Supplementary data

Figure S1. Comparison of *in vitro* release profiles for tenofovir (TFV) gel and RG-TFV gel. The data are the mean±SD from multiple runs of TFV (*n*=3) and RG-TFV (*n*=5) gels.

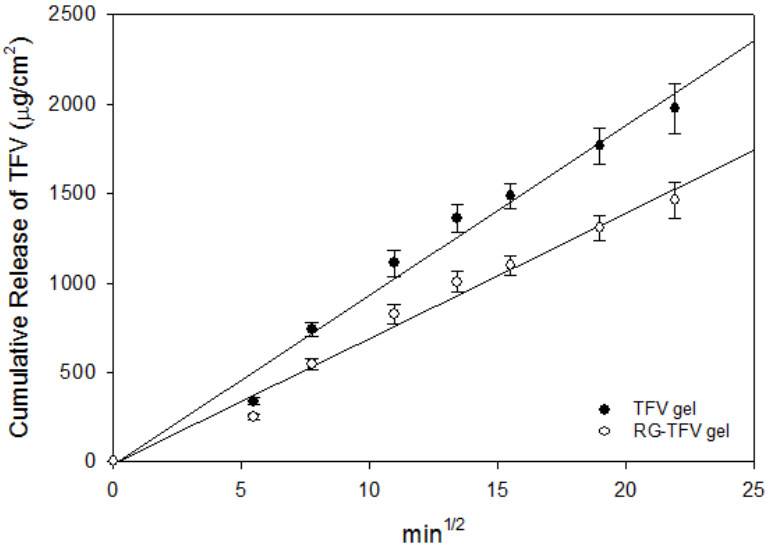

Figure S2. Impact of RG-tenofovir (TFV) gel on retention of epithelial monolayers. Caco-2 and HEC-1-A epithelial cells were grown on transwell supports until stable monolayers developed as measured by a volt meter. Dilutions (1:10) of the RG-TFV and original TFV gels were applied to the apical surface. As controls, no cells, cell with no treatment and a 1:50 dilution of an over-the-counter gel (Gynol II), containing 2% N9, were included. The TER was measured 30 min, 1 h, 2 h, 4 h, 8 h and 24 h after product application. The data shown are the mean±SD from five independent experiments.

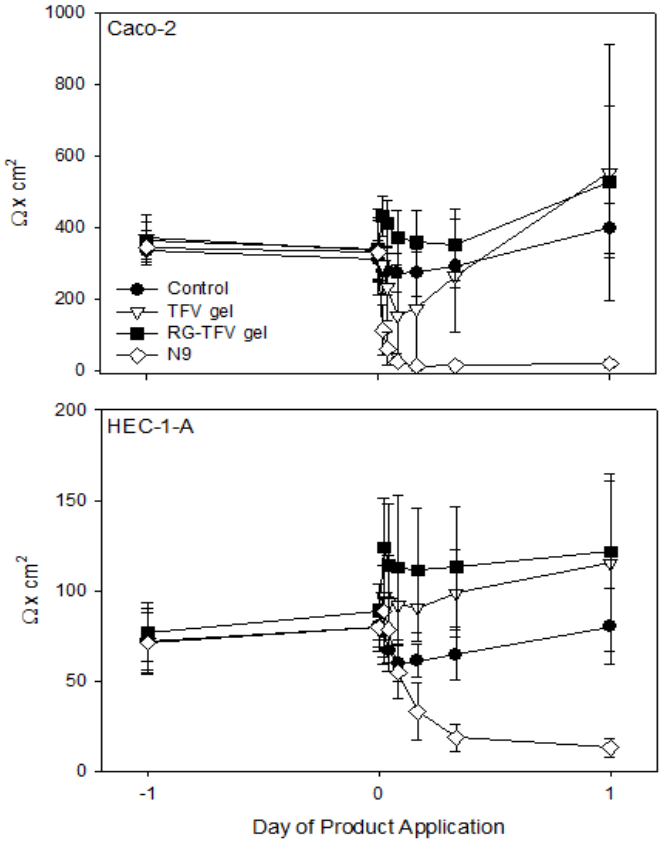

Figure S3. Representative tissue histology and immunohistochemistry after exposure to RG-tenofovir (TFV) gel and the original TFV gel. (a) The effect of RG-TFV gel and original TFV gel on polarized colorectal and ectocervical explant culture viability. Duplicate polarized colorectal and ectocervical explant cultures were treated overnight to 1:5 dilutions of RG-TFV, original TFV or Gynol II (2% N9-containing) gels. Untreated explants were used as the reference control for each tissue. After product exposure, explants were washed and placed in paraformaldehyde for histology. The data shown are representative figures from one of the three independent tissues. (b) Endpoint immunohistochemistry was done to evaluate the anti-HIV-1 activity of the RG-TFV and original TFV gels in ectocervical explant cultures. After overnight exposure to HIV-1 with or without either gel, the explant cultures were washed and followed for 21 days. Shown are representative immunohistochemistry figures from one of the three independent ectocervical tissues.

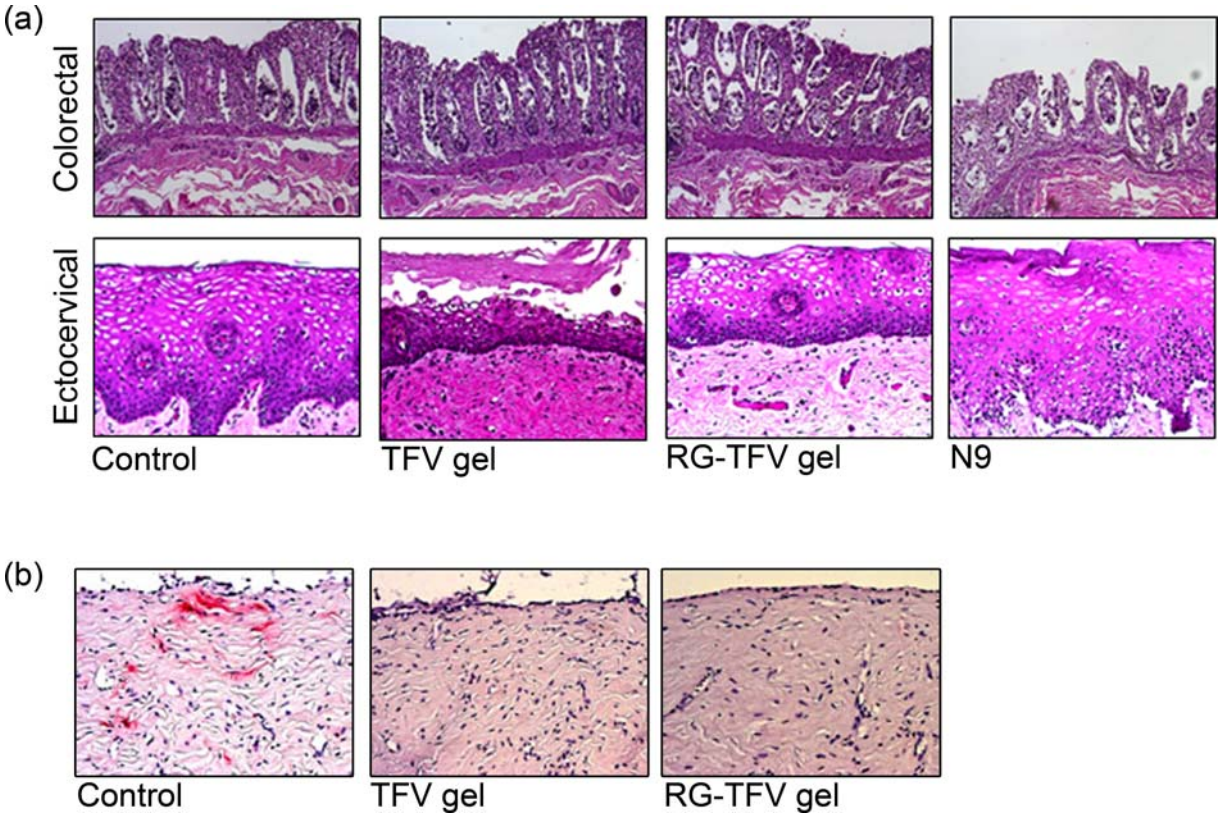

Table S1. Permeability of the original tenofovir and RG-tenofovir gels through ectocervical tissue

	Tenofovir gel (*n*=4)	RG-tenofovir gel (*n*=7)
Tenofovir (μg) in the receptor; 6 h exposure	79.98-257.35	207.72-424.88
P_{app} (cm/s)	2.02±1.12 ($\times 10^{-6}$)	3.02±2.07 ($\times 10^{-6}$)