U.S. FOOD & DRUG ADMINISTRATION

Food Products Incorporating Cultured Animal Cells

Regulatory Perspectives

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Overview of Agenda

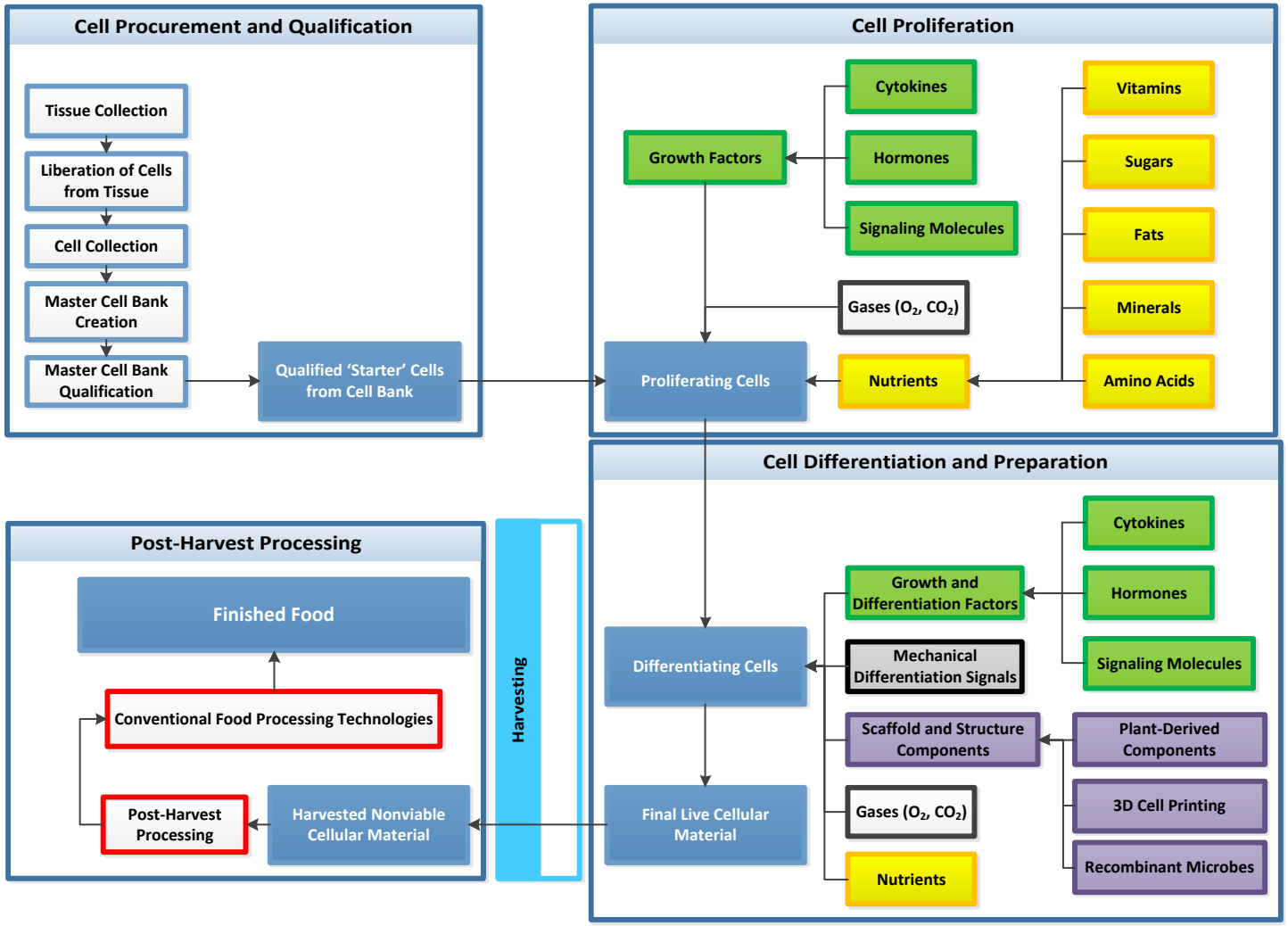
- Animal Cell Culture Overview
- Overview of Joint Framework
- FDA Experience
- Next Steps

Animal cell culture food technology refers to the controlled growth of animal cells from livestock, poultry, fish, or other animals, their subsequent differentiation into various cell types, and their collection and processing into food

Development of Animal Cell Culture Technology

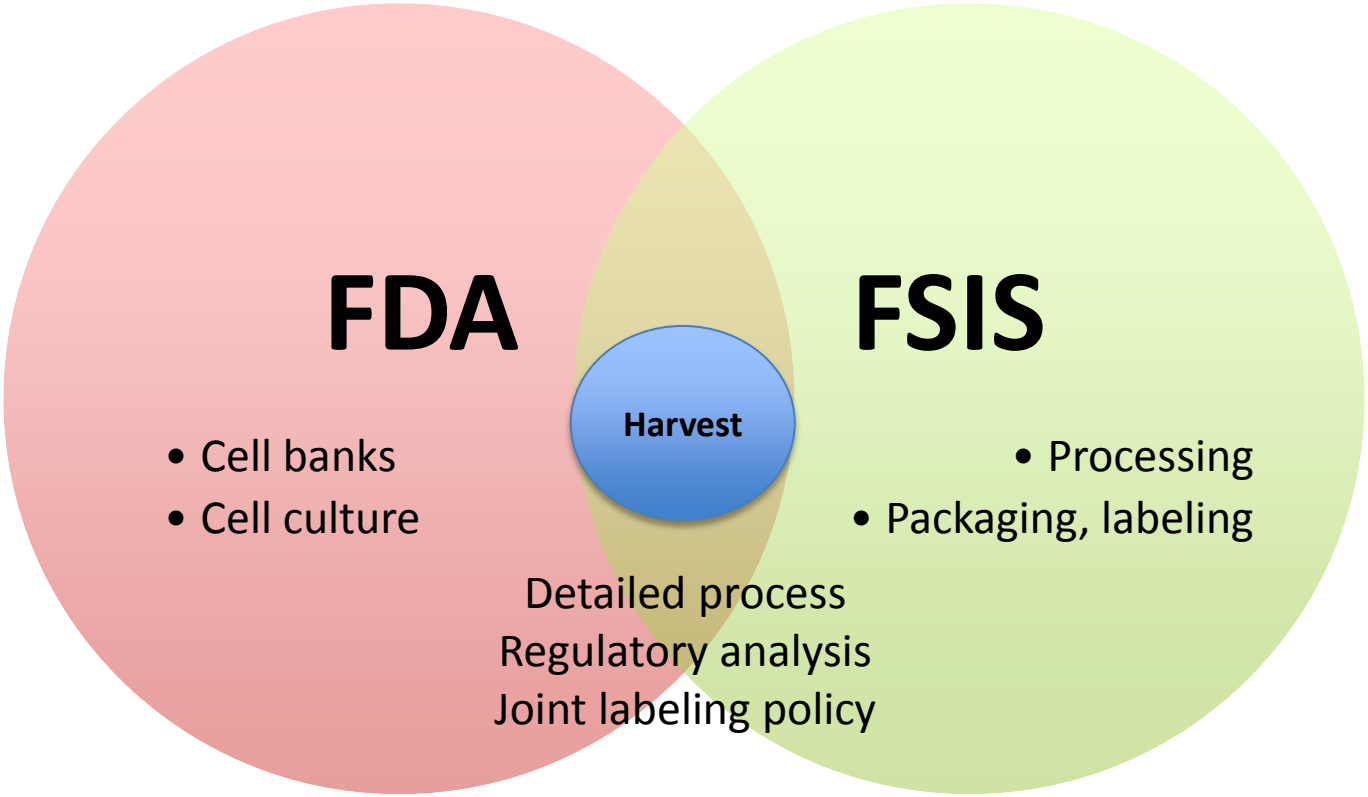
- Research tool
  - Growing animal cells to study basic biology
  - Moving from specialized cells to tissues
- Therapeutic application
  - Production of protein biologics
  - Clinical use of single cells, tissues, and organs
- Food production
  - Tools/methods from therapeutics currently available
  - Challenges remain in scaling production technologies

Overview of Animal Cell Culture Technology



Animal Cell Culture Overview

Joint Framework – Roles and Responsibilities



Overview of Joint Framework

Joint Framework – FDA Roles and Responsibilities

- Conduct premarket assessments for cell culture processes
- Oversee
  - Cell collection
  - Cell bank maintenance
  - Cell proliferation and differentiation
- Conduct inspections and enforcement activities to ensure cell bank and culture facilities are in compliance with FFDCA requirements
- Oversee
  - post-harvest safety of products incorporating cultured fish and seafood cells (except Siluriformes)
  - labeling of products incorporating cultured fish and fishery product cells (except Siluriformes)

Overview of Joint Framework

Joint Framework – USDA Roles and Responsibilities

- To require establishments that harvest and/or process cultured livestock and poultry cells to obtain a grant of inspection
- To conduct inspection in such establishments to ensure that products are safe, wholesome, and properly labeled, as well as
- To require preapproval and verification for labeling of these products

Overview of Joint Framework

Joint Framework – Shared Roles and Responsibilities

- Develop more detailed joint framework for oversight transfer at harvest for cells from amenable species
- Develop coordinated labeling policy to ensure consistent labeling of all foods incorporating cultured animal cells
- Jointly assess future regulatory/statutory needs
- Collaborate on investigation of any food safety issues

Overview of Joint Framework

FDA's Regulatory Framework and Relevant Experiences

- Regulatory approach for food/food ingredients
- Relevant experiences in foods
- Relevant experiences in therapeutics

FDA Experience

Systems-Based Oversight and Mandatory Food Safety Plans

- Hazard analysis
  - Known or reasonably foreseeable
  - Biological, chemical, physical hazards
- Preventive controls
  - Process, allergen, sanitation, other as needed
- Oversight and management of controls
  - Monitoring, correction, corrective action, verification
- Supply chain program
  - If needed based on hazard analysis
- Recall plan

FDA Experience

Food Additives

Any substance the intended use of which

results or may reasonably be expected to result

in its becoming a component

or otherwise affecting the characteristic of any food

including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting or holding food

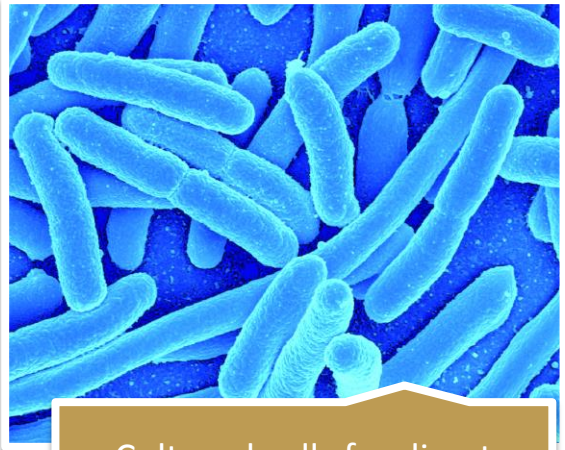
FDA Experience

Reasonable Certainty of No Harm

FDA Experience

Examples from Past Experience

Substances produced by cultured cells

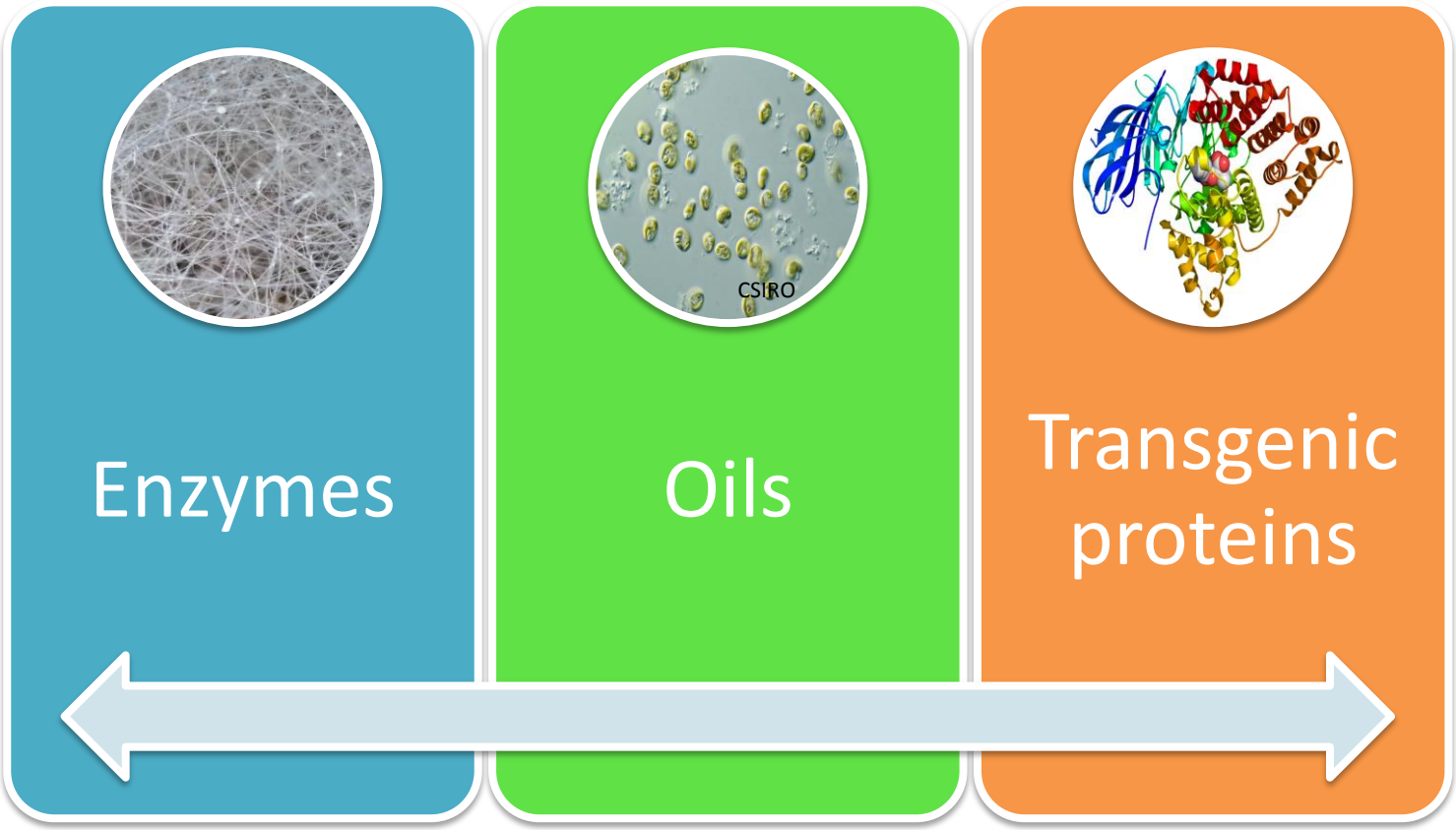


Cultured cells for direct consumption

New plant varieties produced by modern biotechnology

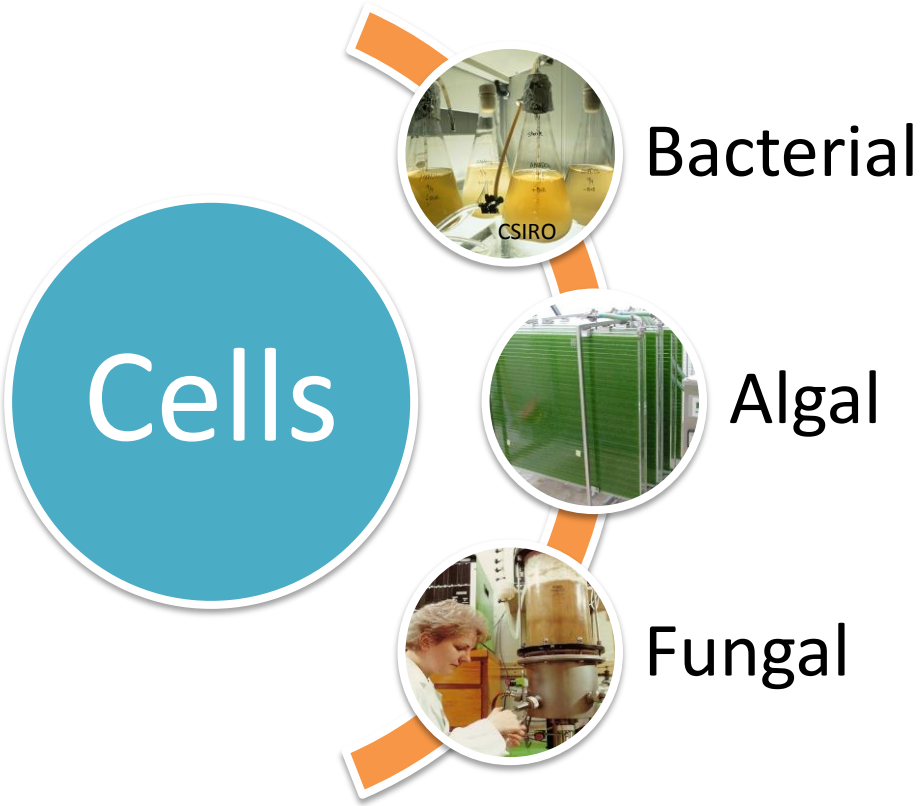
FDA Experience

Substances Produced by Cultured Cells



FDA Experience

Cultured Cells Evaluated as Direct Food Ingredients



FDA Experience

New Plant Varieties Produced Using Modern Biotechnology

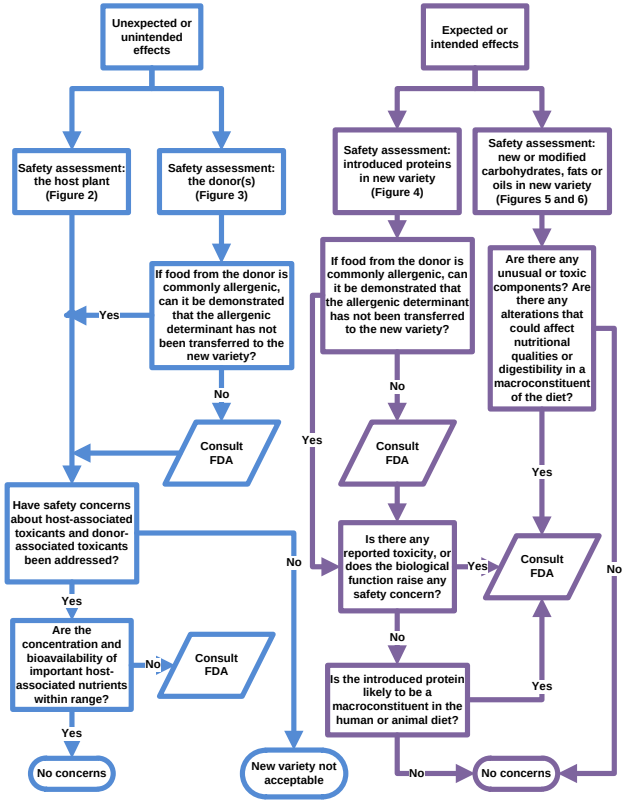


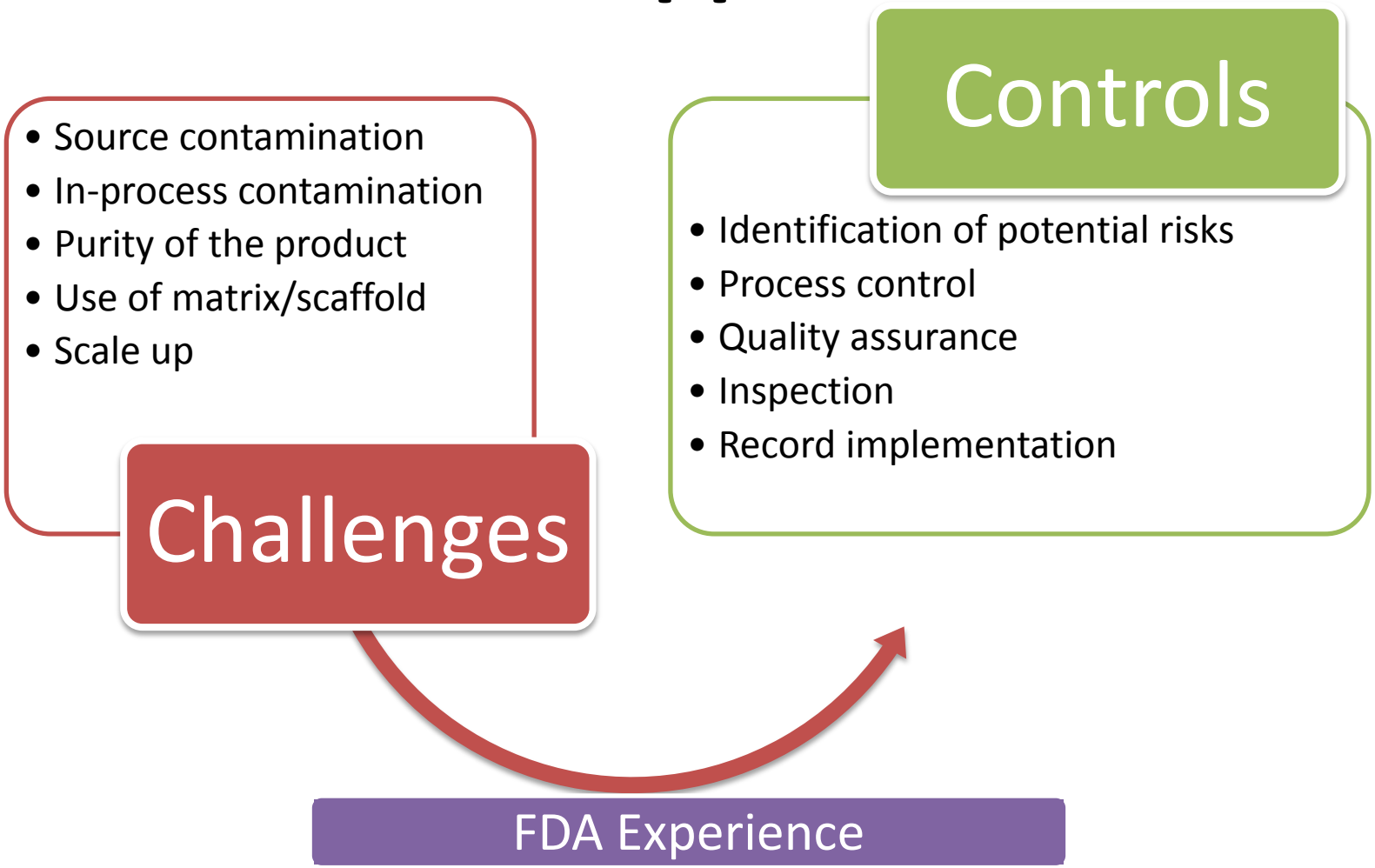
Figure 1. Safety Assessment of New Varieties: Summary

FDA Experience

Current Uses of Cell Culture in Clinical Application

- Cells as a source of production for
  - Recombinant proteins
  - Viruses
  - Vaccines
- Cells as therapies
- Cells that are genetically modified (*ex vivo* modified cells)
- Cells that are grown in materials/scaffolding

Risk-Based Control in Clinical Applications



Observations from Past Experience

- Biological production systems can be complex
- Questions about consistency and control of outcomes often arise during the safety evaluation
- These questions can be successfully addressed during the safety evaluation process prior to market entry
- Risk-based preventive controls can be used to ensure that the process generates safe products

FDA Premarket Assessment

- FDA will develop a premarket assessment process for cellular material production processes to ensure that no issues arise under FFDCA Section 402 or 409
- Includes evaluation of inputs including cells, medium components, scaffolding, as well as properties of pre-harvest cellular material
- Identification of unresolved 409 or 402 issues could render food unlawful
- Also expect to assess facility food safety plans

Next Steps

FDA Verification and Enforcement

- Establishments that conduct cell banking, cell proliferation and differentiation, and cell harvest activities will be required to comply with current GMP and preventive control requirements for food production facilities
- Once a facility is in production, FDA will conduct routine inspections of establishments that conduct preharvest and harvest activities
  - The food safety plan evaluation will guide inspections
  - Ongoing documentation of controls will be required
  - Batch records will be important
  - Records will include information relevant to safety, which we expect to include material inputs, cell sources and qualification, adventitious agent testing, and characterization of cellular material at harvest

Joint Framework – USDA Roles and Responsibilities

- Require establishments that harvest and/or process cultured livestock and poultry cells to obtain a grant of inspection
- Conduct inspection in such establishments to ensure that products are safe, wholesome, and properly labeled, and
- Require preapproval and verification for labeling of such products

Next Steps

FDA's Next Steps

- Develop, in consultation with FSIS
  - a general and systematic assessment for this food production technology to the point of harvest that will support individual premarket assessments.
  - draft guidance on preparing for and participating in premarket assessments for cellular material production processes, and on how manufacturers can ensure that their processes and products are in compliance with the applicable requirements of the FFDCA
- We will seek public comment and other forms of stakeholder input on these documents
- FDA and FSIS also expect to develop more detailed procedures to facilitate coordination of our shared regulatory oversight for cultured cells from amenable species

Next Steps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