

HSV Models

Mouse model of primary HSV-1/HSV-2 challenge

Our primary screening model provides a rapid initial evaluation of antiviral efficacy against HSV primary infection with both clinical and virological endpoints. This model utilizes intravaginal inoculation of female Swiss Webster mice (25 g) with HSV-1 or HSV-2 to evaluate potential antiviral therapies as well as vaccine/adjuvant candidates. Animals are followed daily for signs and symptoms of herpes disease and vaginal swabs are obtained to evaluate the effect of therapy on viral replication. Single or combined antiviral therapies can be administered topically, orally or systemically and can be given at varying intervals begun before or after viral challenge. Dose range studies are also available.

Volume: Dose and route of administration are individualized for each experimental agent. However for each intravaginal dose 15 ul of product is required. Thus for a twice a day therapy for 7 days 210 ul of product at the desired dose is required. **Treatment group size is typically 12-16 mice.**

Microbicide screening model of primary HSV-2 challenge in mice

This model is designed to evaluate the protection afforded by a microbicide candidate against infection with HSV-2. The model utilizes intravaginal inoculation of female Swiss Webster mice for evaluation. The initial trial is usually performed by applying drug 5 minutes prior to challenge with HSV-2. Further evaluation of microbicides in this model either extend the time between microbicide administration and challenge or examine dose range. Promising candidates can be advanced to a secondary species evaluation in the guinea pig model of genital infection. Evaluation includes daily evaluation for signs and symptoms of genital herpes and viral examination of vaginal secretions.

Volume: Intravaginal treatment of the mouse requires a minimum of 15 ul per mouse of candidate drug and placebo formulation, if applicable, applied once. **Treatment group size is typically 12-16 mice.**

Guinea Pig model of primary genital HSV-2 infection

Because genital herpes disease in the guinea pig more closely resembles human disease this animal is used as a second species for therapies with demonstrated efficacy against HSV in mice. As with humans genital HSV infection in guinea pigs is a self limited vesiculoulcerative disease which is followed by healing, the establishment of latency, and then both spontaneous and inducible symptomatic and asymptomatic recurrences. Our model utilizes intravaginal inoculation of female Hartley guinea pigs and provides both clinical and virologic indices to assess both the effect of treatment on primary disease as well as on the frequency or severity of subsequent recurrent infections. Antiviral therapy can be administered orally, topically or systemically and can be given at varying intervals beginning before or after virus challenge. Following intravaginal inoculation animals are followed daily for the development of genital herpes using a validated genital herpes scoring system. Vaginal swabs are also obtained to evaluate the effect against viral replication. Because this is a non lethal model animals can be sacrificed at the conclusion of the experiment to evaluate the effects of treatment on latency. This model can be adapted to evaluate antiviral activity against available drug resistant strains (ACV and Foscarnet).

Volume: Dose, route of administration and duration of treatment are individualized for each experimental agent. Microbicide studies require a minimum volume of 200 uL / guinea pig applied once. For assessing drug requirements the average weight of the animals is 300 gms. **Treatment group size is typically 10-15 animals.**

Guinea Pig model of recurrent genital HSV-2 infection

The guinea pig model of genital herpes is unique in that after recovery from primary genital infection animals experience spontaneous recurrent genital lesions as well as viral shedding in the absence of lesions. This allows a candidate compound to be evaluated for efficacy in controlling recurrent disease. Female Hartley guinea pigs who have recovered from symptomatic primary genital infection are randomized into treatment groups for antiviral treatments beginning on day 21 PI and continued for 21 days after. Treatments can be given orally, topically or systemically. The indices for these studies include quantification and severity assessment of recurrent episodes during treatment and for 21 days following cessation of treatment.

Additionally, vaginal swabs are collected to evaluate any impact on shedding.

Volume: Dose, route of administration are individualized for each experimental agent. . **Treatment group size is typically 10-15 animals.** Duration of treatment is typically 21 days.

Model of neonatal HSV-2 infection in guinea pigs

Our model of neonatal HSV infection mimics the natural history of infection in the human newborn. This model is available to evaluate candidate antiviral drug therapies and combined therapeutic approaches including combination of antivirals or antivirals and immune modulators.

Additionally, this model can be used to evaluate the efficacy of candidate vaccines by measuring the protection afforded by transplacental antibody. In this model newborn Hartley guinea pigs are inoculated intranasally with HSV-2 within 48 hours of delivery. Newborn animals are then randomized to receive experimental drug, placebo or ACV (control). Animals are evaluated daily for evidence of cutaneous herpetic disease and weight gain as well as pulmonary, CNS symptoms and death. Surviving animal are followed for 45 days to assess the effectiveness of therapy on the incidence and frequency of cutaneous herpetic recurrences.

Volume: Dose, route of administration are individualized for each experimental agent. Duration of treatment is typically 10 days or more. **A positive control of ACV (60 mg/kg/day) BID may be used.** Newborn guinea pigs weigh about 125 gms