As described in Section 6.1.2.6 of the draft ICCVAM BRD (http://iccvam.niehs.nih.gov/restrict/ocupanel/mildmod/HETCAM-BRD.pdf), there were four EPA Category III ocular irritants that were classified as Category IV using the HET-CAM test method (i.e., were false negatives, see **Table 3**). Among the four false negatives for the EPA system, 100% (4/4) were EPA Category III substances based on Draize data. For 100% (4/4) of these substances, the categorization was based on conjunctival redness. As noted in Section 6.1.2.6, all of the false negative substances were oil/water emulsions.

**Table 3        HET-CAM False Negative Substances[1] Using the EPA Classification System.**

| Substance | N[2] | In Vivo Scores | |
|---|---|---|---|
| | | Corneal Opacity: score (day cleared)[3] | Conjunctival Redness: score (day cleared)[3] |
| HZA | 6 | - | N=1 2(2) <br> N=1 2(3) |
| HZC | 6 | - | N=1 2(2) |
| HZV | 6 | - | N=2 2(2) |
| HZW | 6 | - | N=4 2(2) <br> N=1 2(3) |

[1] False negative compounds are those that test as nonirritants in vitro but are mild, moderate, or severe ocular irritants/corrosive in vivo i.e. EPA category I, II, and III; GHS 1, 2A, and 2B; and EU R41 and R36.

[2] N: Number of Animals.

[3] For the purposes of this evaluation, clearing is defined in the EPA Hazard Category system as opacity or iritis scores = 0 or redness or chemosis scores = 1.