

IRRITATION TESTING OF CONTRACEPTIVE AND FEMININE-CARE PRODUCTS USING EPIVAGINAL™, AN IN VITRO HUMAN VAGINAL-ECTOCERVICAL TISSUE MODEL

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Normal human vaginal-ectocervical (VEC) cells were cultured to reconstruct VEC tissues in vitro (designated as VEC-100). In some cultures, normal human dendritic cells were also incorporated (designated as VLC-100-FT). Both tissues mimic native in vivo tissue in that they have basal, parabasal, glycogenated intermediate, and the superficial cell layers. To test the utility of the VEC tissue, contraceptives, microbicides, anti-itch agents, and other vaginal-care products (VCP) were topically applied. To mimic heterosexual HIV infection, the VLC tissue was topically exposed to HIV-1 viruses. Quality control (QC) testing on each batch of tissue utilized Triton X-100 (1%) and water as positive and negative controls, respectively. The MTT assay was used to determine the exposure time necessary to decrease the tissue viability to 50% (ET-50) for the positive control and 20 VCP. QC testing showed the tissues to be highly reproducible; the average intra-lot coefficient of variation was <10% and ET-50s averaged 1.26 hr ± 0.23 (n=25 lots). The VEC tissue model discriminated between the mildness of VCP. The ET-50 values ranged between 1.7-2.7 hr for feminine washes, 3.5-7.0 hr for contraceptives, 6.9->18 hr for anti-itch creams, and were > 18 hr for douches, lubricants, and anti-fungal creams. Released cytokines and gene expression levels showed that IL-1a, IL-1β, and IL-8 were associated with toxicity of VCP. Finally, the VLC tissue was infectible with macrophage-tropic and T-cell tropic HIV-1 strains as evidenced by DNA-PCR. Based on these results, it is likely that the VEC tissue model will serve as a useful, highly reproducible, non-animal tool to assess the irritation of VCP. In addition, the VLC tissue will enable studies pertaining to HIV infection, microbicides and drug absorption.

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