

Usefulness and Limitations of the Cytosensor[®] Microphysiometer (CM) Test Method for Ocular Safety Testing

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ICCVAM evaluated CM as a potential replacement for the rabbit eye test for identifying ocular hazards. CM is restricted to water-soluble substances. ICCVAM concluded that substances within a limited applicability domain (water-soluble surfactants, surfactant-containing formulations, nonsurfactants) that are positive for severe effects in CM can be classified as ocular corrosives/severe irritants (EPA Category I, EU R41, GHS Category 1). False positive rates ranged from 0% (0/17, 0/18) to 10% (3/29) and false negative rates ranged from 9% (2/23) to 50% (6/12) depending on the hazard classification system used. ICCVAM also concluded that substances within an even more restricted applicability domain (water-soluble surfactant chemicals and certain types of surfactant-containing formulations, but **not** nonsurfactants) would not require ocular hazard labeling (EPA Category IV, EU Not Labeled, FHSA Not Labeled) without any further testing if they are negative in CM. Although false positive rates were high (50% [3/6] to 69% [18/26]), false negative rates ranged from 0% (0/27, 0/28, or 0/40) to 2% (1/46 or 1/47) depending on the hazard classification system used. CM is not considered valid for identification of mild or moderate ocular irritants (EPA Categories II/III; EU R36; GHS Categories 2A/2B); these substances would require additional testing. ICCVAM also recommended a standardized CM protocol and future studies to expand the applicability domain. Some ICCVAM agencies have endorsed these recommendations, making CM the first *in vitro* test method available in the US for identifying a subset of substances that do not require ocular hazard labeling. A draft OECD TG for CM is currently being considered.

Theme: I-8 Safety Testing for Chemically Induced Eye Injuries: Recent Three Rs Advances

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