

Annual report on the Japanese Center for the Validation of Alternative Methods (JaCVAM) in 2020

Takao Ashikaga, Hajime Kojima and Yoko Hirabayashi

JaCVAM, Biological Safety Research Center, National Institute of Health Sciences (NIHS)

Abstract

In 2020, JaCVAM (Japanese Center for the Validation of Alternative Methods) proposed three test methods accepted by the JaCVAM Regulatory Acceptance Board to the regulatory agency, including: 1) Bhas 42 Cell Transformation Assay: CTA, 2) Performance-Based Test Guideline (PBTG493) for Human Recombinant Estrogen Receptor (hrER) *In Vitro* Assays to Detect Chemicals with Estrogen Receptor (ER) Binding Affinity, 3) Interleukin-8 Reporter Gene Assay (IL-8 Luc assay) for skin sensitization.

Furthermore, JaCVAM contributed to approve OECD (Organisation for Economic Co-operation and Development) three Test Guidelines (TGs) showing below, 1) Stably Transfected Human Androgen Receptor Transcriptional Activation Assay for Detection of Androgenic Agonist and Antagonist Activity of Chemicals: TG458, 2) Short Time Exposure *In Vitro* Test Method for Identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classification for Eye Irritation or Serious Eye Damage: TG491, 3) *In Chemico* Skin Sensitisation: Assays addressing the Adverse Outcome Pathway Key Event on Covalent Binding to Proteins, the Amino Acid Derivative Reactivity Assay (ADRA): TG442C .

In the OECD Work plan, Japan has proposed seven test methods: 1) Amendment of TG439: Including Layer by Layer (LbL) 3D-Skin Skin Irritation Test (SIT), 2) Amendment of TG437: Including of histopathological examination on Bovine Corneal Opacity and Permeability (BCOP) test method, 3) Amendment of TG494: Expansion of the applicability domain of Vitrigel-Eye Irritation Test (EIT), 4) Amendment of TG442C: Modification of ADRA for skin sensitisation, 5) Integrated Approaches to Testing and Assessment (IATA) for photosafety test, 6) Detailed Review Paper (DRP) for *in vitro* immunotoxicity test and 7) DRP for *in vitro* reproductive and developmental toxicity test using pluripotent stem cell. JaCVAM is cooperating with OECD in the development and review process regarding TGs and Guidance Documents (GDs) for their approval after 2021.

Additionally, JaCVAM is coordinating, along with several other international collaborators, in ongoing validation studies and peer reviews, which include Multi-ImmunoTox assay (MITA) IL-2 Luc assay, MITA IL-2 Leukocyte Toxicity Test (LTT) assay and MITA IL-1 β Luc assay for immunotoxicity, EpiSensA for skin sensitisation, LbL 3D- SIT and ADRA.