Reviewer's report

Title: Microbicide excipients can greatly increase susceptibility to genital herpes transmission in the mouse

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Reviewer: Brian Wigdahl

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Summary: This manuscript centers on the use of a mouse model to determine whether active components of microbicides, and inactive ingredients, including preservatives and other excipients, increase the susceptibility of HSV-2 transmission as a measure of potential toxicity. The following comments are provided to the authors:

1. The authors test the two components of “Astroglide”, a personal lubricant, which in the slug irritation model reported toxicity. The authors proceed to test formulations of 10% glycerol and 10% propylene glycol. The authors do not include a rationale behind why these concentrations were chosen for their studies. This information needs to be included. It would seem that concentrations more characteristic of what is included in Astroglide should be included.

2. Because 5% GML in KYWJ and KYWJ alone both caused nearly all of the treated animals to become infected, a lower dose of virus was used to challenge treated animals. This low dose challenge should also have included 5% GML colloidal suspension in PBS as well as PBS. The inclusion of the colloidal GML would have given an additional direct comparison of increased susceptibility to infection with regard to what is being caused by GML alone and KYWJ alone. The authors did include the PBS control, however at the higher challenge dose of 1.0 ID50. For the sake of completeness, PBS challenged at the low dose should also be included, to allow the readers to make a direct comparison.

3. One issue with the manuscript, is that the data is presented in a fashion that is merely “screening” of compounds and excipients. Although the authors include some information on osmolality, a more mechanistic research approach should be pursued so that the authors can strengthen the “overall impact” and determine why they got the results they did and how they can alter future experimental directions.

4. In general, the manuscript presented is well written, with interesting experiments that lead to conclusions that are relevant for the field of microbicides. However, a more mechanistically driven results section would greatly enhance the quality of the manuscript.

Level of interest: An article of importance in its field

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.