

### **SUPPORT DOCUMENT III: Antiviral Penetration of Topical Antiviral Agents**

Topical antiviral agents vary in their ability to penetrate the cornea and achieve adequate aqueous humor concentration. Adequate aqueous concentrations of trifluridine, for example, can only be achieved when the cornea has been debrided or damaged. The corneal penetration of trifluridine doubles in patients with debrided or damaged corneal epithelium when compared to patients with an intact corneal epithelium (Pavan-Langston 1979, Sugar 1973, Poirier 1982). However, topical acyclovir has been proven to achieve adequate aqueous humor concentrations in humans with an intact corneal epithelium (Poirier 1982). Topical ganciclovir, at doses 20 times the currently marketed strength, achieved adequate aqueous humor concentration levels in rabbits with normal corneas (Schulman 1986). There are no studies with intact or debrided corneas demonstrating corneal penetration measured by adequate aqueous humor concentration levels of ganciclovir gel 0.15%. Given the penetration data, topical antivirals (ganciclovir and trifluridine) may not be useful in the treatment of deeper herpes simplex keratitis infections, especially when the corneal epithelium is intact.