Eye injury is a leading cause of visual impairment in the U.S., with up to 50,000 new cases reported each year. To evaluate the potential of chemicals to cause eye irritation, the protocol most widely accepted by regulatory agencies is based on the Draize rabbit eye test method. Since current ocular test guidelines state that users must ensure that the topical anesthetic does not affect test results, pain medications are often not used. However, for over 20 years CPSC has recommended pre-application of a topical anesthetic for all rabbit eye toxicity studies. Therefore, ICCVAM recently conducted a comprehensive evaluation of the usefulness and limitations of routinely using topical anesthetics, systemic analgesics, and earlier more humane endpoints to minimize pain and distress in ocular toxicity testing. Following this evaluation, which included recommendations from an international independent peer review panel, ICCVAM concluded that a balanced preemptive pain management protocol should always be used when the Draize rabbit eye test is conducted for regulatory safety testing. This protocol should include pre-treatment with a topical anesthetic and systemic analgesic, and routine post-treatment with systemic analgesia. ICCVAM also recommends several additional humane endpoints that should be used to end studies earlier. To ensure timely and accurate detection of humane endpoints in ocular studies, ICCVAM recommends routine examination with a slit-lamp biomicroscope to characterize the nature, severity, and progression of any corneal lesions. ICCVAM also recommends routine observations for clinical signs of pain and distress at least twice daily, or more often if needed. Implementation of these ICCVAM recommendations should avoid or significantly reduce pain and distress associated with ocular safety assessments while continuing to support the protection of human health.