Recombinant Animal-Free Albumin Enhances Infectious Lentiviral Vector Yields

By Stabilizing Viral Particles During Downstream Processing and Final Formulation

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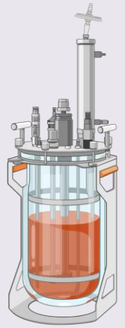
InVitria, Junction City, KS

Lentiviral Vector Downstream Processing Workflow

Lentivirus titer loss through all of the DSP processes including hold times is significant due to sensitive nature of lentiviruses

DSP Est. Cumulative Titer Loss
70-80%

Post-Harvest Hold

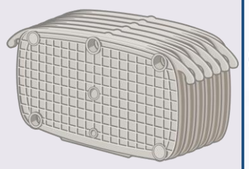


Thermal decay of envelope; spontaneous capsid disassembly

~10-50% Loss

HOLD

Clarification

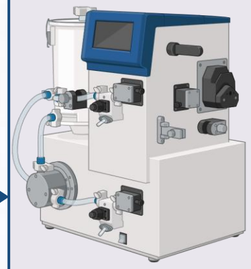


Adsorption to depth filters & tubing surfaces

~10-40% Loss

HOLD

TFF #1
(Buffer exchange / Concentration)



Membrane adsorption + shear stress

~20-60% Loss

HOLD

Chromatography
(Capture)

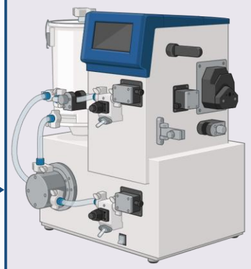


Column-resin binding; envelope destabilization in ~1 M NaCl

~20-60% Loss

HOLD

TFF #2
(Final concentration / formulation)



Membrane adsorption + shear stress

~10-30% Loss

HOLD

Sterile Filtration
(0.2 µm)



Non-specific adsorption + shear at PES membrane

~30-70% Loss

HOLD

Fill / Finish



Second freeze-thaw cycle; ice and envelope damage

~10-50% Loss

HOLD

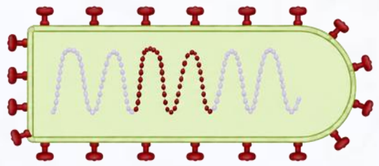
Process Holds Typical holds between unit operations (at 2-25 °C) contribute to cumulative thermal stress and LVV titer loss throughout the downstream process.

RECOMBINANT ALBUMIN — PROVEN IN AN ENVELOPED VIRAL VECTOR

One Stabilizer. Multiple Failure Modes Addressed.

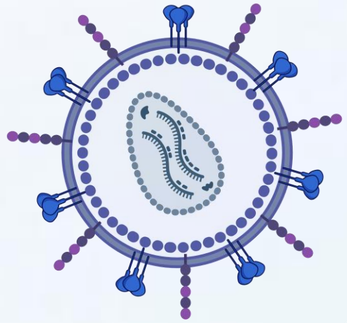
- ✓ Shear Protection
- ✓ Surface Passivation
- ✓ Anti-Aggregation
- ✓ Cryoprotection
- ✓ Thermal Stabilization

Similar Enveloped Viral Stability Challenges



rVSV-ZEBOV

same lipid envelope · same surface glycoprotein · same fragility



VSV-G LVV



Regulatory Precedent

MERCK ERVEBO (Ebola Zaire Vaccine, Live)

- ✓ Stabilizer: InVitria recombinant albumin
- ✓ Approval: FDA, EMA, PMDA — December 2019
- ✓ Vector class: VSV-pseudotyped enveloped virus

rHSA Properties

Optibumin 25

- ✓ Source: Animal-free, chemically defined rHSA
- ✓ Quality: cGMP excipient grade · consistent lot-to-lot
- ✓ Format: 25% w/v · Stabilizer-free · 99% reduced Cys34

References: Burke & Volkin US 6,210,683 · EMA 606159/2019, Carmo 2009, Bandeira 2012, Moreira 2021

EXPERIMENTAL DESIGNS AND METHODS

Hypothesis:

Optibumin 25 recombinant HSA will stabilize LVV particles across multiple DSP unit operations by addressing shear, surface adsorption, thermal stress, and freeze-thaw stress in a similar manner that it stabilizes VSV particles in ERVEBO



Experimental Setup:

VSV-G Pseudotyped LVV samples were exposed to the following stressors relevant to commercial virus manufacturing with or without the addition of 1% (m/v) rHSA and LVV titer measured

Unit Operation	Stress Condition
Hold time	24 hour hold at RT or 4 ºC
TFF buffer exchange	5x concentration with TFF
Cryopreservation	Freeze thaw at -80 ºC
Sterile Filtration	Controlled flow through 0.2 micron PES filter

Titer Measurement:

Absolute genomic titer was measured by RT-qPCR of viral samples relative to an RNA standard of known concentration

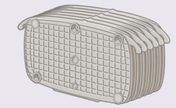
Infectious titer was measured by transduction of HT-1080 cells with LVV encoding GFP using live cell imaging

To minimize variability, all virus samples were derived from the same batch, titer was compared to an unstressed control sample, and titer was measured using the same cell sample for all conditions within an experiment

OPTIBUMIN 25 — CLARIFICATION

Optibumin Protects LVV Through Clarification — Near-complete Genomic Preservation, ~4× Infectious Recovery

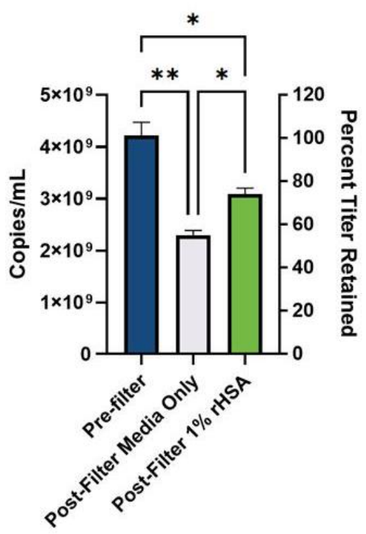
Virus samples were harvested from cell culture and passed through Millistak depth filters
1% Optibumin significantly improved genomic and infectious titer recovery



Depth Filtration

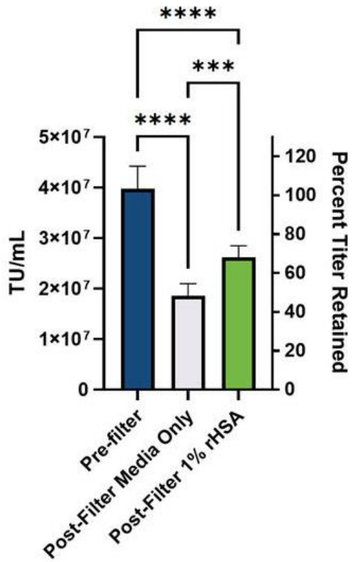
Genomic Titer

(RT-qPCR)



Infectious Titer

(HT-1080 Transduction)



~55%
Genomic titer retained with Optibumin

~75%
Genomic titer retained without albumin

~70%
Infectious titer retained with Optibumin

~50%
Infectious titer retained without albumin

~70%
Genomic titer retained after clarification

~70%
Infectious titer retained after clarification

~1.4×
Higher infectious recovery vs buffer-only control (70% vs 50% retained)

~50%
Genomic titer lost without rHSA in a clarification

OPTIBUMIN 25 — TANGENTIAL FLOW FILTRATION

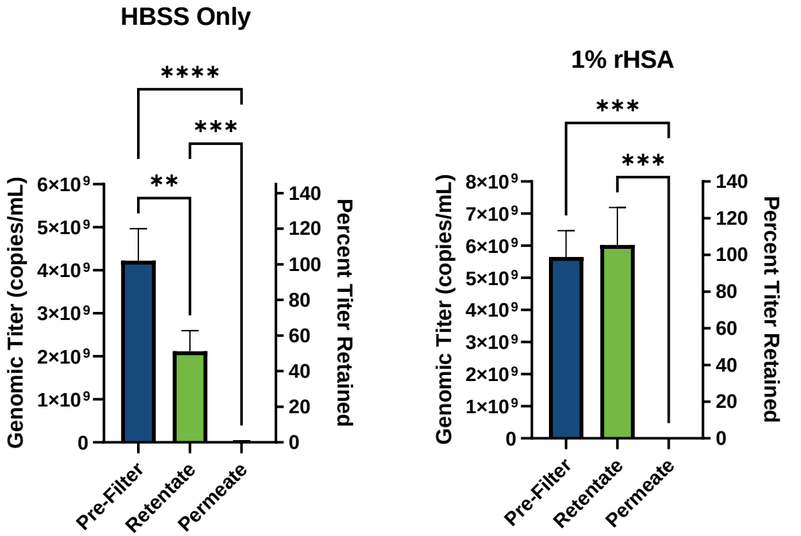
Optibumin Protects LVV During TFF Buffer Exchange by Coating the Membrane

Viral samples were dilute 5-fold in HBSS then concentrated back down using a 500 kDa membrane
~1.5× higher infectious recovery with 1% Optibumin, and 100× less virus lost to permeate — direct evidence of cassette passivation.

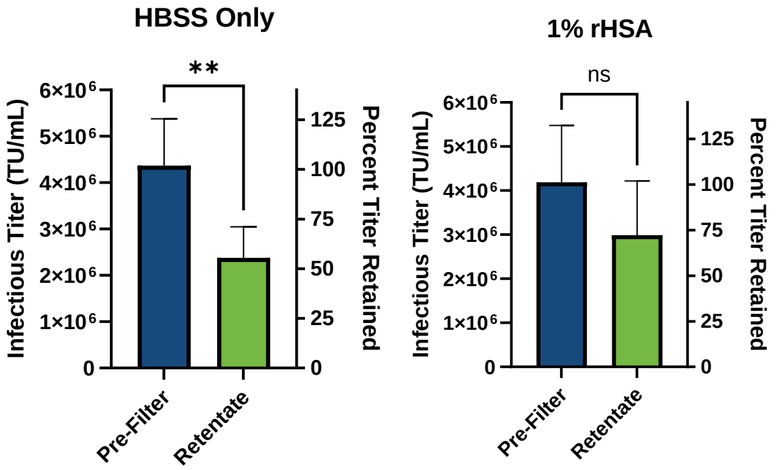




Genomic Titer
(RT-qPCR)



Infectious Titer
(HT-1080 Transduction)



~1.5×
Retained without albumin (genomic)

~100%
retained with Optibumin (genomic)

~50%
retained without albumin (infectious)

~70%
retained with rHSA (infectious)

~1.5×
Higher recovered infectious titer vs no-albumin TFF

100×
Reduction in virus lost to permeate - direct evidence of cassette membrane coating

0% vs ~50%
Genomic titer loss with 1% rHSA vs without albumin during TFF

Drop-in compatible
Tested in standard TFF cassettes (500 kDa MWCO) for buffer exchange prior to chromatography

OPTIBUMIN 25 — HOLD TIME PROTECTION

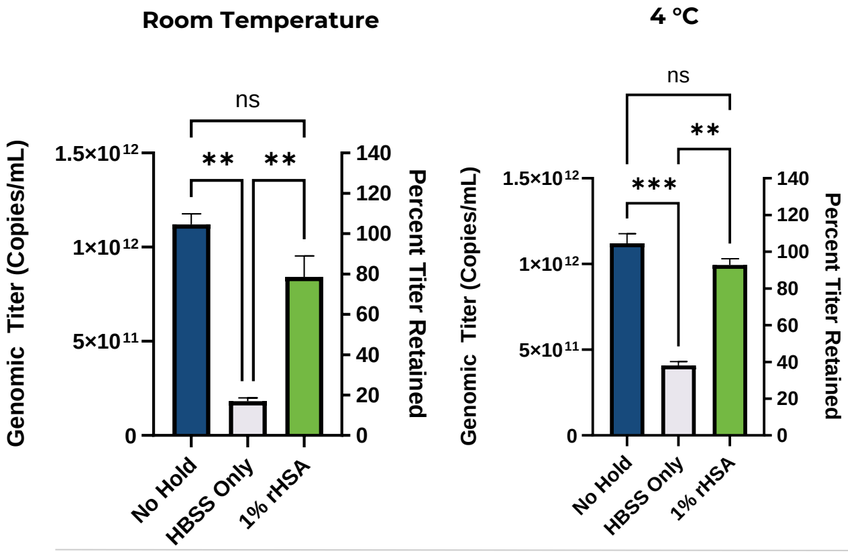
Optibumin Preserves LVV Titer During Process Hold Steps at Both RT and 4 °C

Virus was diluted in HBSS with or without rHSA and held for 24 hours

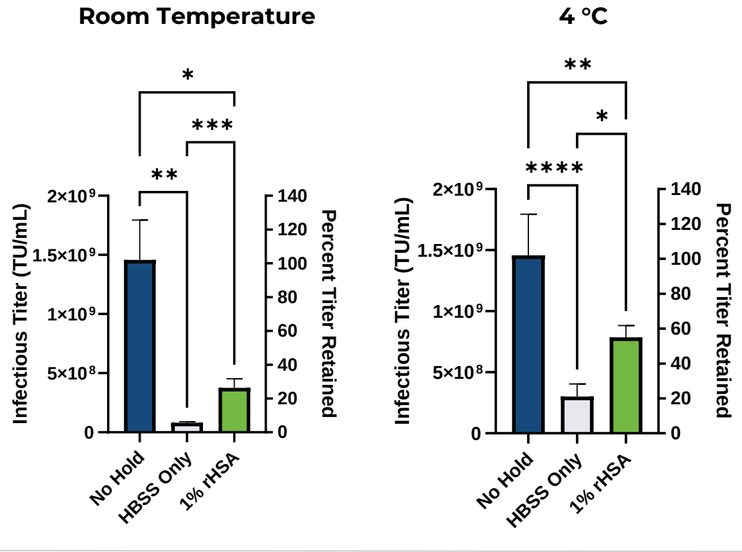
Genomic titer fully restored to no-hold control at RT and 4 ºC
infectious titer significantly recovered vs buffer-only control at RT and 4ºC



Genomic Titer (RT-qPCR)



Infectious Titer (HT-1080 Transduction)



~75%
Genomic titer retained at RT with Optibumin

~87%
Genomic titer retained at 4 °C with Optibumin

~33%
Infectious titer retained at RT with Optibumin

~47%
Infectious titer retained at 4 °C with Optibumin

~4×
Higher genomic titer at RT vs no rHSA

~2.5×
Higher genomic titer at 4 °C vs no rHSA

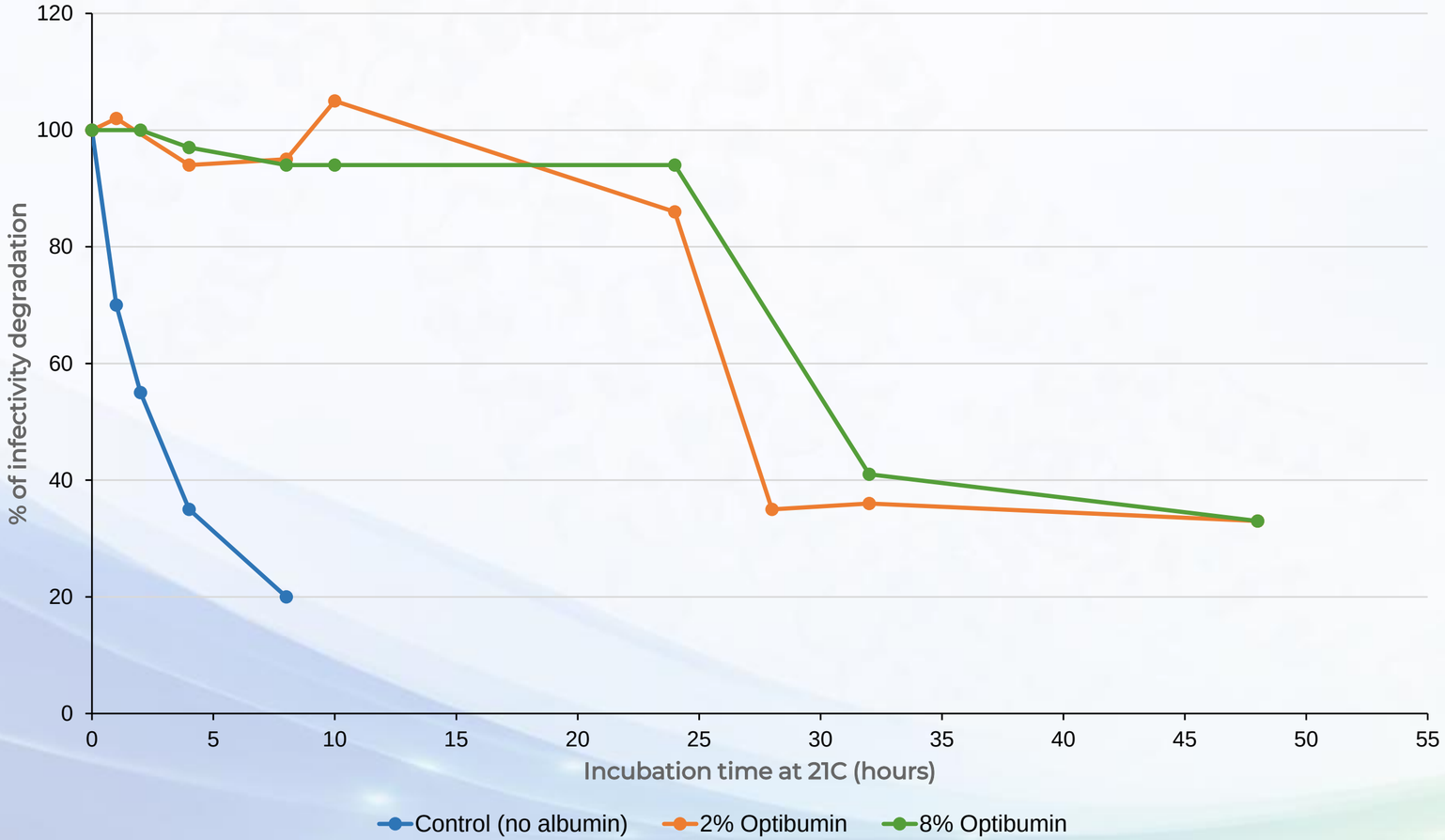
~2.5×
Higher infectious recovery at both temperatures tested

~50%
Infectious titer preserved after 24 hours at 4ºC

OPTIBUMIN 25 — ROOM-TEMPERATURE HOLD STABILITY

Optibumin Preserves Infectious LVV Titer During Extended Room-Temperature Holds (Third Party Collaborator Data)

VSV-G pseudotyped LVV held at 21 °C (room temperature) with 0%, 2%, or 8% Optibumin — infectious titer (TU/mL) by transduction, expressed as % of time-zero titer



~86%
Infectious titer retained at 24 h with 2% Optibumin

<LOQ
Without albumin, LVV infectivity falls below detection by 24 h

~100%
Infectivity fully preserved through the first 10 h with Optibumin

≥48 h
2% Optibumin extends usable LVV stability out to 48 h at room temperature

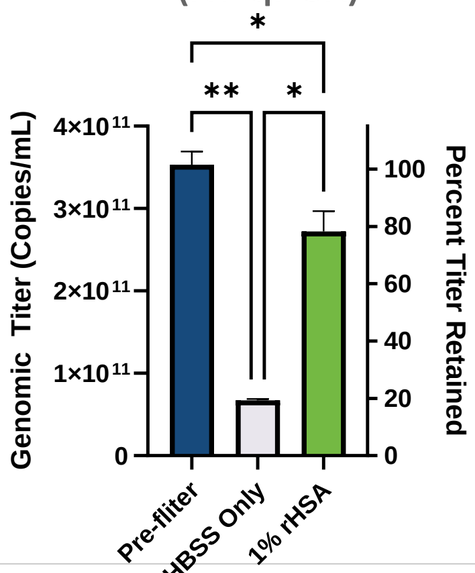
OPTIBUMIN 25 — STERILE FILTER PRE-TREATMENT

Optibumin Pre-Coats 0.2 µm Filters to Prevent Lentivirus Loss During Sterile Filtration

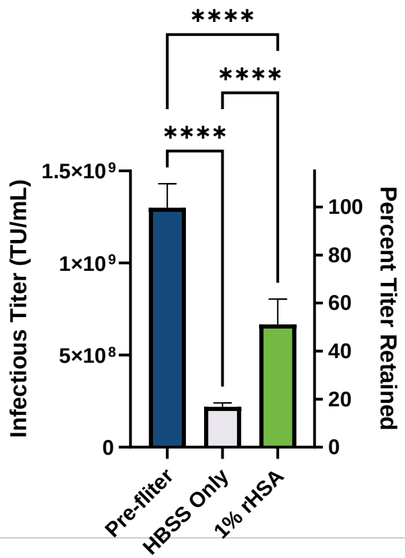
Viral samples were passed through a PES filter at a controlled flow rate using a peristaltic pump
~3× higher infectious titer recovery and ~4× higher genomic titer retention with 1% Optibumin pre-coat — consistent with filter passivation in just 5 minutes.



Genomic Titer
(RT-qPCR)



Infectious Titer
(HT-1080 Transduction)



~75%
Genomic titer retained with 1% Optibumin

~19%
Genomic titer retained without albumin

~49%
Infectious titer retained with 1% Optibumin

~17%
Infectious titer retained without albumin

~3×
Higher infectious titer recovery vs HBSS-only filtration.

~4×
Higher genomic titer retention with 1% Optibumin pre-coat.

5 minutes
Effective filter passivation time — minimal process disruption.

0.36%
Infectious-to-genomic ratio preserved — within typical 0.1–1% range, confirming particle quality.

OPTIBUMIN 25 — CRYOPRESERVATION

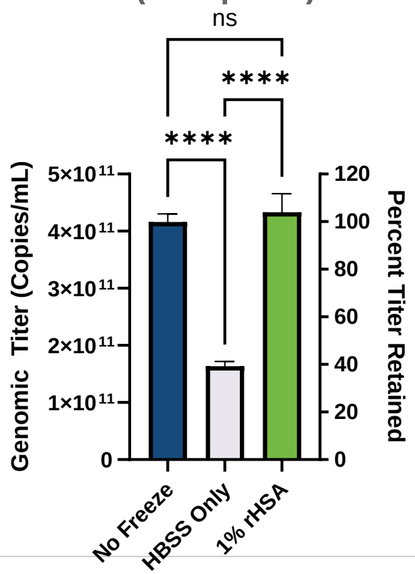
Optibumin Protects LVV Through Freeze-Thaw — Near-complete Genomic Preservation, ~4× Infectious Recovery

Viral samples were frozen in a 50 mL tube at -80 ºC and thawed at RT
1% Optibumin matches no-freeze reference for genomic titer
recovers ~4× more infectious titer than buffer only.

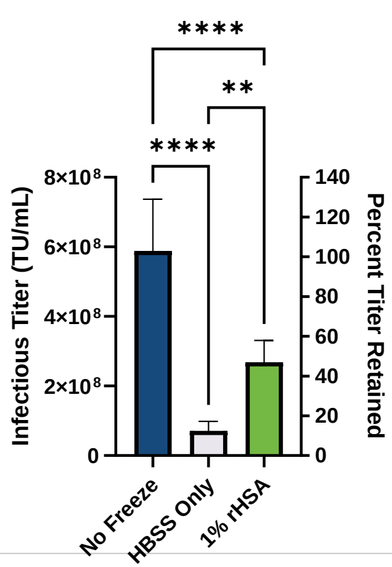




Genomic Titer
(RT-qPCR)



Infectious Titer
(HT-1080 Transduction)



~100%
Genomic titer retained with Optibumin

~37%
Genomic titer retained without albumin

~47%
Infectious titer retained with Optibumin

~12%
Infectious titer retained without albumin

~100%
Genomic titer retained — matches No Freeze reference

~50%
Infectious titer retained after cryo

~4×
Higher infectious recovery vs buffer-only control (47% vs 12% retained)

~62%
Genomic titer lost without rHSA in a single cycle

InVitria

Performance. Defined.

Thank you!

Any questions?

No questions will be lost to non-specific adsorption.

InVitria, Inc.
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Email: **info@invitria.com**
www.invitria.com