Annual report in 2011 on the Japanese Center for the Validation of Alterative Methods (JaCVAM)

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Summary
In November 2005, the Japanese Center for the Validation of Alternative Methods (JaCVAM) was established at the Biological Safety and Research[0] Center affiliated with the National Institute of Health Sciences (NIHS) in Japan. The JaCVAM's mission is to facilitate the 3Rs (Reduction, Refinement and Replacement) with regard to animal testing, with special priority in Japan given to reduction and replacement. Specifically, the key objectives of JaCVAM are:
1) To ensure that new or revised tests are validated through comparison with domestically developed or internationally certified standard tests, peer reviewed, and officially accepted by the regulatory agencies.
2) To work towards harmonization of international alternatives to animal testing. Each validation center has signed a Memorandum of Cooperation with the International Cooperation on Alternative Test Methods (ICATM). Countries and regions participating in ICATM include JaCVAM; the European Union Reference Laboratory for Alternative Methods to Animal Testing (ECVAM)[0]; the United States NTP Interagency Center for the Evaluation of Alternative Toxicological Methods/Interagency Coordinating Committee on the Validation of Alternative Methods (NICEATM/ICCVAM); Health Canada; and, as of March 2011, the Korean Center for the Validation of Alternative Methods (KoCVAM). Under the ICATM framework, JaCVAM expects to experience more efficient test validation and review, as well as more rapid national and international acceptance of scientifically valid methods.

In the six years that JaCVAM has been active, seven methods have been accepted by the JaCVAM regulatory acceptance board, including: 1) the bovine corneal opacity and permeability (BCOP) test for identifying ocular corrosives and severe irritants; 2) the isolated chicken eye (ICE) test for identifying ocular corrosives and severe irritants, 3) the local lymph node assay (LLNA): DA, a non-radioactive modification to the LLNA, which quantifies adenosine triphosphate (ATP) content via bio-luminescence as an indicator of lymphocyte proliferation; 4) the LLNA:BrdU-enzyme linked immunosorbent assay (ELISA), a non-radioactive modification to the LLNA test method, which utilizes non-radiolabelled 5-bromo-2-deoxyuridine (BrdU) in an ELISA-based test system to measure lymphocyte proliferation; 5) the Reconstructed Human Epidermis Test Method, EPISKIN for *in vitro* skin irritation testing; 6) the Human Skin Model Test, Vitrolife-Skin, EpiDerm for *in vitro* skin corrosion testing; and 7) an *in vitro* cytotoxicity test for estimating starting doses for acute oral systemic toxicity tests.

In February 4, 2011, the Ministry of Health, Labour and Welfare of Japan was notified that data obtained with alternative testing methods approved by the JaCVAM Steering Committee could be used for the submission of quasi-drug applications or for petitions to include ingredients in the Standards for Cosmetics. Therefore, JaCVAM decided to accelerate new *in vitro* testing methods to take advantage of this opportunity to strongly impact testing throughout Japan. Accordingly, JaCVAM is currently coordinating the validation studies and peer review of several tests. Most of the tests are for the safety assessment of cosmetic ingredients and/or products. The methods currently undergoing national or international peer review include the Bhas cell transformation assay and the short time exposure (STE) assay for eye irritation testing. Additionally, JaCVAM is participating, along with several other international collaborators, in ongoing validation studies, which include the human cell line activation test (h-CLAT), *in vivo/in vitro* Comet assays, the stably transfected transactivation assay (STTA) antagonist test for screening of endocrine disruptors, and an a reactive oxygen species (ROS) assay for phototoxicity.

Furthermore, we started the validation study on the IL-8 Luc assay for the skin sensitization and SIRC-CVS for the eye irritatiion under the ICATM framework this year.