also noted the need to review the document and established an electronic working group chaired by Singapore and co-chaired by China, Republic of Korea and Saudi Arabia to improve the project document. The Terms of References of the EWG agreed in CCFA are to:

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- Determine specific areas requiring FAO and WHO scientific advice for the purpose of developing risk assessment frameworks for cell culture media components.

Importance of establishing internationally harmonised guidelines

12 With the potential to contribute to a global food system, several countries including Australia, Canada, China, India, Israel, Japan, Republic of Korea, Singapore, United Kingdom, United States and some European countries, 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 potential safety concerns whilst fostering innovation and facilitating trade. The industry's anticipated growth underscores the need for a global consensus on safety standards and regulations of food made using this technology. Given Codex Alimentarius' mandate to protect consumer health and facilitate trade, there is an opportunity for the organisation to address these challenges proactively.

13 Although trade in cell-based foods is currently very limited in comparison to other traded commodities, there has been interest from the World Customs organisation to explore the development of a Harmonised Commodity Description and Coding System (HS) code to classify such products.

14 By developing harmonised guidelines for cell culture media components used in the production of cell-based foods, Codex can ensure consumer safety as the sector continues to evolve. Such alignment will facilitate international trade by standardising regulatory approaches across countries, support innovation through defined regulatory pathways and accommodate 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.

Addressing food safety challenges of cell culture media components at CCFA

15 Cell culture media is essential in the production of cell-based foods and comprises a complex mixture of individual components that may include salts, sugars, vitamins, amino acids, acids and bases, growth factors, hormones, small molecules, antimicrobials and others for the cells to grow. The cell culture media components confer a range of functions in the culture media such as providing nutrients, encouraging cell proliferation, and if relevant, inducing differentiation from stem cells to specialised cell types. Some of these cell culture media components are already present in conventional foods (e.g. amino acids and vitamins), while others have no prior history of use in food. While most cell culture media components will be either utilised by cells or removed during the production process, some could remain in the cells and may present potential food safety risks that will need to be managed.

16 Currently, there is a lack of internationally harmonised guidelines for assessing the safety of cell culture media components when they are used for the production of cell-based foods. The development of a guideline

for conducting 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, some of which have not been previously used for food production. As such, Singapore, China, Republic of Korea and Saudi Arabia are putting forth the development of a guideline to manage conducting food safety assessment of cell culture media components used in the production of cell-based foods as part of risk management measures (**Appendix 1**).

17 As cell culture media components are diverse and numerous, the proposed guidelines could potentially include an assessment 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.

18 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 conducting food safety assessment of cell culture media components used in production of cell-based food.

Recommendations

19 CCFA56 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**). The project document in revision mode, updated based on FA55/CRD06, is accessible [here](#).

20 A draft guideline for the conduct of food safety assessment of cell culture media components used in production of cell-based foods has been developed (**Appendix 3**) which demonstrates the categorisation framework for cell culture media component. The technical information in the draft is not intended to be discussed in detail at CCFA56 but will form the basis for the new work once the proposal is approved. A list of questions was consolidated from the EWG members to seek technical advice from FAO and WHO once the new work is supported (**Appendix 4**).

PROJECT DOCUMENT⁶**NEW WORK PROPOSAL FOR DEVELOPMENT OF A GUIDELINE 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 foods⁷. During the production process of cell-based foods, animal cells are cultured in cell culture media that comprises a complex mixture of individual components that may include salts, sugars, vitamins, amino acids, acids and bases, growth factors, hormones, small molecules, antimicrobials and others for the cells to grow. Where used, antimicrobials could also contribute antimicrobial resistance when used in excess

As these cell culture media components may remain in the cultivated cells, there is a need to assess the food safety risks where warranted. Currently, there are no internationally harmonized best practice guidance for assessing the safety of components used in cell culture media for food production. As such, establishing a Codex guideline that defines the most appropriate methods, can serve as a reference and allow for a more efficient application process. While trade volumes of cell-based foods remain limited and research into their sustainability is ongoing, Codex work in this area anticipates potential global developments and supports the goal of building safe and resilient food systems.

2. Purposes and scope of the standard

The purpose of the proposed new work is to develop guidelines for the food safety assessment for cell culture media components, including components such as buffering agents, cryoprotectants, and dissociation agents, used in the production of these foods. This will cover the process from cell isolation and cell line establishment to harvest⁸. It does not apply to feed application and scaffolds. The scope of the guidance would include a framework on the general considerations required to assess the safety of different types of cell culture media components. To provide clarity, a glossary of terms that would be used would also be included to improve understanding and comprehension of the guideline.

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.

Moreover, the production of cell-based foods could align with the global shift towards environmentally friendly food sources and may contribute to a more sustainable and resilient food system for the future. In addition, this also potentially aligns with the United Nation's Sustainable Development Goal 2: Zero Hunger which aims to ensure a sustainable food production system. Moreover, cell-based foods mitigate risks associated with animal-borne diseases by producing protein in controlled, sterile environments, thereby reducing the risk of outbreaks and enhancing biosecurity. They also offer the flexibility to improve nutritional profiles, such as by increasing beneficial fatty acids and reducing unhealthy fats, which supports better public health outcomes.

An increasing number of countries are granting regulatory approvals and conducting regulatory evaluations for the commercial sale of cell-based foods with more regulatory approvals and completed regulatory evaluations anticipated in the near future. As of mid-2025, cell-based foods have either received regulatory approval or completed regulatory evaluation in Australia, Israel, New Zealand, Singapore, and the United States of America. Other Codex members such as India, Republic of Korea, Switzerland, Thailand, UAE, United Kingdom, 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.

It is important to assess the safety of the cell culture media components to ensure it will not pose a food safety risk if present in the final product. The proposed new work aims to outline the evidence needed for cell culture media components regarding potential food safety risks associated with their presences in the final product, to support safety assessment. This provides assurance to consumers that cell culture media components if

⁶ For the version with track changes from the project document at CCFA55, please check [here](#).

⁷ In this document, the term "cell-based foods" is used as a working terminology to indicate food and/or food ingredients produced through the culturing of cells isolated from animals. This includes, but is not limited to, cells isolated from poultry, bovine, porcine, caprine, ovine, game meat, fish and crustacean sources.

⁸ "Harvest" refers to the collection of cells for downstream food processing, formulation and packaging.

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 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 promoting a unified standard that can streamline international market access for such products.

4. Main aspects to be covered

The guidance document will encompass a framework outlining the types of evidence for various types of culture media components. It will provide regulators and industry stakeholders with a reference for general considerations needed to assess the safety of these components.

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 support competent authorities 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 improving the safety of cell-based foods for consumers.

Criteria applicable to general subjects

a) Diversification of national legislation 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 on the requirements but could 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 newly emerging technology of cell-based food presents an exciting opportunity 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 will require regulatory approval or evaluation. Clear and well-defined regulatory frameworks are essential for the cell-based food industry to support its growth and innovation without creating unnecessary barriers or costs. The Codex guidelines would represent the shift towards international harmonization 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 ensure 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. More than 160 companies are currently seeking approval to market cell-based food products, but differences in regulatory processes and uncertainties regarding data requirements across regions present challenges. The establishment of international guidelines 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 cell-based foods.

6. Relevance to Codex Strategic Objectives

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

- Goal 1: 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

With cell-based food production being an emerging industry, the guidance will act as a base reference for member countries that do not already have clear criteria for establishing the safety of cell-culture media components. Furthermore, it provides a unique opportunity to be proactive and address the food safety challenges in a timely manner. The guidance will also leverage expertise from various FAO expert committees/meetings. This ensures that scientific advice is used consistently in line with Codex risk analysis principles.

- Goal 4: 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 guidelines for cell-based foods to develop their own risk assessment framework for cell-based foods, 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 relevant Codex documents, such as:

- 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)
- Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant DNA Plants (CAC/GL 45-2003)
- Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant DNA Animals (CAC/GL 68-2008)
- Guidelines for Risk Analysis of Foodborne Antimicrobial Resistance (CXG-77-2011)
- Guidelines on Integrated Monitoring and Surveillance of Foodborne Antimicrobial Resistance (CXG-94-2021)

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 and WHO for inputs on the information needed for the risk assessment required of cell culture media components.

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

Technical inputs could be sought from The Good Food Institute Asia-Pacific and Vireo Advisors LLC. They recently published a manuscript⁹ proposing a framework for the streamlined safety assessment of cell culture media component for cell-based food production which incorporates significant industry input and feedback.

⁹ Ong, K. J., Kuk, K., Powell, D. J., Chen, W. N., Goh, S., & Shatkin, J. A. (2025). Development of a Safety-Assessed Media Ingredient (SAMI) Framework for Streamlined Safety Assessment of Cultivated Meat and Seafood Products. *Trends in Food Science & Technology*, 105209.

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 GUIDELINE FOR THE CONDUCT OF FOOD SAFETY ASSESSMENT OF CELL CULTURE MEDIA COMPONENTS USED IN PRODUCTION OF CELL-BASED FOODS**1. INTRODUCTION**

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

The general process for the production of cell-based food can be divided into four main steps, consisting of: 1. Cell selection: cell sourcing, preparation and storage 2. Cell proliferation and differentiation (if relevant), 3. Harvesting, and 4. Food processing, formulation and packaging. In this process, cell culture media components are used from step 1 to step 3 .

Cell culture media is essential in the production of cell-based foods and comprises of a complex mixture of individual components that may include, salts, sugars, vitamins, amino acids, acids and bases, growth factors, hormones, small molecules, antimicrobials and others for the cells to grow. The cell culture media components confer a range of functions in the culture media such as providing nutrients, encouraging cell proliferation, and if relevant, inducing differentiation from stem cells to specialised cell types.

Many of these cell culture media components are already present in conventional foods (e.g. amino acids and vitamins), while others have no prior history of use in food. While most cell culture media components will be either utilised by cells or removed during the production process, some could remain in the cells and may present potential food safety risks that will need to be managed. It is also recognized that the cell culture media may impact the composition (e.g., fatty acid/vitamin/mineral composition) of the cells cultured in the media. Evaluation of the intended use of cell culture media components is an important part in assessing the food safety of a cell-based food.

The guideline aims to facilitate assessment and management of food safety risks associated with these cell culture media components to improve consumer safety and facilitate international trade by aligning approaches and provide clear regulatory pathways

2. SCOPE

The guideline provides a framework for assessing the food safety of different cell culture media components used in cell-based food production.

3. DEFINITIONS

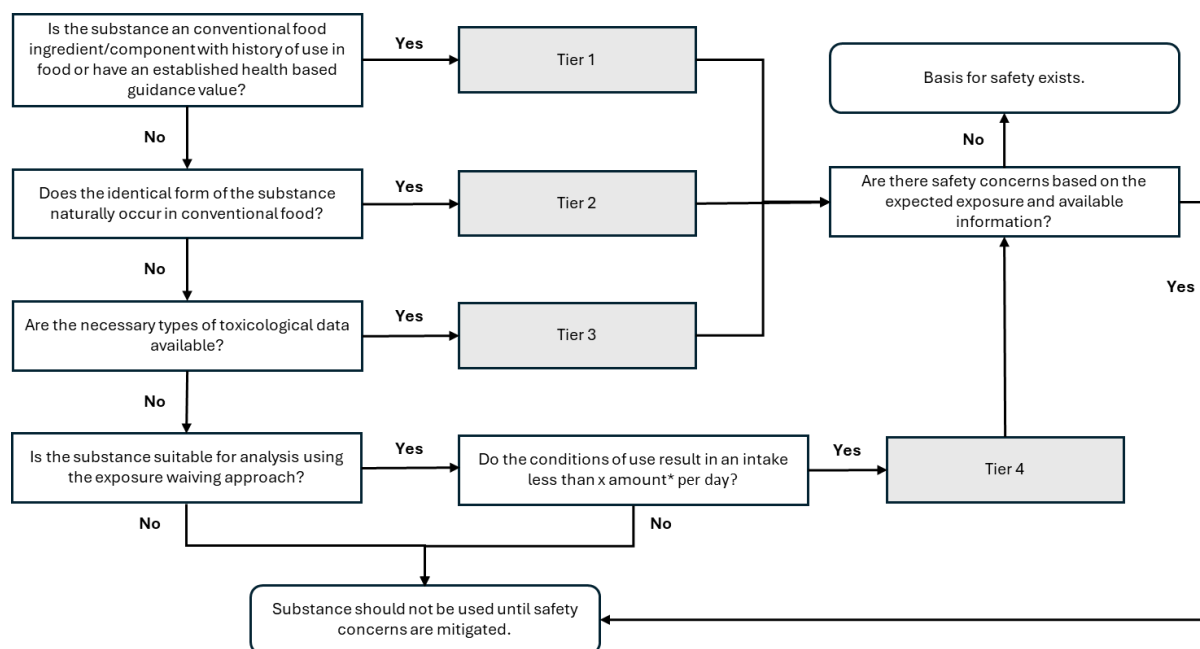
The definitions below apply to this guideline:

- **“Cell-based foods”** refers to food and/or food ingredients produced through the culturing of cells isolated from animals. This includes, but is not limited to, cells isolated from poultry, bovine, porcine, caprine, ovine, game meat, fish and crustacean sources.
- **“Harvest”** refers to the collection of cells for downstream food processing, formulation and packaging.

4. ASSESSMENT OF CELL CULTURE MEDIA COMPONENTS

Cell culture media can contain a diverse range of substances, some naturally present in food or with an established history of use in food production while others are novel ingredients that have not been used for food production before. A systematic framework has been developed to categorise these various cell culture media components, to support the safety assessment of the cell culture media components.

The framework takes into consideration the following key factors: the substance's history of use in food (natural occurrence in food, intentional addition to food, or novel substances not previously used in food), availability and adequacy of toxicological data, production methods, and intake levels compared to established thresholds. Through this tiered approach, components with different risk profiles undergo structured safety assessments, with components not conventionally added to food undergoing additional scrutiny. If safety concerns cannot be mitigated, the component should not be used.



*The intake amount to be discussed further when the new work is supported

Figure 1: Flowchart to categorise cell culture media components

5. GENERAL CONSIDERATIONS FOR EACH CATEGORY

This section provide details on the different considerations and information required to assess safety of the cell culture media components.

The following information should be provided for the cell culture media components used in the production of cell-based foods. Further information may be required depending on the tier level of the component.

The following information should be provided for all cell culture media components:

- Identity of substance
- Concentration in the cell culture media
-

5.1. Tier 1

Tier 1 cell culture media components consist of conventional food ingredients/components that either have an established history of use in food and/or possess established health-based guidance values.

The following information should be provided to assess the safety of Tier 1 cell culture media components:

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5.2. Tier 2

Tier 2 cell culture media components include substances that naturally occur in conventional foods with a history of use.

The following information should be provided to assess the safety of Tier 2 cell culture media components:

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5.3. Tier 3

Tier 3 cell culture media components comprise substances that, despite having no history of use or natural presence in foods, have sufficient toxicological data to demonstrate their safety for consumption.

The following information should be provided to assess the safety of Tier 3 cell culture media components:

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5.4. Tier 4

Tier 4 cell culture media components refer to substances that lack sufficient toxicological data for a comprehensive safety assessment but is undetectable / present in low levels in the final product.

The following information should be provided to assess the safety of Tier 4 cell culture media components:

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Appendix 4**PROPOSED QUESTIONS TO SEEK INPUTS FROM FAO/WHO**

The following questions listed be raised to FAO/WHO should the work be supported. We invite member countries and observers to consider these questions and to include any further relevant questions that could be raised to FAO/WHO for the purpose of developing risk assessment frameworks for cell culture media components.

Scientific questions

- Specific to the framework
 - Is the proposed framework sufficient to categorise the different types of cell culture media components used in cell-based food production?
 - What kind of information is needed at each tier to adequately address the food safety concerns about the use of cell culture media components?
 - Are the thresholds based on the Threshold of Toxicological Concern (TTC) approach sufficient to address Tier 3 cell culture media components?
 - Under Figure 1 of Appendix 2, should there be a fixed intake amount applied to all components, or should it vary according to the function of each cell culture media component?
 - Is the Toxicological Threshold of Concern approach appropriate for evaluating cell culture media components? Are other approaches, such as Quantitative Structure-Activity Relationship be appropriate as well?
- Others
 - Should exposure studies for certain cell culture media components be reconsidered if they have dual purposes such as nutrients and food additives?
 - Can FAO/WHO propose methods to evaluate cumulative exposure?
 - Should immunogenicity and allergenicity be considered more prominently for novel proteins?
 - Should components that are commonly deemed safe for consumption such as sugar, vitamins and sodium chloride be subjected for safety assessments?
 - Are there any methodologies for detecting trace levels of media components?
 - Can FAO/WHO provide guidance on assessing synergistic or antagonistic effects between multiple media components present in the final product?
 - Are there validated models or in vitro systems that can simulate human digestion and absorption of residual media components?

General questions

- Is there interest from FAO and WHO in expanding the scope of foods in the food category system to include cell-based foods? If so:
 - Would there be capacity to incorporate evaluations related to cell-based foods by a FAO/WHO scientific body?
 - Would there be a recommendation on which committee would be best positioned to manage cell-based foods?
 - Would there be capacity by FAO and WHO to develop a reference document (e.g., a general standard) for cell media components?
- How can JECFA assist in the development of the new work proposal?
- Should a global database of pre-evaluated media components be created?
- Would the nomenclature of “cell culture media components” be sufficient to distinguish these substances from other types of substances, especially for components that have multiple purposes in foods?
- Will it be necessary to evaluate the entire culture medium when some of the components cannot be disclosed by the industry?