Japanese Center for the Validation of Alternative Methods (JaCVAM)

Proposal for Engagement Rules

May 1, 2007

## I. Organization Name, Policy, and Mission

Organization Name: Japanese Center for the Validation of Alternative Methods (JaCVAM)

JaCVAM's activities are conducted by the Office of New Testing Method Assessment, Division of Pharmacology, National Biological Safety Research Center (NBSRC), National Institute of Health Sciences (NIHS). Provision 51 (6) of the NIHS statute book specifies "The Office of New Testing Method Assessment is responsible for research and evaluation of testing methods to ensure the safety of industrial materials" and JaCVAM is responsible for this evaluation.

Policy and Mission: JaCVAM's policy and mission is to promote the 3Rs in animal experiments (see glossary) for the evaluation of chemical substance safety in Japan and establish guidelines for new alternative experimental methods through international collaboration.

## II. Purpose of This Document

To pursue JaCVAM's mission, this document defines engagement rules that specify JaCVAM's activities and the role of affiliated organizations.

## III. Glossary

**Appendix 1**

## IV. JaCVAM Activities

The Office of New Testing Method Assessment is assigned as the Secretariat of JaCVAM.

A) Evaluation of new and revised testing methods and establishment of their guidelines

The evaluation of new and revised testing methods and establishment of guidelines for such methods are processed in the following order: open recruitment, receiving applications, selection for evaluation, preparation of Background Review Document (BRD) by an oversight committee, evaluation by a peer review panel, evaluation by a regulatory

acceptance board, and proposal to regulatory bodies.

Each evaluation process is described in the following subsections.

(1) Open recruitment of new/revised testing methods to be evaluated

- Preparation of documents for open recruitment
- Preparation of application forms
- Distribution of information via web sites and public relations magazines issued by affiliated academic societies

(2) Receiving applications

(3) Selection of testing methods to be evaluated

(4) Preparation of BRD by an ad hoc oversight committee

- Selection of oversight committee members
- Collection of information necessary for evaluation with oversight committee members
- Holding oversight committee meetings
- Preparation of BRD

(5) Evaluation of testing methods by an ad hoc peer review panel

- Organization of a peer review panel
- Preliminary evaluation of oversight committee reports and accompanying information by a peer review panel
- Holding peer review panel meetings
- Preparation of peer review reports

(6) Evaluation of testing methods by a regulatory acceptance board

- Selection of regulatory acceptance board members
- Preliminary evaluation of BRD and peer review reports by an regulatory acceptance board
- Holding board meetings
- Preparation of regulatory acceptance board reports

(7) Proposal to regulatory bodies

- Publication of reports prepared by regulatory acceptance board
- Preparation of proposals for guidelines of new/revised testing methods
- Submission of proposals to regulatory bodies

B) Outsourcing the validation of new and revised testing methods

If a validation result is found to be unsatisfactory in the evaluation process and a further validation is deemed necessary, JaCVAM will outsource the validation to an appropriate scientific society, such as the Japanese Society for Alternatives to Animal Experiments (JSAAE). JaCVAM will ask them to form an ad hoc management team for the validation study of each method and to perform a comprehensive validation process including the preparation of reports. The secretary will support the smooth execution of the validation study. In addition, the oversight committee will collaborate with them to make validation results available for the peer review panel when appropriate.

C) Promotion of the 3Rs and international collaborations

(1) Promotion

To promote the 3Rs in Japan, JaCVAM collects information about the 3Rs from Japan and abroad and broadcasts this information through scientific societies, web sites, and publications, as well as by to holding symposia as the occasion demands. Additionally, the secretary distributes publications that summarize the JaCVAM's activities to the relating organizations.

(2) International collaboration

JaCVAM collaborates on promotion of the 3Rs with international organizations for research and associated activities in many areas, including evaluation and validation of new/revised testing methods.

## V. Affiliated committees and their roles

The Office of New Testing Method Assessment is in charge of being the secretariat of each committee.

A) Committees to provide support and advice to JaCVAM

(1) Advisory Committee

The advisory committee provides advice on the strategy and policy of JaCVAM's activities according to reports on JaCVAM's plans and achievements, which are provided at least once a year.

The advisory committee consists of approximately eight members, including toxicologists not affiliated with NIHS, animal experimentalists, alternative methods experimentalists, representatives recommended by industry groups, clinicians, representatives of citizens, and regulatory officers. Each member's term is two years starting in January and he/she can be reappointed indefinitely. JaCVAM selects the members and the director general of NIHS appoints them. The deputy director general of NIHS serves as the chair of committee meetings.

(2) JaCVAM steering committee

The steering committee supports JaCVAM's activities by providing advice regarding the

overall guiding principles of JaCVAM as well as the evaluation of new and revised testing methods. JaCVAM then reviews this advice. The secretary hosts periodical steering committee meetings and seeks their advice regularly.

The steering committee consists of the deputy director general of NIHS, a director of the NBSRC, a head of Division of Pharmacology, a chief of the Office of New Testing Method Assessment, a representative of JSAAE, and other representatives appointed by the steering committee. A director of the NBSRC serves as the chair of the steering committee.

Specific tasks of the steering committee include:

- Advice on the validation and execution of evaluations of new/revised testing methods
- Advice on selecting advisory committee members
- Advice and requests for selecting regulatory acceptance board members
- Advice on selecting peer review panel members
- Advice on selecting oversight committee members
- Contact with support groups of NIHS
- Support of the secretary
- Advice on strategy, plans and reports prepared by JaCVAM

(3) JaCVAM Support Group

The support group provides practical assistance and advice to the secretary for pursuing JaCVAM's objectives. For example, the secretary holds meetings with experts of each subject who are members of the support group and asks them for assistance and advice to pursue the tasks regarding the evaluation procedure.

The support group of JaCVAM consists of representatives of the divisions in NBSRC including Cellular and Molecular Toxicology, Pathology, Pharmacology, Genetics and Mutagenesis, Risk Assessment, and Laboratory Animal Control. A director of NBSRC leads the support group.

JaCVAM holds meetings to share perceptions about plans and achievements of JaCVAM and about trends in animal welfare in foreign countries with the support group members at least once a year, as well as with outside representatives as the occasion demands.

B) Groups to participate in the evaluation of new and revised testing methods

(1) Oversight committee

The oversight committee prepares BRD based on the validation reports on new and revised testing methods, which are prepared by the validation management team. The oversight committee also supports the execution of validations study by providing advice for improvement in new and revised testing methods and further experiments.

The oversight committee consists of the applicants of the new or revised testing method

and several selected experts appointed by the validation management team of the testing method. A secretariat supports the oversight committee.

The secretary submits the BRD prepared by the oversight committee to the peer review panel to request its review. The oversight committee is dismissed upon acceptance of the report by the peer review panel.

(2) Peer Review Panel

The peer review panel reviews the BRD prepared by the oversight committee from a scientific point of view and prepares review reports for new and revised testing methods.

JaCVAM selects several experts to evaluate and validate the testing method and organizes the peer review panel. Concurrent assignment with the oversight committee is not allowed. A chair is elected by a vote of panel members. The secretary submits the review report prepared by the peer review panel to the regulatory acceptance board to request its review. The peer review panel is dismissed upon acceptance of the report by the regulatory acceptance board.

(3) Regulatory acceptance board

The regulatory acceptance board reviews the reports prepared by the oversight committee and the peer review panel, evaluates them from a standpoint of administrative application and social diffusion, and submits board reports to the secretariat.

The regulatory acceptance board consists of approximately ten members including representatives of NIHS, experts of alternative methods, toxicologists, representatives recommended by industry groups, biostatisticians, and regulatory officers.

Each member’s term is two years starting from January and he/she can be reappointed indefinitely. JaCVAM selects the members and the director general of NIHS appoints them. Concurrent assignment with either the peer review panel or the oversight committee is not allowed. A regulatory acceptance board meeting is hold as the occasion demands and it is effected upon the attendance of greater than or equal to a half of the members. The chair is elected by a vote of regulatory acceptance board members.

Steering committee members, peer review panel members, oversight committee members, and representatives involved in validation study may be called to the regulatory acceptance board meeting as the occasion demands. However, the chair of the meeting has a right to ask any member to leave the meeting if the chair thinks he/she is not appropriate for the meeting.

**Appendix**

Glossary

The 3Rs in animal experiments:

Refer to OECD GD34