The WHO Collaborating Center for Smallpox and other Poxviruses at the Centers for Disease Control and Prevention Atlanta, GA: 2006 report on *in vitro* evaluation of the antiviral compound ST-246.

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As recommended by the U.S. government, antiviral compounds are under current investigation as therapeutic options for the treatment of smallpox in the event of an intentional or accidental release of variola virus. ST-246 is a compound that specifically targets a viral assembly protein which is required for extracellular virus formation. Variola virus C17L mediates the envelopment of intracellular mature virus to yield enveloped virions (EV) which are believed to be responsible for dissemination of the virus within a host. C17L is the homolog of vaccinia virus F13L which has been identified as the target for ST-246 through resistance mapping studies. To evaluate ST-246 as an antiviral therapy, its activity was characterized *in vitro* against live variola virus infection. Comet reduction assays were performed to measure the level of variola EV production in Vero E6 cells treated with ST-246 post-infection. Comet formation was completely inhibited in cells that received concentrations of 0.5 – 0.05uM and was reduced at a concentration of 0.015uM. In addition, the effective concentration of ST-246 to protect cell monolayers by 50% from virus-induced cytopathic effects (EC_{50}) was calculated. Cell monolayers were infected with Variola virus at an MOI of 0.1 which causes 90% cytopathic effect at 3 days post-infection. Cytopathic effects were quantified by staining cell monolayers with crystal violet and measuring absorbance values at 570nm. Inhibition curves were generated and showed the EC_{50} is approximately 0.05uM. Additional animal model testing will be performed to further characterize the effect ST-246 has on live Variola virus infection.