Food safety considerations for cultivated meat

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Accelerating the shift to a sustainable, healthy, and just food system through three key areas of work:

**Science and Technology**
Advancing and open-sourcing the foundational science of plant-based and cultivated meat

**Corporate Engagement**
Consulting with the world’s biggest food companies to help them capitalize on opportunities in the plant-based market

**Policy**
Advocating for fair regulation of plant-based and cultivated meat and lobbying for governmental investment in sustainable protein R&D

We act as a force multiplier, bringing the expertise of our departments to the rest of the world.

90+ staff in 6 countries

- UNITED STATES
- EUROPE
- BRAZIL
- ASIA PACIFIC
- ISRAEL
- INDIA
How will we feed 9.7 billion people by 2050?

Sustainably  Efficiently  Safely
Global land use for food production

- Earth’s surface: 29% land, 71% ocean
- Land surface: 71% habitable land, 10% glaciers, 19% barren land
- Habitable land: 50% agriculture, 37% forests, 11% shrub, 1% freshwater, 1% urban
- Agricultural land: 77% livestock, 23% crops
- Protein supply: 33% Meat & dairy, 67% Plant-based food

Adapted from OurWorldInData.org and based on UN FAO statistics
Animals are inefficient processors

9 ENERGY CALORIES = 1 FOOD CALORIE

11% CONVERTED
Intensive farming presents numerous risks

- 14.5% GLOBAL GREENHOUSE GAS EMISSIONS
- NO.1 USER OF FRESHWATER RESOURCES ON THE PLANET
- NO.1 CAUSE OF DEFORESTATION DUE TO CATTLE RANCHING AND SOY PRODUCTION
- MANURE & FERTILIZER RUNOFFS ARE CAUSING WIDESPREAD LAND & WATER POLLUTION
- NO.1 GLOBAL USER OF ANTIBIOTICS, INCLUDING SHARED-CLASS ANTIBIOTICS
- HEALTH HIGH RISK OF NON-COMMUNICABLE DISEASES & FOOD-BORNE ILLNESS
- LABOUR POOR VISIBILITY OF SUPPLY CHAINS
- WELFARE CLOSE CONFINEMENT AND MUTILATIONS

This slide is reproduced courtesy of the FAIRR initiative, a global investor network focused on risk and opportunity in protein supply chains. For more information please see www.fairr.org
... and yet, global meat demand shows no sign of slowing
Meat consumption is correlated with income

Source: UBS, The Food Revolution 2019
Meat made in a better way

<table>
<thead>
<tr>
<th>PLANT-BASED PROTEINS</th>
<th>FERMENTATION</th>
<th>ANIMAL CELL CULTURE</th>
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</thead>
</table>

- **PLANT-BASED PROTEINS**
- **FERMENTATION**
- **ANIMAL CELL CULTURE**
What is cultivated meat?

Cultivated meat is genuine animal meat that can replicate the sensory and nutritional profile of conventionally produced meat because it’s comprised of the same cell types arranged in the same three-dimensional structure as animal muscle tissue.
B2B Startups
Technology Type

- Bioreactor/Cultivator Design: MeaTech
- Scaffolding
- Cell Culture Media: biftek.co, multis media
- Cell Line Development: CUBIQ FOODS, CELL FARM

Note: For instances in which companies are pursuing various strategies, such as B2C and B2C, we categorized based on best-guess analysis of publicly available information.
Source: GFI Startup Database, Crunchbase, manufacturer websites

B2C Startups
Product Type

- Beef
- Chicken
- Pork
- Seafood
- Pet Food
- Other

Source: GFI Startup Database, Crunchbase, manufacturer websites
Cell-Based Meat Production at Scale
Outline

- Overview of process stages involved in cultivated meat manufacturing
  - Shared considerations across stages
  - Stage-specific considerations and testing

- Specific considerations
  - Antibiotics
  - Use of animal serum or other animal-sourced ingredients
    - Prions
  - Genetic modifications

- What this means for food safety
Different stages have different safety considerations

NOVEL FOODS FRAMEWORKS (many regions)

UNITED STATES FDA

USDA

STAGE 1: CELL LINE SELECTION & BANKING

STAGE 2: PROLIFERATION SCALE UP

STAGE 3: DIFFERENTIATION & MATURATION

STAGE 4: HARVEST

STAGE 5: PACKAGING

Food safety concerns are mostly product-focused, other considerations are process-focused

* Stages and considerations are hypothetical and could be viewed differently by different regulatory agencies
Some safety considerations are shared across multiple stages

Cell culture media may contain recombinant proteins and/or small molecules

Cells may produce substances at higher levels than in an intact animal

Risk of contamination from adventitious agents (i.e. viruses, pathogens)

Testing of new cells

Process monitoring

Testing

Residue testing

Allergenicity and/or residue testing

* Stages and considerations are hypothetical and could be viewed differently by different regulatory agencies
Priority Stage 1 safety considerations

**STAGE 1: CELL LINE SELECTION & BANKING**

1. Procure cells from healthy animals
2. Validation of cell identity
3. Test for adventitious agents (i.e. viruses, pathogens)
4. Genome modifications
5. Small molecules & recombinant proteins in media

**Relevant Guidelines**

- US FDA: [Points to consider in the characterization of cell lines to produce biologicals](https://www.fda.gov)
- US FDA: [Characterization & Qualification of Cell Substrates & Other Biological Materials Used in the Production of Viral Vaccines for Infectious Disease Indications](https://www.fda.gov)
- US FDA: [Guidance for industry: enzyme preparations](https://www.fda.gov)
- EMA ICH Q5D: [Quality of Biotechnological Productions](https://www.ema.europa.eu)
- Barone et al (2020). *Viral contamination in biologic manufacture and implications for emerging therapies*
- Gombold et al (2014). *Systematic evaluation of in vitro and in vivo adventitious virus assays for the detection of viral contamination of cell banks and biological products*

**Relevant Testing**

- **Adventitious Agents**: PCR and PERT assays, immune-based assays*
- **Cell Identity**: STR profiling*, COI gene assays*, immune-based assays
- **Media substances**: Tested at Stage 4
- **Genome modification**: discussed later

*some tests may need to be developed for species used in cultivated meat
Priority Stage 2 safety considerations

STAGE 2: PROLIFERATION SCALE UP

1. Process monitoring for adventitious agent contamination
2. Small molecule & recombinant proteins in media
3. Potential harmful substances produced by cells

Relevant Guidelines

- US FDA: Validation of cleaning process 7/93
- US FDA: Guidance for industry: enzyme preparations
- Barone et al (2020). Viral contamination in biologic manufacture and implications for emerging therapies

Relevant Testing

- **Adventitious Agents**: Routine process monitoring, cleaning, and sterilization (discussed in antibiotics review)
- **Media substances**: Tested at Stage 4
- **Harmful substances**: Tested at Stage 4
Priority Stage 3 safety considerations

STAGE 3: DIFFERENTIATION & MATURATION

1. Process monitoring for adventitious agent contamination
2. Small molecule & recombinant proteins in media
3. Potential harmful substances produced by cells
4. Food-safe scaffold materials

Relevant Guidelines

US FDA: Validation of cleaning process 7/93
US FDA: Guidance for industry: enzyme preparations
Barone et al (2020). Viral contamination in biologic manufacture and implications for emerging therapies

Relevant Testing

Adventitious Agents: Routine process monitoring, cleaning, and sterilization (discussed in antibiotics review)

Media and scaffold substances: Tested at Stage 4

Harmful substances: Tested at Stage 4
Priority Stage 4 safety considerations

STAGE 4: HARVEST

1. Contamination of adventitious agents
2. Validation of cell identity
3. Small molecule & recombinant proteins in media
4. Potential harmful substances produced by cells
5. Food-safe scaffold materials

Relevant Guidelines

US FDA: Validation of cleaning process 7/93
US FDA: Guidance for industry: enzyme preparations
EFSA: Scientific opinion on the evaluation of allergenic foods and food ingredients for labelling purposes
US FDA: Guidance for industry: enzyme preparations
EMA ICH Q5D: Quality of Biotechnological Productions
USDA: Residue sampling, testing, and other verification procedures under the national residue program for meat and poultry products
Barone et al (2020). Viral contamination in biologic manufacture and implications for emerging therapies

Relevant Testing

Adventitious Agents: PCR assays, PERT assays, immune-based assays
Cell Identity: STR profiling, COI gene assays
Media substances: Allergy testing (database analysis, IgE serum challenges, enzyme digestibility), Residue testing*

*may require new safety data for specific proteins/small molecules
Priority Stage 5 safety and nutrition considerations

Relevant Guidelines

US FDA: Animal cloning: a risk assessment

US FDA GRAS Notices #313 “Beef protein” and #168 “Poultry protein”

EFSA Novel Food Guidance: some aspects on in vitro meat

Rudenko et al (2007). Animal cloning and the FDA—the risk assessment paradigm under public scrutiny

Relevant Testing

Nutritional composition: ash, moisture, fat, protein, and others as needed

Shelf life: microbiological and physicochemical testing (e.g. TBARS)

STAGE 5: PACKAGING

1. Comparative nutritional analyses of end products
2. Proposed uses and use levels
3. Shelf-life characteristics
How is contamination prevented or detected?

1. Preparation and sterilization of media components in separate vessels
2. Filtration or sterilization at medium and gas inlets/outlets
3. Positive pressure maintained in vessel
4. Adherence to common “good manufacturing practices”
5. Process monitoring: changes in oxygen use, pH, or density measurements can indicate a contamination event

Entire industries rely on these methods to deter contamination and eliminate antibiotics use
Will antibiotics be used?

Contamination is always a risk, but prophylactic antibodies are not the solution. Why?

1. Robust systems of prevention exist
2. Antibiotic use at scale is expensive!
3. Antibiotics can be detrimental to the viability of cell cultures
4. Misaligned with goals of the industry

When might antibiotics be used?

1. To prevent contamination and the loss of precious tissues at Stage 1
The use of animal serum

- Serum is variable by region & batch, a potential contamination source, misaligned with animal welfare, **an economic non-starter.**

- 6 companies have **already declared** themselves serum-free and all have stated they would never sell a product using serum

> "We in fact are now using growth media without any FBS, or any other animal products." - Mosa Meat, Nov. 2019
The use of animal serum

- FBS prices have increased nearly 300% in recent years
- FBS profits go to the slaughterhouse, not the farmer → no incentive to increase herd size to match FBS demand
- Cultivated meat will accelerate serum-free innovation

“Peak Serum”

Brindley et al. 2012
The use of animal serum and consideration of prions

When might serum be used?

1. To assist in the growth of new cell lines at Stage 1 that have no documented methods for handling -- serum works well for this purpose

2. For previous reasons stated, it will be highly discouraged

If serum is used, are prions a threat?

1. Prions are the causative agents behind transmissible spongiform encephalopathies (TSEs), documented in cows, sheep, goats, elk, deer, cats, and mink.

2. Prions are primarily found in the brain and central nervous system (not in serum or tissues to be used by the industry)

3. Majority of FBS comes from regions with no previous history of prions

4. There is a preponderance of evidence suggesting TSEs cannot be transmitted by blood (WHO Guidelines on Tissue Infectivity Distribution in TSEs, 2006)
The use of genome modification

1. Cultivated meat production does not require genome modification, but it could improve the efficiency and/or productivity of the process, the nutritional characteristics of a product, or how a product is marketed (i.e. by removing an allergen)

2. Some patents filed to date by cultivated meat companies describe various genome modifications to cell lines

3. Regulations have not kept pace with scientific advancement. Recent regulations in plant crops have focused on the final attributes rather than the methods.

4. A similar approach would make it likely for gene edits and some other forms of modifications permissible or permissible on a case-by-case basis
Implications for food safety and food externalities

- Cultivated meat will not contain harmful enteric food pathogens (E. coli, salmonella) and is likely to have lower incidence of foodborne illness

- Cultivated products may have longer shelf lives and reduced spoilage

  “Left at room temperature the conventional meats were completely spoiled in less than 48 hours; after four days, the lab-grown meats had barely decomposed because there was no trace of bacteria”
  - Uma Valeti of Memphis Meats describes initial testing

- Cultivated seafood will not contain mercury or microplastics

- Cultivated products have several food safety-related advantages compared to conventional meats
Conclusions

- We expect **cell culture technology** to enable the production of **high-quality cultivated meat and seafood** without posing risks that cannot be **managed effectively** through the use of well understood and established controls by responsible producers.
- The **core technology** for cultivated meat production is well understood.
- **Cellular events** unique to cultivated meat can be characterized and assessed with **existing, well established tests**.
- **Documented guidelines and tests** exist that can be applied to cultivated meat to **identify and characterize potential hazards and assess risks**.
- A balance of **science- and risk-based regulatory approaches** can ensure consumer safety for new products while not being overly burdensome to companies.