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 hereby established as part of the Biological Safety Research Center (BSRC), the National Institute of Health Sciences (NIHS). The BSRC director serves as head of JaCVAM.

1-2. JaCVAM is called the Japanese Center for the Validation of Alternative Methods in English.

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

2-1. JaCVAM was established to promote the use of alternative methods to animal testing in regulatory studies, thereby replacing, reducing, or refining (the 3 Rs) the use of animals wherever possible while meeting the responsibility of the BSRC to ensure the protection of the general public by assessing the safety of chemicals and other materials, as stipulated in the regulations of the NIHS. JaCVAM activities are also beneficial to application and approval for the manufacture and sale of pharmaceutical and other products as well as to revisions to standards for cosmetic products.

2-2. For this purpose, JaCVAM assesses the utility, limitations, and suitability for use in regulatory studies of test methods for determining the safety of chemicals and other materials and also performs 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. To ensure proper management of JaCVAM activities, an Advisory Council, Steering Committee, and Regulatory Acceptance Board are to be established. The Steering Committee requests the organization of Peer Review Panels and Validation Management Teams when necessary.

3-2. Members of each of these bodies are appointed by the NIHS director general and receive renewable two-year terms.

3-3. A secretariat to provide administrative support for these organizations is to be provided by the Section for the Evaluation of the Novel Methods, Division of Pharmacology, BSRC, NIHS.

3-4. A quorum of two-thirds of the membership of a body is required in order to transact business at a meeting, and in principle decisions are to be made by consensus of those in attendance. In cases where a consensus cannot be reached, decisions can be made by a majority vote of two-thirds of those in attendance. Meeting reports are to include information on issues for which a consensus was not achieved.

Article 4: **The Advisory Council**

4-1. The Advisory Council receives reports from the Steering Committee once or more each year, on which it deliberates and for which it provides advice.

4-2. The Advisory Council consists of approximately 10 members. The NIHS director general serves as the chairperson, and the rest of the Council includes the BSRC director, administrators from related government agencies, experts on animal welfare, representatives from related academic societies, and industry representatives, as well as other persons judged necessary by the chairperson.

Article 5: **The Steering Committee**

5-1. The Steering Committee deliberates on the selection of novel and modified methods for study by JaCVAM as well as finalizes budgetary and manpower allocations necessary to determine scientific validity and implement evaluation of the methods selected for study. It also deliberates on reports from the Regulatory Acceptance Board, establishes the official policy of JaCVAM regarding test methods judged to be suitable for regulatory studies, and issues documentation of the results of these activities, which are then submitted to relevant agencies at the Ministry of Health, Labour and Welfare (MHLW) as well as made available to the public. In addition, the Steering Committee appoints the chairpersons of Peer Review Panels and Validation Management Teams.

5-2. The Steering Committee consists of the NIHS director general, the members of the BSRC Steering Committee (which includes the BSRC director as well as the directors of the Division of Cellular and Molecular Toxicology, the Division of Pathology, the Division of Pharmacology, the Division of Genetics and Mutagenesis, the Division of Risk Assessment, and the Head of the Animal Management Section of the Division of Cellular and Molecular Toxicology), a representative from the MHLW, a representative from the Pharmaceuticals and Medical Devices Agency, and the head of the Section for the Evaluation of Novel Methods in the Division of Pharmacology, BSRC, NIHS. The BSRC director serves as the chairperson. In addition, other persons may participate as observers when judged necessary by the chairperson.

Article 6: **The Regulatory Acceptance Board**

6-1. The Regulatory Acceptance Board examines reports provided by Peer Review Panels, background information, and other relevant opinion obtained from public comment in deliberating on the scientific validity, regulatory utility, and potential for acceptance by society in general of the test method under consideration, after which it issues a final report.

6-2. The Regulatory Acceptance Board consists of the BSRC director, experts on the safety of chemical substances and statistical analysis, and other persons judged necessary by the chairperson. The chairperson is to be elected by the members of the committee from among themselves. If deemed necessary by the chairperson, the number of committee members may be increased slightly.

Article 7: **Peer Review Panels**

7-1. Peer Review Panels evaluate from a disinterested standpoint test methods under consideration, and prepare draft evaluation reports, which are then presented for public comment. When necessary, a Peer Review Panel proposes implementation of a validation process and recommends topics of interest for the validation. After deliberating on the results of this process, the Peer Review Panel issues a report to the Steering Committee.

7-2. A Peer Review Panel is to be commissioned by the Steering Committee each time a test method is submitted for consideration, and consists of experts on the safety of chemical substances and statistical analysis, who were not involved in the development or validation of the test method under consideration. After the Steering Committee appoints a chairperson, additional panel members are named by the chairperson in consultation with the secretariat.

Article 8: **Validation Management Teams**

8-1. Validation Management Teams are responsible for planning and implementing validation processes. In addition, Validation Management Teams deliberate on results obtained from validation processes and prepare validation reports that include recommended protocols for submission to the Steering Committee. A Validation Management Team is to be commissioned

whenever a Peer Review Panel determines that a validation process is necessary.

8-2. After the Steering Committee appoints a chairperson, additional members are named by the chairperson in consultation with the secretariat.

Article 9: **Secretariat**

9-1. The secretariat handles all administrative issues related to the operation of JaCVAM, provides support for activities undertaken by the bodies prescribed in Articles 4 to 8, and cooperates and collaborates with domestic and international academic societies and other organizations involved in the evaluation of alternative methods to animal testing in assessing the safety of chemicals and other substances. The Secretariat also assembles, organizes, and makes available to others a wide range of information on the evaluation of test methods. If necessary, the Secretariat will provide the Steering Committee with recommendations for candidates for a chairperson of a Peer Review Panel or Validation Management Team. In addition, the Secretariat provides the chairperson of each body with advice on the selection of other members.

Article 10: **Other details**

10-1. Other details necessary to JaCVAM activities are determined separately by the Steering Committee.

Article 11: **Revisions to these rules**

11-1. These rules are subject to revision as determined by deliberation of the Steering Committee and approved the NIHS director general.

Article 12: **Revision history**

12-1. These rules are effective as of May 1, 2007.

12-2: Portions of these rules were revised effective July 31, 2009.

12-3: Portions of these rules were revised effective April 20, 2011.

12-4. Portions of these rules were revised effective April 2, 2012.