## JaCVAM statement on
## *in vitro* cytotoxicity assay for estimating acute oral toxicity

At a meeting held on 24 April 2019 at the National Institute of Health Sciences (NIHS) in Kanagawa, Japan, the Japanese Center for the Validation of Alternative Methods (JaCVAM) Regulatory Acceptance Board unanimously endorsed the following statement:

**Proposal:** Provided that thorough consideration is given both to the characteristics of the test method and to its applicability domain as well as with the further stipulation that the protocol used during the validation study is followed with the greatest care, this test method can be used in a regulatory context in order to identify test chemicals not having an $LD_{50}$ for acute oral toxicity of 2,000 mg/kg or less. We recommend that the results of this test method be used in a weight-of-evidence approach together with other sources of highly reliable information on chemical substances that are already in the market and for which there is plentiful evidence indicating low oral toxicity or on chemical substances that very closely resemble other substances of known oral toxicity in terms of structure, physicochemical properties, *in vivo* behavior, and other characteristics.

Also, considering the characteristics of this test method, it should be used when considering applications for exemptions of formulations containing deleterious substances under the Poisonous and Deleterious Substances Control Law, applications for approval of manufacture and sale of quasi-drugs, and requests for revisions of the Positive List of Cosmetics.

This statement was prepared to acknowledge that the results of a review and study by the JaCVAM Regulatory Acceptance Board have confirmed the usefulness of this assay.
Based on the above, we propose *in vitro* cytotoxicity assay as a useful means for estimating acute oral toxicity by regulatory agencies.

Yasuo Ohno
Chairperson
JaCVAM Regulatory Acceptance Board

Yoko Hirabayashi
Chairperson
JaCVAM Steering Committee

April 24, 2019

The JaCVAM Regulatory Acceptance Board was established by the JaCVAM Steering Committee, and is composed of nominees from the industry and academia.

This statement was endorsed by the following members of the JaCVAM Regulatory Acceptance Board:

Mr. Yasuo Ohno (Kihara Memorial Yokohama Foundation for the Advancement of Life Sciences): Chairperson
Mr. Yoshiaki Ikarashi (National Institute of Health Sciences: NIHS)
Mr. Noriyasu Imai (Japanese Society for Alternatives to Animal Experiments)
Mr. Tomoaki Inoue (Japanese Society of Immunotoxicology)
Mr. Yuji Ishii (Center for Biological Safety and Research: CBSR, NIHS)
Ms. Yumiko Iwase (Japan Pharmaceutical Manufacturers Association)
Mr. Takeshi Morita (Japanese Environmental Mutagen Society)
Mr. Shunji Nakai (Japan Chemical Industry Association)
Ms. Ruriko Nakamura (National Institute of Technology and Evaluation)
Mr. Akiyoshi Nishikawa (CBSR, NIHS)
Mr. Satoshi Numazawa (Japanese Society of Toxicology)
Ms. Maki Noguchi (Pharmaceuticals and Medical Devices Agency) *
Mr. Kazutoshi Shinoda (Pharmaceuticals and Medical Devices Agency)
Ms. Mariko Sugiyama (Japan Cosmetic Industry Association)
Mr. Hiroo Yokozeki (Japanese Society for Cutaneous Immunology and Allergy)

Term: From 1st April 2016 to 31st March 2018
*: From 1st April 2017 to 31st March 2018

Mr. Yasuo Ohno (Kihara Memorial Yokohama Foundation for the Advancement of Life Sciences): Chairperson
Ms. Yoko Hirabayashi (CBSR, NIHS)
Mr. Yoshiaki Ikarashi (NIHS)
Mr. Noriyasu Imai (Japanese Society for Alternatives to Animal Experiments)
Mr. Kunifumi Inawaka (Japan Chemical Industry Association)
Mr. Tomoaki Inoue (Japanese Society of Immunotoxicology)
Mr. Yuji Ishii (CBSR, NIHS)
Ms. Yumiko Iwase (Japan Pharmaceutical Manufacturers Association)
Mr. Fumihiro Kubo (Pharmaceuticals and Medical Devices Agency)
Mr. Kenichi Masumura (Japanese Environmental Mutagen Society)
Ms. Ruriko Nakamura (National Institute of Technology and Evaluation)
Mr. Akiyoshi Nishikawa (CBSR, NIHS/ Saiseikai Utsunomiya Hospital)
Mr. Jihei Nishimura (Pharmaceuticals and Medical Devices Agency)
Mr. Satoshi Numazawa (Japanese Society of Toxicology)
Ms. Mariko Sugiyama (Japan Cosmetic Industry Association)
Mr. Hiroo Yokozeki (Japanese Society for Cutaneous Immunology and Allergy)

Term: From 1st April 2018 to 31st March 2020

This statement was endorsed by the following members of the JaCVAM steering Committee after receiving the report from JaCVAM Regulatory Acceptance Board:

Ms. Yoko Hirabayashi (CBSR, NIHS): Chairperson
Mr. Manabu Fuchioka (Ministry of Health, Labour and Welfare)
Mr. Osamu Fueki (Pharmaceuticals and Medical Devices Agency)
Mr. Akihiko Hirose (Division of Risk Assessment, CBSR, NIHS)
Mr. Koichi Hiruta (Pharmaceuticals and Medical Devices Agency)
Mr. Masamitsu Honma (Division of Genetics and Mutagenesis, CBSR, NIHS)
Mr. Koji Ishii (National Institute of Infectious Diseases)
Mr. Yasunari Kanda (Division of Pharmacology, CBSR, NIHS)
Mr. Satoshi Kitajima (Division of Toxicology, CBSR, NIHS)
Mr. Kouichirou Koike (Ministry of Health, Labour and Welfare)
Ms. Kumiko Ogawa (Division of Pathology, CBSR, NIHS)
Mr. Haruhiro Okuda (NIHS)
Mr. Taku Oohara (Ministry of Health, Labour and Welfare)
Mr. Atsuya Takagi (Animal Management Section of the Division of Toxicology, CBSR, NIHS)
Mr. Masaaki Tsukano (Ministry of Health, Labour and Welfare)
Mr. Hajime Kojima (Division of Risk Assessment, CBSR, NIHS): Secretary