1. Were the submitted test method and supporting validation data subjected to a transparent and independent peer review process?

Prinsen et al as well as Balls et al performed validation according to GLP, and the published results of five validation tests were reviewed by ICCVAM,[1] an independent organization promoting alternatives to animal experiments.
In addition to the results of the above-mentioned five tests, the isolated chicken eye (ICE) method has also been reported on, but was eliminated from consideration due to a lack of information on substances tested, a lack of numerical data, and problematic individual data.
The JaCVAM peer review panel on alternatives to ocular irritation testing based its review on this data.

2. Does the data generated by the test method adequately measure or predict the end point of interest? For replacement test methods, does the data show a linkage between the proposed test method and an existing test method, and/or the proposed test method and effects in the target or model species?

This test method involves the assessment of damage (swelling, opacity, fluorescein retention) to the cornea of an isolated chicken eye as an alternative method for assessing corrosion and severe irritation that can replace the Draize rabbit eye test for toxicity assessment of ocular irritation in humans.

This test method demonstrates sufficient agreement with Draize test classification of ocular corrosion and severe irritation caused by chemical substances. Indices of these changes indicate irreversible effects on the eye and are useful in assessing ocular corrosion and severe irritation caused by chemical substances.

Given that there are, however, significant anatomical and physiological differences in rabbit and chicken corneas, combined with the fact that this test method involves the use of an isolated eye, the application of this method for uses other than the prediction of corrosion and severe irritation is limited.

3. Does the test method generate data useful for hazard/risk assessment purposes?

This test method is useful for hazard assessment of ocular corrosion and severe irritation caused by chemical substances. There are no judgment criteria for use in risk assessment nor is any analysis of concentration and reactivity performed.

4. Do the submitted test method and supporting validation data adequately cover a spectrum of chemicals and products representative of those administered by the regulatory program or agency for which the test method is proposed? Are the applicability and limitations of the test method clearly described?

The supporting validation data for this test method includes a total of 175 chemical substances or products, 90 of which are single chemical substances and 85 of which are commercial products or preparations comprising chemical compounds. A variety of chemical structures, characteristics, properties, and irritation potencies were measured across a clearly defined spectrum of applicable substances.

This test method is capable of assessing the potency of corrosion and severe irritation across a wide spectrum of substances. It is not, however, sufficient for predicting potency of alcohol, surface-active agents, or solids.

This test method assesses changes in the cornea immediately after exposure but does not assess recovery or other aspects thereafter.

5. Is the test method sufficiently robust (relatively insensitive to minor changes in protocol) and transferable among properly-equipped laboratories with adequately-trained staff?

This test method is can be performed at any properly-equipped laboratory with an adequately-trained staff. Based on the need for specialized devices as well as the need for acquisition of testing techniques, it would be difficult to transfer to Japan at this time.

The protocol is considered sufficiently robust.

6. Is the test method both time and cost effective as well as likely to be used in a regulatory context?

The cost of this test does not differ significantly from that of the Draize test, but the time required to perform the test is significantly shorter.

The EU currently accepts ICE tests for use to positively identify and label chemical substances as severe eye irritants (R41). The US EPA[2] has indicated its acceptance of this test method for identifying the corrosion and severe irritant potency in chemical substances being assessed for ocular severe irritation.

This test method has been judged to be useful as a test for ocular irritation in determining corrosion and irritation potency of substances in accordance with GHS,[3] which leads us to conclude that it should be acceptable as for use in a regulatory context in Japan, as well.

Although ordinary use in Japan is impracticable at this time, there is an overseas laboratory to which these tests could be subcontracted.

7. Can scientific, ethical, and economic justification be provided for the new or updated test method in light of existing test methods?

This test method can be used to ascertain irreversible damage to the cornea caused by chemical substances, which provides scientific justification for its use in the assessment of ocular corrosion and severe irritation.

This test method is ethically preferable to the Draize test method.

This test method could potentially be a more economical alternative to animal testing.

8. The test method should be suitable for use as regulatory documentation in the assessment of safety.

This method is capable of assessing direct corrosion and severe irritant potency of chemical substances. Within that limitation, it is suitable for used in a regulatory context.

Based on the above, the JaCVAM Regulatory Acceptance Board has determined that correct application in accordance with all precautions stipulated by the isolation chicken eye (ICE) test method for assessing ocular irritant potency as an alternative to animal testing is a scientifically-valid means of assessing ocular irritant potency of chemical substances.

Notes:

1. Interagency Coordinating Committee on the Validation of Alternative Methods, USA (ICCVAM)

2. U.S. Environmental Protection Agency (EPA)
3. Global Harmonized System of Classification and Labeling of Chemicals (GHS)