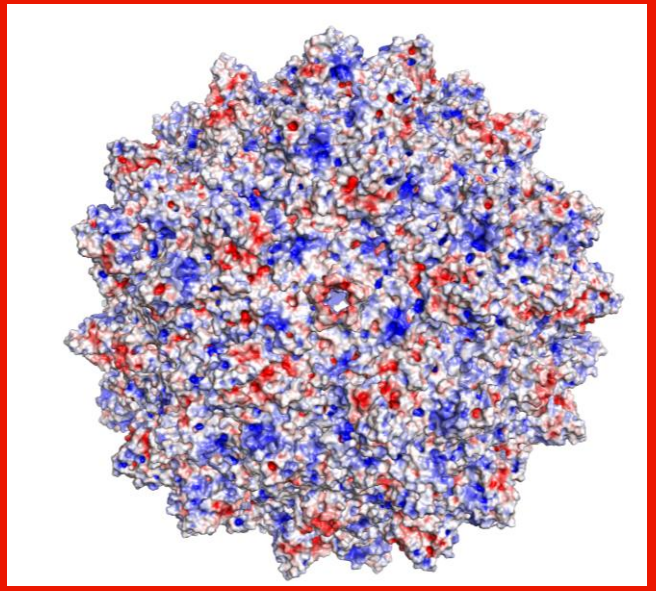
Modeling Strategies to Accelerate and De-Risk Viral Vector Development



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Drug Product Development
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June 9 – 11
Cell and Gene Therapy Products 2026 Symposium
Rockville, MD, USA

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An exclusive focus on healthcare empowers us to tackle the world's toughest health challenges.
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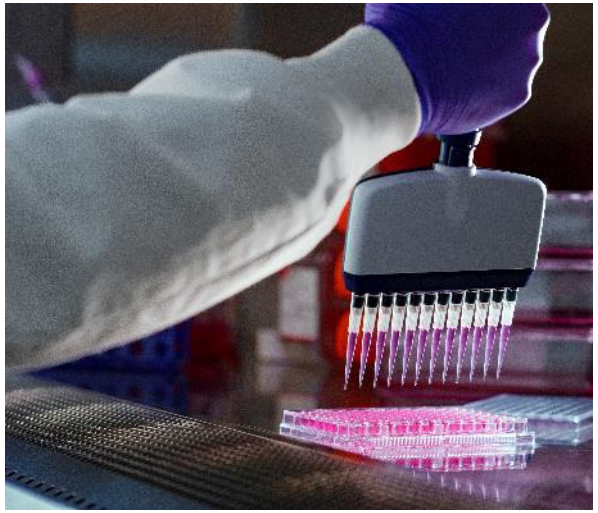
J&J Innovative Medicine



Leading where medicine is going.

Patients will always inform and inspire our science-based innovations, which continue to change and save lives. Applying rigorous science with compassion, we will continue to confidently address the most complex diseases of our time and unlock the potential medicines of tomorrow.

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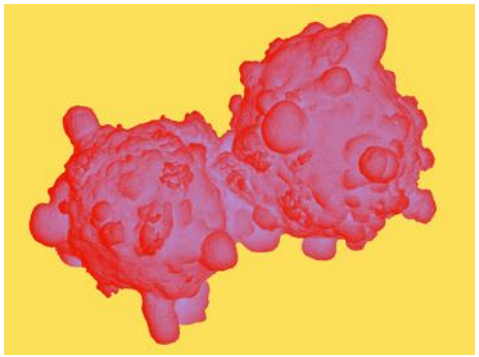
We’re focused in areas where patient need is high, and our expertise is deep



Oncology

- Multiple Myeloma
- Lung Cancer
- Bladder Cancer
- Prostate Cancer
- B-Cell Lymphoma

Immunology

- Crohn’s Disease
- Ulcerative Colitis
- Psoriasis
- Psoriatic Arthritis
- Rheumatoid Arthritis
- Maternal-Fetal Diseases
- Rare Autoimmune Diseases

Neuroscience

- Schizophrenia
- Depression
- Alzheimer’s Disease
- Myasthenia Gravis
- Specialty Ophthalmology
- CIDP

Select disease areas

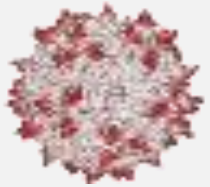
- Thrombosis
- Retinal Disease
- Pulmonary Hypertension

Overview

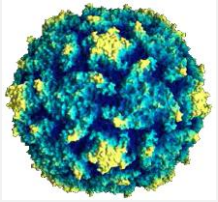
01	Shared challenges in viral vector drug product development
02	How modeling can address these challenges and enable faster, lower-risk early development
03	Areas where modeling adds significant value
04	Key takeaways

Shared Viral Vector Challenges in Drug Product Development

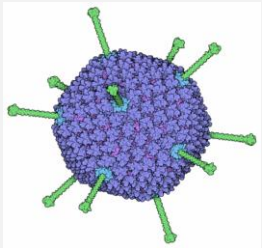
Recognizing common challenges allows us to build transferable knowledge and modelling approaches across viral vector platforms



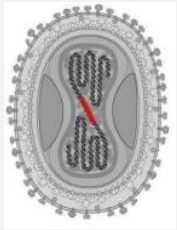
Adeno associated virus (AAV)
Non-enveloped virus
Size *25 nm*



Inactivated Poliovirus (IPV)
Non-enveloped virus
Size *30 nm*

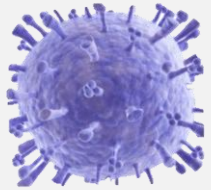


Adenovirus
Non-enveloped virus
Size *90-100 nm*



Modified Vaccinia virus Ankara (MVA)
Enveloped virus
Size *400 nm*

Herpes simplex virus 1 (HSV-1)
Enveloped virus
Size *155-240 nm*



Lentivirus
Enveloped virus
Size *80-120 nm*

C&G Therapy Viral vectors span a wide range of sizes and structural properties

Challenges:

Stability

Surface Interaction & Adsorption

Formulation & Packaging

Process-Induced Stress

Characterization

Main Factors Driving Stability of Viral Vector Drug Products

Intrinsic Particle Properties

Viral particles are inherently fragile

Sensitivity to temperature

Multiple, parallel degradation pathways:

- Aggregation / clustering
- Disassembly / dissociation
- Genome release

Formulation & Packaging

Buffer composition and excipient choice

High concentration requirements amplify instability risks

Primary packaging interactions (glass, plastics, elastomers)

Surface interaction & Adsorption

Non-specific adsorption to:

- Plastic and glass surfaces
- Filtration and chromatography membranes

Cumulative losses during:

- Filling, transfers & hold steps

Process-Induced stress

Shear stress during mixing, filtration and filling

Aggregation and titer loss linked to handling conditions

Batch-to-batch variability driven by process sensitivity

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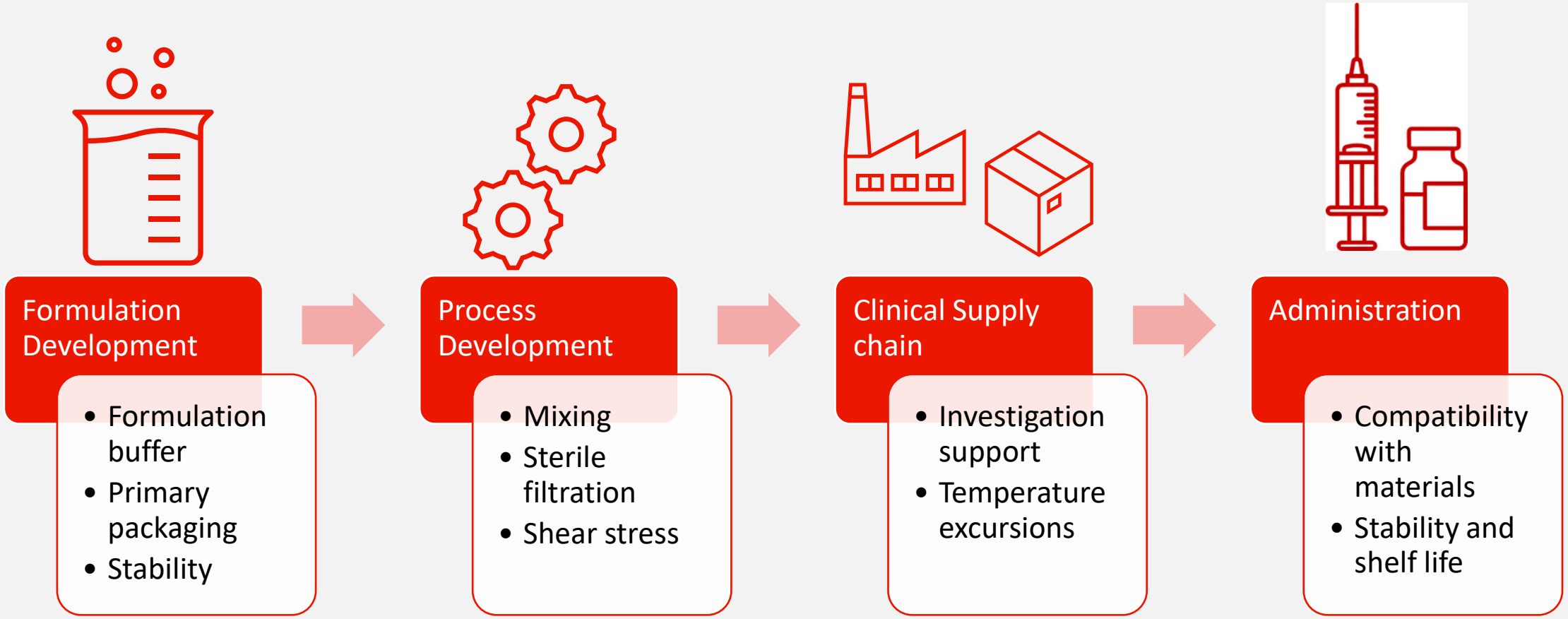
Viral vector drug products face challenges from multiple sources, making predictive tools crucial for efficient development.

How can modeling enable faster, lower-risk early development of viral vector drug products?

From stability and adsorption to shear stress and process design — predictive tools bridge the gap between challenges and solutions.

Modeling Across Drug Product (DP) Development

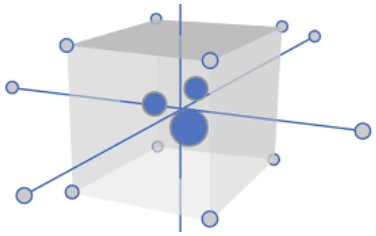
Overview of how modeling can be applied across DP development lifecycle

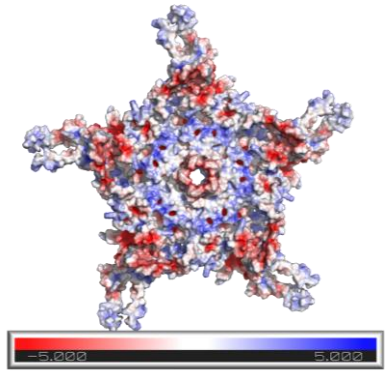


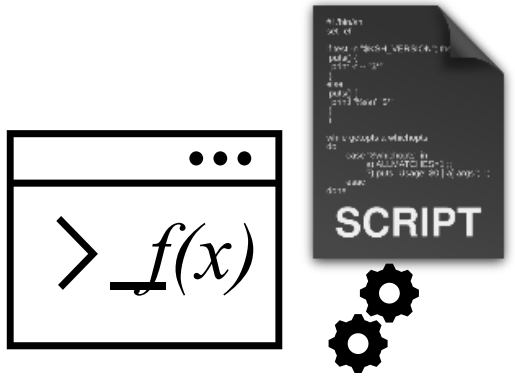
Modeling is crucial early in DP Development. The key is integrating modeling early in development to make informed decisions before committing significant resources.

Using Modeling to Maximize Learning with Limited Material

- Fundamental understanding how factors affect an outcome
- Prediction of the best settings for a certain process/formulation
- Fewer experiments, less material and time
- Modelling increases process/product understanding
  - Process improvements and scale-up
  - Cost savings



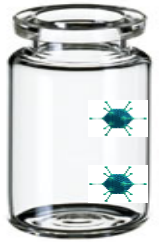
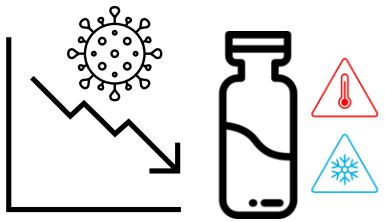
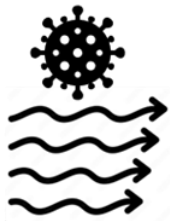




Accelerated development and deeper product understanding

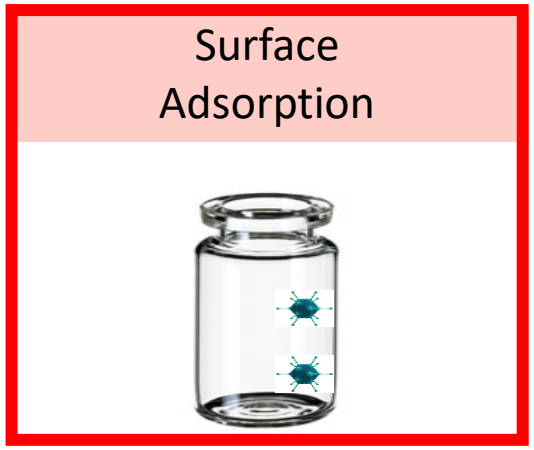
Design of Experiments combined with statistical modeling is a powerful approach that helps us explore large design spaces efficiently.

Areas Where Modeling Adds Significant Value

Surface Adsorption	Predictive stability	CFD- modeling	Shear stress
			

DP Stability and Interactions with Primary Packaging

- **Product-Packaging Interactions:** Viral vector drug products interact with primary packaging materials (glass vials, plastic containers, elastomer closures), making compatibility a critical development consideration
- **Surface Adsorption and Titer Loss:** Viral particles adhere to glass and plastic surfaces through non-specific binding, leading to significant titer loss during storage and potentially compromising dose accuracy
- **Mitigation is Essential:** Understanding and addressing these surface interactions early in development is key to achieving stable, commercially viable drug products with reliable potency throughout shelf life

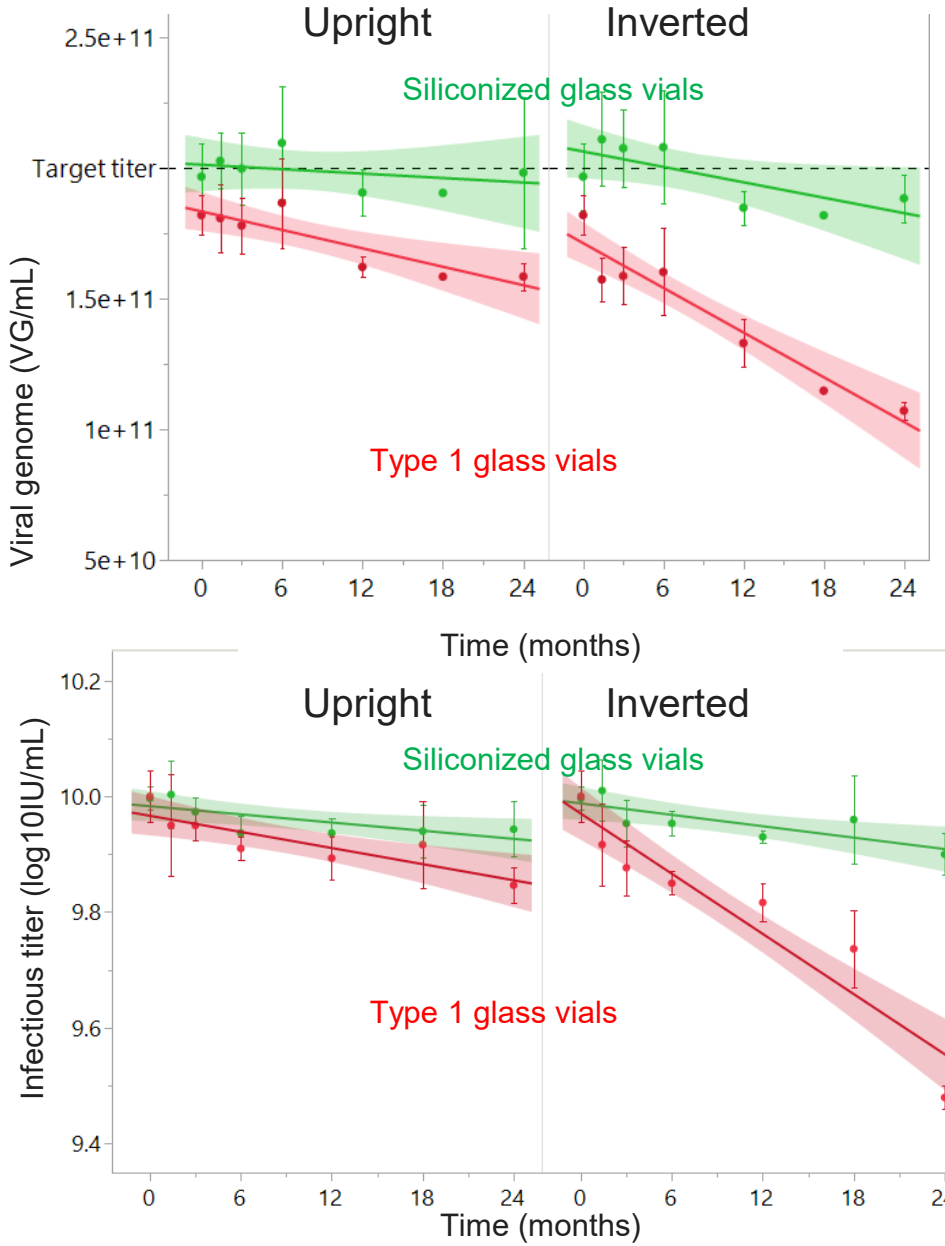


Glass Vials & Syringes

Primary Packaging Materials

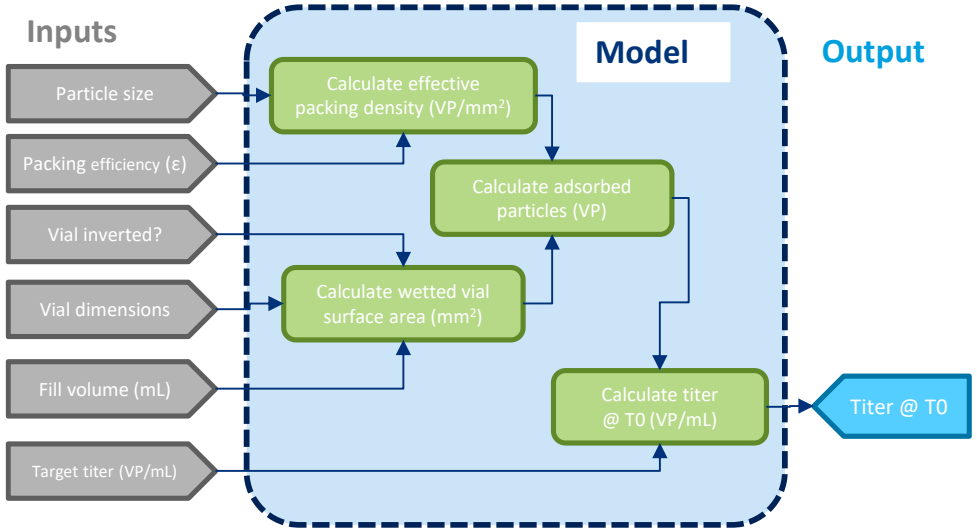
Mitigation of Viral Particle Interaction with Glass Surfaces

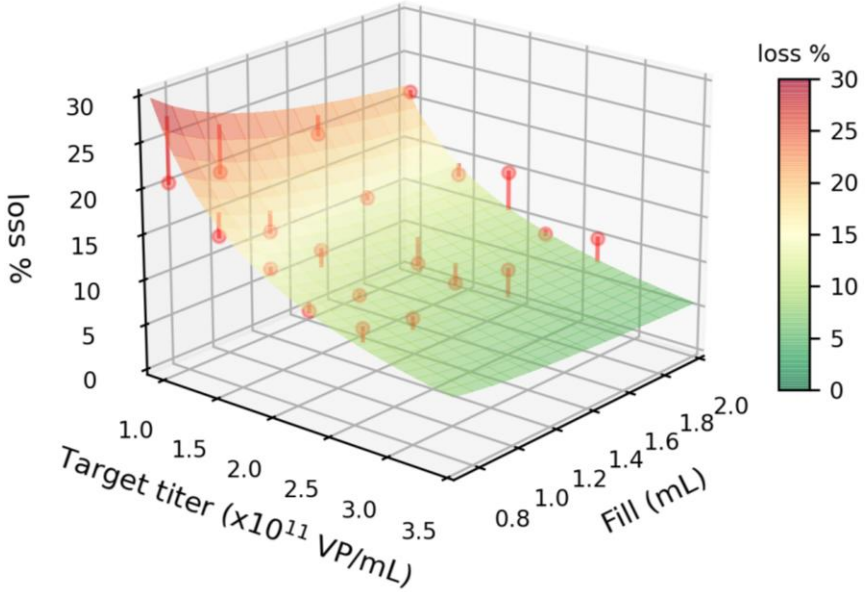
- **2 year 5°C stability** data show for Ad26 only a minimal decline in potency, unprecedented for a viral vector based vaccine
- Elimination of adsorption, in combination with earlier process and formulation improvements, resulted in a **thermostable Ad26 vaccine**, suitable for field deployment



Mönkäre J. et al., "Mitigation of viral particle interaction with glass surfaces improved Ad26 vaccine quality and long-term stability," Eur. J. Pharm. Biopharm., 2025.

Predicting Titer Loss from Glass Surface Adsorption





- Model created based on experimental data to understand impact of fill volume and Ad26 titer on adsorption
- Assumptions:
  - Vial is cylinder
  - Wetted surface uniformly covered by adsorbed particles
  - Adsorbed particles are spherical and form monolayer

- Model can indicate loss of Ad26 titer due to adsorption on glass surface
- Model can be utilized to evaluate different manufacturing scenarios with minimal experimental work
- Example scenario shows decreasing adsorption with increasing target titer and fill volume

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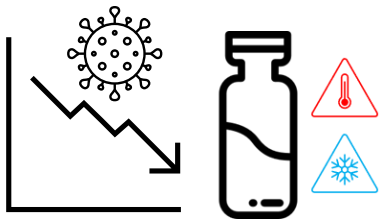
Mönkäre J. et al., "Mitigation of viral particle interaction with glass surfaces improved Ad26 vaccine quality and long-term stability," Eur. J. Pharm. Biopharm., 2025.

Areas Where Modeling Adds Significant Value

Surface Adsorption

Predictive stability

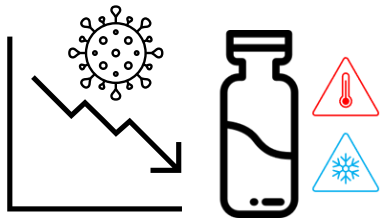


CFD- modeling

Shear stress

Predictive Stability Towards Accelerating Patient Access

Predictive stability



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Review

Predictive stability in biopharmaceuticals and vaccines: perspectives and recommendations towards accelerating patient access

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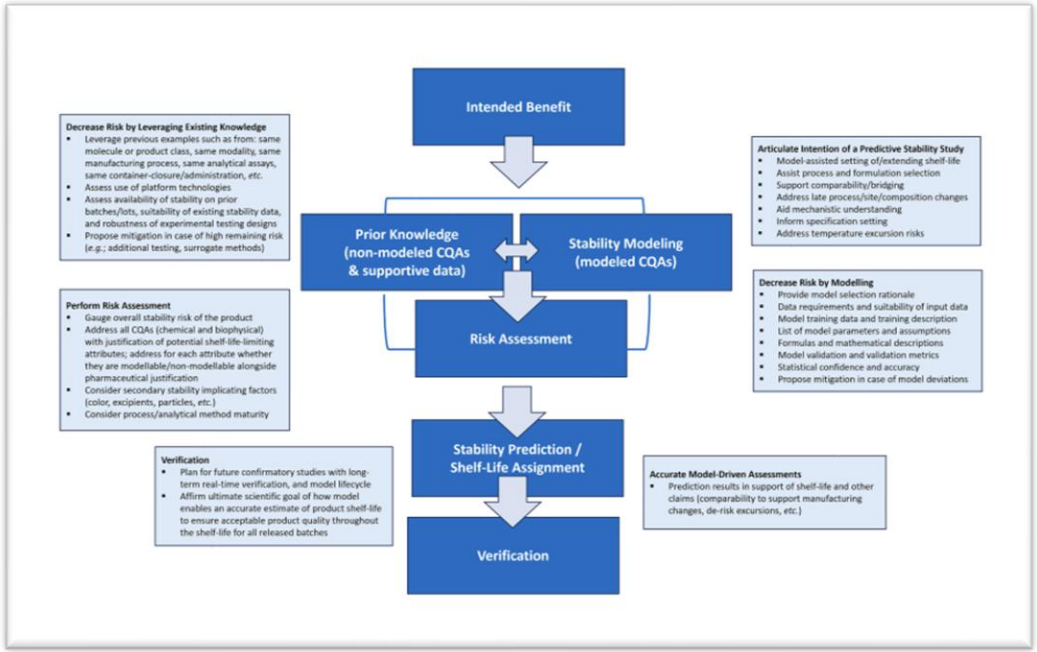
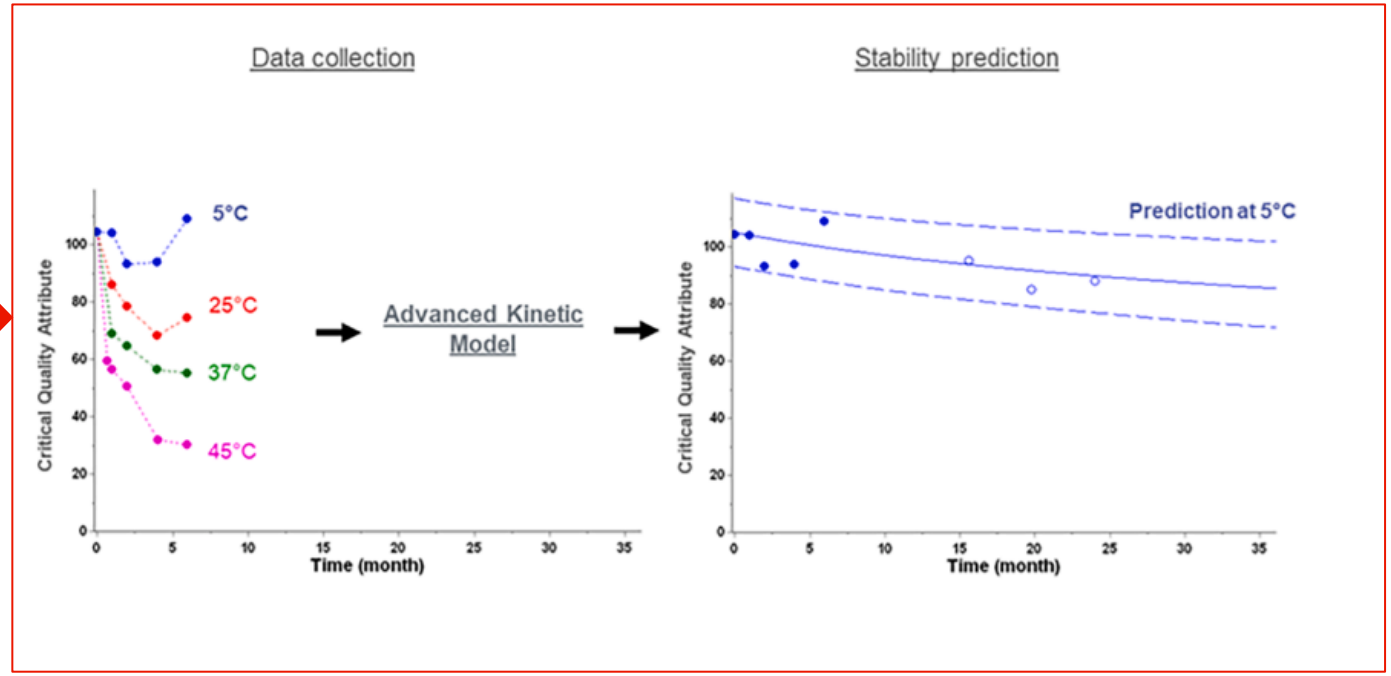
Modeling approach particularly valuable in pandemic response scenarios where speed to market is critical.

Predictive Stability Towards Accelerating Patient Access

Integrating modeling, prior/platform knowledge, and risk assessment for accurate shelf-life prediction



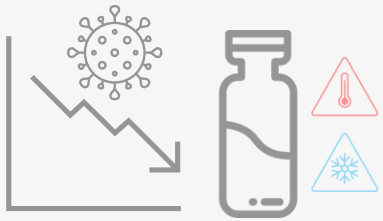


Model incorporates potential multiple degradation pathways and environmental factors to provide robust shelf-life predictions

Areas Where Modeling Adds Significant Value

Surface Adsorption

Predictive stability



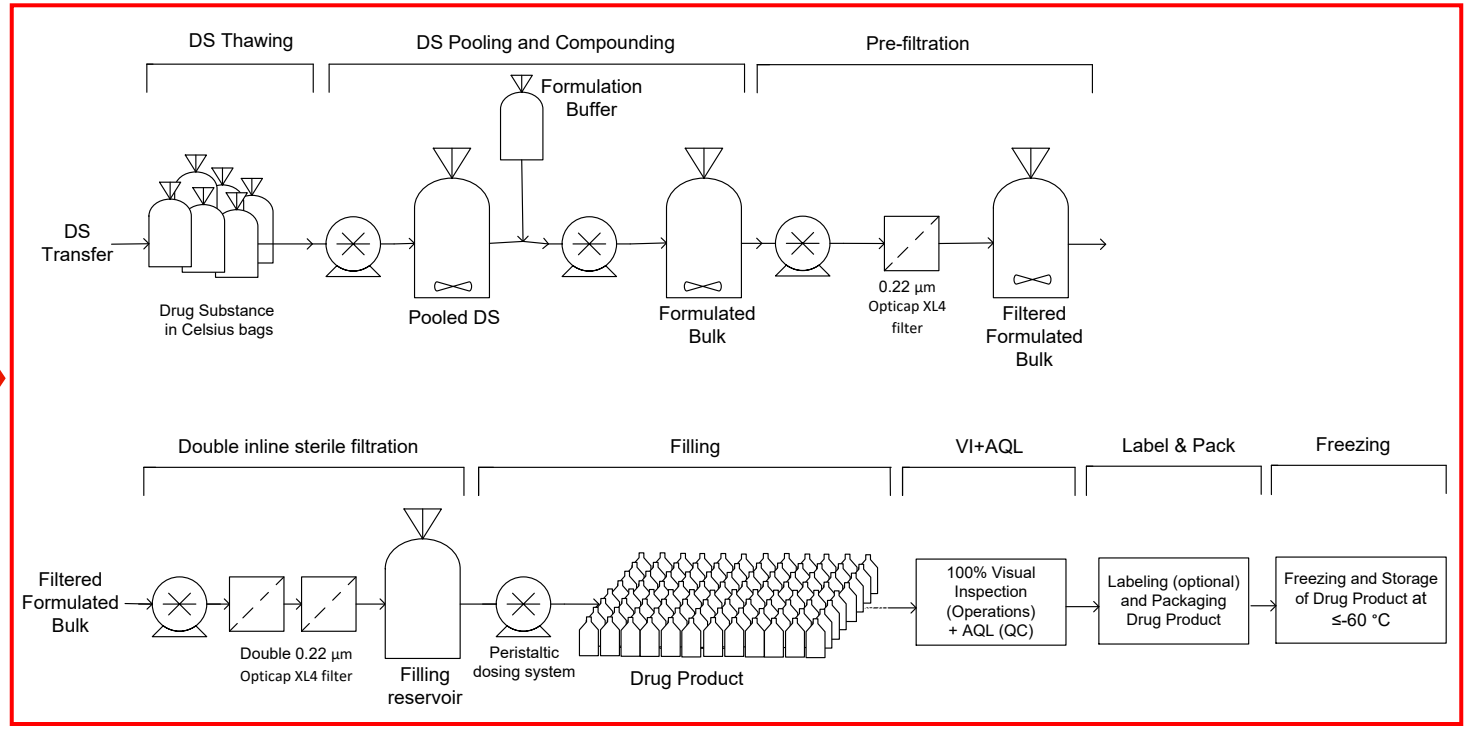
CFD- modeling

Shear stress

Computational Fluid Dynamics Modelling for Process Design

Computational Fluid Dynamics (CFD): a powerful simulation tool to model fluid flow behavior in process equipment

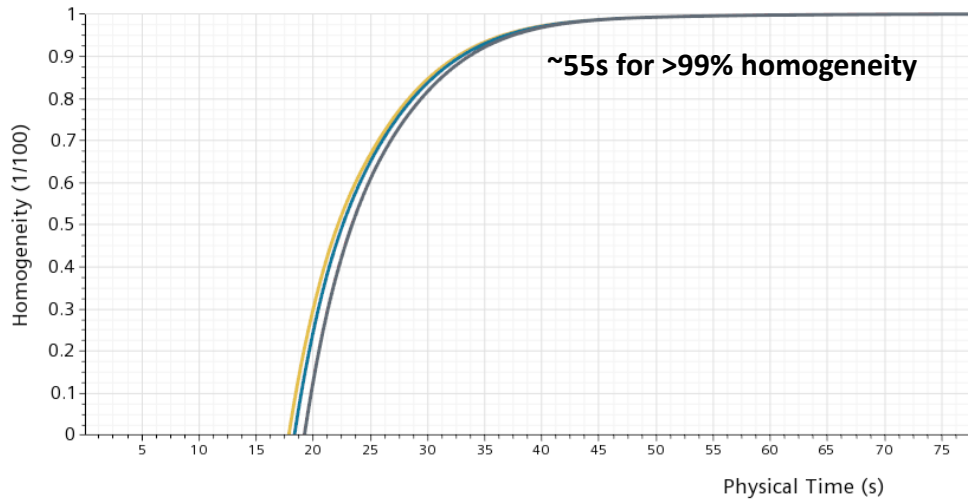
CFD- modeling



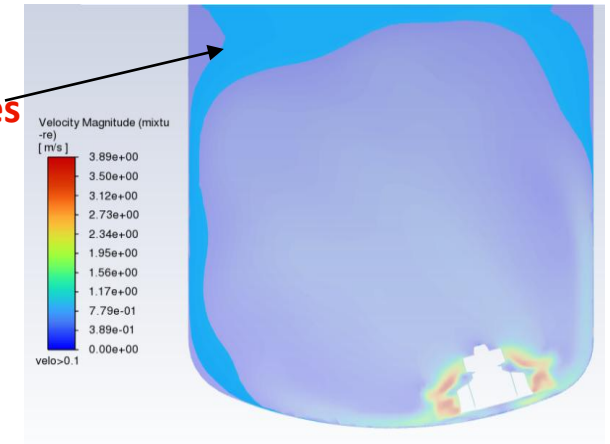
- CFD provides detailed insight into mixing patterns, shear forces, and flow distribution.
- Application: process parameters optimization before committing to physical experiments.

Application of CFD to Mixing in Single-Use Mixers/Tanks

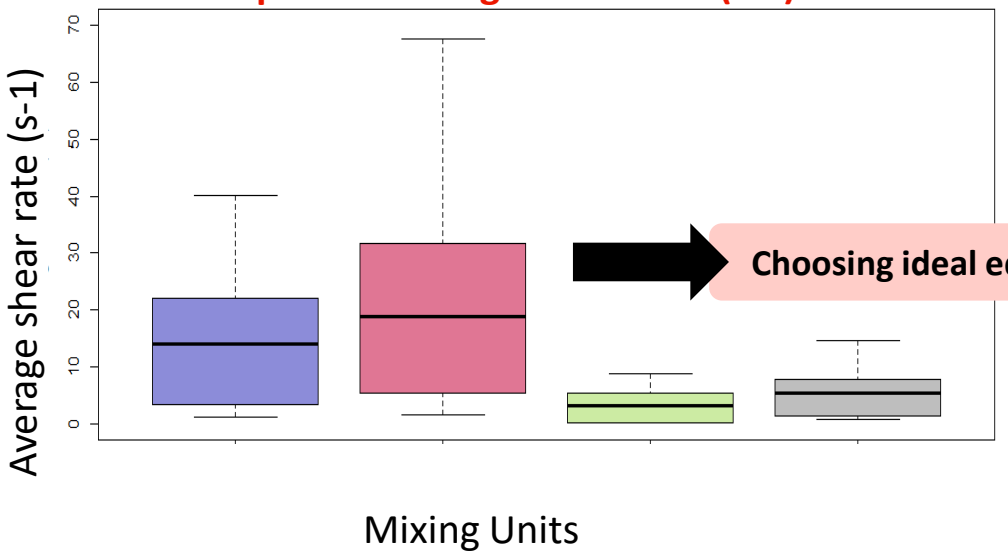
Tracking homogeneity of DP and DS with real time



Identifying dead zones (velocity < 0.1m/s)

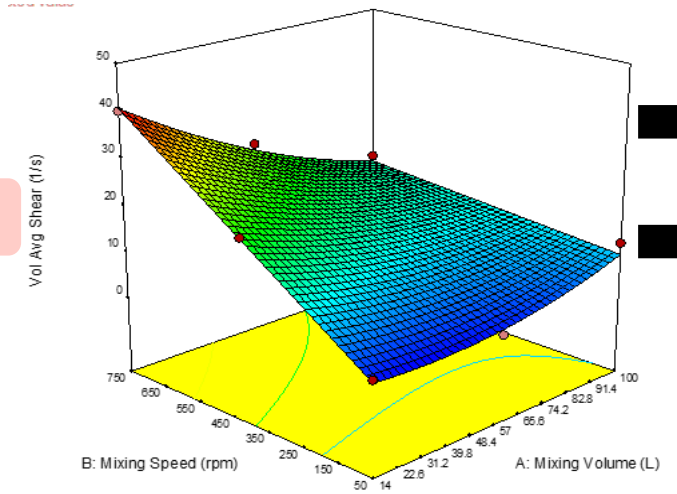


Boxplot of average shear rate (s-1)



Choosing ideal equipment

Design space for shear rate varying with speed and volume



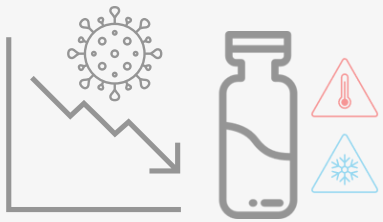
Process optimization

Scale-up

Areas Where Modeling Adds Significant Value

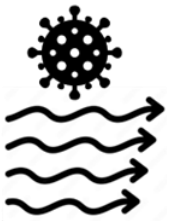
Surface Adsorption

Predictive stability



CFD- modeling

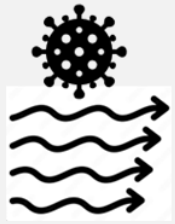
Shear stress



Shear Stress Modelling for Process and Product Understanding

This modeling approach links the mechanical shear experienced during processing to measurable changes in product quality attributes. By establishing this quantitative link, we can set meaningful process limits and design processes that minimize product impact.

Shear stress

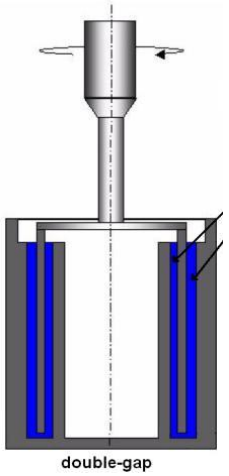


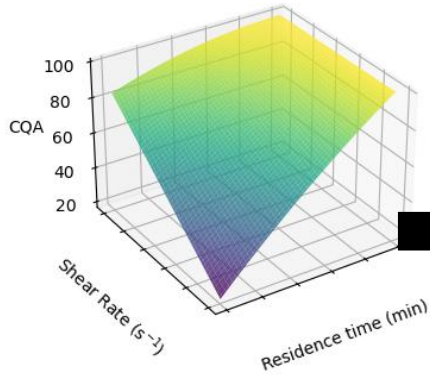
Link between shear and product impact

Shear Stress in Fill Finish Line

Product quality **Shear**

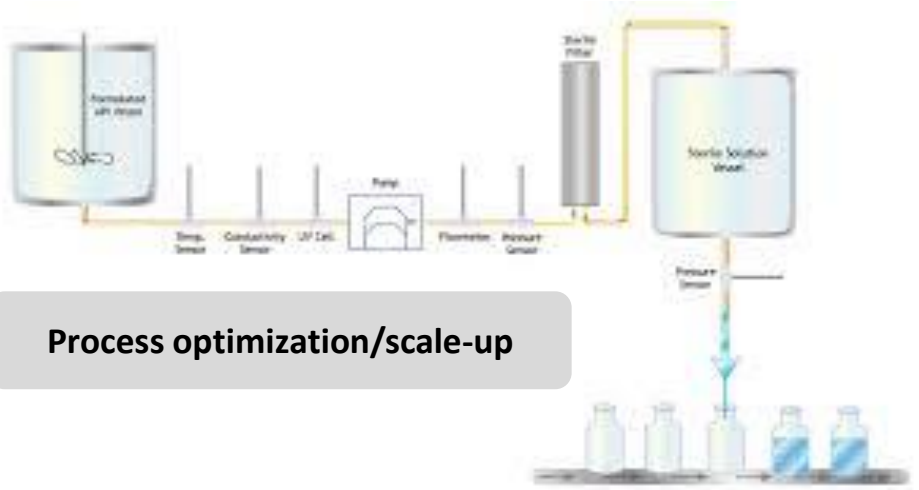
Rheometer delivers controlled amount of shear for defined durations





DoE with shear rate and residence time as factors

Process optimization/scale-up



- CFD model distribution of shear in transfer of DP during filling (tubing, needles, junctions, etc.)
- **Input** on process parameters such as **flow rate, tubing and needle diameter**
- Model **output**: **Shear stress, accumulated shear** = Shear rate x Residence time
- Rheometer used to validate the model + measurement of resulting product impact

Key Takeaways

Leveraging Modeling to De-Risk Viral Vector Development

01

Deeper Insight

Modeling reveals product and process behavior— from adsorption mechanisms to shear stress distribution.

02

Time Savings

Computational tools reduce experimental cycles, enabling faster development timelines by predicting outcomes

03

Material Savings

Conserve valuable viral vector material in early development when supply is limited — model instead of running exhaustive experiments.

Integrate modeling early in your development program to maximize impact and accelerate the path to patients.

Computational tools are indispensable for modern viral vector drug product development

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