Rules of Operation at the Japanese Center for the Validation of Alternative Methods

Article 1. **Establishment of the Japanese Center for the Validation of Alternative Methods**

1-1. The Japanese Center for the Validation of Alternative Methods (JaCVAM) is established as part of the Center for Biological Safety and Research (CBSR) at the National Institute of Health Sciences (NIHS). The director of the CBSR also serves as director of JaCVAM.

Article 2. **Roles and responsibilities of JaCVAM**

2-1. JaCVAM has been established to promote the use of alternatives to animal testing in regulatory studies, thereby replacing, reducing, or refining (the Three Rs) the use of animals wherever possible while meeting the responsibility of the CBSR, as stipulated in the NIHS regulations, to ensure the protection of the general public by assessing the safety of chemicals and other substances. JaCVAM activities are also beneficial to the application and approval for manufacture and sale of pharmaceutical and other products as well as for revisions to standards for cosmetic products.

2-2. For this purpose, JaCVAM assesses the utility, limitations, and suitability for use in a regulatory context of test methods for determining the safety of chemicals and other substances as well as organizes validation studies when necessary. In addition, JaCVAM cooperates and collaborates with similar organizations in related fields, both in Japan and internationally.

Article 3. **Committees and other bodies necessary to carry out JaCVAM activities**

3-1. A Steering Committee, Advisory Council, and Regulatory Acceptance Board as well as Editorial Committees, Validation Management Teams, and Peer Review Panels are to be established in order to ensure that JaCVAM activities are managed and implemented properly.

3-2. The members of these committees and other bodies are named to renewable two-year terms by the director of the NIHS.

3-3. The Secretariat for these committees and other bodies is provided by Section 2 of the Division of Risk Assessment, CBSR, NIHS.

3-4. A quorum of two-thirds of the members of a committee or other body is necessary to hold meetings, and a consensus of all those in attendance is necessary to finalize decisions. In cases where a consensus cannot be reached, a decision may be finalized with the consent of two-thirds of those in attendance. Any points of dispute, however, are to be recorded and reported in the meeting minutes.

Article 4. **The Steering Committee**

4-1. The Steering Committee determines which novel or derivative test methods are to be selected and assessed by JaCVAM as well as allocates both financial and human resources necessary to undertake the scientific validation and assessment of such test methods. It also reviews final reports issued by the Advisory Council, issues JaCVAM statements on test methods that have been determined to be suitable for use in a regulatory context, and reports these results to the appropriate agencies within the Ministry of Health, Labour and Welfare as well as to the general public. In addition, the Steering Committee appoints members of the Advisory Council and the Regulatory Acceptance Board as well as the chairs of each Editorial Committee, Validation Management Team, and Peer Review Panel.

4-2. The Steering Committee is chaired by the director of the CBSR and comprises the director of the NIHS, members of the CBSR Steering Council (which includes the director of the CBSR; the heads of the Toxicology, Pathology, Pharmacology, Mutation Genetics, and Risk Assessment Divisions; and the head of the Animal Management Office), representatives from the National Institute of Infectious Diseases, the Ministry of Health, Labour and Welfare, the Pharmaceuticals and Medical Devices Agency, and the Secretariat. Additionally, observers may participate in the committee as necessary at the discretion of the chair.

Article 5. **Advisory Council**

5-1. The Advisory Council receives at least once per year reports from the Steering Committee on JaCVAM operations, planning, and achievements, which it reviews and provides advice as necessary.
5-2. The Advisory Council is chaired by the director of the NIHS and comprises roughly 10 members, including the director of the NIHS, the director of the CBSR, representatives from regulatory agencies, animal welfare groups, academic societies, or the private sector, and other individuals as necessary at the discretion of the chair.

Article 6. **Regulatory Acceptance Board**

6-1. The Regulatory Acceptance Board examines reports provided by Editorial Committees and background information relevant to the test method under consideration in deliberating on the scientific validity, utility in a regulatory context, and potential for acceptance by society, after which it issues a final report that is made available for public comment.
6-2. The Regulatory Acceptance Board comprises the director of the CBSR, experts on material safety and statistical analysis, and any other individuals as necessary at the discretion of the chair. The members of the Regulatory Acceptance Board elect a chair from among themselves. Additional members may be added as necessary at the discretion of the chair.

Article 7. **Editorial Committee**

7-1. The Editorial Committee examines validation reports, peer review panel reports, and background information relevant to a test method under consideration and provides this information to related organizations worldwide.
7-2. The Editorial Committee for each test method comprises experts in material safety and statistical analysis for the related fields. After the Steering Committee appoints a chair for an Editorial Committee, additional committee members are named by the chair in consultation with the Secretariat.

Article 8. **Validation Management Team**

8-1. Validation Management Teams are responsible for planning and implementing validation studies. In addition, Validation Management Teams review the results obtained during the validation studies and prepare a validation report that includes recommended protocols. Validation Management Teams are established when the Steering Committee determines that a validation study is necessary.
8-2. After the Steering Committee appoints a chair for a Validation Management Team, additional team members are named by the chair in consultation with the Secretariat.

Article 9. **Peer Review Panels**

9-1. Peer Review Panels evaluate from a disinterested standpoint validation reports and relevant background information in performing a scientific evaluation of the reliability and suitability of the test method under consideration. Peer Review Panels propose the implementation of additional validation testing and subject matter requiring further study. The Peer Review Panels then review these results and prepare a peer review report.
9-2. The Peer Review Panel for each test method comprises experts in material safety and statistical analysis for the related fields. After the Steering Committee appoints a chair for a Peer Review Panel, additional panel members are named by the chairperson in consultation with the Secretariat.

Article 10. **The Secretariat**

10-1. The Secretariat manages the operation of JaCVAM, providing support for activities undertaken by the committees and other bodies stipulated in Articles 4 to 9 as well as cooperating and collaborating with academic societies and other organizations that are involved in the evaluation of alternative methods to animal testing in assessing the safety of chemicals and other substances, both in Japan and around the world. The Secretariat also assembles, organizes, and makes available to others a wide range of information on the evaluation of test methods.
10-2. The Secretariat provides the Steering Committee with recommendations for candidates for members of the Advisory Council, the Regulatory Acceptance Board, and Editorial Committees as well as chairs for Validation

Management Teams and Peer Review Panels. In addition, the Secretariat provides the chair of each committee or other body with advice on the selection of members.

Article 11. **Other Details**

11-1. Other details necessary to JaCVAM activities are determined separately by the Steering Committee.

Article 12. **Revisions to these Rules of Operation**

12-1. These rules are subject to revision as determined by the Steering Committee and approved the director of the NIHS.

Article 13. **Revision history**

13-1. These rules are effective as of May 1, 2007.

13-2. Portions of these rules were revised effective July 31, 2009.

13-3. Portions of these rules were revised effective April 20, 2011.

13-4. Portions of these rules were revised effective April 2, 2012.

13-5. Portions of these rules were revised effective January 5, 2014.

13-6. Portions of these rules were revised effective August 3, 2015.