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The Performance Characteristics of the *In Vivo* Rabbit Eye Test

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Alternative *in vitro* test methods proposed to substitute or replace an *in vivo* assay should provide equivalent or improved protection of human or animal health to gain regulatory and general acceptance. The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) is evaluating four *in vitro* ocular test methods as partial replacements for the detection of severe ocular irritants (i.e., those that induce or are likely to induce irreversible ocular damage). Integral to this evaluation and to the future evaluation of *in vitro* ocular toxicity test methods that are proposed as full replacements is an assessment of the performance characteristics of the current *in vivo* rabbit eye test. Ideally, this analysis would evaluate the ability of the rabbit eye test to correctly predict ocular toxicity in humans. However, due to the absence of adequate human data, estimating the likelihood of underpredicting a positive response in the *in vivo* rabbit eye test is the best approach for assessing the performance of this assay. Relevant *in vivo* rabbit eye test method data have been obtained from U.S. Federal agencies and published literature. The underprediction rate for the *in vivo* rabbit eye test depends on the regulatory classification system used. For this analysis, the UN Globally Harmonized System of Classification and Labeling of Chemicals and the U.S. Environmental Protection Agency Ocular Toxicity Classification Scheme are the regulatory approaches being used to distinguish between nonirritants and various classes of ocular irritants. More than 500 chemicals were assigned to ocular irritation categories based on the observed responses in 3 to 6 animals. Based on this distribution of animal responses within each irritation classification level, the underprediction rate associated with a sequential testing strategy (maximum of three animals) was evaluated. The results and implications of these analyses will be presented and discussed.
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SOT Itinerary Information:

ID#	662
Location:	Room R03
Date/Time:	March 8, 2005 / 9:10 – 9:40 AM
Session:	Current Status and Future Considerations for the Development and Validation of *In Vitro* Alternatives to the Draize Rabbit Eye Test