

Perspective from the USDA-CVB Future Directions

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Animal and Plant Health Inspection Service
Veterinary Services
Center for Veterinary Biologics



Purpose and Intent of Engagement



Purpose: *Obtain public input as CVB aims to develop practical, science-based guidance*

Guidance: *Clarify risk-based practices to minimize contamination from EA*

Engagement: *Public engagement to ensure guidance is practical and adaptable to real-world scenarios while ensuring standards for purity are met*

Global Supply Chain Considerations: *Guidance addresses diverse material origins; promotes internationally harmonized approaches to contamination control*

Framework Overview: 4 Material Groups

Master Seeds and Cell Stocks

MS and MCS are foundational biological systems with the highest impact on product safety and quality, requiring thorough risk characterization.

Ingredients of Animal Origin

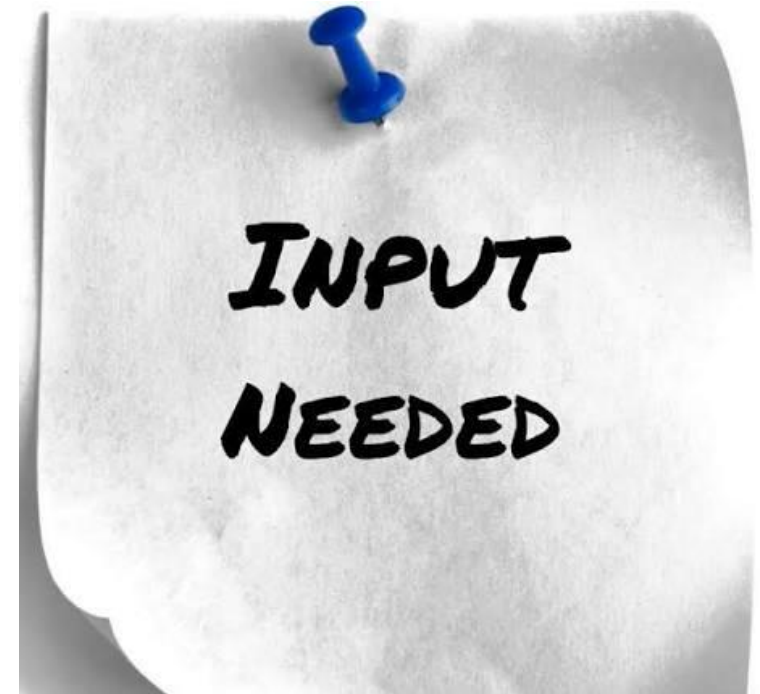
IAO materials like serum and tissues carry higher extraneous agent risks, needing supplier qualification and contamination prevention.

Non-Ingredients of Animal Origin

Non-IAO materials contain no animal components or exposure, posing lowest risk managed by foundational quality practices.

Non-IAO Exposed to IAO

Non-IAO materials exposed to animal-derived substances during processing require documentation, exposure tracing, and decontamination.



Framework Overview: International Standards



International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medical Products (VICH)

Draft VICH GL60: GMP for active ingredients used in veterinary medicinal products—Scientific guideline



ICH Q5A(R2): Guidelines on viral safety evaluation of biotechnology products derived from cell lines of human or animal origin—Scientific guideline



**World Organisation
for Animal Health**

WOAH Manual of Diagnostic Tests and Vaccines for Terrestrial Animals



EU Pharmacopoeia: 5.2.5 Management of extraneous agents in immunological veterinary medicinal products



Framework Overview: Materials Management

Common themes across international standards:

- Strong emphasis on end-to-end materials management
- Controls based on documented processes, traceability and risk assessment

Key Questions:

- How do current CVB expectations align with global models?
- Should international standards be adopted by CVB in total? What are the pros and cons?
- What guidance can CVB provide to manufacturers to support innovation while maintaining purity, safety and efficacy of the veterinary biologic?



Performance Standards

Requirement	Performance Standard	Representative examples as evidence
Supplier & Material Qualification	Materials originate from qualified, reliable sources and meet defined specifications	Summary of supplier approval. qualification process and criteria. Approved supplier list. Supplier audits. Supplier quality accreditation document Risk assessments supporting reduced or risk-based inbound testing of raw ingredients.
Receipt, ID & Status Control	Materials are correctly received, uniquely identified and assigned an appropriate status to prevent unintended use	Categorization of biological vs. non-biological Receiving flow description. Label formats showing unique ID/lot #. Warehouse maps indicating quarantine, approved, rejected lots. Inventory system; records showing status changes over time. Procedures for handling un/mis-labeled
Sampling, Testing & Release	Materials are evaluated for identity and suitability before use; release decisions are documented	Sampling and testing procedures. Risk-based testing rationale. COA verification logs. Documentation of release decisions (i.e., QA sign off)



Performance Standards

Requirement	Performance Standard	Representative examples as evidence
Storage, Handling & Material Protection	Materials are protected from contamination, mix-ups, and degradation	Temperature/environmental monitoring logs. Segregation controls. Storage maps for hazardous, temp-sensitive, or IAO. Procedures for spills or damaged containers.
Use of Materials in Manufacturing	Material use is traceable to every batch, with identity confirmed at point of use	Batch records showing material lot numbers. Batch reconciliation records. Procedures describing identity confirmation before use. Traceability system or matrix
Disposition (Rejection, Destruction, Returns)	Nonconforming materials are controlled and prevented from use; disposition is documented	Nonconformance reports. Rejection tags or status codes. Destruction logs/Certificates. Segregation procedures for rejected materials.

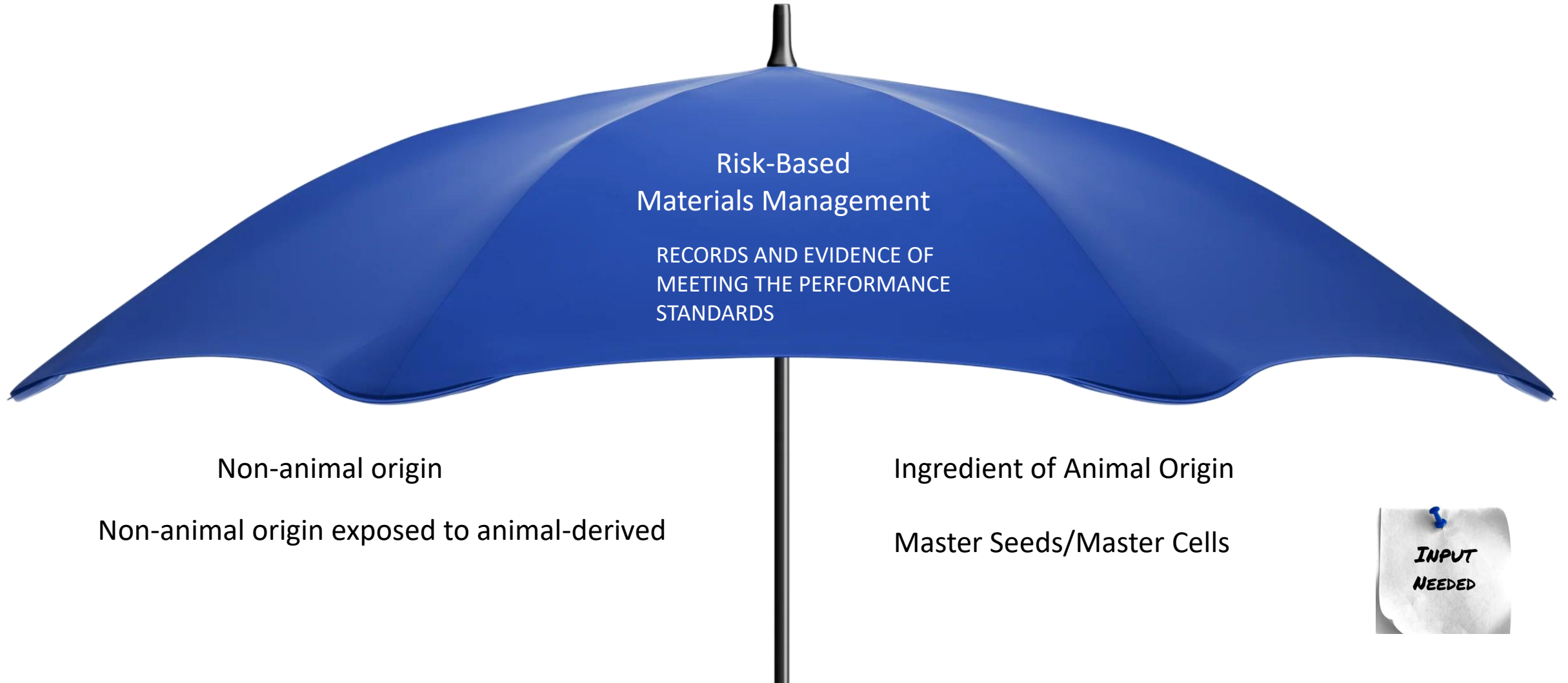


Performance Standards

Requirement	Performance Standard	Representative examples as evidence
End to End Traceability	Ability to trace a material lot from supplier>receipt>testing>storage>use>disposition	Traceability map/flow. Completed traceability exercise or mock-recall report. Inventory management histories. Case studies tracing a lot through production. Lot numbers linked to batches.
Records and Data Integrity	Records are accurate, complete, contemporaneous, and protected	Description of records management system and data integrity controls. Backup schedules. Examples of controlled forms. User access control procedures.



MM&T Framework



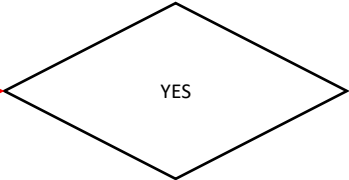
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Master Seed/Master Cell

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6. Use /
Disposition (OOP)



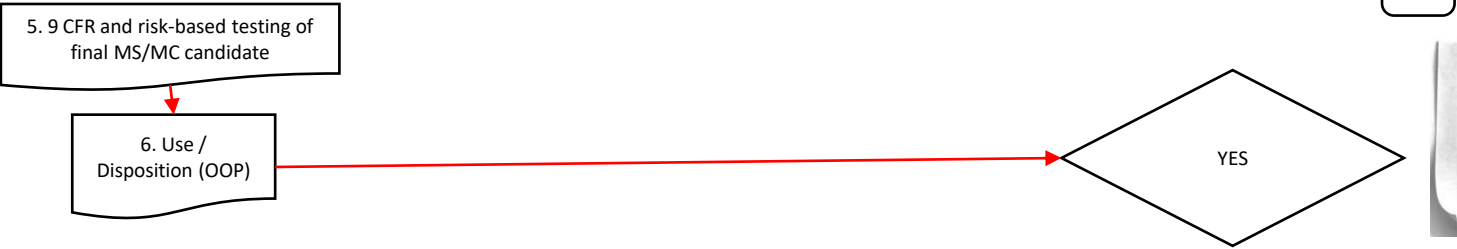
Risk Assessment

Risk Controls / Mitigation

Master Seed/Master Cell

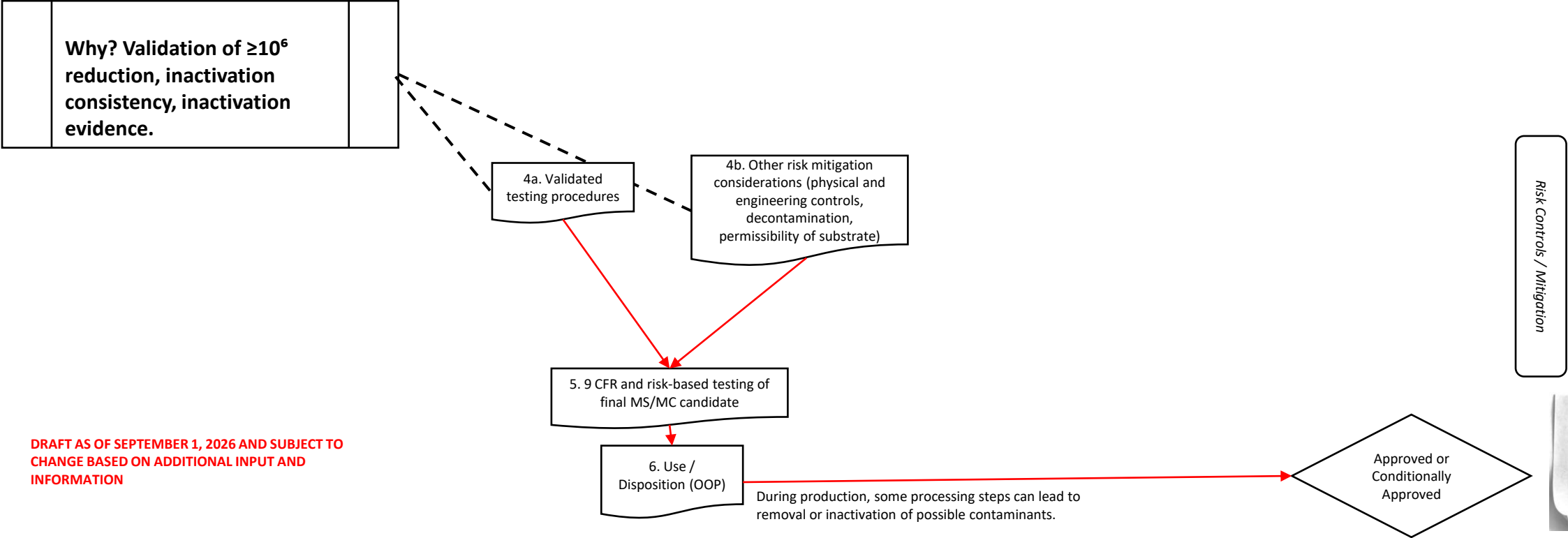
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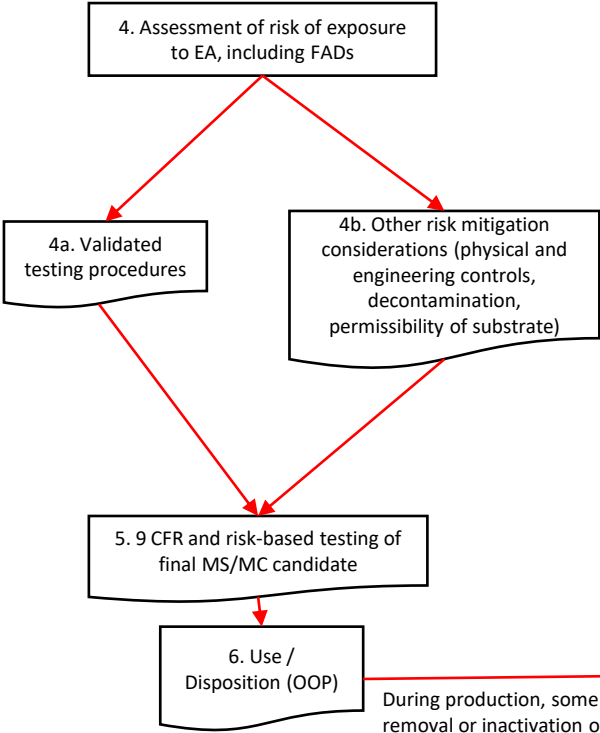
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Risk Assessment

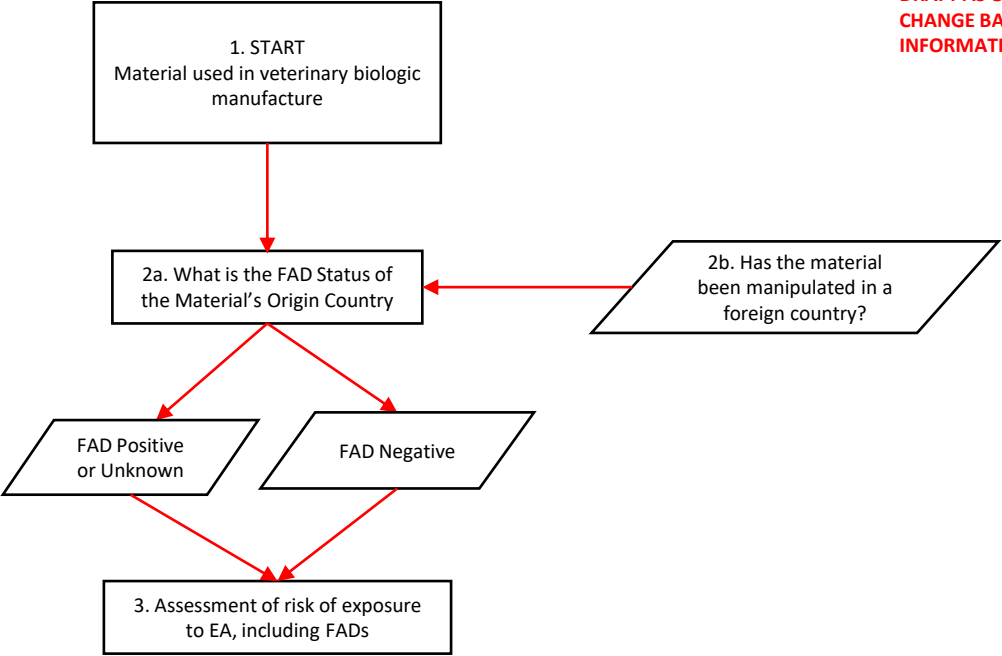
Risk Controls / Mitigation



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Master Seed/Master Cell

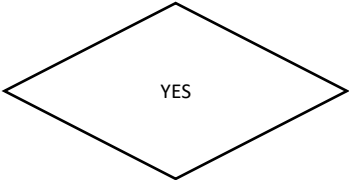
Countries that do not report
FAD status to WOAHA and/or
APHIS may require additional
risk controls to ensure materials
are free of EA.



Risk Assessment

Risk Controls / Mitigation

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Master Seed/Master Cell

	<i>Performance Standards</i> • Supplier and Material Qualification • Receipt, Identity and Status Control Why? Materials must have documented origin, suitability and qualification.	
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Countries that do not report FAD status to WOA and/or APHIS may require additional risk controls to ensure materials are free of EA. This uncertainty may require additional evidence of controls.

	<i>Performance Standards</i> • Sampling, Testing and Release • Storage, Handling and Protection • Use of Materials in Manufacturing Why? Validation of $\geq 10^6$ reduction, inactivation consistency, inactivation evidence.	
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	<i>Performance Standards</i> • Storage, Handling and Protection • Sampling, Testing, and Release • Use of Materials in Manufacturing Why? Upstream use with purification lowers risk; late-stage addition increases risk and documentation requirements.	
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1. START
Material used in veterinary biologic manufacture

2a. What is the FAD Status of the Material's Origin Country

2b. Has the material been manipulated in a foreign country?

FAD Positive / Unknown

FAD Negative

3. Assessment of risk of exposure to EA, including FADs

4a. Validated testing procedures

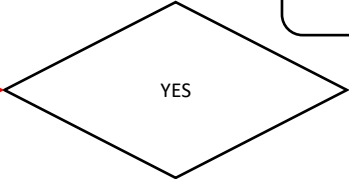
4b. Other risk mitigation considerations (physical and engineering controls, decontamination, permissibility of substrate)

Treatment and Test Pathway

5. 9 CFR and risk-based testing of final MS/MC candidate

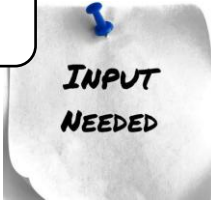
6. Use / Disposition (OOP)

During production, some processing steps can lead to removal or inactivation of possible contaminants.



Risk Assessment

Risk Controls / Mitigation



Questions

- Are the risks appropriately characterized?
- Would VICH GL60 and ICH Q5A(R2) have applicable concepts that can support US manufacturers?
- What other standards should CVB review?
- What challenges should we be aware of when considering concepts in international standards?



Questions

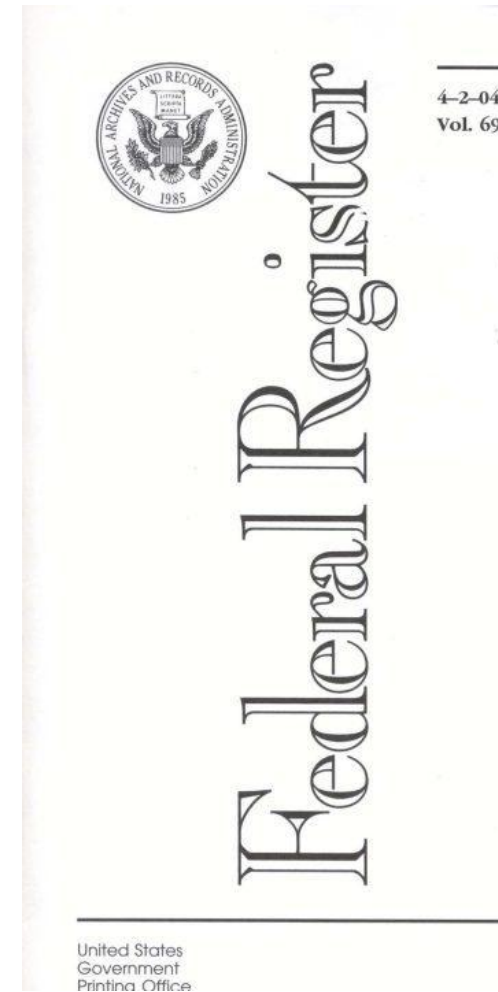


- How could CVB alignment with internationally recognized guidelines and standards help your organization?
- Are there international guidelines or standards that inhibit innovation or otherwise complicate product development?
- What additional guidance, definitions, or supporting material would industry find useful?



Federal Register: USDA Office of the Secretary

- Docket No: USDA-2026-0298
 - Solicit public input
 - 9 CFR parts 101-118, 123-124
 - Modernization of regulations





Questions?

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