



Use of Bovine serum in the manufacture of veterinary medicinal products

Status and challenges

Perspective from the veterinary pharmaceutical industry

IABS-Bovine Serum Online Meeting -29-30 September 2026

Benjamin Hatat

🐦 @animalhealthEU

📘 /animalhealthEU

🌐 AnimalhealthEurope

animalhealtheurope.eu

Discussion Topics

To keep in mind: When requirements exceed risk, supply resilience suffers.

Introduction

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Sourcing considerations

Regulatory compliance & Documentation

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Reflection on experiences

Key takeaways

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Why bovine serum still matters?

- Bovine serum remains a critical raw material
 - ✓ Supports growth of a wide variety of cell substrates
 - ✓ Essential for many veterinary vaccine production processes
 - ✓ Alternatives remain product-specific and difficult to implement at industrial scale
 - ✓ Supply continuity directly impacts vaccine availability

Continuously evolving field

- Disease situation is changing globally and locally → Risk assessment is subject for revision
 - ✓ e.g., HPAI H5N1 detected from FBS in the US, Feb 2025
- Regulatory requirements
 - ✓ global regulatory requirements increase and remain only partially harmonized
- Animal welfare considerations
 - ✓ e.g., US requirement to test in sheep all imported serum batches
- Technological advancements
 - ✓ Serum manufacturing and control methods

=> The industry objective is to maximize safety while preserving supply resilience

- Example for Regulatory ref.: [FBS Exporting Countries: Comparing Regulation - BioProcess International](#)

Serum sourcing - from qualification to routine importation

- Some figures

- ✓ ⌚ typical supplier qualification timeline = **2-4 years**
- ✓ ⌚ Typical timeline from purchase to usable lot: **2-9 months**
- ✓ 📄 Typical documentation accompanying each lot: **~40 documents**

- Key challenges

- ✓ Lengthy qualification process
- ✓ Import and customs complexity
- ✓ Need to maintain large inventories (with possible storage constraints)
- ✓ Difficulty in establishing true dual sourcing (see next slide)

Supply dynamics & purchasing power

- Serum suppliers' priority order
 - ✓ Human pharma sector is in priority vs. Vet - unless demand justifies priority
 - ✓ Volumes of order matter but regulatory requirements apply equally to large and small volume orders
 - ✓ Purchase orders may differ in level of regulatory requirements -a large consumer may require less QC and documentation vs. a small consumer
- Serum collection vary among sourcing geographies - pressure on forecasting
 - US continuous production through the year
 - NZ once a year (typically August- September; or NBCS July to September) - require purchase order a year before
 - FCS supply can be negatively impacted by rearing considerations of farmers (beef price vs. value for a Veal)
- What matter most for serum suppliers and pharma industry equally
 - Precise forecast of serum purchase and vaccine demand (pull and push)
 - Flexible use (less types and same grade of serum use for more vaccines)
 - Less exception/specific requirement for specific vaccines due to custom made or regulatory requirements

Industry capabilities vs. Regulatory requirements

- Serum suppliers and vaccine manufacturers already implement multiple layers of control
 - Supplier qualification
 - Traceability
 - Testing programs
 - Risk assessments
 - Validated irradiation and manufacturing processes
- Critical elements such as EDQM CEPs are widely recognized
- However, global regulatory requirements remain only partially harmonized



Consequently, similar information is reviewed repeatedly by multiple authorities

Industry capabilities vs. Regulatory requirements

- The same serum lot may need to satisfy:

- Different documentation packages
- Different veterinary certificates
- Different testing expectations
- Different irradiation expectations
- Different interpretation of similar risks

- Administrative burden increases without a proportional increase in safety

- Up to dozens of supporting documents
- Repeated regulatory assessments
- Slower implementation of new suppliers
- Reduced supply flexibility



„Global regulatory divergence reduces flexibility and delays access to supply.”

Regulatory Compliance does Not Guarantee Interchangeability: A challenge often underestimated

- Even when suppliers meet identical regulatory requirements:
 - ✓ compliant origin
 - ✓ compliant testing
 - ✓ compliant documentation
 - ✓ compliant irradiation
- Differences remain in:
 - ✓ Cell growth performance
 - ✓ Process robustness
 - ✓ Product yield
 - ✓ Manufacturing consistency

“Biological equivalence is more challenging than regulatory equivalence.”

Viral Safety is the Regulatory Focal Point

Current framework relies on three pillars

1. Origin & animal health status:

- ✓ Country of origin
- ✓ Traceability
- ✓ Surveillance systems

2. Testing strategy:

- ✓ Supplier testing
- ✓ Manufacturer testing
(verification and/or
supplementation)

3. Ionizing irradiation:

- ✓ Additional viral risk
reduction step

“The industry fully supports this objective; The goal is not less safety. The goal is a more pragmatic/proportionate demonstration of safety.”

Documentation (Typical in EU for each serum batch)

- **Certificate of analyses from supplier**

Catalog no.

Batch no.

Date of manufacture

Final batch volume

Shelf life

Exclusively of bovine origin

Statement: "Obtained from normal fetuses from dams / animals fit for human consumption"

- **TSE Certificate of Suitability from supplier**

CEP no.

Country (-ies) of origin.

- **Gamma irradiation documentation**

Dosimetry showing a dose between 25 and ...kGy

- **Health Certificate from supplier**

Supplied with each batch

Example of Documentation focusing on testing (Typical for EU)

- Testing data (differ between FBS and other type of bovine serum) from supplier

- Appearance

- Identity

- Osmolality

- Total protein

- Haemoglobin

- Sterility before irradiation

- Mycoplasma before irradiation

- Extraneous agents before irradiation (8 agents)

- BVD before and after irradiation

- Anti-BVD-1 (and anti-BVD-2) antibodies

- Testing data performed by vaccine manufacturer

- Interference with growth of specified viruses

- Growth promoting quality with cells

- Specified Extraneous agents

- Sterility, mycoplasma, endotoxin, osmolarity, identity, total protein

- BVD before and after irradiation

- + overall risk assessment

- Summary of all information from supplier

- Summary of all information from vaccine manufacturer

- Justification for agents not tested by exclusion

- Using:

- Geographical origin of serum sourcing

- Herd origin of serum sourcing

- Biological characteristics of the agent

- Effectiveness of manufacturing process to remove agent

- Effectiveness of manufacturing process to inactivate agent

- Some (not all) of the requirements:

- PhEur 2262 ([under revision](#)),

- PhEur 0062, 5.2.5, 9CFR etc....

Certification of suitability vs. Risk assessments

○ Serum with a Certification of suitability (CEP)

- Issued by EDQM
- Recognized in EU also Internationally
- After thorough review of serum supplier application documentation
- Based on risk assessment - apart from safety, high focus on traceability
- Vaccine manufacturers are using for vaccine dossier submissions



Responsibilities

EDQM - Serum supplier

○ Serum supplied with Risk assessment without a CEP

- Subject for evaluation by each competent Regulatory Authority
(as part of each vaccine dossier application & life cycle management)
- Prepared by vaccine manufacturer/applicant who submits vaccine dossier
- National permits might be needed for handling of GMO's and might take up to several months



Responsibilities

Regulatory Agency - Vaccine manufacturer - Serum supplier

- Recognition & Responsibilities differ

Reflection on experiences

○ Upon a non-EU country Regulatory Authority request for a dose of ≥ 30 kGy

- "All of our current Serum customers, mainly Vaccine Manufacturers, accepting irradiation ≥ 25 to 40kGy
- "Therefore I suggest checking with your Regulatory & Quality people for the reason of irradiation ≥ 30 kGy.
- "In case you insist on irradiation ≥ 30 kGy, we need to set up a "Custom item",
- "Custom Serum" will certainly be more expensive."

/PhEur 2262 (under revision): ... "For bovine serum intended for use in immunological veterinary medicinal products, for inactivation by gamma irradiation a minimum dose of 30 kGy is applied, unless otherwise justified and authorised.".... /

○ HPAI H5N1 isolated from FBS

- Rebelo et al. (2026; Cornell/USDA) reported isolation of infectious HPAI H5N1 virus from FBS lot during routine adventitious agent testing. https://wwwnc.cdc.gov/eid/article/32/8/26-0077_article
 - Contamination levels were low and associated with the 2024-2025 U.S. dairy cattle outbreak
 - Heat treatment (56°C/30 min) completely inactivated the virus. → supporting risk mitigation for vaccine manufacture
- However,
- Could still be a biosecurity risk for using such serum to diagnostics purposes

Reflection on experiences

- Serum importation to US
 - Any batch of bovine serum is subject for testing prior entry to US
 - At present USDA is applying general safety testing by injecting the serum to sheep
 - Industry is questioning the adequacy and necessity of such testing (animal welfare, redundancy and benefit above other measures)
 - It is a Barrier when the relevant Sheep is not available for testing like it did happen recently:
<https://content.govdelivery.com/accounts/USDAAPHIS/bulletins/3e57dd6>

Reflection on expériences: Examples from a USDA 3rd party assessment

○ 35. Seed/Cell Testing Requirements

- Challenge: Seed and cell substrate testing expectations appear to have expanded beyond published requirements, creating uncertainty and inconsistent treatment of pre-master materials.
- Opportunity: Establish a transparent, risk-based framework defining when additional PCR or extraneous agent testing is scientifically justified.

○ 36. Serum Importation & Animal-Based Testing

- Challenge: Current serum importation requirements and animal-based testing approaches are viewed as outdated, burdensome, and misaligned with supply chain realities and the 3Rs principles.
- Opportunity: Adopt scientifically validated alternative methods and clarify irradiation expectations through harmonized, risk-based guidance.

○ 40. PCR Detection of BVDv

- Challenge: Detection of BVDv nucleic acid by PCR may trigger restrictions even when no infectious or replicating virus can be demonstrated.
- Opportunity: Implement a science-based decision framework distinguishing nucleic acid detection from viable virus and supporting risk-based assessments

Key takeaways

- **Manufacturers repeatedly submit to multiple authorities:**
 - ⇒ Animal Health Information
 - ⇒ Test methods & Validation reports
 - ⇒ Production descriptions
 - ⇒ Traceability data
- **Non harmonized Irradiation requirements**
 - ⇒ Commercial standard is ≥ 25 kGy, but manufacturers may request a tailored product since requirements may reach beyond 30 kGy and even 55 kGy (Australia, but **(too high irradiation may reduce serum performance)**)



Need for Improvements

- **Not harmonized Risk-Based Regulation**
 - ⇒ While it is in place in EU, some geographies put in place automatic exclusion when outbreaks of some specific diseases like FMD occur
- **Lack of sourcing and post approval Flexibility**
 - ⇒ Evolving disease situations and market availability→
 - ⇒ Leading to change in sourcing countries and qualified suppliers→
 - ⇒ Need for post-approval changes related to serum sourcing



How to strengthen consistent supply of safe Bovine serum while keeping admin and logistic burden minimum

Opportunities for Improvements

Perspective from the veterinary pharmaceutical industry

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Gergely Hamar

🐦 @animalhealthEU

📘 /animalhealthEU

🌐 AnimalhealthEurope

animalhealtheurope.eu

Recommendations for safe supply & regulatory compliance

Promote International Reliance of serum
supplier dossiers

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02

Promote Global Consensus on Irradiation

Further Promote Risk-Based Approaches

03

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Conclusion

Recommendations for safe supply & regulatory compliance

- Recommendation 1: Promote International Reliance of serum supplier dossiers

Develop/extend a certification process at supplier's level, including extraneous agents purity risk assessment

- ⇒ performed by trusted bodies (successful example in the past with EDQM developing the BSE/TSE certification in the early 2000')
- ⇒ Encouraged recognition frameworks among regulatory authorities

- Benefits

- ⇒ Vaccine manufacturers can then focus on the supplementary safety aspects, which fit with a specific use (see recommendation 3)
- ⇒ Less duplication (e.g., batch testing, regulatory assessment...)
- ⇒ Faster supplier onboarding
- ⇒ Reduced burden for suppliers
- ⇒ Unchanged safety expectations



Evaluate once, use many times

Recommendations for safe supply & regulatory compliance

- Recommendation 2: Promote Global Consensus on Irradiation

Compile/supplement a validated scientific reference of irradiation dose that maximizes viral safety while preserving serum functionality

⇒ Global recognition of the scientific reference to achieve consensus

⇒ AnimalhealthEurope is working on a report similarly to the verification report on steam sterilization (<https://www.vitacyte.com/wp-content/uploads/2024/07/IFAH-Europe-Sept-2012-Virbac-Laboratories.pdf>)

- Benefits

⇒ Replace multiple local re-demonstrations

⇒ Limit (ideally waive) the need of custom products



Evaluate once, use many times

Recommendations for safe supply and regulatory compliance

- Recommendation 3: Further Promote Risk-Based Approaches

Focus controls on the actual risk posed by the agent and intended use of the serum

Demonstrate viral risk mitigation rather than geographic exclusion alone /

⇒ Consider biological characteristics of the agent rather than disease status alone

⇒ Consider process steps during serum and vaccine manufacture for effectiveness of removal and inactivation of agents

(HPAI H5N1 example illustrate the effectiveness of serum process treatments)

- Benefits

⇒ Avoid requirements that add burden without a measurable improvement in safety

⇒ Replace multiple local re-demonstrations

⇒ Remove geographical barrier if related risk proven to be negligible

Increase serum supply flexibility
and prediction on forecast



Reduce supply logistics complexity
to secure vaccine availability

What success would look like?

○ Today

- Duplicate assessments
- Variable documentation
- Different irradiation expectations
- Limited supplier flexibility

○ Tomorrow

- ⇒ Harmonized data package
- ⇒ Recognised supplier certification
- ⇒ Consensus irradiation guidance
- ⇒ Science-based risk management
- ⇒ More resilient vaccine supply



Same serum, Same science, Same safety expectations,
Fewer administrative barriers

Conclusions

- **Current situation**
 - Divergent regulatory requirements accross different geographies
 - Leading to paralell assessments
 - Burdening safe supply of serum → Impact vaccine availability
- **Vaccine manufacturers proposed 3 recommendations**
 - To significantly reduce administrative burden and resources implications
 - Ease current logistics and forecasting pressure for securing vaccine availability

One single assessment by a trusted Regulatory Authority → through a recognition scheme