

ICCVAM Recommendations on the Usefulness and Limitations of the Cytosensor Microphysiometer® (CM) Test Method For Ocular Safety Testing

J Merrill¹, D Lowther¹, A Layton², J Redden³, M Wind², W Stokes⁴

¹U.S. FDA, Silver Spring, MD; ²U.S. CPSC, Bethesda, MD; ³U.S. EPA, Washington, DC; ⁴NICEATM/NIEHS/NIH/DHHS, RTP, NC

ICCVAM recently evaluated several *in vitro* test methods as potential replacements for the rabbit eye test for identifying potential ocular hazards. None of the methods were considered adequate as complete replacements. However, ICCVAM concluded that test substances within a defined limited applicability domain (water soluble surfactants, surfactant-containing formulations and nonsurfactants) that are positive for severe effects in the 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 from 9% (2/23) to 50% (6/12) depending on the hazard classification system used. ICCVAM also concluded that test substances within an even more restricted applicability domain (water soluble surfactant chemicals and certain types of surfactant-containing formulations) can be considered as not classified for ocular hazards (EPA Category IV, EU Not Labeled, FHSA Not Labeled) without any further testing if they are negative result in the 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% (1/42 or 1/47) depending on the hazard classification system used. A chemical that produces a response in CM between these two extremes would require additional testing (*in vitro* and/or *in vivo*) to establish a definitive classification. The CM test method is not considered adequately valid for identification of mild or moderate ocular irritants (GHS Categories 2A/2B; EU R36; EPA Categories II/III). ICCVAM also recommended a standardized CM protocol and future studies to expand the applicability domain of the CM. These recommendations have been forwarded to Federal agencies and if accepted, the CM will be the first *in vitro* test method available in the U.S. for identifying substances that do not require ocular hazard labeling.

Keywords: ocular safety; *in vitro*; eye irritation

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