

# Comment

## The Need for the Establishment of a Brazilian Centre for the Validation of Alternative Methods (BraCVAM)

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**Summary** — Brazil has recently approved legislation for regulating experimental animal use. On the other hand, it is a requirement that the safety of many products on the market is controlled on the basis of animal testing. Some groups at official laboratories, universities and industries are studying alternative methods, but there is no approved mechanism for funding collaborative studies, nor is there an institution responsible for coordinating these studies. These shortcomings obstruct the development of these assays in Brazil. The creation of a Brazilian Centre for the Validation of Alternative Methods (BraCVAM) would facilitate the development and validation of tests in all the institutions working on alternative methods in Brazil, and could also offer support to other Latin American countries.

**Key words:** *alternative methods, regulatory acceptance, validation.*

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### Introduction

The use of animals in research goes back to ancient times, since it was referred in *Corpus Hippocraticum* in around 350 BC. Ferguson's pre-occupation about this subject in 1767 (1), the deliberations of Jeremy Bentham in late 18th century ("The question is not, 'Can animals reason?', nor, 'Can they talk?', but, 'Can they suffer?'" [2]), the foundation of the first animal protection society, the Society for the Prevention of Cruelty to Animals, in Britain in 1824 (3), and the first ethics code proposed by Marshall Hall in 1831 (4), were important events in the development of consciousness among researchers of the need to search for alternatives to the use of animals in experimentation (5).

In 1959, after the introduction of the Three Rs (*Replacement, Reduction and Refinement*) concept by Russell and Burch in their book, *The Principles of Humane Experimental Technique* (6), it became more possible to combine quality science with the ethical conduct of experiments (5, 7). However, only at the end of 1970s, due to the increase in anti-vivisectionist activity against the use of animals by cosmetic industries, was the search for alternatives intensified.

The use of animals in various scientific fields is still a reality throughout the world, including the

European Union (EU; 8), where much effort is being concentrated on the quest for alternative methods. On the other hand, since the publication of the *6th* and *7th Amendments to the EU Cosmetic Directive 76/768/EEC* (Council Directives *93/35/EEC* [9] and *2003/15/EC* [10], respectively), the use of animals in the development of cosmetics has shown a downward trend (11).

### European Centre for the Validation of Alternative Methods (ECVAM)

ECVAM was created in 1991, as part of the European Commission's Joint Research Centre (JRC), in order to fulfil the requirements outlined in Article 23 of *EU Directive 86/609/EEC*, which aimed to stimulate the development and validation of alternative methods which would be able to supply at least the same level of information given by existing animal assays, but which would use fewer animals, or significantly reduce their suffering, or replace their use altogether (12). ECVAM's role in achieving these aims is mainly via the coordination of the validation of these alternative methods.

ECVAM was located in the JRC in Ispra, Italy, since the JRC is a multilingual establishment,

with a history of acting for the promotion of international scientific cooperation. This factor facilitated the design of the correct technical structure needed for ECVAM's work, besides providing a basis for expanding the role of the JRC in research (12).

### **Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM)**

ICCVAM was founded in September 1994, as an *ad hoc* committee for presenting a report to support the requirements of the *1993 NIH Revitalization Act*. In this Act, the National Institute of Environmental Health Sciences (NIEHS) was required to establish criteria for the validation and regulatory acceptance of toxicological alternative methods (13). This committee became permanent in December 2000, and nowadays comprises representatives from 15 US Federal regulatory and research agencies.

At present, ICCVAM receives scientific support from National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM), which is part of NIEHS, located at Research Triangle Park, NC, USA. ICCVAM's mission is to promote the development, validation and regulatory acceptance of alternative methods, emphasising the Three Rs principles, while scientific quality and human, animal and environmental health are upheld and promoted (13).

### **Japanese Centre for the Validation of Alternative Methods (JaCVAM)**

JaCVAM was established in November 2005, and is affiliated to the Japanese National Centre for Biological Safety and Research (NCBSR), of the National Institute of Health Sciences (NIHS; 14).

The mission of JaCVAM is to propose and improve the validation of alternatives and to establish international cooperation, besides developing new alternative methods (15).

### **The Current Situation in Brazil**

The need to validate and establish alternative methods according to the Three Rs principles — motivated by the search for technical improvement and by the pressure applied by animal rights groups — has compelled a large number of laboratories to perform studies in this field.

In Brazil, however, no organisation exists which is responsible for the coordination of validation

studies. The current research in this field is due to particular initiatives by public or private institutions, which, motivated by the precedent in other countries, have started working on the development of alternative methods.

*Decree Number 4725*, dated June 9th 2003, dictates that one of the activities of the National Institute of Quality Control in Health (INCQS) is to establish the quality control rules and procedures for the health laboratory network (16). However, except when methods are already internationally validated, it is impossible to comply with this ruling without conducting a collaborative study to harmonise the procedures and to define the parameters for the interpretation of the results they provide.

Although Brazilian *Resolution No. 899*, dated May 29th 2003, published the *Guideline for the Validation of Analytical and Bioanalytical Methods* (17), the whole process is not defined, nor is the role of each entity during the various steps established, as originally stated in the EU initiative which established ECVAM (12) and subsequently in the OECD Guidance on validation (18).

Therefore, the creation of a Brazilian Centre, comparable to ECVAM, ICCVAM and JaCVAM, would be an important step for such studies, which could then be coordinated in the correct manner. In addition, the Centre would be invaluable for important contact and interaction with other similar organisations in other countries throughout the world.

### **A Brazilian Centre for the Validation of Alternative Methods (BraCVAM)**

The Oswaldo Cruz Foundation (FIOCRUZ) possesses all of the attributes necessary for it to become the headquarters of a BraCVAM, since it is an internationally-recognised scientific institution that unites a vast range of scientific and medical fields, including basic and applied research, drug and vaccine production, quality control and teaching. This is an important aspect, since the multidisciplinary scientific infrastructure of FIOCRUZ could be used to form a working platform with a wide range of available knowledge in many relevant subjects.

INCQS, and a number of other groups in FIOCRUZ, have been studying alternative methods for a long time. Since INCQS is the official laboratory of the Brazilian Ministry of Health, it has to perform assays to guarantee that products that are on the market are sufficiently safe. For this purpose, INCQS routinely performs animal toxicological tests, and, since 1989, has tested most of these products with alternative methods, comparing results and evaluating correlations between animal and non-animal data.

INCQS has frequently participated in Brazilian and international congresses, including the *World Congress on Alternatives and Animal Use in the Life Sciences*. It comprises a group of approximately 20 professionals and students, who are working on alternative methods, mainly for the replacement of animals in testing for skin, eye and mucous irritation, and in sensitisation and pyrogen testing, as well as in vaccine control. A range of activities, such as poster presentations, lectures, organisation of meetings and roundtables, paper publications, and post-graduate studies, have also been undertaken by INCQS.

Once established, the activities of a BraCVAM could include:

- the development of new methods;
- the coordination of studies on the development of alternative methods;
- the coordination of the validation of alternative methods;
- the proposal and evaluation of test protocols;
- the analysis and evaluation of results obtained from studies;
- participation in international cooperation;
- the creation, maintenance and management of data bases of technical procedures, substances, raw materials, finished products, and any other aspects relevant to alternative methods;
- the promotion of meetings, congresses, workshops, or any other route of disseminating scientific information to regulatory organisations, industries, academia, and any other institutions related to alternatives;
- the publication of reports about the progress of studies; and
- the improvement of any procedure that could help in the development of alternative methods.

## Conclusion

The creation of a Brazilian Centre for the Validation of Alternative Methods (BraCVAM) would be very important, not only for Brazil, but for the whole of Latin America, since there is no such institution in this part of the world.

Once established, BraCVAM should determine its structure, take all necessary steps to become officially viable, and determine the start-up period for its activities.

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