

# FDA Animal Rule Models for Orthopoxvirus Monkeypox & Rabbitpox

## OUR EXPERTS ARE READY TO SUPPORT YOUR ORTHOPOXVIRUS TESTING NEEDS

Given our past & current experience in orthopoxvirus models, SR is fully cognizant that the FDA requires the performance of parallel Animal Rule Efficacy Studies which should include the following phases:

**PHASE 1:** To include model development, proof-of-concept, & early immunogenicity studies

**PHASE 2:** To include further immunogenicity, develop bridging data, dose-ranging & vaccine regimen, preliminary challenge studies & continue to develop efficacy studies, validation of associated assays, equipment, etc.

**PHASE 3:** To include definitive or pivotal efficacy studies to be conducted in accordance with 21 CFR Part 58 GLP regulations, use of final formulation, bridging animal and human immunogenicity data, statistical plan, and use of validated assays, equipment, etc.

With these considerations in mind, and responding to needs of our clients, SR has validated a wide range of small and large animal models to mimic human orthopox diseases.

Infections	Host Species	Pathogen Strain	Challenge Route	Disease Endpoints	Stage of Development
Monkeypox	Macaque	MPXV Zaire	Intravenous	Survival morbidity	Available
Monkeypox	Macaque	MPXV Zaire	Intravenous	Survival morbidity	Available
Rabbitpox	NZW rabbit	RPXV Utrecht	Intranasal	Survival morbidity	Available
Mousepox	Mouse	ECTV Moscow	Intranasal	Survival morbidity	Available
Vaccinia	Mouse	VACV-IHDJ	Intranasal	Survival morbidity	Available

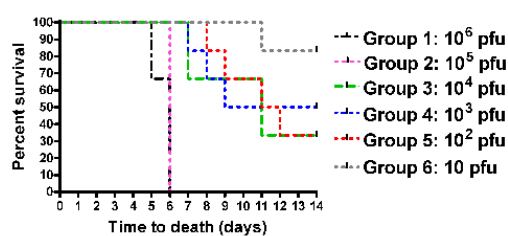
### MODEL DETAILS

- Established SOPs
  - Pivotal GLP-regulated studies
- Clinical endpoints
  - Established euthanasia criteria
- Standardization challenge dose-Lethal Dose<sub>50</sub> studies
- Parenteral & respiratory challenge routes (Intravenous, Intratracheal, Intranasal)

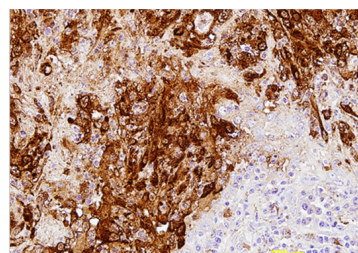
### VALIDATED ASSAYS

- Viral load
  - HA-gene-targeted real-time PCR
- VACV ELISA
- Plaque Reduction Neutralization Test (PRNT)
  - MPXV, RPXV, & VACV
- Orthopoxvirus Plaque Assay
- ELISA
- ELISpot
- Clinical chemistry & hematology

Kaplan-Meier survival curves of groups of 9-week old NZW rabbits challenged intranasally with 10-fold serial dilutions of RPXV



Immunohistochemical Evaluation of the Lungs Post MPXV Challenge- Day 13



Mortality following Intratracheal Challenge of Cynomolgus macaques with MPXV, NR-2324

