Food and Agriculture Organization of the United Nations

CELL-BASED FOOD: ITS SAFETY AND ITS FUTURE ROLE

STAKEHOLDER ROUNDTABLE MEETING REPORT

TEL AVIV, ISRAEL, 7 SEPTEMBER 2022

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ACKNOWLEDGEMENTS

The Food and Agriculture Organization of the United Nations (FAO) would like to express its appreciation for active participation of the stakeholders participated in the stakeholder meeting held in July 2022 in Tel Aviv, Israel. The report has been jointly drafted by Maura Di Martino and Masami Takeuchi. The meeting was co-organized by Ministry of Health, Israel and FAO, and coordinated by Ziva Hamama (Israel), Masami Takeuchi (FAO) and Mia Rowan (FAO) under the overall guidance of Markus Lipp (FAO). Technical and editorial inputs were provided by various FAO colleagues, and technical editing was provided by Jeannie Marshall.

ABBREVIATIONS AND ACRONYMS

AMPS	Association for Meat, Poultry and Seafood Innovation
BC	bacterial cellulose
CBD	cellulose binding domain
CEFET MG	Federal Center of Technological Education of Minas Gerais
CFSA	China National Center for Food Safety Risk Assessment
DNA	deoxyribonucleic acid
FAO	Food and Agriculture Organization of the United Nations
FBS	fetal bovine serum
GAP	good agricultural practices
GLP	good laboratory practices
GMO	genetically modified organism
GMP	good manufacturing practices
HACCP	hazard analysis and critical control points
HARPC	hazard analysis and risk-based preventive controls
ISO	international Organization for Standardization
TTC	threshold of toxicological concern
WHO	World Health Organization

EXECUTIVE SUMMARY

Cell-based food production involves culturing cells isolated from animals to develop products such as meat, poultry, aquatic products, dairy and eggs. Currently, many companies around the world are developing a wide range of cell-based foods using a variety of different production methods.

In collaboration with the Ministry of Health, Israel, the Food and Agriculture Organization of the United Nations (FAO) held a stakeholder meeting to come up with a technical reference document on the food safety aspects of cell-based food. Developers and producers of cell-based foods were invited to present the different cell-based production processes used for chicken nuggets, hamburgers, beef steak and sushi salmon, and to present their input materials, such as scaffolds, cell lines and growth media, that in certain cases are consumed along with the cell-based food product.

All the participants stated that food safety is of foremost importance, and many presenters explained their cell-based food production processes with relevant food safety considerations in flowcharts, which have been included in this report. Some participants stressed the importance of having clear guidance from regulators to ensure safety and to move the development process forward. They acknowledged the importance of communicating with consumers using simple and concise messages, granting access to detailed food safety information. They further emphasized the importance of transparency during the discussion session on effective food safety communication strategies.

The meeting provided an opportunity for stakeholders from different parts of the world to learn from one another, and to share their experiences and challenges. As a result, the presentations delivered in the meeting provided an overview of the 2022 status of the topic of cell-based food development and presented the potential complexities of conducting food safety hazard identifications for cell-based food.

Keywords: food safety, cell-based food, cultured meat, cultivated meat, research and development, food production process, input materials, hazard identification, risk assessment, risk communication, food technology

1. INTRODUCTION

1.1. Background

The global demand for animal protein is growing enormously due to population increases. According to the latest United Nations projections, the world population is expected to reach 9.7 billion by 2050. The spread of the middle class across the world is creating a higher demand for meat and other protein-rich foods, increasing the pressure to scale up the production of livestock, which has a negative impact on the environment and on animal welfare. Feeding the world in a sustainable way is one of the most urgent challenges in the coming years and cell-based food products has the potential to play an important role.

Cell-based food production involves culturing cells isolated from animals under controlled conditions, which, when combined with other ingredients, can achieve an appearance, texture, taste, and nutritional value similar to its conventionally produced counterparts such as meat, poultry, aquatic products, dairy and eggs.

As many companies around the world are already developing various cell-based foods using different production technologies, understanding the wide range of cell-based food production processes currently in use is the first step toward identifying the potential food safety implications of cell-based food to protect consumer health. Researchers, developers and producers were asked to present their cell-based food products at the stakeholder meeting organized by the Food and Agriculture Organization of the United Nations (FAO) and to explain step by step the relative production processes, using flowcharts. Also, input materials, that are key elements for the cell-based food production process, were presented to provide a better understanding of the entire manufacturing process.

This meeting provided an opportunity for cell-based food stakeholders to discuss concrete food safety assurance issues as well as the potential benefits and challenges of cell-based food production. In addition, stakeholders discussed transparent, and useful food safety communication strategies on the topic.

1.2. Overview

FAO collaborated with the Ministry of Health of Israel to organize a stakeholder roundtable meeting entitled "Cell-based food and the future of food security and food safety". A total of 48 participants, including 16 presenters, 23 government representatives and four officers from FAO and the World Health Organization (WHO) participated in this one-day meeting at the Dan Tel Aviv Hotel in Tel Aviv-Yafo, Israel on 7 September 2022. The final list of participants is attached as Annex 1. The specific objectives of the meeting were: 1) to develop a technical reference on food safety aspects of cell-based food by understanding the different production processes that exist to produce various cell-based food products as well as their input materials; 2) to provide a forum for stakeholders to discuss the opportunities and challenges in the industry; and 3) to consider effective food safety communication strategies on the topic of cell-based food. Note that any stakeholder company names, individuals, products, materials and methods for the production processes appear in this report have been discussed at the meeting as they are described in the text, and it does not mean they are approved / endorsed by FAO nor the Government of Israel.

2. PROCEEDINGS

2.1. Opening session

Ziva Hamama, Head of the Food Risk Management Department at the National Food Service, Ministry of Health in Israel, welcomed the 43 participants, saying that research and development in the cell-based food industry is of strategic interest to the country. “Israel is a fertile ecosystem for new technologies, and together with knowledge and experience we believe we have a good platform for the introduction of cell-based foods,” she said, while emphasizing that the safety aspects of foods are essential. Later in the day, Sharon Elroi Preiss, Head of the Public Health Division at Israel’s Ministry of Health provided an official address emphasizing the importance of holding this proactive discussion in Israel by stating that "what you are doing it is fascinating: you are inventing the future, so I hope you are all proud in this.” She also said that the biggest challenge we face is that the new foods we are creating must be safe, tasty, sustainable and healthy. She acknowledges that this is not easy and said that the most effective way to do it is through partnerships with different professions from around the world. She concluded her speech by thanking FAO for holding the meeting in Israel and expressing her hope that this meeting opens a new opportunity for all the participants to collaborate.

Markus Lipp, FAO Senior Food Safety Officer, officially opened the day-long session by emphasizing the importance of the meeting. “At the international level, we have different challenges – and I believe the one in front of us today is to define a common language to talk about these new products and new technology. Here we have a platform to hold a discussion that can lead to a common language and ultimately find fit-for-purpose solutions together.” Masami Takeuchi, FAO Food Safety Officer, presented an overview of FAO's work on cell-based foods, in particular noting three publications on terminologies, production processes and current regulatory frameworks. “Many food safety authorities are working, often in tandem, to identify and address the potential food safety implications so that appropriate regulatory frameworks can be set up to protect consumers.” She pointed out that many other stakeholders, including researchers studying the food safety issues of cell-based food, private cell-based food developers and producers and non-governmental organizations are all working in this space to advance our collective knowledge.

2.2. Technical presentations

2.2.1. Producing cell-based meat in China

Ziliang Yang and Ning Xiang from CellX, a China-based startup company that aims to be the first company to commercialize cell-based food in China, presented their three products in development. CellX to date has developed more than ten cell lines from different animal species as well as in-house edible scaffolds, in collaboration with various universities and companies within and outside China. According to Yang and Xiang, China has the advantage of serving the largest market with all the necessary infrastructure, reducing costs to scale up for consistent production. Their presentation was structured in two main parts where part A described the production processes of their cell-based food products, and part B focused on regulations and commercialization in China.

Xiang explained the production process of cell-based meat (**Figure 1**), which consists of three phases: cell isolations from animals, cell cultures in bioreactors and the final product. The final product can be combined or structured. A combined product mixes the output with plant-based protein, while a structured product creates the shape of whole-cut meat by using scaffolding technology or 3-D printing. Their cell banks contain different cell types, such as satellite cells, adipocytes, myoblast and fibroblasts from bovine, porcine, avian and fish species.

For the product development of the structured whole-cut pork, a prototype was created with a plant protein-based scaffold with directional pores. These cells, specifically porcine satellite cells, are cultured on an edible scaffold with alignment where the cells have good differentiation into myoblast. In the last step, the product is processed with food colouration to look like a cut of pork.

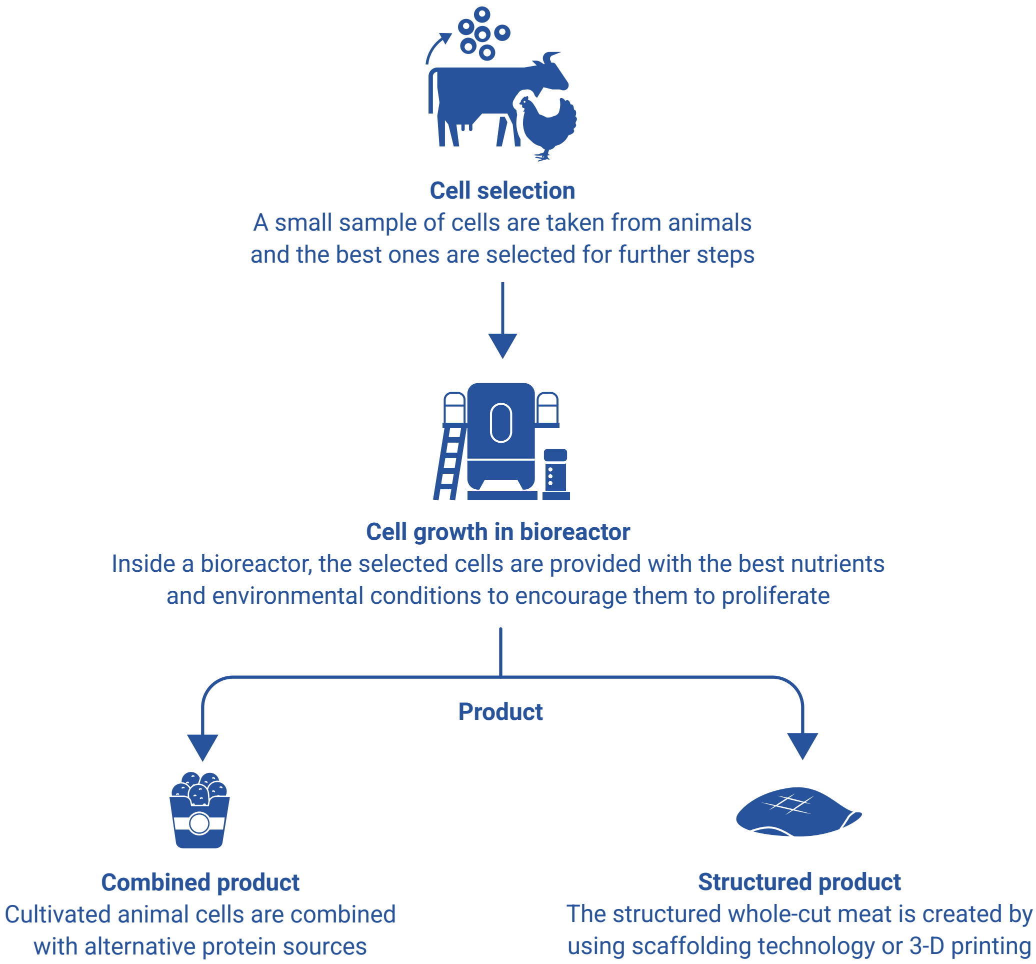
For the production of textured chicken strips and nuggets from fibrous protein, they used a spinning technology that was developed in-house. The chicken cells, which provide the flavour components, are cultured on the scaffold, which offers the mechanical strength and the texture properties in the final product. Both chicken products that they developed have the structure and the sensory profile of raw chicken. Indeed, in the sensory evaluation, people on the panel were unable to distinguish between the conventionally produced chicken nuggets and the cell-based chicken nuggets.

The company also produces a 3-D printed product, where bovine cells are cultured on microcarriers developed in-house, which are edible and animal free. After the quantity of cells is assured, 3-D printing technology is used to produce a marbled beef product, where the white spots are the fat tissues, and the red sections are the muscle tissues. CellX held its first tasting event in September 2021 with those three products, and more tasting events are being planned in 2022 and 2023.

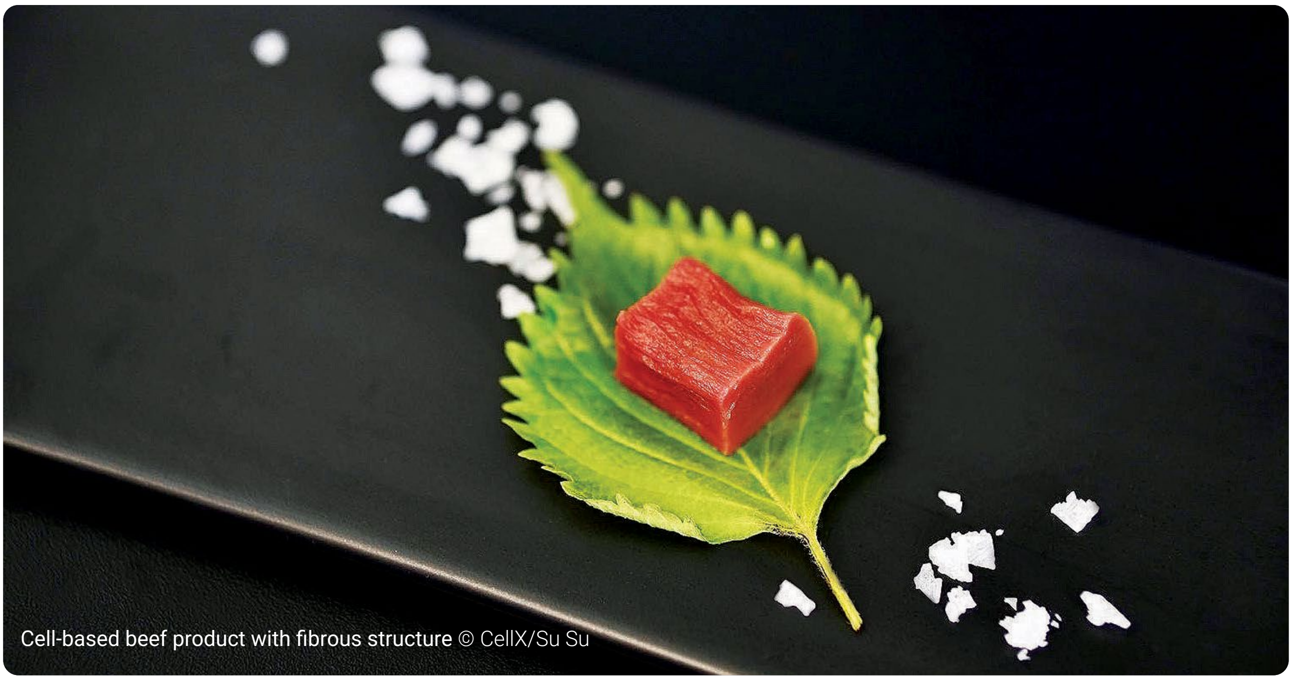
Yang addressed the regulatory landscape and commercialization in China, where he has seen increasing support from the central government. The breakthrough came at the end of 2021 when cell-based food production technology was announced as part of the 14th Five-Year Plan in China. The Government stated that China should adopt a "greater food" approach and look at plant-based, fermented and cultivated animal protein to protect the environment and achieve sustainable development goals. This accelerated research and development in the relevant industry in China, and around ten companies have been active.

CellX is currently working with companies and research institutions in China to establish a working group with CFSA for regular discussions, paving the way for the first application to be submitted. The application process in China is expected to take about two to three years after the submission. Any global efforts to facilitate discussions would be beneficial for all the stakeholders in China.

Figure 1. Overview of the production process of cell-based cut pork and chicken strips and nuggets



Source: Adapted from Yang, Z. and Xiang, N. 2022. *Producing cultivated meat in China: Approaches and Challenges*. Presented at the Stakeholder roundtable meeting. Cell-based food and the future of food security and food safety. 7 September 2022. Tel Aviv.



Cell-based beef product with fibrous structure © CellX/Su Su

2.2.2. Inventing entirely new meat

George Peppou from Vow, a cell-based food company in Australia, introduced a unique perspective in a presentation on inventing foods that do not yet exist. Peppou is a chef and a biochemist by training. He came to cell-based food production when his signature product, Morsel, was just an idea. Today consumers think of meats as associated with a single animal that has been grown, fished or hunted. Consumers think that they need to choose meat from poultry, fish, shellfish and so forth. Instead, by flipping this on its head, Peppou asked himself "what would we make if we did not have the constraints of meat as just a single animal?" He wondered if creating something that has not existed before could fundamentally change the behaviour of consumers and potentially increase the level of satisfaction and nutrition.

Plant-based products can become high-quality replicas of meat, but that is just about making the same food differently. Peppou said that consumers still consider plant-based food as a "poor" replication of animal meat. In this context, the idea of cell-based meat has the potential to be different. Plant-based meat may have a positive impact on climate and on animal welfare and it can create more options for food supplies and food security. However, there are two main challenges in replicating things that people already know: 1) matching the price to the conventionally produced counterparts; and 2) meeting the expectations and satisfaction of consumers who have a great deal of understanding, appreciation and attachment to the existing conventionally produced food products. Therefore, Vow has initiated research to develop a brand-new type of animal protein food product.

The Vow product aims to attract chefs and hotel management looking for unique and novel dining experiences to provide to their customers. The production process consists mainly of two parts: the upstream bioprocessing that involves cell culture in bioreactors, and the downstream process that creates finished textured products (Figure 2).

Simplifying the production process and selecting cells that either produce or accumulate more bioavailable nutrients both reduces production costs and increases the premium that can be charged for these products. In the long run, this process will allow for a new food item to be produced with increased nutrient density and availability. That food item will be tasty and nutritious and be available at a reasonable, and potentially lower, price than conventionally produced meat products.

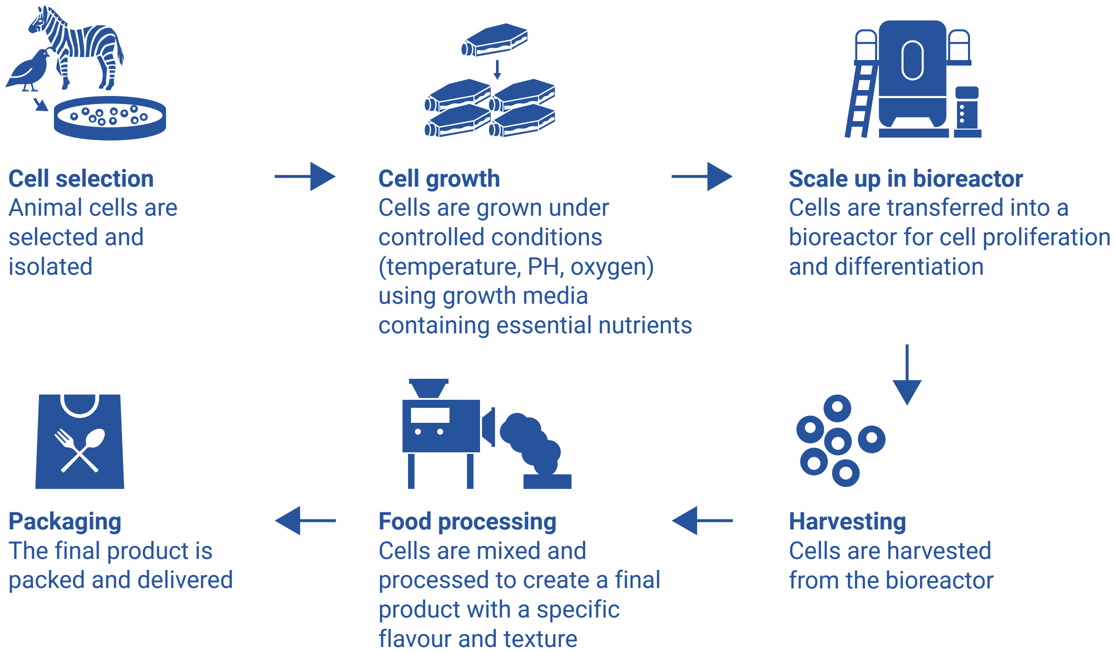
Vow has already submitted draft food safety assessment dossiers to regulatory agencies in Australia, and they are considering two key issues:

1) There must be a careful implementation of food safety basics through Hazard Analysis and Critical Control Points (HACCP) or Hazard Analysis and Risk-Based Preventive Controls (HARPC) so that critical control points can be checked each time in the production line and monitored throughout the production process. The current challenge is that, when taking precautionary approaches, there are numerous control points identified due to the nature of cell-based food production. However, in cell-based food production, zero-microorganisms control is essential because any contamination can overtake the growth of the targeted cells, preventing the final product from being produced. However, extremely low levels of microbiological growth are a feature of every successfully harvested batch and do not require further, additional control.

2) There is the potential for novel hazards in the cell-based food production process such as (epi)genetic drift and growth media residues in the final products. An abnormal rate of repeated mutations could possibly cause a new allergenicity issue or activate biochemical pathways that may trigger the toxicity that has not been expressed. Hence, genetic drift studies in the final cell culture media are important to demonstrate that the mutations are at a slow enough phase and in place within the genome, so that it does not a high risk for food safety. For the residue, all the growth media at Vow are compound-free and controlled using the Threshold of Toxicological Concern (TTC) approach to qualitatively assess the risk of residues, such as the low-level presence of substances in the media. Regarding biological components, like growth factors, Vow takes a similar approach, hypothetically assuming that 100 percent of the growth factors end up in the final product to run the simulations. With this approach, it is possible to compare the data obtained against the available data in the literature related to growth factor concentrations in conventionally produced meat products.

Currently, the relevant regulations, at least those that exist, assume that cell-based food products are the ones that have been grown out of the cells of animals that already exist. There could be a regulatory challenge, since Vow's product is completely new and there may be some uncertainties around food safety. However, any novel risks, would come from the cell-line growth and development as the rest of the production processes are quite common among any other food production. It is also important to consider that if microbiological contaminations happen at any step before cell harvesting, there would be no growth of the cells, making it impossible to obtain the final product. The cell-based production process is self-limiting. The risk of microbiological cross-contamination post-harvest and during food processing is a very traditional food safety risk, and there are several mitigation measures (i.e. good practices, HACCP, etc.) and tools are already available.

Figure 2. Biological and post-harvest production process steps



Source: Adapted from Peppou, G. 2022. *Vow: Inventing Entirely new meats.* Presented at the Stakeholder roundtable meeting. Cell-based food and the future of food security and food safety. 7 September 2022. Tel Aviv.

Laab-style salad made with cell-based food © Vow/Aidan De La Plaz

2.2.3. Bovine meat burger: Brazilian technology

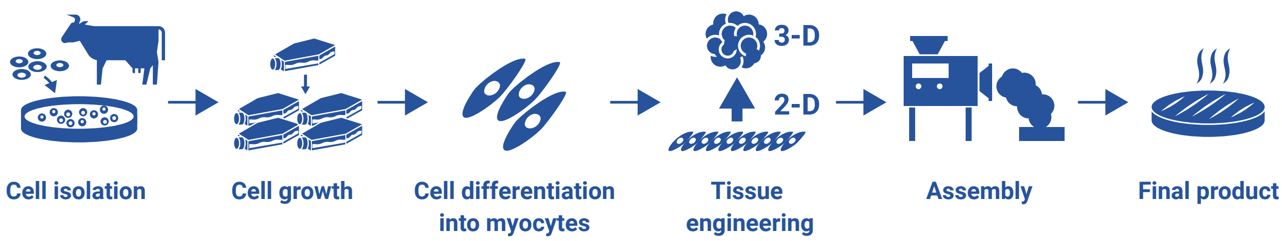
Bibiana Matte, founder of Ambi Real Food in Brazil, presented a cell-based bovine meat product using a combination of cell biology and tissue engineering techniques to create the first cell-based food in the country. She introduced a combined product containing bovine cell-cultured meat, which is right now being produced on a laboratory scale, following five production steps (Figure 3). As step one of the process, cells are isolated and grown in culture media and subsequently differentiated into myocytes. After applying a tissue engineering technique, it transitions from the 2-D cell culture to the 3-D texture. The result is an aggregate of bovine muscle cells. The cells are then harvested and assembled into the final product, which is ready to be cooked.

It is extremely important to minimize potential food safety risks and develop good food safety plans. To collect healthy cells, the crucial steps are to first verify the health of the donor animal by assuring that it does not have any diseases. Also, it is fundamental to implement good practices, including good laboratory practices, good cell culturing practices and good manufacturing practices to ensure sterile conditions, and to use certified sterile materials. Additionally, it is essential to have a visual analysis of the cells being cultured to identify any types of contamination. A molecular biology analysis is conducted to verify the absence of mycoplasma and other viruses.

Matte is currently trying to change the cell growth media to increase the assurance of food safety in terms of residues. While the currently used media does not pose any immediate concerns, additional measures to verify the applicability of the growth media for food production can be quite positive. Evaluating cell characteristics during the whole production process provides an opportunity and poses a challenge, since it is essential to verify the cell proliferation as any mutations can become a potential hazard. However, mutations in cells are not new in biology, so it is particularly important to understand how this phenomenon could occur in the process. The product is currently being developed in a laboratory. Bringing the whole process into a real-life food production facility would be a huge task. Also, once the production starts, there can be no trials with human subjects, unlike in the pharmaceutical industry, and the production must be truly sustainable.

For the composition analysis, the data showed an equal protein value with the conventionally produced meat. However, Matte's combined product has a lower percentage of moisture compared to its conventionally produced counterparts, and there is room to improve the texture. The ash percentage analysis, which is usually correlated with the number of minerals, shows that conventionally produced meat has a higher percentage, while the plant-based product has the lowest. Cell-based meat was found to be in-between, indicating that combined products may add value to the plant-based product. Matte concluded her presentation by saying that it is extremely important to ensure all food safety and quality issues have been met before the products enter the market. More discussion on safety and quality is very important to advance the technology and consider approaches for such assurance processes.

Figure 3. Cell-based burger production process flow chart



Source: Adapted from Matte, B. 2022. *Bovine meat burger: Brazilian technology*. Presented at the Stakeholder roundtable meeting. Cell-based food and the future of food security and food safety. 7 September 2022. Tel Aviv.

Cell-based beef burger © Ambi Realfood/Kamila Santos

2.2.4. Building consumer trust with a strong food safety culture

Neta Lavon from Aleph Farms, a cell-based food company in Israel, introduced a thin-cut beef steak as their first product, which will be launched in 2023. The key aim is to develop quality meat products with a strong commitment to net-zero carbon.

Lavon explained that the company uses pluripotent stem cells, which are embryonic stem cells derived from the blastocyst-stage early mammalian embryo from cows. This type of cell does not have to be genetically modified to maintain the proper conditions of proliferation in culture and it can differentiate into the necessary cell types. Moreover, non-surgical procedures are used to collect these blastocysts and the cells derived have an indefinite potential to grow in culture, showing a very long and stable proliferation. These cells have a relatively short population doubling time, they multiply every 24 hours, which is an advantage compared to other cell types.

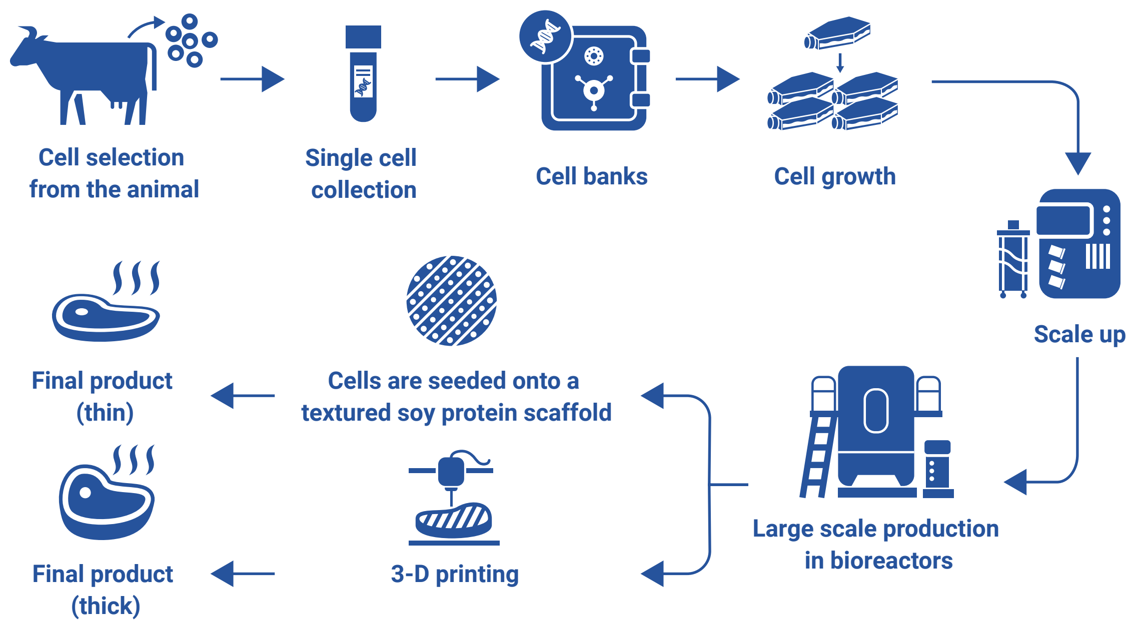
Aleph Farms owns cell banks, and this allows it to fully characterize the stem cells at once, making sure that all the cell batches coming from the same bank are genetically identical and are clear of any microbiological contaminants. After the full analysis, cells can be used time after time, enhancing the reproducibility of the product, which is important for the scaled-up processes. This high reproducibility lowers cost, as well as safety risks. Moreover, means production is independent of seasonal changes or any disease outbreaks that may happen in the world.

There are eight steps in the entire production process (Figure 4) that moves the frozen cells from the bank into flasks and then into bioreactors in a scalable system. The growth in suspension makes sure that all the cells have the same composition of growth media. It is crucial to use fully controlled conditions (temperature, pH and nutrients) to scale up and to have a homogeneous culture at different stages. In this system, the cell mass increases in free-floating aggregates expanded in bioreactors without microcarriers. It is important to monitor the number of cells and their viability during the process to show the stability of the cells through the different steps. The stability of the cells is clear since the traceability system is concrete and the history of the mother cow, where the blastocyst was taken, is known. From this single-cell collection, raw materials can be developed to produce thousands of tonnes of steaks.

Different cell types can become the initial components to make cell-based meat. Cells can turn into different types of tissues to create a steak with all the elements such as fat, muscle and collagen. The company developed a methodology for growing the cell on a textured vegetable protein scaffold to support cell growth and mimic the extracellular matrix. These scaffolds are edible and part of the final product. They are made of a high-value protein to maintain a certain percentage of protein content in the final product so that the ratio is similar to conventionally produced meat. The scaffold has many pores that allow the cell to grow into it, creating a tissue of a few millimetres. To make it thicker, it is necessary to use platforms that support the active transfer of growth media and bring oxygen to the cells within a thicker structure. Aleph Farms developed such a thick product 3-D bio-printing cells within supporting hydrogel, to replace the scaffold. The growth media is an essential part of their products, and Lavon's company uses animal-free containing media with the necessary ingredients that have already been used in conventionally produced food products, such as amino acids, vitamins, minerals, fatty acids and proteins. Those elements in the growth media are essential for the cells to grow, and in conventional beef, these come from the blood of the cow.

Food safety strategies have two main parts: 1) intrinsic safety, which relates to the safety risk around the cell growth, the growth media and the nutritional values; and 2) operational safety, which is related to the manufacturing processes with the critical points for monitoring the cell harvest, the final product preparation, packaging, release, shelf life, and finally the transport and marketing.

Figure 4. Flow chart of the production process of cell-based beef steak



Source: Adapted from Lavon, N. 2022. *Driving Consumer Trust with a Strong Food Safety Culture.* Presented at the Stakeholder roundtable meeting. Cell-based food and the future of food security and food safety. 7 September 2022. Tel Aviv.

Cell-based ribeye steak, thick cut © Aleph Farms/Daniel Lailah

2.2.5. On a mission to create the cleanest, most sustainable seafood on the planet

Aryé Elfenbein, co-founder at Wildtype, an American company that produces cell-based fish, explained that their main product is a cell-based salmon.

According to FAO's *The State of World Fisheries and Aquaculture 2022,* the global production of aquatic animals has been slightly decreasing. This can be an indicator of the possible unsustainability of the global fishing industries. It is often highlighted that conventional approaches in the industry can be environmentally destructive and can contribute to greenhouse gas emissions at a similar level to the entire global aviation sector. Another example of potential sustainability concerns is the limitation of coastal aquaculture sites. Salmon prices have increased as a direct economic consequence of all these issues, making this type of animal protein more inaccessible to consumers.

Conventionally produced fish and fishery products can be contaminated with various microbiological and chemical hazards. Microplastics and heavy metals such as mercury are also of concern. Cell-based salmon production could be an option for producing very similar nutritional benefits to the most pristine wild-caught fish while providing precisely controlled safety assurances.

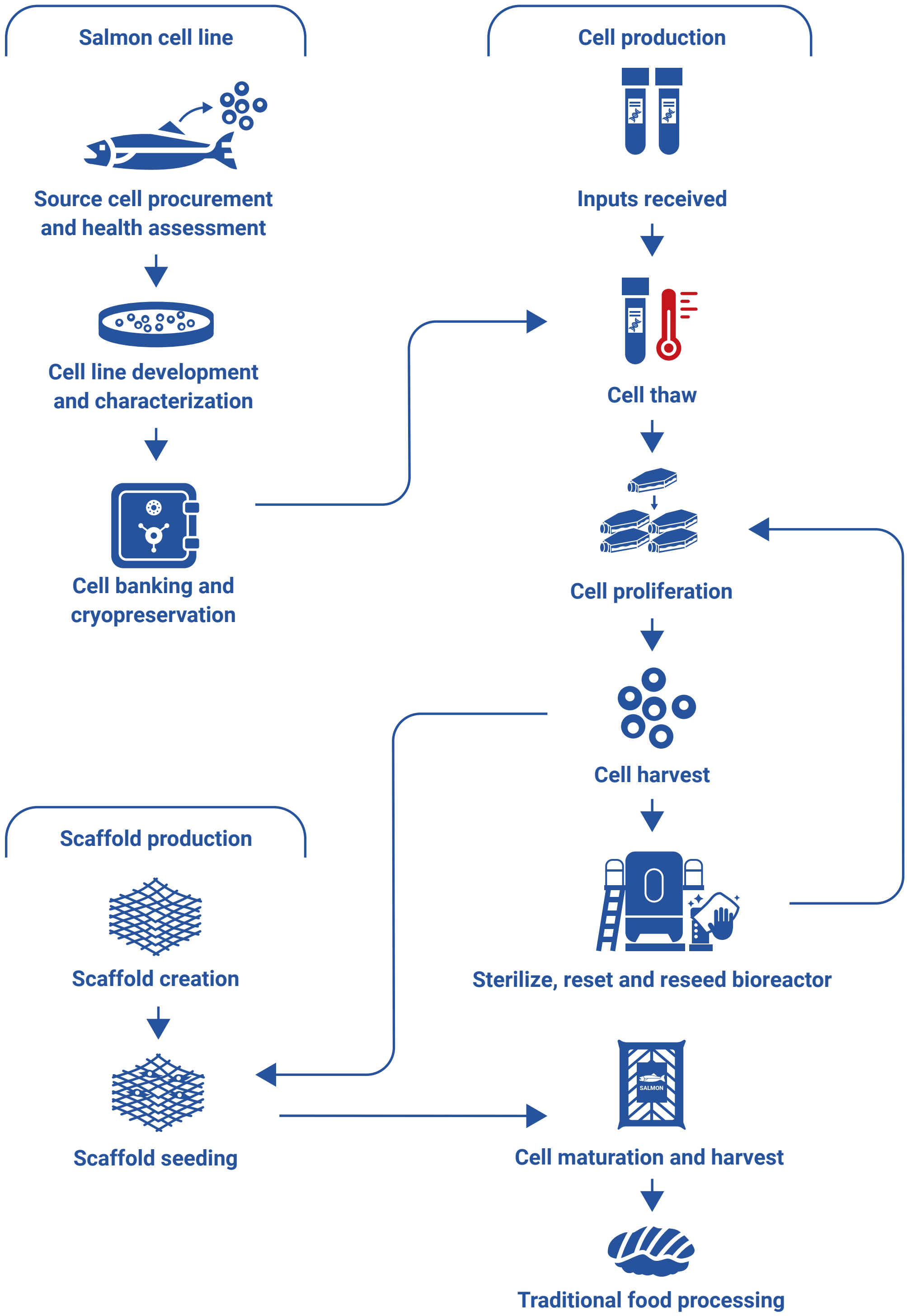
Cell sourcing is the first step of the production process. Living cells from Pacific salmon are sourced from a species called Coho (*Oncorhynchus kisutch*), also known as Silver Salmon, living in the North Pacific area and the coastal rivers and streams from Alaska to California.

The next step is to grow the cells in bioreactors using specific conditions (controlled temperature, pH and nutrients) that enable the cells to mature as they would in the wild. The last step is to harvest the cells from the bioreactor and seed them into a plant-based scaffold, which provides a structure for the product and becomes the shape of a cut of salmon. The nutritious fats, including Omega-3 fatty acids, are adjusted to create a desirable texture.

To assure food safety, it is important to consider all the steps of the production process. The stepwise hazard analyses, preventative controls, input monitoring and environmental monitoring programmes are all essential for food safety assurance.

Most countries currently lack a regulatory precedent for cell-based foods. There could be some regulations on some inputs such as growth factors. It is important to shift the approach and have food-centred discussions and regulatory considerations. The concern over genetic modifications with cell lines can be both regulatory and consumer-perception issues. Also, the nomenclature is always problematic for labelling. The big philosophical question is: Can a food grown from salmon cells as the main ingredient also be called salmon?

Figure 5. End-to-end production process overview of cell-based sushi salmon



Source: Adapted from Elfenbein, A. 2022. *On a mission to create the cleanest, most sustainable seafood on the planet, starting with salmon*. Presented at the Stakeholder. Cell-based food and the future of food security and food safety. 7 September 2022. Tel Aviv.

Cell-based salmon saku © Wildtype/Rebekah Mackay

2.2.6. Plant cellulose-based nanofibres as a matrix to grow cultivated meat

Professor Aline Bruna da Silva from the Federal Center of Technological Education of Minas Gerais (CEFET MG) in Brazil, presented the steps for producing structured cell-based chicken, which is a three-dimensional chicken product created by stacking edible films of primary skeletal chicken muscle cells that have been grown in cellulose acetate nanofibres.

The product uses tissue engineering principles and performs on a lab scale. The main goal of this project is to create a thick piece of meat. The research is focused on developing the scaffold.

There are three main steps in the production process (Figure 6). First, the satellite chicken cell lines are isolated for production. Second, the scaffold of cellulose-based nanofibres are produced through an electrospinning technique. The scaffolds consist of a non-oven mat of nanofibres with a diametre between 100 to 200 nanometres, with a smooth surface that is highly porous and with enough space for the cells to grow between the fibres. Thirdly, the chicken cells from the first step are seeded into the nanofibre scaffolds, developed as edible sheets composed of grown chicken muscle cells, into the cellulose-based nanofibre scaffolds. The stratification is done layer by layer, allowing the cells to grow in the previous stratum before the next one is seeded. It takes six days for the three-dimensional product composed of cultivated chicken muscle cells and a cellulose-based nanofibres matrix to develop. During this process, chicken cell adhesion, proliferation and differentiation as well as cell viability throughout the thickness of the 3-D structure is validated.

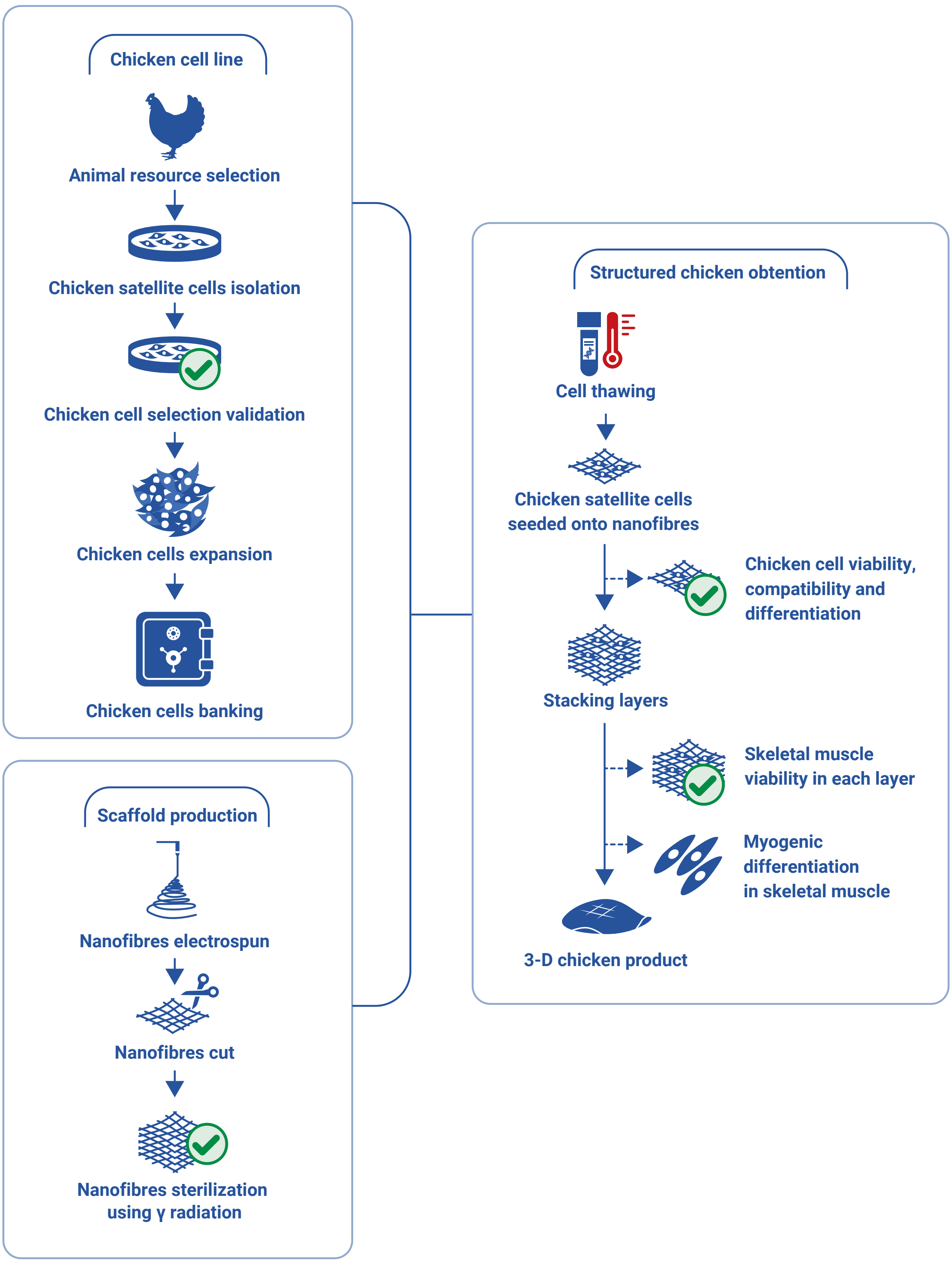
Through the microscope, the cells appear to be aligned with the nanofibre structure and the differentiation is visible within the scaffold. Also, after cooking, the size of the product does not change, thus the cell growth in the scaffold is considered to be successful.

At a laboratory scale, the food safety assurance procedures and approaches can be different from those at a scaled-up production level. A carbon-dioxide incubator is used exclusively for cultivated meat in the laboratory, a biological safety cabinet class II is used during the different procedure steps, and periodic mycoplasma tests are run for product safety. For the scaffold, a differential scanning calorimetry test to the solvent residue is verified, and before seeding the cells, sterilization is performed using gamma radiation.

Professor da Silva emphasized that food safety is one of the most important issues for cell-based food and that every single potential hazard must be evaluated. Safety of growth factors, growth media including fetal bovine serum (FBS), possible antibiotic residues in the final product, food allergens from scaffold materials and the presence of foodborne pathogens contaminated post-harvest are usually the major food safety issues.

As the next technical challenge, she is aiming to obtain 3-D chicken products through stacked edible films of primary skeletal chicken muscle cells in cellulose acetate nanofibres and alginate microparticles with microencapsulated canola oil as the fat. Microencapsulation can be an exciting yet ambitious project since many other nutritional substances, such as minerals and vitamins, could be microencapsulated in the product.

Figure 6. 3-D Chicken production process using a scaffold of cellulose-based nanofibres



Source: Adapted from da Silva, A.B. 2002. *Structured Cultivated Chicken - Cellulose-Based Nanofibers as a Matrix to Grow Cultivated Meat.* Presented at the Stakeholder roundtable meeting. Cell-based food and the future of food security and food safety. 7 September 2022. Tel Aviv.

3-D product composed of cell-based chicken muscle cell and cellulose nanofibers matrix © CEFET MG/UFMG/Leonardo Dutra Luz

2.2.7. Bacterial cellulose-based biomaterials for cell-based meat production

Ximing Zhang from Zhejiang University in China explained that there are currently two reasons for using scaffolds for cell proliferation: one is to achieve a desired high cell density; and the second is to properly align the cells with the scaffold. While the previous speaker discussed plant-based cellulose, Professor Zhang's research focuses on the use of bacterial cellulose (BC) as a primary source, which can generate four types of scaffold with various morphologies and characteristics.

To develop a microcarrier, BC is combined with calcium alginate, which has a spherical shape and is used for high-density suspension cultures. The film scaffold is composed of BC and chitosan, which is used for high-density culture in a bioreactor. The porous scaffold is developed with BC that has been freeze-dried for the proliferation of adipocytes. The fibrous scaffold created with BC-oriented proliferation is for preparing myofibroblasts and whole meat.

There are several reasons why BC could be an effective material for scaffolding for cell-based food productions: 1) functionally, BC has already been used in tissue engineering for decades as scaffold material due to its good mechanical properties; 2) for food, this scaffold is not made from animals, and it is edible; 3) the material is already used in the food industry, especially in China, and it is likely to be accepted by consumers ; and 4) commercially, it is relatively low cost and can be produced on a large-scale.

The first product explained was a cellulose-based aligned scaffold (Figure 7). In this process, the activated bacteria are inoculated in a tube bioreactor containing the BC scaffold and the cultured BC medium. This bioreactor is an O2-permeable silicone tube. Since bacteria proliferation requires a lot of oxygen, this system allows for control of the demand of this parameter. After the incubation time, it is possible to see cells aligned to the BC scaffold. Then the scaffold is taken out for cell proliferation and viability. There are two ways to do so: 1) immersing the BC directly with the chitosan; or 2) *in situ* component BC with chitosan. The results showed that the proliferation was successful with the desired density and alignment.

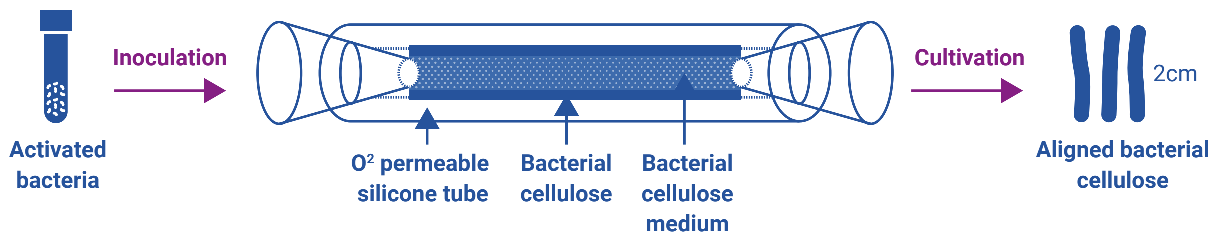
The second product explained was a cellulose-based porous scaffold and microcarrier made by freeze-drying a cellulose dispersion (Figure 8). This approach allows for control of all growth parameters, such as temperature, pH, and oxygen, which is an important aspect of industrial production for reproducible results. The freeze-drying process in different conditions allows for control of the size of the microcarrier pores diameter. Indeed, the functioning of the cells is highly dependent on scaffold pore sizes, which play an essential role in nutrient and oxygen supply. Smaller pores, called secondary pores, of the microcarriers are for the cells to settle inside, while larger pores are for the nutrients to go through. One of the major advantages of this system is that it avoids the transformation of the media inside the microcarrier having a continuous flow, resulting in good cell proliferation outside and inside the microcarrier.

The third product explained was a cellulose basket disk carrier (Figure 9). This product is made through the process of oven-drying cellulose dispersion. This system was also found to be stable for reproducibility on a large scale. The output is a good cell density where all cells receive adequate nutrients, and they function to their fullest potential.

The fourth product explained was a cellulose-based spherical carrier with a diameter of 300 to 400 μm prepared by combining electrostatic spraying with microfluidic (Figure 10). This system is hard to commercialize since it requires specific, laborious, and complex fabrication techniques. However, at the lab scale, the BC is well dispersed inside and outside the microsphere.

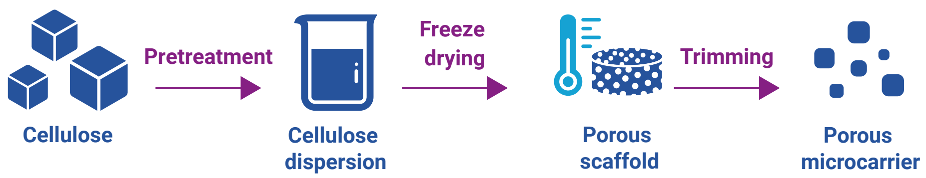
The BC-based scaffold material can allow cell-based food developers to use enzymes to make differentiation on cellulose mechanical strength, changing accordingly the texture of the final product. BC is widely used in the food and food packaging industry in China and various safety assurance programmes have already been established in the sector. The current challenge for the cell-based meat production process is the high price of FBS free media. Satellite cells used in cell-based food have traditionally relied on FBS, a notoriously expensive, unsustainable and inconsistent component, and which is essentially opposed to the aims of cell-based meat. Developing an FBS-free recyclable growth media, where nutritional values and pH can be adjusted after use, could be an option for reducing production costs.

Figure 7. Product 1: cellulose-based aligned scaffold



Source: Adapted from Zhang, X. 2022. *Cellulose-based biomaterials for the application of cultured meat production*. Presented at the Stakeholder roundtable meeting. Cell-based food and the future of food security and food safety. 7 September 2022. Tel Aviv.

Figure 8. Product 2: cellulose-based porous scaffold and microcarrier

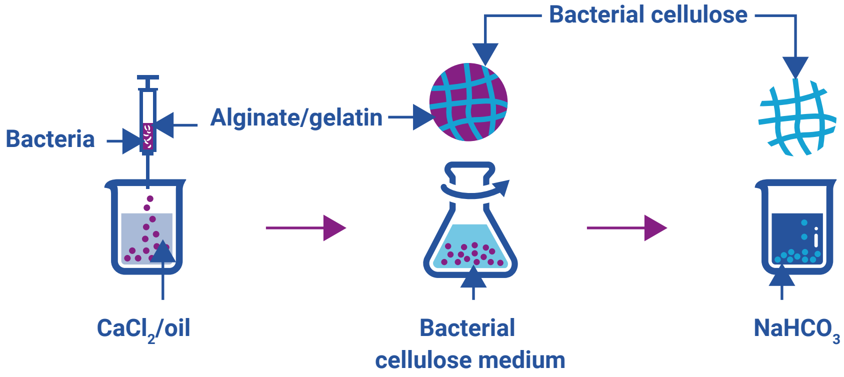


Source: Adapted from Zhang, X. 2022. *Cellulose-based biomaterials for the application of cultured meat production.* Presented at the Stakeholder roundtable meeting. Cell-based food and the future of food security and food safety. 7 September 2022. Tel Aviv.

Figure 9. Product 3: cellulose-based disk carrier

Source: Adapted from Zhang, X. 2022. *Cellulose-based biomaterials for the application of cultured meat production*. Presented at the Stakeholder roundtable meeting. Cell-based food and the future of food security and food safety. 7 September 2022. Tel Aviv.

Figure 10. Product 4: Cellulose-based spherical carrier



Source: Adapted from Zhang, X. 2022. *Cellulose-based biomaterials for the application of cultured meat production*. Presented at the Stakeholder roundtable meeting. Cell-based food and the future of food security and food safety. 7 September 2022. Tel Aviv.

Directional fibrous scaffold made by bacterial cellulose © Zhejiang University/Ximing Zhang

2.2.8. Structured cell-based meat products

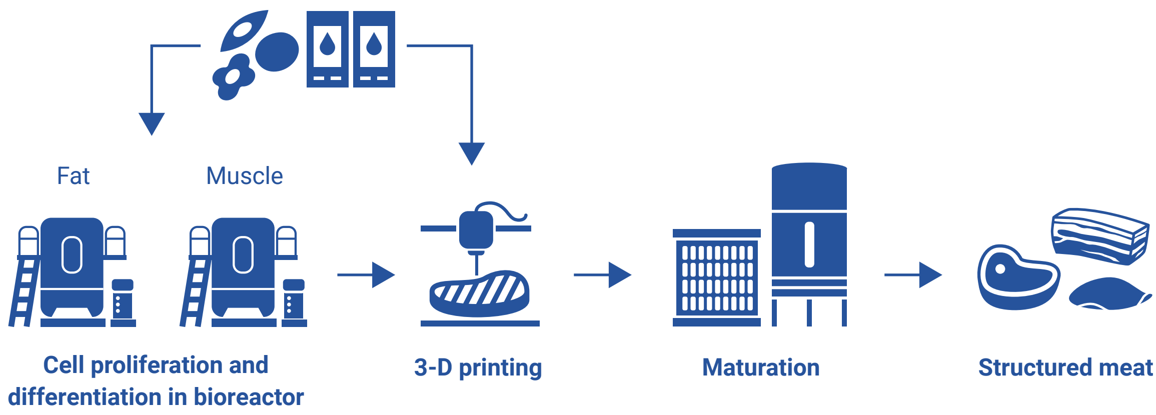
Dan Kozlovski, Chief Technology Officer at Steakholder Foods, illustrated the evolving landscape of meat alternatives in relation to their organoleptic properties. The first products planned for commercialization are those that combine cell-based meat biomass and plant-based ingredients. With this Steakholder Foods' system, it is possible to enhance the taste so that it is similar to the animal product. Eventually, the company would like to produce cell-based structured meat cuts using a 3-D printer.

Orit Goldman, Vice President of Biology at Steakholder Foods, presented detailed steps of the production process. Currently, the company's species portfolio includes bovine, porcine, avian and piscine. The first step is cell isolation. To scale up the process and reach a large amount of biomass, cells are cultured in bioreactors for proliferation. These cells then differentiate into fat and muscle cells. To 3-D print structured products, the company designed and built an industrial scale 3-D printing machine. Once the meat is printed, it is then incubated until it matures (Figure 11).

Cell-based food production has the advantage of freely designing the shape of the products and its fat to muscle ratio so that the final product can be lean or fatty, based on customer preferences. For the combined product using fat animal cells, the chicken fat biomass from cells is grown in bioreactors and then mixed with plant-based products. In this way, different types of products, such as chicken-like nuggets or roasted pita bread can be developed. However, the company's main aim is to create a structured product with a solid taste, texture and the same nutrients as is found in the native tissues. In 2021, the first 100 g piece of 3-D printed steak was successfully produced in the pilot plant. It is the largest 3-D printed steak with both fat and muscle cells.

While the success of such production lines is exciting, it is also essential to ensure food safety. Food safety strategies would include: stabilizing the cells, issues of toxicity, genotoxicity and allergenicity. Following good practices and implementing HACCP is fundamentally important to minimize any food safety risks. Full regulatory compliance is essential for all printer components used for food production processes.

Figure 11. Production process for 3-D printed tissue of cell-based beef steak



Source: Adapted from Zhang, X. 2022. *Cellulose-based biomaterials for the application of cultured meat production*. Presented at the Stakeholder roundtable meeting. Cell-based food and the future of food security and food safety. 7 September 2022. Tel Aviv.

Combined product of chicken-like nuggets ©Steakholder/Dudi Moskowitz

2.2.9. Development and application of the HACCP plan for food safety

Amanda Leitolis from the Good Food Institute, a nonprofit organization that supports alternative protein innovation, talked about her work on the food safety assessment of cell-based food. The main objectives are to design a generic HACCP-based food safety plan aiming to facilitate the future product development and implementation of a company's food safety system.

The study models a theoretical process flow diagram based on 27 production steps (Figure 12) to produce a cell-based meat burger. The product was defined as a patty consisting of cultivated bovine muscle cell biomass, an aggregate of poly galacturonic acid microcarriers and bovine muscle cells, produced in bioreactors, with some plant-based ingredients added later, which is shaped and subjected to a food technology process. The product is frozen and intended for use in restaurants.

The partial results show that foodborne pathogens were the main hazard in the initial production, especially from the environment where contamination could happen during sampling. There are different possible control measures, such as concentration of antimicrobials, control temperature and time of sample transportation. In addition to trichotomy, it is essential to clean, and use an antisepsis on the animal's muscle sampling area, using sterile material for the sampling procedure.

There are three main hazards in the biomass production step:

1) Foodborne pathogens, although theoretically controlled for in the cell procurement steps, can cause contamination to occur in the manipulation. The control measures were: visual inspection of the cells and cultures under a microscope, sterilization of the bioreactors, and ensuring the use of a sterile culture medium to prevent those hazards.

2) The residues of growth factors and the human serum albumin, which are used in the differentiation medium formulation, can become chemical hazards as they could remain in the final product. The cells biomass validated washing procedure and the residual test control after harvesting could be effective control measures for those hazards in the study. A food allergen declaration on the packaging for the presence of albumin is a control measure.

3) In the food process production, it is possible that foreign materials such as plastics and metals from raw material packaging or the metal components of bioreactors could become contaminated. For these hazards, inspecting the packaged product using an x-ray or making a visual examination could be a concrete control measure.

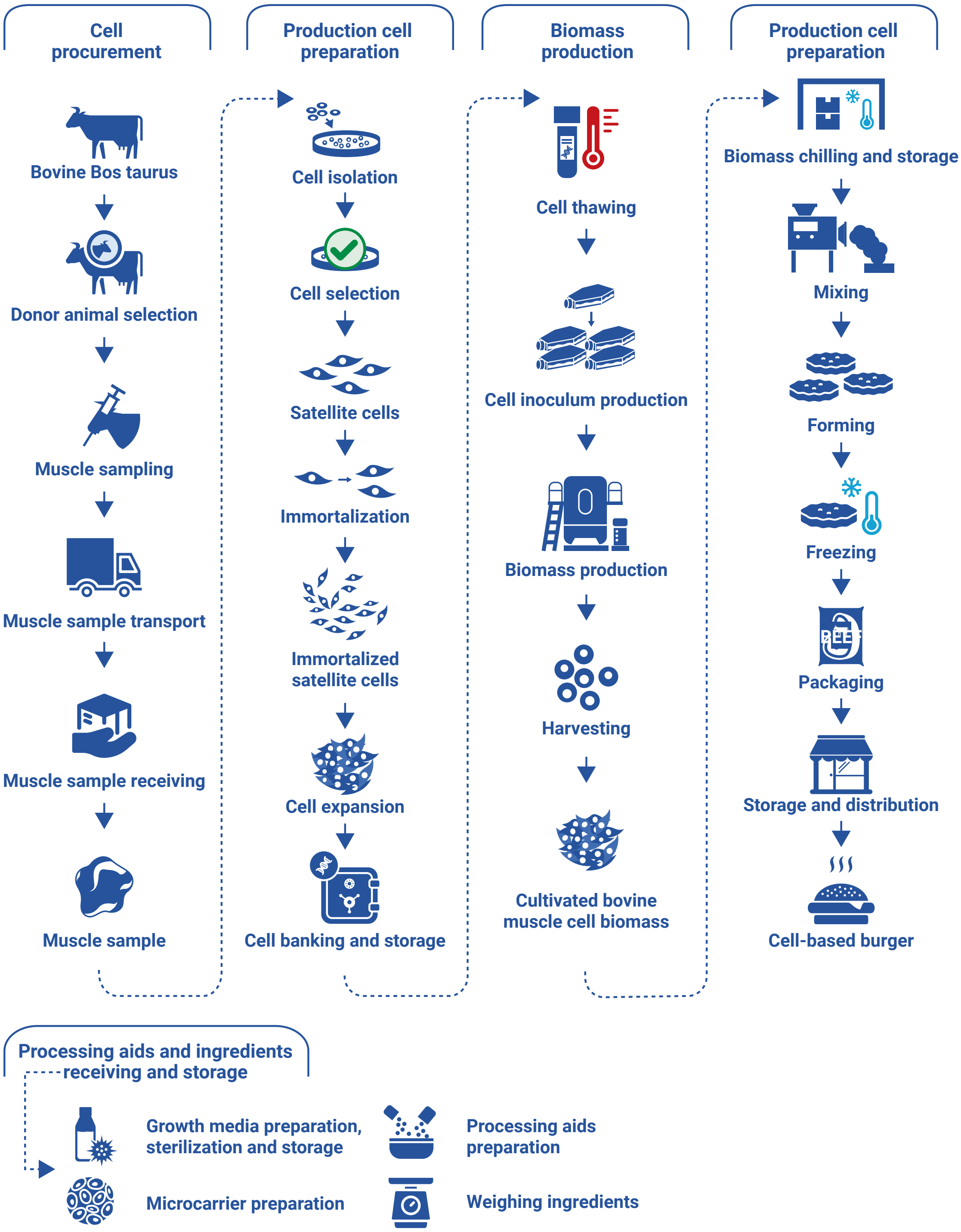
Fifty different inputs such as culture medium ingredients, microcarriers, enzymes, processing aids, texturized pea protein, among others, were evaluated during the study. Seven critical control points were identified according to the hazard analysis that was developed. Some of the inputs were considered critical since they have not been used in non-cell-based foods.

For inputs used at the early steps of the production process or inputs used in a trace amount, it is important to quantify the substances precisely before proceeding with a safety assessment. For the inputs used in later steps of the production process, such as growth factors, it is necessary to understand the safe levels of such residues (maximum residue limits). A prerequisite for this process is to verify whether currently available methodologies for residue analysis are sufficient or whether new analytical methodologies must be developed to analyse potential residues.

Leitolis concluded that, for the biological hazard, donor animal selection and muscle sampling steps need special attention. It is important to follow good agricultural practices (GAP) and to control for the potential of biological hazards from the animal; however, the sampling procedure in larger animals such as cattle, which occurs in open fields, can be problematic in terms of cross-contaminations. Therefore, it may be necessary to create specific control measures for each case. Detailed risk assessments of all inputs and concentrations used in cell-based food production enable developers to map critical ingredients so that control points can be set and monitored.

As HACCP is product/processed-based, developing an effective HACCP system is a complex process requiring various analyses with different methodologies and tools. A HACCP plan for cell-based food involves multidisciplinary efforts requiring professionals with experience in all relevant industries, such as conventional meat industries, veterinarians, microbiologists, chemists, quality assurance experts in the food industry, etc. Identifying research gaps is critical to ensure the safety of cell-based food products. As food safety is everyone's responsibility, collaboration among different stakeholders including companies, regulatory agencies, scientists, and researchers is useful for sharing the results of food safety assurance approaches and methodologies.

Figure 12. Theoretical process flow diagram for producing a cell-based burger



Source: Adapted from Leitolis, A. 2022. *Assuring Safety of Cultivated Meat: Development and application of the HACCP plan*. Presented at the Stakeholder roundtable meeting. Cell-based food and the future of food security and food safety. 7 September 2022. Tel Aviv.

2.2.10. Human milk for babies

Katariina Koivusaari from BIOMILQ, an American early-stage startup company, discussed the development of cell-cultured human milk products. While BIOMILQ is working towards a whole infant nutritional option, it does not aim to replace breastfeeding. Rather, BIOMILQ is trying to harness the power of mammary cells to produce cell-cultured human milk as an option in addition to breastfeeding babies. It could be used when breastfeeding is not possible.

Fewer than 50 percent of the babies in the world are exclusively breastfed for the first six months, as is recommended by WHO. There are many reasons why a child may not receive breast milk, and other options are extremely limited. Many caregivers rely on infant formula. This conventional formula, which is available commercially, is currently the most used alternative to breastfeeding. However, formula companies openly acknowledge that conventional infant formula falls short of providing the full constellation of proteins, fats and sugars that make human breast milk so extraordinary. Furthermore, most commercial infant formulas are soy- or dairy-based, two of the most common childhood allergens.

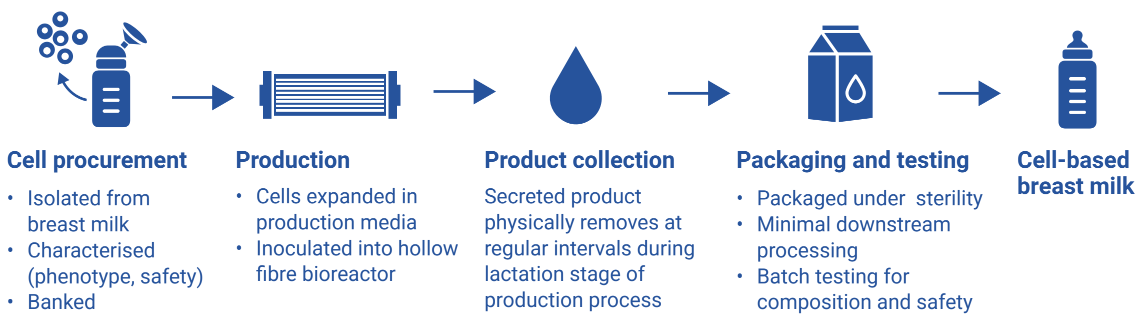
In addition to conventional infant formula, milk banks offer pasteurized, donated breast milk, but the supply is limited, and its use is prioritized for premature infants and infants with medical needs. It has also become increasingly more common to share breast milk. However, this is an informal and unregulated system and quite a large share of this milk fails to meet milk bank safety standards.

Koivusaari explained that infant feeding is not one size fits all and caregivers need additional nutritious, safe and accessible options. It's important to note that BIOMILQ's products cannot perfectly replicate the dynamic complexity of human milk. Breast milk is highly variable and contains various antibodies and beneficial microbes that BIOMILQ's product will not contain. Yet, its cell-based production system provides unique advantages. For example, BIOMILQ's products may contain nutritive and functional components that current infant formulas cannot offer. They are produced in a sterile environment and are free of cow's milk and soy, two of the most common childhood allergens.

BIOMILQ's cell-based production system uses the biological functionality of mammary epithelial cells to produce human milk components. The system provides the cells with an environment that allows them to produce milk similar to how they do in the body. As with any new product or production platform, especially one for such a vulnerable population, the importance of safety is highly recognized. The stability and sterility of process inputs are critical for safety and maintaining product consistency. The nutritive media composition must be well defined to assure safety and to have a targeted nutritional composition for the final product. Sterility must be maintained during the whole production process using the appropriate good manufacturing practice (GMP) guidelines. At the end of the process, the final product will be tested to make sure that it meets all criteria that have been set for composition and safety.

At present, there is no clear guidance on regulatory requirements in countries where BIOMILQ would like to seek approvals, including the information on requirements for safety assessment parameters. Technical guidance from relevant authorities and experts to jointly assure the safety of the products is needed. A clear, predictable and science-based safety framework encourages responsible innovation and competition across the field.

Figure 13. Scheme of the production process of cell-based human milk



Source: Adapted from Koivusaari, K. 2022. *Human milk for babies: The potential of cell-cultured human milk and safety considerations*. Presented at the Stakeholder roundtable meeting. Cell-based food and the future of food security and food safety. 07 September 2022. Tel Aviv.

2.2.11. Cell-line development: A single cell can make a world of difference

Joe Mee from Roslin Technologies, a food-tech company based in Edinburgh, presented various cell-line products that Roslin Technologies considers to be key elements for the success of the end-to-end cell-based meat production process. They specifically focus on proliferation potential and differentiation capacity to develop high-quality cell lines. One of their main products is self-renewing pluripotent stem cells (Figure 14).

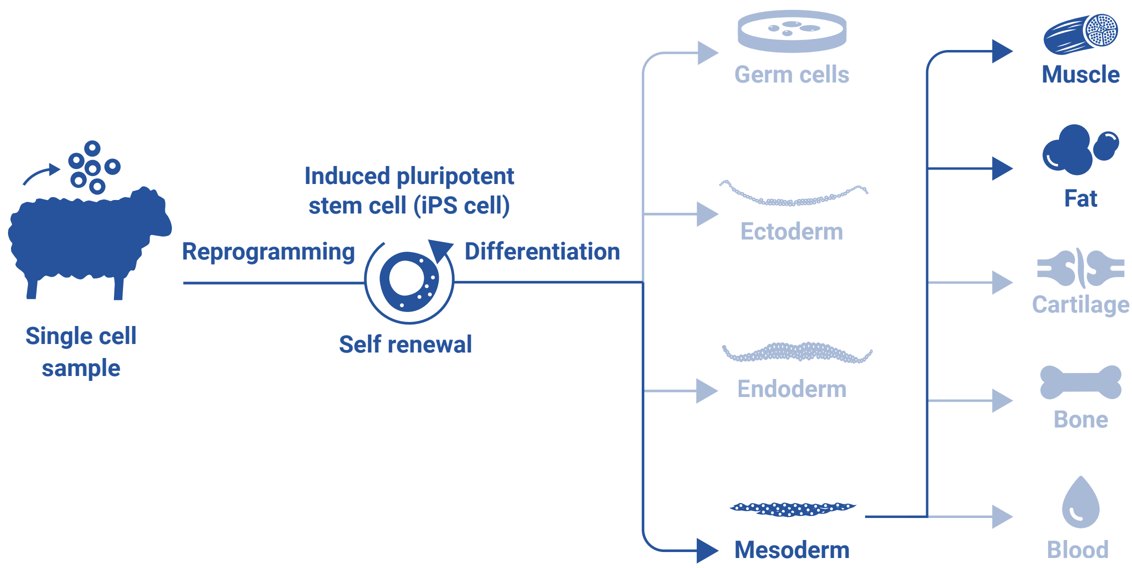
Currently, the company's cell lines come from different animal sources such as porcine, avian and ovine. They also have new lines from bovine and crustaceans in the pipeline. The pluripotent cells they use are an effective source of cell-based meat products, as those cells grow indefinitely, maintain chromosome stability and can differentiate into muscle and fat cells. Model products made from their cell lines include chicken nuggets, dumplings and sausage prototypes, which were products that combined plant-based ingredients with 10 percent animal cells.

As for the safety assurance process, when somatic cells are first sourced from an animal, establishing traceability is a crucial step. Then during the cell culturing process, it is important to record every step to be able to assess every risk. In addition, full characterization of the cell lines is important to provide confidence in the quality and safety of the cells. All the data with all the recorded characteristics linked to a specific cell line can be made available by the company to its clients to support their regulatory efforts.

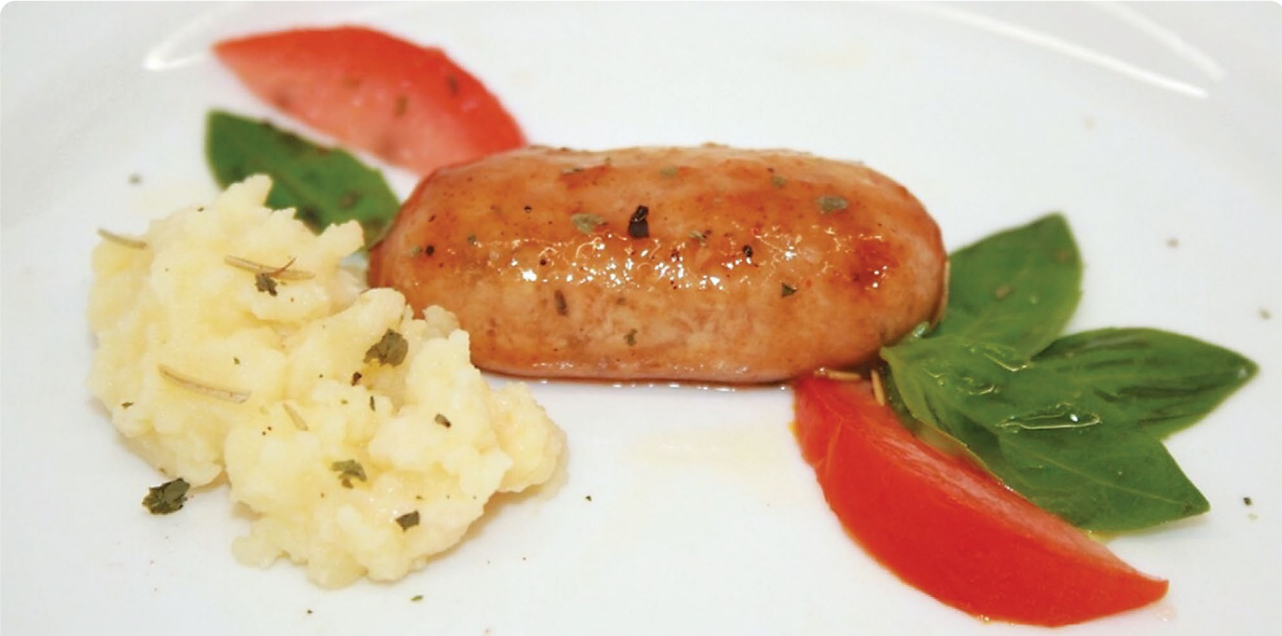
As part of the cell line derivation and characterization process, all cell colonies, their growth rate, morphology, stains and the effectiveness of their cell differentiation are critically assessed, assuring that they respond in the same way when these cells are scaled up in the bioreactor. The genetic stability of the cells is also verified, using molecular biology techniques (RNAseq, qPCR, flow cytometry, etc.), and the specific growth rate and longevity are monitored.

While regulatory requirements are still uncertain in many countries, the company considers it important to have in place precise cell line traceability and standard screening methodologies. The growth media compositions must be disclosed and comply with regulations. Working with food safety advisors and regulatory bodies is very important for identifying any potential food safety issues.

Figure 14. Production process of pluripotent stem cells



Source: Adapted from Mee, J. 2022. *A single cell can make a world of difference*. Presented at the Stakeholder roundtable meeting. Cell-based food and the future of food security and food safety. 7 September 2022. Tel Aviv.



Prototype of pork sausage for demonstration of cell lines to customers © Roslin Technologies/Jacqui Matthews

2.2.12. Key growth factor in the future of food

Amit Yaari from BioBetter, an Israeli agritech start-up company, introduced their plant-expressed growth factors developed for cell-based food production. The growth factors are an essential input that plays a critical role in cell proliferation and differentiation. Currently, the high cost of such growth factors, due to limited availability, is one of the biggest challenges that cell-based food producers are facing.

As of September 2022, the cell-based food industry was still relatively small, thus the demand for growth factors has not largely exceeded the supply. However, it is expected that the cell-based food industry may drastically expand with scaled-up larger productions soon, and the existing facilities may not be able to provide a sufficient quantity of high-quality growth factors.

BioBetter inserts the deoxyribonucleic acid (DNA) sequence coding for the molecular machinery into tobacco plants, which are then transformed into a plant bioreactor system that grows and stores growth factors until harvest. The aim is to achieve large-scale open-field cultivation of the plants, to maximize the advantages of molecular farming and economies of scale. A small investment is required for protein production since existing tobacco farms are already equipped with all the necessary infrastructure, land, machinery and technical know-how to grow the plants. Western tobacco farmers are facing a crisis due to the steep decline in smoking around the world and are desperate to find alternative uses for tobacco cultivation that can make good use of their farming practices.

However, the tobacco-based production platform faces three significant challenges: 1) difficulties associated with genetically modified plants. In general, genetically modified organisms (GMOs) are not perceived positively and are not well accepted by consumers when applied to food, and they may pose various regulatory challenges in some countries; 2) tobacco has an extremely negative reputation, and although it is not meant to be smoked and, therefore, does not harm human health, there is still a negative public perception; and 3) the regulatory requirements of growth factor production and use for food are still not very well established, as many growth factors have been considered as potential therapeutic agents.

The process starts with generating the transgenic tobacco plant line, cloning DNA vectors and incorporating them into the plant genome. The parent lines are validated by sequencing to ensure that no sequence changes occur and the insert genomic location is maintained. The proteins are characterized to insure functionality, activity and sequence. The parent lines are hermetically quarantined to avoid cross-pollination or disease. Full sequencing is performed before every seed batch is generated to validate the stability of the genetic materials in the seeds.

An overview of the growth factor production steps is illustrated in Figure 15. In the open field, biomass production, weather conditions and environmental parameters, such as water and air quality, are monitored. Subsequently, the biomass is harvested and transported to different locations for extraction and purification.

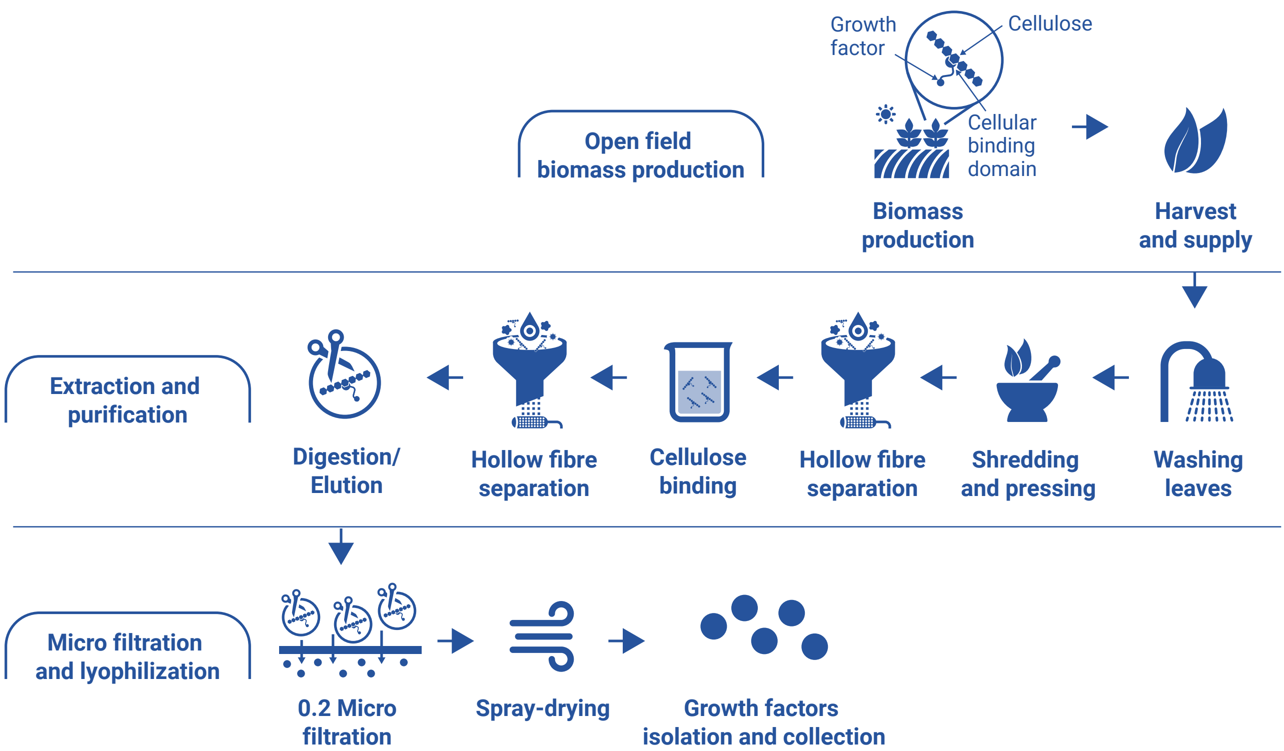
For the protein purification process, the growth factor is expressed in the plants with a peptide linker that connects it to a cellulose binding domain (CBD), a protein domain that binds cellulose strongly and specifically. To enable the separation of the factor from the CBD, the peptide linker contains a proteolysis site.

After biomass harvest, the leaves are washed clean and crushed using an extraction machine, and the extracts are filtered through a 0.2 micron filtration system to remove any insoluble particles and bioburdens such as bacteria or dust from the fields. Immediately afterwards, cellulose particles are added, and the CBD-bound growth factors are specifically separated from the rest of the proteins and small molecules. A second filtration stage immediately follows, but this time the growth factors are retained because of their large size, while any other elements pass through. For elution, a protease is added that releases the growth factor from the CBD, allowing it to pass through the membrane and be collected, concentrated and dried.

A food safety plan is being implemented for this new production facility, including setting up safety and quality standards and monitoring points. For biomass production, the standard to be followed is the global GAP. Monitoring focuses on the use of pesticides, expression levels and quality during plant growth before harvesting. The safety of GMOs is also assessed in line with local regulations. For extraction, purification, filtration and packaging, ISO22000 standards and HACCP are followed.

While the company would like to use a GMO-free system, the current situation does not allow them to use non-transgenic plants. The use of tobacco has the advantage of it not being an edible plant, thus accidental consumption of plants containing growth factors, which can pose a high risk, is not a concern. Furthermore, the risk of a transgene escaping into the ecosystem or neighbouring fields is greatly reduced.

Figure 15. Overview of the growth factors production steps in a plant system



Source: Adapted from Yaari, A. 2022. Key growth factor in the future of food. Presented at the Stakeholder roundtable meeting. Cell-based food and the future of food security and food safety. 7 September 2022. Tel Aviv

In vitro culture of plants used for growth factor production © BioBetter/Alexander Selexnyov

2.2.13. Customized, plant-based, edible scaffolding and microcarriers

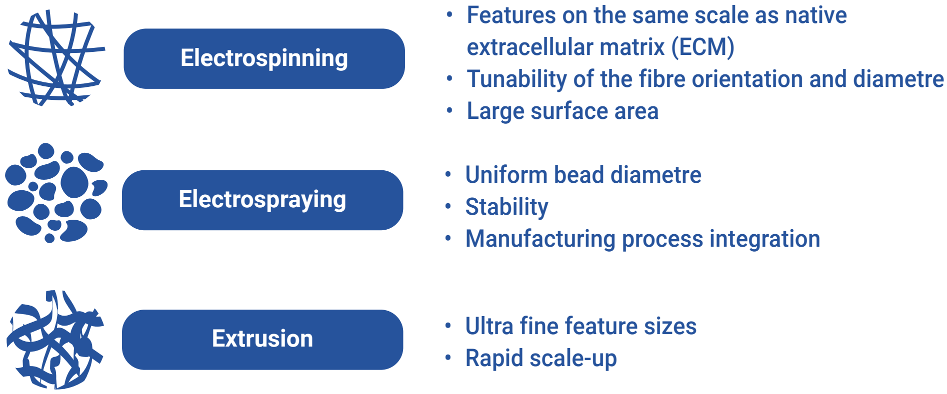
Heidi Coia, from Matrix Food Technologies in the United States of America, introduced Matrix's plant-based, edible nanofibre scaffolds for the cell-based food industry. The products are animal component-free and designed to be customizable with 3-D structures. The customization parameters include the surface treatment, size, composition, colour and fibre alignment.

The company's major product lines also include scaffolding, microbeads and microcarriers and the production process can be categorized into three systems (Figure 16) electrospinning – a low-cost technique where the solution of polymers passes through a spinneret needle during the application of a high electric field, creating a porous fibre network with tunable diameters and high surface area; 2) electrospraying – cell and food compatible biomaterials are electro-sprayed, yielding droplet deposition, which provides a uniform bead diametre as well as good stability; and 3) extrusion – a methodology to dispense larger filaments made by natural and/or synthetic biomaterials, allowing both scaffold-based or scaffold-free production, a technology also used to create high cell density bio-inks, printed spheroids, or cell-laden microcarriers in similar applications. This system has an ultra-fine feature size and a rapid scale-up.

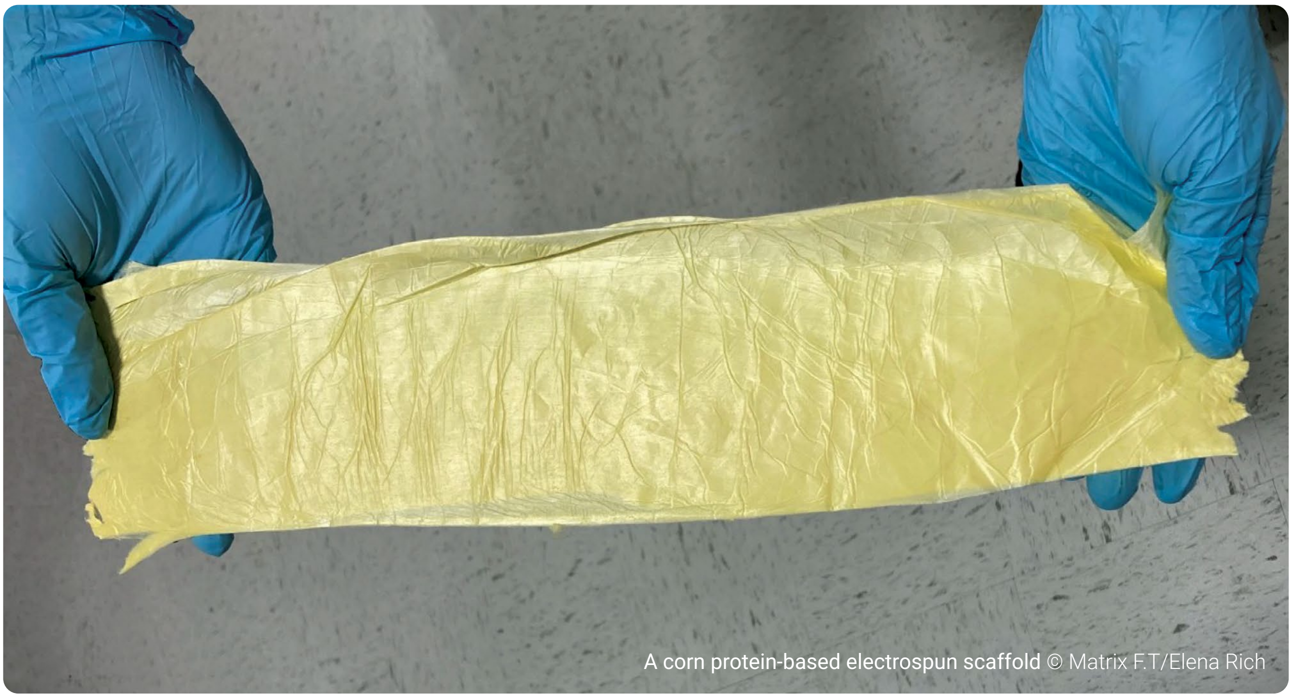
The surface is prepared for cell adhesion and can be made unique and specific for different user applications, for example, a more aligned cell structure is achieved in the scaffolding, while microcarriers are treated for optimal cellular attachment. Various applications can be considered for these products, and the specificity of each scaffold can be uniquely designed according to the desired final product. The research and development team are conducting advanced cell culture research to better optimize cell-based food production using scaffolds and cell characterization.

The company wants to comply with all the regulatory requirements and to ensure that all the materials they used are compliant. They regularly train their employees on GMP standards to ensure the GMPs are strictly followed. The company awaits more precise technical regulatory guidance.

Figure 16. Production processes of plant-based, edible nanofibre scaffolds



Source: Adapted from Coia, H. 2022. *Customized, plant-based, edible scaffolding and microcarriers for cultivated meat*. Presented at the Stakeholder roundtable meeting. Cell-based food and the future of food security and food safety. 7 September 2022. Tel Aviv.



A corn protein-based electrospun scaffold © Matrix F.T/Elena Rich

2.3. Communication strategies on food safety aspects of cell-based food

During the meeting, a special session on communication was organized by FAO. Unlike any other health-related topics, food is personal for almost all people. Talking about it in terms of pure science may not be the best strategy for effective communication concerning food safety. Culture, tradition, family and personal preferences play much bigger roles, and even the soundest science can only communicate a part of the story.

Communication about cell-based food is currently focused on the potential benefits the technology and the products may offer, such as food security, environmental sustainability and contributions to animal welfare. While such advantages are recognizable by many people, others may focus only on the strong novelty of the topic of cell-based food. When food is unfamiliar, communication about it is not straightforward, and the topic can be overwhelming and difficult to grasp. Providing scientific and technical information is not enough to bring an understanding of the big picture.

Basically, any food safety communication is a challenge because people usually want 100 percent safety to be assured when that is not realistically possible. There is always a certain level of risk in any food items and their production processes, and food safety efforts are there to minimize the risks, not to eliminate them. Risk communication, based on the foundation of the risk-based approach, is often considered too complex and vague because it is impossible to make a simple black-and-white statement. Our current digital era prefers concise and simple communication without complexity. Scientific communication almost always accommodates the need to explain the technical background, which is often complex. It is difficult to hold the public's attention long enough to get to the point of the key message, and people might draw ill-considered conclusions.

Some people will find cell-based food exciting and will be interested in the potential of the technology and products, while others will be extremely skeptical or frightened. Some may demand all the technical information available. With or without a basic understanding of the relevant science, people may request complete transparency with regard to technologies, methodologies, materials, equipment and ingredients used in all different types of production processes for different commodities. People may request all the safety assessment results with detailed laboratory data. At the same time, there could be a large group of people who demand a simple and short answer about whether or not cell-based food is safe to eat, wanting 100 percent certainty, which is impossible for any regulators to provide.

The session touched upon various communication methodologies and approaches based on a hypothetical case study to facilitate the discussion: Let's say you are teaming up with your government authorities to talk about the food safety aspects of cell-based food. The public is asking vague questions such as "Is cell-based food safe?" "How do we know it is safe to eat?" How do you strategize your communication plan? The following three key issues were the main discussion points of the session.

Transparency: Many participants suggested the importance of showing a readiness to disclose the necessary information, rather than communicating everything in detail from the start. For example, the initial communication can be prepared in a simple and short message, while technical and knowledge resources can be made available elsewhere (i.e. website) where people who want more detail can be referred.

Inclusiveness: Participants stressed the importance of having early-stage consultations with various stakeholders, especially with consumers. It serves to "test the water", and at the same time, it is a good opportunity to understand what people want to know, as well as to identify what people need to know from the regulatory standpoint.

Public-private collaboration on communication: Most of the participants noted that people from the cell-based food and its inputs industries in the private sector have first-hand knowledge and experience of technical matters in developing cell-based food. But, it is the regulators in the public sector who are the ones who understand the key elements and issues that need to be regulated and addressed to protect consumers. When it comes to a communication strategy on the safety of cell-based food, it makes sense to have the two sectors work together.

2.4. Discussion

The meeting provided an open and global dialogue on cell-based food and its inputs technologies, and participants found it useful. All presenters agreed that there is a strong need for clear guidance at both the international and national levels in terms of food safety assessments and assurances, as well as on the relevant regulatory requirements. They also stated that it would be useful to have a forum or a platform where regulators from various countries could meet and share their regulatory experiences regarding cell-based food, making their assessment results publicly available. Moreover, participants would like to see a specific contact point in each regulatory agency in various countries where cell-based food products could be produced so that industry people could consult on safety assurance, standards, regulatory compliance and monitoring issues. Nomenclature is one of the biggest issues and the participants would like to see a global effort led by an international organization like FAO to achieve harmonization in the terminology. The following is an informal list that participating stakeholders have made during the meeting.

- It would be helpful to collaborate with various regulators who can check the production process prior to the safety assessment dossier submission so that the production steps can be developed aligned with the regulatory requirements.
- It would be useful if the novel food regulatory standards including specific topics such as the safety of growth media, safety assessment on possible genetic drifts, etc., could be unified among countries.
- A clear regulatory pathway for the approval of growth factors to be used in food production will be extremely helpful.
- Many regulators in various countries are unaware of the need to make the regulatory route accessible, thus a global effort in awareness raising would be helpful.
- As this stakeholder meeting it was useful to have an opportunity to talk with the Israeli regulators who are open to discussion. FAO could coordinate more interactions among companies and regulators to share relevant experiences on safety assessments and the regulatory approval processes.
- The public is unaware of the full picture of cell-based food and its production, as well as the science behind it. Education programmes and awareness raising for the general public are needed.
- The topic of cell-based food should be discussed clearly and thoroughly, including the topics of sustainability, environment, use of resources, food safety, nutrition, etc., rather than discussing only one topic.
- FAO can help facilitate open discussions with regulators around the world to compile regulatory questions from the industry so that regulators can prepare their answers.
- A publication from FAO on the topic, including the report of the meeting, is useful for raising awareness.
- It will be useful for the industry to have more opportunities to discuss food safety issues with international organizations and regulatory agencies from various countries.
- An internationally developed technical guidance for safety assurance would be useful.
- Public and private partnerships are essential to creating a regulatory environment where innovation is supported while safety is assured.
- FAO should provide technical assistance to develop a roadmap of cell-based food production focusing on regulators in low- and middle-income countries, as they are likely to need a stepwise approach.
- Codex Alimentarius might be the right place to discuss the governance and standard-setting for cell-based food, but the current structure of Codex limits the possibility.
- Considering likely public criticisms on the novelty of cell-based food, which are often fueled by fear rather than substantiated by data, are there are opportunities for companies to work with regulators on something other than safety or other regulatory requirements? This could involve working together to better understand the root of mistrust that many groups of people (consumer groups, non-governmental organizations, etc.) feel for companies and regulators. It would be helpful to understand how behaviours, attitudes and preconceived notions differ geographically and how companies and regulators can work together to build greater consumer trust.

3. CONCLUSIONS

The stakeholder roundtable meeting on cell-based food provided the opportunity to establish contacts and build networks among participants from different backgrounds in industry, academia, government authorities and regulatory agencies. The presentations provided a wide overview of the 2022 state-of-the-art on this topic from the perspectives of developers and companies around the world. Moreover, it facilitated in-depth discussions specifically on food safety aspects of cell-based food. The special communication strategy session highlighted both the opportunities and challenges of communicating about the food safety aspect of cell-based food. Overall, the meeting provided a set of resource materials that presenters provided to facilitate a deeper understanding of the technical details of various production processes of different cell-based food products and their input production methodologies.

Asian style dish made with thin cell-based beef steak © FAO/Oded Antman

ANNEX 1. LIST OF PARTICIPANTS

Presenters

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- Arye Elfenbein, Wildtype, United States of America
- Orit Goldman, MeaTech3D, Israel
- Katariina Koivusaari, BIOMILQ, United States of America
- Dan Kozlovski, MeaTech3D, Israel
- Neta Lavon, Aleph Farms, Israel
- Amanda Leitolis, the Good Food Institute, Brazil
- Bibiana Matte, Ambi Realfood, Brazil
- Joe Mee, Roslin Technologies Ltd., the United Kingdom of Great Britain and Northern Ireland
- George Peppou, Vow, Australia
- Ning Xiang, CellX Ltd. Co., China
- Amit Yaari, BioBetter Ltd., Israel
- Ziliang Yang, CellX Ltd. Co., China
- Dana Yarden, BioBetter Ltd., Israel
- Ximing Zhang, Zhejiang University, China

Government of Israel representatives

The Prime Minister's Office

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- David Yamin, Legal Advisor to the Better Regulation Department

Ministry of Health

- Pnina Oren-Schneider, Director of the National Food Service
- Ruth Yishai, Director, Department of Laboratories, Public Health Services
- Noa Tejman-Yarden, Deputy Director Dep. of Laboratories, Public Health Services
- Yossi Sadeh, Chief Food Engineer, Food additives unit, National Food Service
- Shay Reicher, Head of Risk Assessment Section, the Risk Management Department, National Food Service
- Yogev Magen, Head of Novel Food Section, the Risk Management Department, National Food Service
- Joseph Haskin, Head of Food Contaminants Section, the Risk Management Department, National Food Service
- Avi salmon, District Manager of Food Control Service, Tel Aviv District
- Inbal Benari, Senior food inspector, Central District
- Ronit Endevelt, Head of the Nutrition Division
- Menashe Soffer, Official Government Veterinarian, Veterinary Unit
- Meirav Shtenzler, Director of the Food Service in the north district
- Shirly Drai-Last, District Manager of Food Control Service, Ashkelon District
- Naomi Fliss Isakov, Head of Nutrition Research, Nutrition Division
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- Dana Shakh, Head of the Microbiology Unit

Israel Innovation Authority

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- Alexander Meshoulam, Israel Innovation Authority
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Ministry of Innovation, Science and Technology

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