



RSV CLINICAL CHALLENGE STOCK: RSV M37




RSV is the most important cause of pneumonia and bronchiolitis in infants and small children and is the most common respiratory pathogen in young children and infants accounting for over 50% of hospitalizations due to lower respiratory track infections in this age group. RSV also causes significant morbidity and mortality in premature infants, the elderly, immune compromised adults, patients with pre-existing chronic lung disease, and individuals with underlying heart defects. No vaccine currently exists and the only approved therapeutic (ribovirin) is associated with severe side effects. Antibodies to RSV do not prevent re-infection and current RSV control measures are inadequate. There is a critical need for the development of new vaccines and anti-viral therapeutics which can be enabled through the use of Meridian's RSV M37 challenge virus.

Product #88023 - Product Description and Specifications:



Summary	cGMP manufactured live Respiratory Syncytial Virus Challenge Stock (RSV M37): RSV M37 consists of an RSV high titer stock produced in characterized Vero cells infected with an RSV virus strain isolated from an original pediatric clinical sample.
Infectivity / Intended Use	RSV M37 has been used in four separate Phase I clinical studies where it successfully generated a human infectivity model (See publications below). When further propagated, RSV M37 can infect Mice, African Green Monkeys, and Lambs for use in preclinical studies.
Clinical Utility	<u>Vaccines:</u> RSV M37 enables precisely controlled clinical studies to demonstrate protection (vs. implied protection via neutralizing Ab response). Patient sample size may be reduced and protection demonstrated in vaccinated vs. placebo groups. <u>Anti-viral Therapeutics:</u> RSV M37 enables precisely controlled clinical studies to show therapeutic efficacy in eliminating or mitigating the effects of the disease in patients who have developed a controlled RSV infection as compared to control.

Product Specifications (Product #88023):



Passage History*	RSV isolate was plaque purified and passaged 4 times in Vero cells.
Infectivity	Titer > 1×10^6 pfu/ml, by plaque assay in Vero cells. Infectious in humans.
Volume / Storage	1mL per vial in 1.8mL cryovials. Store below -60°C.
Viral Bank Testing & Contaminants	Bank tested for identity, sterility, mycoplasma, viral contaminants, retroviruses; and no bacteria, fungus, or mycoplasma detected. No viral contaminants detected by cell culture and PCR analysis. Endotoxin < 10EU/ml.
Cell Bank Testing	Sterility, mycoplasma, adventitious agents by cell culture, <i>in vivo</i> adventitious agents, karyology, isoenzymes, bovine viruses, <i>in vitro</i> assay for porcine viral contaminants, and transmission electron microscopy.
Availability	RSV M37 is available for use in R&D studies or in minimum lot sizes for use in human clinical studies. Clinical M37, grown to higher titer in Vero or HEP-2 cells, has been shown to infect Mice, African Green Monkeys and Lambs.
Publications	<i>Proceedings of the National Academy of Sciences, May 11, 2010, vol. 107, No. 19, pp 8800-8805:</i> The authors show proof of efficacy of a novel RNA interference therapeutic targeted to RSV using the RSV M37 human infection model. <i>American Journal of Respiratory Critical Care Medicine, 2010 Jul 9:</i> Article provides a detailed evaluation of the human infectivity model in adult volunteers and showed that the model parallels natural RSV infection.

Sales Terms and Conditions: Requires Material Transfer and Quality Agreements. Includes full document package: Cell Line Expansion, Accession Bank, Batch Record, COA's for Viral Bank and Cell Line. Includes rights for one human clinical trial. Additional rights available.

* Compared to NIH challenge virus: Passaged 27 times in 5 different cell lines.
F.E.-H. Lee et al. / Antiviral Research 63 (2004) 191-196.

RSV M37 HIGH TITER R&D/PRECLINICAL STOCKS

Meridian has manufactured three versions of the M37 Challenge virus, one for clinical use and two higher titer stocks for R&D/preclinical studies. Multiple animal species are susceptible to RSV infection and have been used as models of RSV pathogenesis or in the development of vaccines and anti-RSV therapeutics. Due to the fact that only small volumes of material can be administered in most mammalian models, and that not all animals used as potential models are as permissive to RSV infection as humans, the need for higher titer RSV challenge materials is warranted. Meridian has developed two higher titer RSV challenge stocks derived from the original clinical challenge material, which can be used for *in vitro* or preclinical *in vivo* studies.

Product #EV9508** - High Titer RSV M37 Grown in Vero Cells:

- Summary** Vials of clinical RSV M37 (Product #88023) were expanded through three additional passages in qualified Vero cells outside of the cleanroom environment to achieve a higher titer stock suitable for preclinical animal challenge studies.
- Infectivity / Intended Use** Titer > 2×10^7 pfu/ml, by immunofluorescence assay in HEp-2 cells. Infectious in Mice, African Green Monkeys, and Lambs. NOT SUITABLE FOR USE IN HUMANS; FOR RESEARCH USE ONLY.
- Volume / Storage** 1mL per vial in 1.8mL cryovials. Store below -60°C.
- Availability** High Titer RSV M37 (Vero) is available for use in R&D studies or preclinical animal challenge studies and is available for purchase.
- Publications / Data** Data on mouse and African Green Monkey infectivity shared from clients who have purchased M37 previously which is available upon request.

Product #EV9510** - High Titer RSV M37 Grown in HEp-2 Cells:

- Summary** Vials of clinical RSV M37 (Product #88023) were expanded through three additional passages in HEp-2 cells outside of the cleanroom environment to achieve a higher titer stock suitable for preclinical animal challenge studies.
- Infectivity / Intended Use** Titer > 2.1×10^8 pfu/ml, by immunofluorescence assay in HEp-2 cells. Infectious in Lambs (no data available at this time in mice and non-human primates). NOT SUITABLE FOR USE IN HUMANS; FOR RESEARCH USE ONLY.
- Volume / Storage** 1mL per vial in 1.8mL cryovials. Store below -60°C.
- Availability** High Titer RSV M37 (HEp-2) is available for use in R&D studies or preclinical animal challenge studies and is available for purchase.
- Publications / Data** Ackermann, M. et al. In newborn lambs, wild-type, low passage, human respiratory syncytial virus strain Memphis 37 (RSV M37) causes lung infection and pathology paralleling that of infants. *Presentation given at the 7th International Respiratory Syncytial Virus Symposium. (December 2-5, 2010. Rotterdam, Netherlands.)*

Custom Services - RSV Manufacturing:

- Summary** Meridian has the capability and experience to successfully propagate human clinical isolates of RSV for your experimental studies and we can generate dedicated high titer stocks of RSV M37 in cell lines of your choosing upon request.