

Food safety considerations for cultivated meat

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The Good Food Institute

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.



UNITED STATES
BRAZIL
ISRAEL

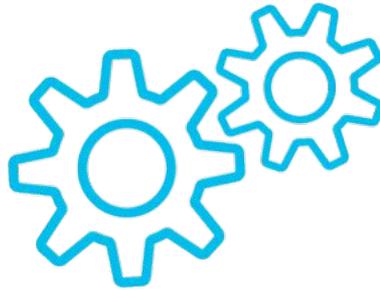
EUROPE
ASIA PACIFIC
INDIA

90+ staff in 6 countries

How will we feed 9.7 billion people by 2050?



Sustainably

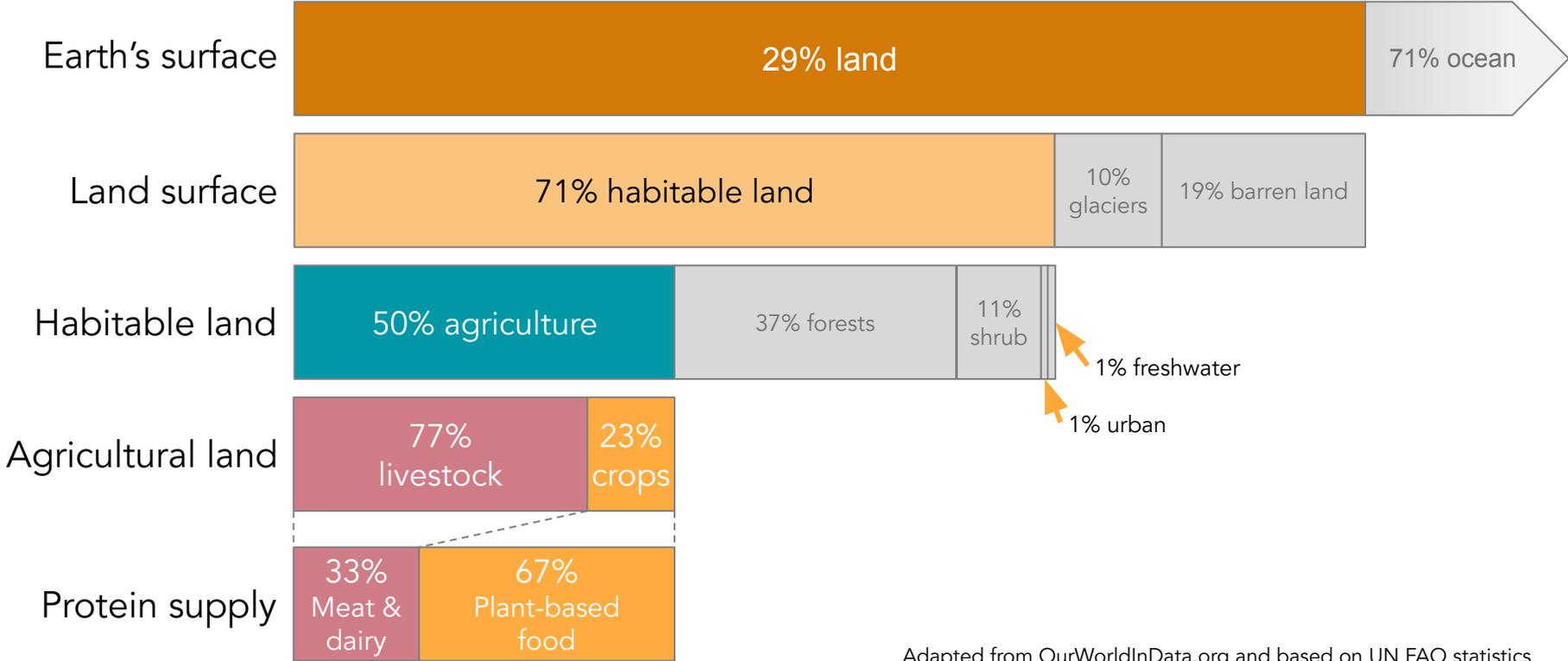


Efficiently



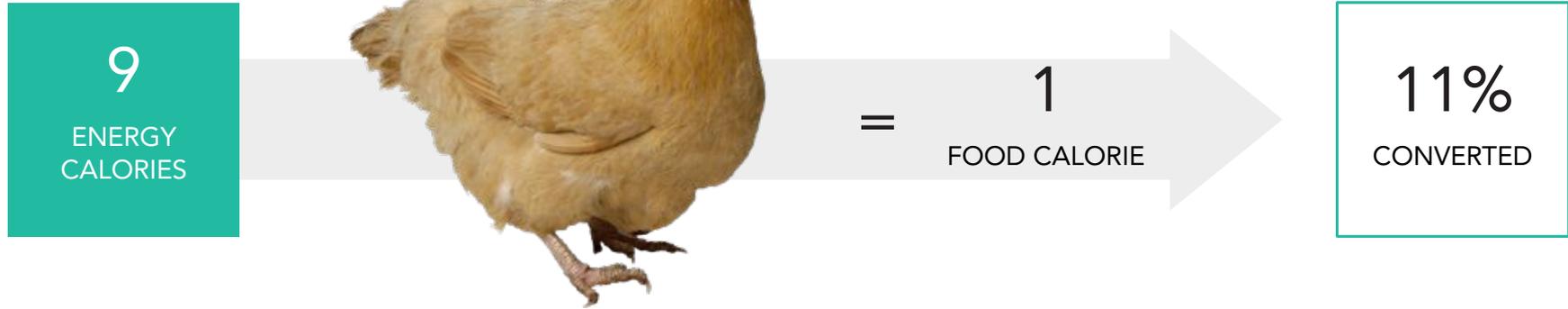
Safely

Global land use for food production



Adapted from OurWorldInData.org and based on UN FAO statistics

Animals are inefficient processors





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



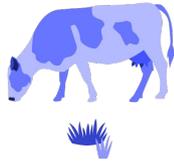
HEALTH

HIGH RISK OF NON-COMMUNICABLE DISEASES & FOOD-BORNE ILLNESS



LABOUR

POOR VISIBILITY OF SUPPLY CHAINS

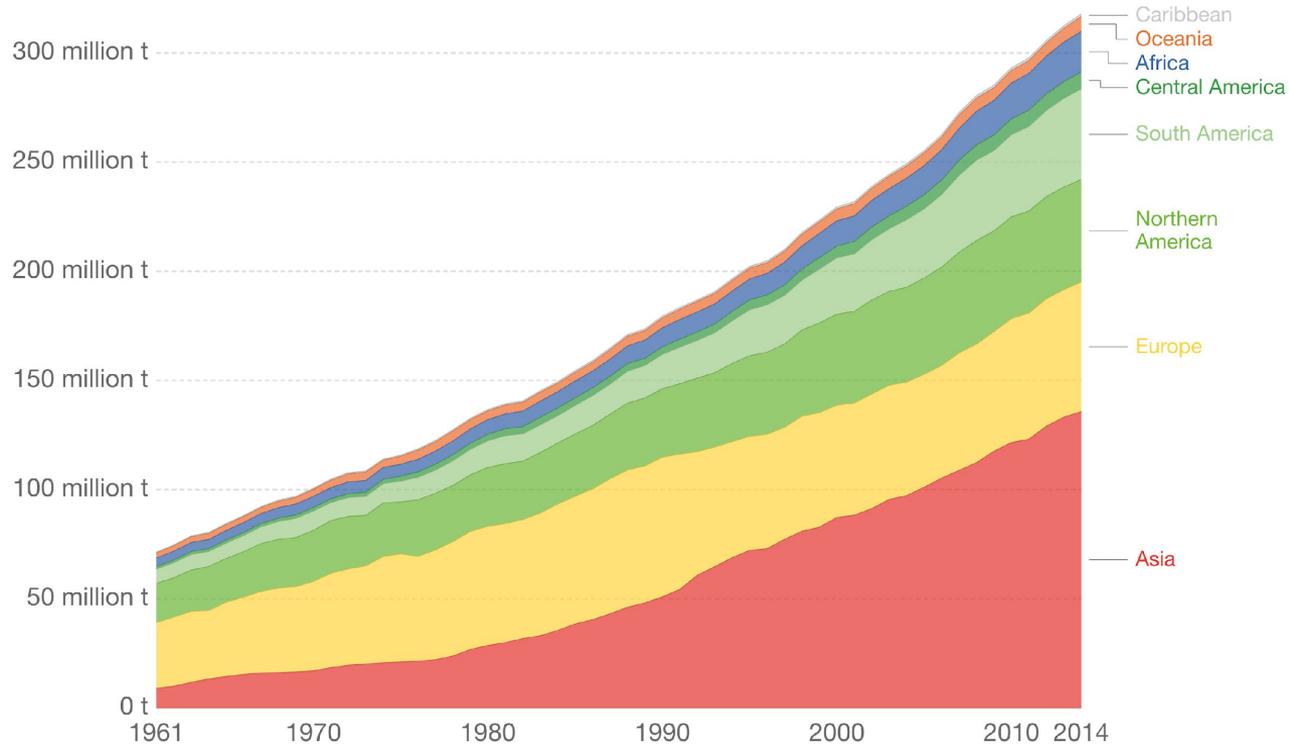


WELFARE

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

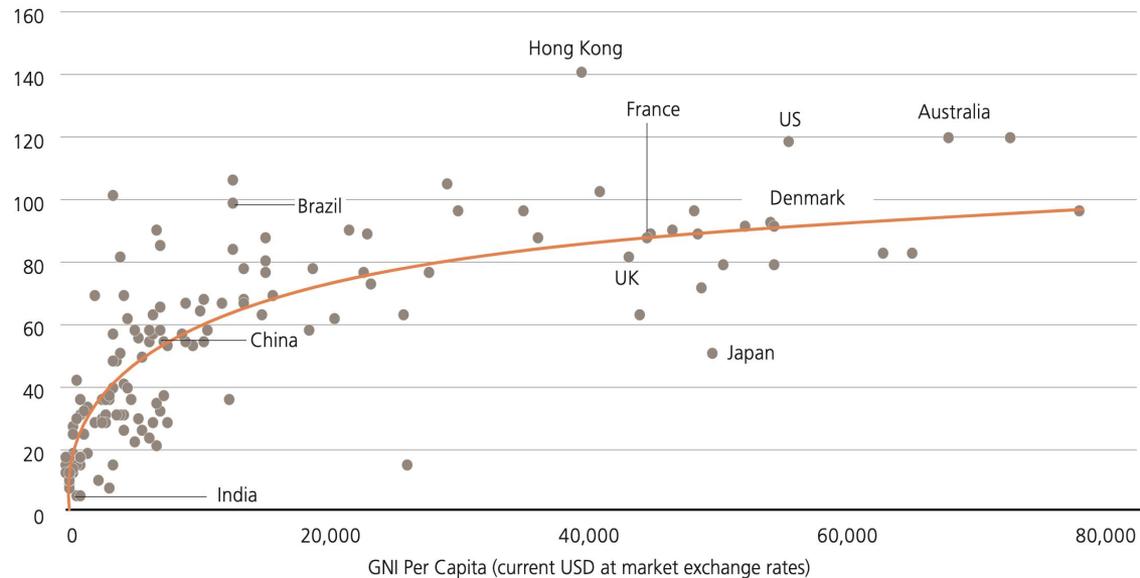
... and yet, global meat demand shows no sign of slowing



Meat consumption is correlated with income

Per capita meat consumption

In kg/year



Meat made in a better way

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

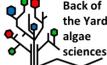
Technology Type

Bioreactor/
Cultivator Design  **MeaTech**

Scaffolding  **Biomimetic**
SOLUTIONS

Cell Culture Media  **biftek.co**
beef tech!

 **Heuros**  **AGULOS**
BIOTECH

 **FUTURE FIELDS**  **Back of the Yards**
algae sciences

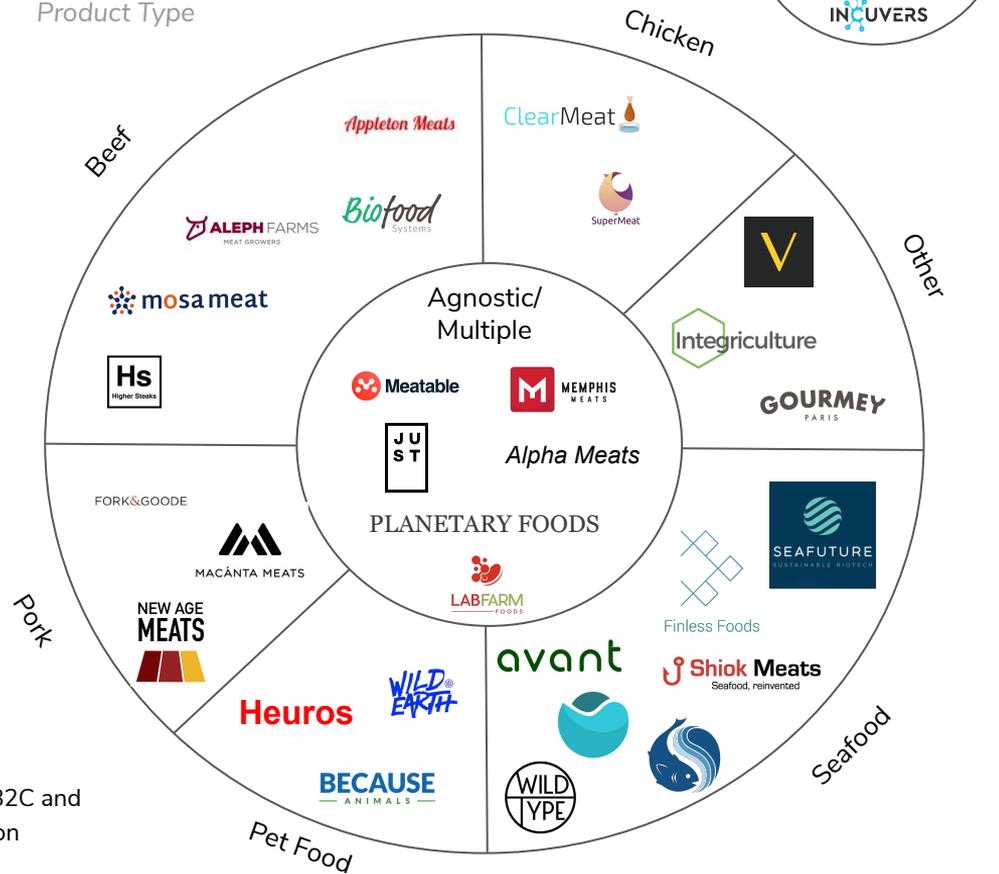
Cell Line Development  **CELL FARM**
Food Tech

 **CUBIQ**
FOODS
Smart fat solutions

 **MISSION**
BARNES

B2C Startups

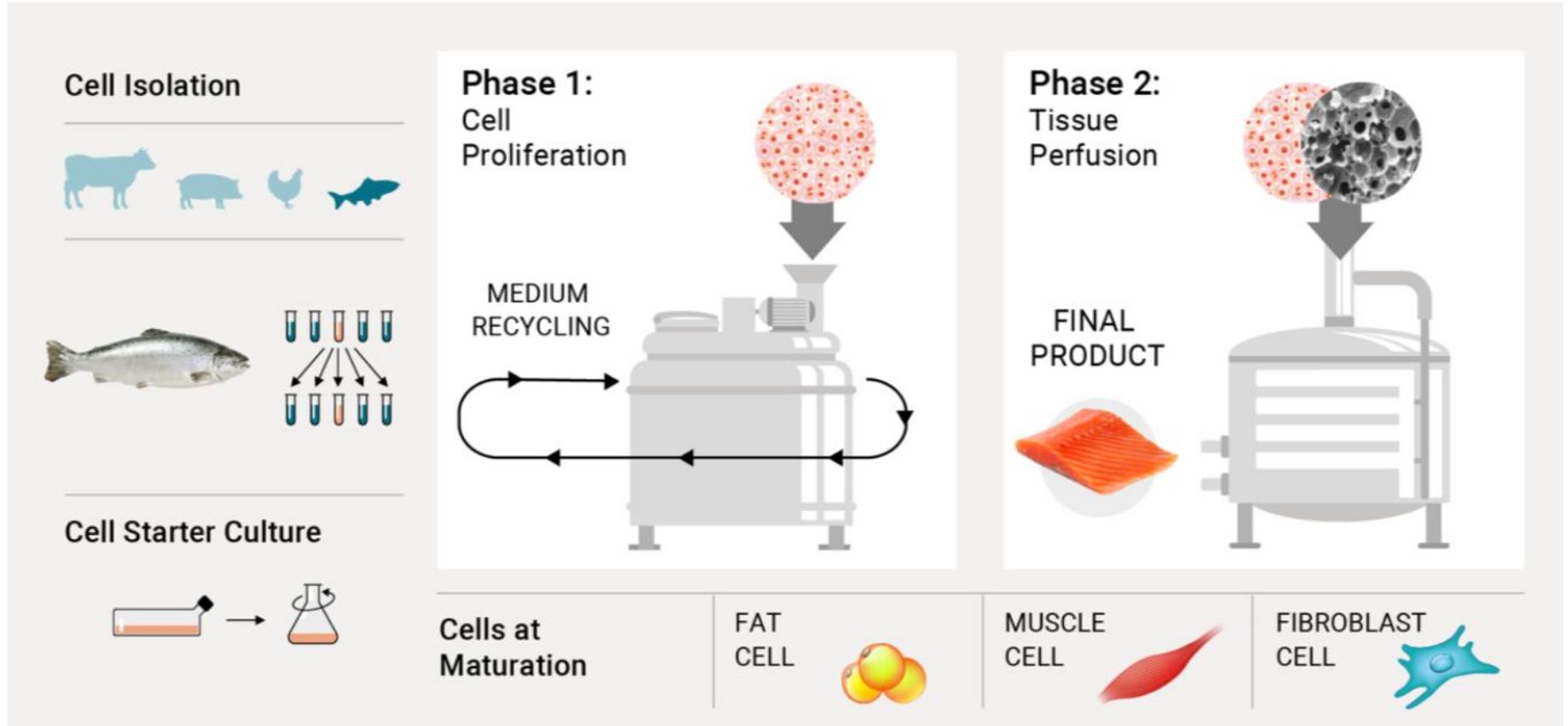
Product Type



Note: For instances in which companies are pursuing various strategies, such as B2C and B2B, we categorized based on best-guess analysis of publicly available information

Source: GFI Startup Database, Crunchbase, manufacturer websites

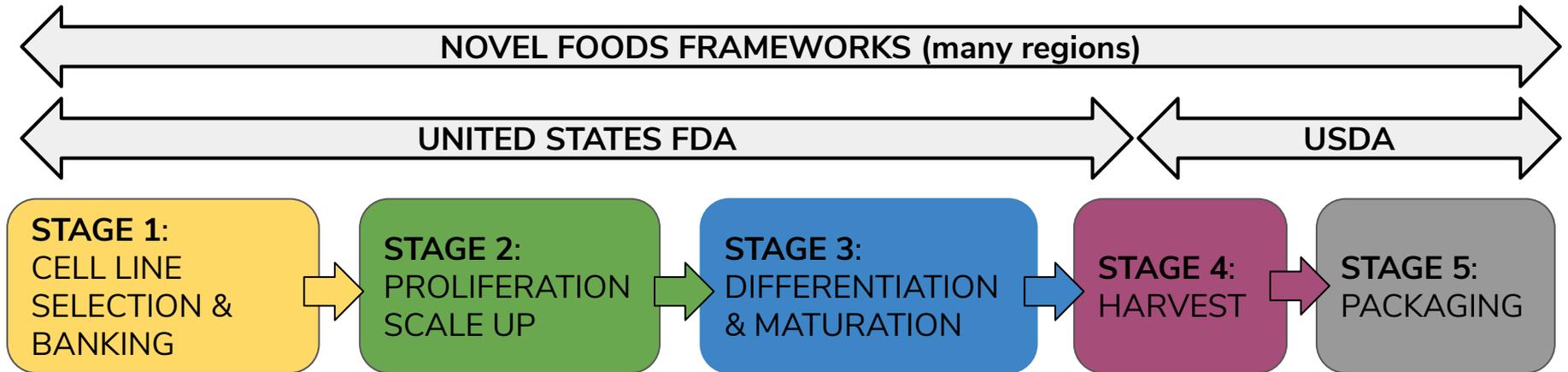
Cell-Based Meat Production at Scale



Outline

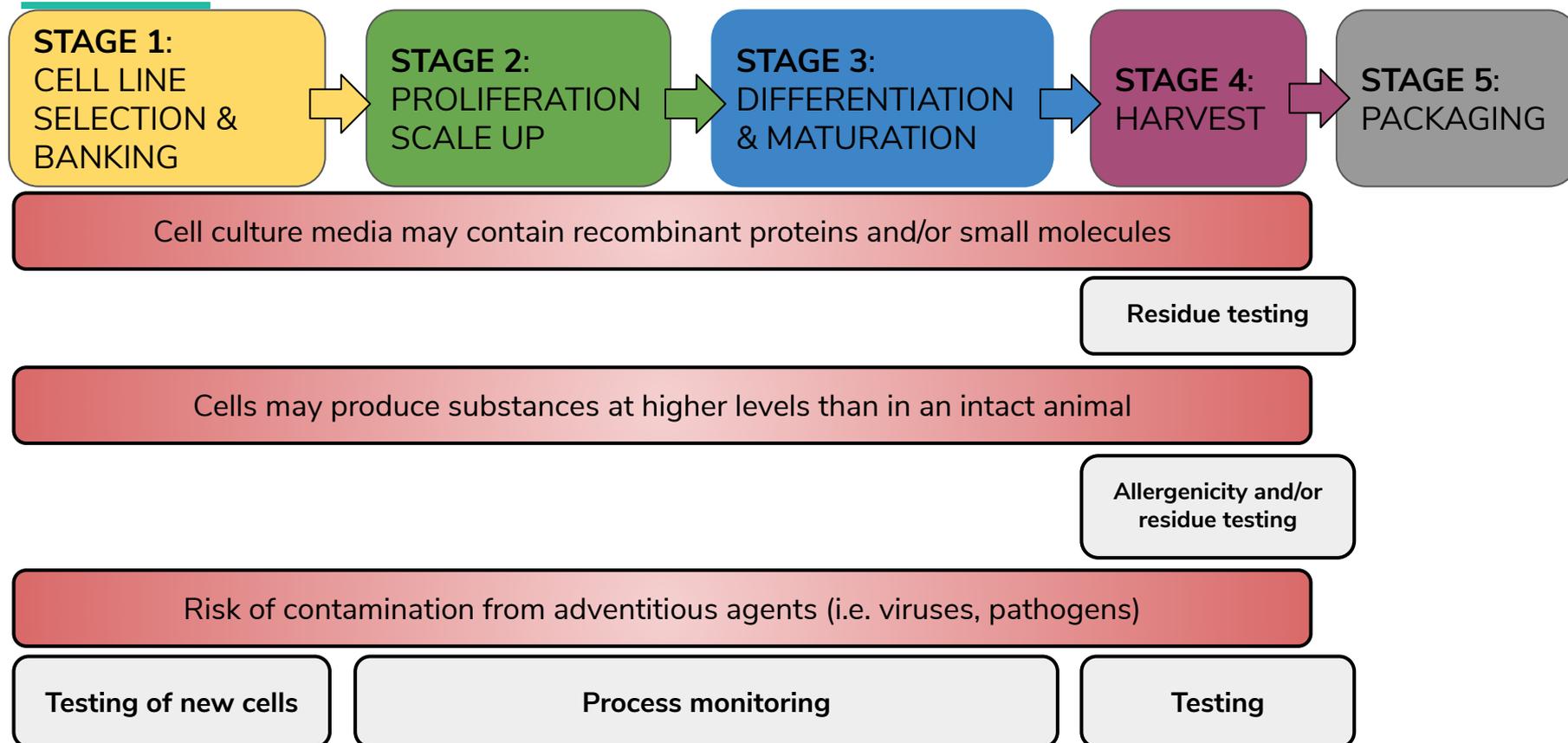
- Overview of process stages involved in cultivated meat manufacturing
 - Shared considerations across stages
 - Stage-specific considerations and testing
- Specific considerations
 - Antibiotics
 - Use of animal serum or other animal-sourced ingredients
 - Prions
 - Genetic modifications
- What this means for food safety

Different stages have different safety considerations



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

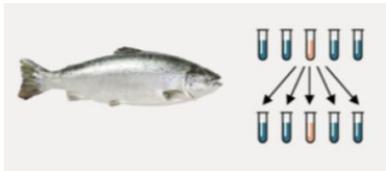
Some safety considerations are shared across multiple stages



* 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](#)

US FDA: [Characterization & Qualification of Cell Substrates & Other Biological Materials Used in the Production of Viral Vaccines for Infectious Disease Indications](#)

US FDA: [Guidance for industry: enzyme preparations](#)

EMA ICH Q5D: [Quality of Biotechnological Productions](#)

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

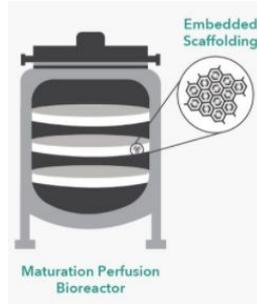
Adventitious Agents: Routine process monitoring, cleaning, and sterilization (discussed in antibiotics review)

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

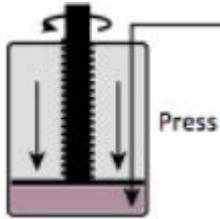
Adventitious Agents: Routine process monitoring, cleaning, and sterilization (discussed in antibiotics review)

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](#)

Mazzuchelli et al (2018). [Current food allergenic risk assessment: Is it fit for novel foods?](#)

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

STAGE 5: PACKAGING



1. Comparative nutritional analyses of end products
2. Proposed uses and use levels
3. Shelf-life characteristics

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](#)

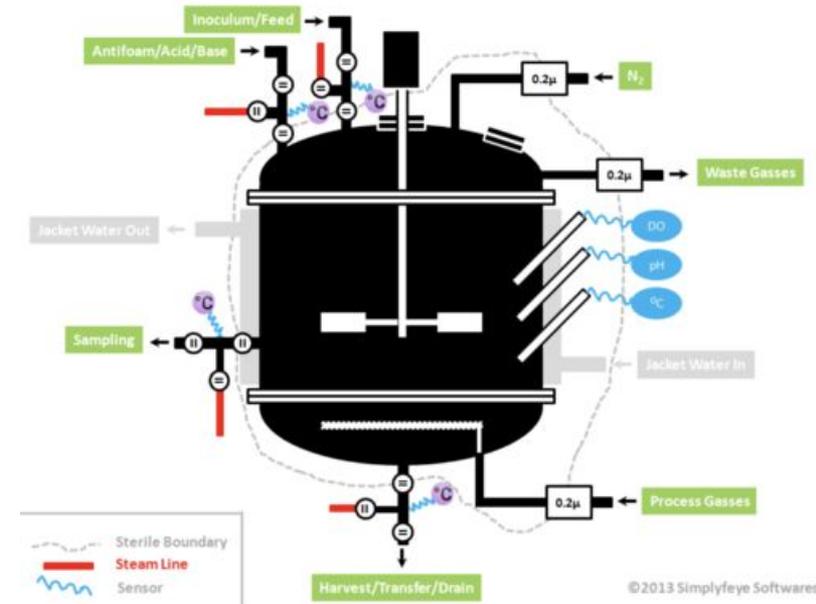
Relevant Testing

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

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

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 antibiotics 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

FBS contains growth factors, hormones, and other molecules that aid cellular proliferation

The use of animal serum

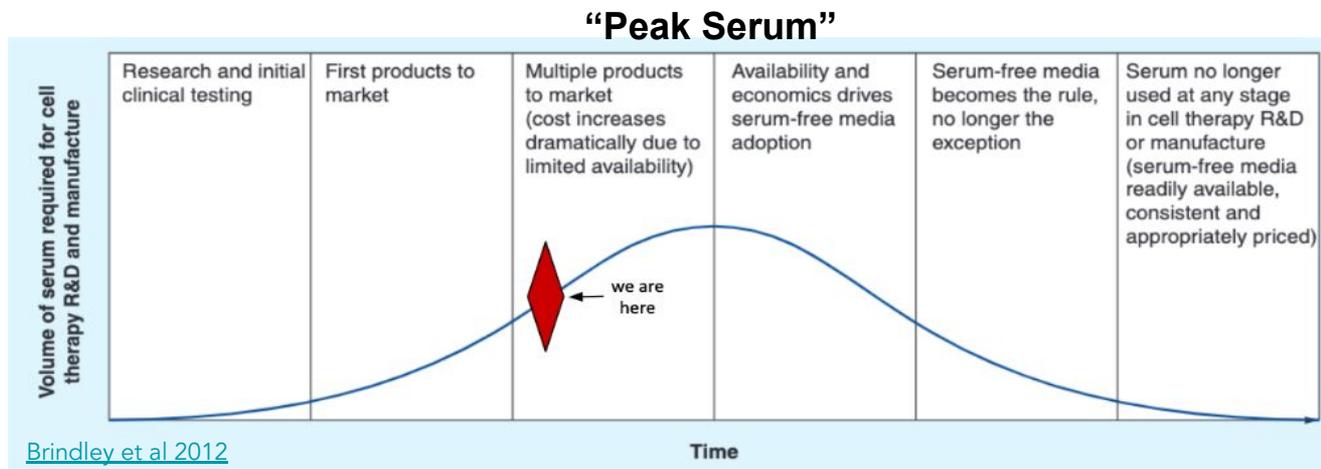
- Serum is variable by region & batch, a potential contamination source, misaligned with animal welfare, **an economic non-starter.**
- 6 companies have [already declared](#) themselves serum-free and all have stated they would never sell a product using serum

"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



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

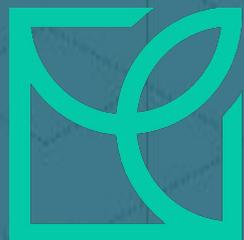
“Left at room temperature the conventional meats were completely spoiled in less than 48 hours; after four days, the lab-grown meats had barely decomposed because there was no trace of bacteria”

-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.



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