

# Summary of the Workshop on Training for the Implementation of Alternative Test Methods<sup>1</sup>

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**Summary** — Over the last two decades, emphasis has been on new method validation, acceptance criteria and international harmonisation, and in recent years, several scientifically validated alternative test methods have been accepted. The objectives of this workshop were to review the various training programmes related to *reduction*, *refinement* and *replacement* (the Three Rs) and validated alternative methods, the obstacles to such training and ways to overcome them. In general, training in the Three Rs should be a continuous exercise. Whenever the regulators accept an alternative test method, specific training should be offered in order to overcome the reluctance to change and to expedite the implementation of the new test method. It is essential that funds be made available for this purpose, e.g. via regulatory agencies and international organisations.

**Key words:** *alternative test methods, implementation, Three Rs, training.*

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## Introduction

Over the last two decades, emphasis has been on acceptance criteria and international harmonisation for new test method validation. As a number of scientifically-validated new test methods have been accepted over the last few years, the question arises about how effectively these test methods are being implemented.

Some of the questions addressed during a discussion of this issue at the Fourth World Congress Workshop included:

- What happens following new method acceptance?
- How do regulatory agencies implement new test methods?
- What are the obstacles to implementation?
- How do training programmes enhance the implementation process?

During the workshop, discussions centred on the obstacles to training programmes. These triggered

positive discussions about ways to overcome these obstacles and to provide better training in general.

## Presentations on Training Activities

This workshop substantiated that the need for training is of widespread concern and has been recognised by various organisations, as well as by individual scientists. Some of the current training activities are dedicated to individual methods, while others have a more general or global training goal.

Denise Sailstad summarised the International Life Sciences Institute (ILSI)/Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) workshop on the implementation of the murine local lymph node assay (LLNA) for assessment of the potential for chemicals to cause allergic contact dermatitis. The LLNA was the first test method to undergo the ICCVAM review. It has been accepted by ICCVAM, US government agencies and by the scientific and international communities. As implementation of the LLNA began, it became apparent that there was a need to provide additional information (guidance, training, support and interpretation) to expedite its implementation. A

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workshop proposal was developed in cooperation with the stakeholders in the assay, including peer-review panel members and working group members from the ICCVAM review, sponsors of the assay, and immunotoxicologists familiar with the LLNA. These stakeholders supported the workshop concept and worked directly with the programme committee. Continual work with ICCVAM and ILSI resulted in a workshop that provided practical advice and conceptual information that were essential for the assay to be implemented. There were approximately 100 participants from diverse backgrounds (government agencies, industry, contract laboratories and research institutes). The workshop provided guidance and technical information about procedures and data interpretation and provided abundant opportunity for formal and informal discussion. Hands-on participation through smaller breakout groups allowed the participants to evaluate actual data sets by using case studies. Additionally, the *in vivo* assay was demonstrated through a video insert used in a PowerPoint presentation. The limitations and uses of the assay were emphasised throughout. US regulatory agency representatives provided an update on their guidelines and implementation process, and provided answers to questions on the application of the LLNA for their agencies. The LLNA Training Workshop successfully provided the opportunity for specific questions and concerns to be addressed. The workshop engaged a large number of facilitators and provided a template for future workshops as new test method alternatives become accepted.

Gisela Murillo (Laboratory for Alternative Methods, Center for Toxicology and Biomedicine [TOXIMED], Medical University of Santiago de Cuba, Cuba) provided information on ProALt (Project for the Promotion of Alternative Methods in Latin America and the Caribbean), initiated by her institute. The main goals of ProALt are to implement a system for the dissemination of information about alternatives to animal studies in toxicity testing, biological and medical research and teaching; to create awareness and to promote activity relating to the Three Rs within the educational and scientific sectors of this geographical region. Attention to the ProALt goals will encourage increased use of alternatives, leading to a reduction in the overall use of laboratory animals and the refinement of procedures for reasons of ethics, economy and science. TOXIMED also runs training courses on non-animal testing methods that are established in its laboratories and organised *The First Workshop on Alternative Methods in Latin America and the Caribbean* (4–5 December 2001, Santiago de Cuba).

Marlies Halder and Miroslav Cervinka (Charles University Faculty of Medicine, Hradec Králové, Czech Republic) presented the European Centre for the Validation of Alternative Methods (ECVAM's) activities on promotion of alternative testing meth-

ods, involving twelve Candidate Countries (CCs) for membership in the European Union (EU) (Bulgaria, Cyprus, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Malta, Poland, Romania, Slovakia and Slovenia). During 2001 and 2002, ECVAM has sponsored, within the Joint Research Centre (JRC) Enlargement Project, the training of individual scientists from CCs in alternative methods at ECVAM, three training workshops (20–30 participants) on validation, the use of alternative test methods in higher education, and the use of quantitative structure–activity relationships (QSARs) in risk assessment. ECVAM also conducted three larger workshops (60–100 participants), which reviewed the ethical and legal background to the Three Rs concept (e.g. *Directive 86/609/EEC*), the principles of validation, and the status of alternatives in the EU. Miroslav Cervinka stressed the need for involving academia in the process of implementation.

Coenraad Hendriksen (National Vaccine Institute, Bilthoven, The Netherlands) reported on his experience, gained as an organiser of and lecturer in training courses on good laboratory animal practice and vaccine quality control. He underlined that training courses are an excellent platform for discussion and networking. The planning of a training course should cover several aspects, e.g. sufficient financial support, a well-developed programme with alternative topics in case of eventualities, well-instructed trainers, facilities and equipment. Before the course, participants should receive background information in the form of a reader/course book, including Standard Operating Procedures (SOPs), handouts of the presentations, etc. The organisers and trainers in the course should also have information about the level of training and expertise of the participants. A course that lasts for several days helps build camaraderie.

## Discussion

The overview of training workshop experiences provided by the speakers stimulated discussion of training obstacles and effective tools for productive workshops.

### Need for and creation of training workshops

The need for training workshops is typically determined by the need for better communication and the sharing of technical expertise on a specific method. Once this need is identified, it is important to partner with appropriate stakeholders, both to gain support and perhaps to provide funding. This need should be sufficiently justified to make the rationale for cost and effort clear. Care should be taken in forming the programme committee. Those involved in the training programme will need to share a common goal in the process and be advocates for an effective work-

shop. It is important the desired end-product be clearly stated and understood.

### **Announcement of workshops**

Workshops can be announced through professional organisations, newsletters, websites, journals, mailing lists, etc.

### **Participants**

While training a large number of individuals is desirable, the nature of the method and type of training creates practical limits to the number of participants. If a wet-lab approach is taken, facilities may not be adequate to handle large numbers that can be effectively trained at one time. Participants should be encouraged to ask questions. Particular attention to communication should be made when the training workshop is not in the native language of the participants. Additionally, the number of facilitators available may determine the appropriate number of participants. Another factor is the mix of the participants. While, the LLNA training workshop was directed at a broad audience, other training programmes should focus only on those individuals or staff who will work directly with the test method. Participants may need background information prior to attending a workshop.

### **Costs and logistics**

Costs and logistics are major obstacles for training workshops. Some ideas were mentioned that might bridge the funding obstacle. While ICCVAM and ECVAM focus on validation and review, funds set aside for training through these organisations was discussed. That these organisations have already sponsored and held workshops of this type, was also discussed. Additional suggestions included the use of professional organisations to sponsor training workshops at annual meetings.

The format of a training workshop is important. Efficient use of time and funds is essential. Additionally, attention must be placed on any safety issues or animal welfare concerns that involve the training process.

Alternatives to direct training include the potential for making training manuals, software (CD-

ROM) or videos available. Other suggestions included providing training workshops that adequately prepare participants to train others once they complete the workshop. These are all alternatives that will reduce funding needs and make training more available to a larger audience.

### **Special considerations**

What are the lessons learned from previous training workshops conducted to date? The format of a training workshop may be an important factor in its success. Some training workshops are better suited for two phases, where staff attend an initial session and then return at another time to complete the training. Non-industrialised countries are confronted with a number of additional obstacles. Barriers such as political environment and language may make travel and participation in international workshops difficult. In order to allow new test methods to be fully implemented, it is essential that workshops for training be provided. The international harmonisation of test methods and procedures, such as experiential or historical controls, Good Laboratory Practice (GLP), unified software, recordkeeping, etc., will require less training and more-efficient use of funds.

### **Conclusions**

This training workshop session at the Fourth World Congress on Alternatives provided the opportunity for discussion about the issues that impede the implementation and active use of new test methods that may be beneficial alternatives to animal methods. However, essential elements of scientific method training in general were also discussed. The formal presentations and audience discussion provided the basis to better understand the diversity of obstacles that face those who wish to provide training programmes. This discussion along with the identification of successful features of each workshop provided positive and supportive ideas that participants may use as they carry out training in the future. As the international community gains experience in providing training workshops for the implementation of alternative test methods, additional opportunities for discussion, such as this session, will be of immense value.