

FINAL AT 28 DECEMBER 2010**DISCUSSION PAPER****Animal Use in Regulatory Testing****A strategic approach to encouraging international adoption of scientifically validated non-animal alternatives****Purpose**

The purpose of this discussion paper is to assist the OIE Laboratory Animal Welfare *ad hoc* Group in formulating a possible strategic approach to encouraging and facilitating (at an international level) the replacement of live animal use in regulatory testing, where scientifically- validated, non-animal tests exist.

This paper is a revised version of an earlier paper, of 26 July 2009, discussed at LAWAHG 3 and reflects both discussion at that meeting and subsequent discussions involving *ad hoc* group members. The paper also takes note of recent developments in the subject area, including the outcome of General Session 78.

Background

Laboratory animals are used for regulatory testing to assess the safety, efficacy and/or potential adverse health effects of new chemicals and products such as vaccines, medicines, food additives, pesticides and industrial chemicals. These regulatory tests are required by law in most countries, and companies performing these tests have to comply with the regulatory protocols.

At the May 2010 General Session of the World Assembly of Delegates, OIE members adopted for inclusion in the Terrestrial Animal Health Code, as Chapter 7.8, "The use of animals in Research and Education". This text is considered to underpin Guiding Principles relevant to the use of animals in regulatory testing detailed in Appendix 1. Likewise, it is considered that relevant OIE definitions are included in existing OIE documents, with the exception of those included in Appendix 2.

The original discussion paper "Issues and options regarding a future international role for the OIE in laboratory animal welfare" identified "facilitating the regulatory acceptance and adoption of internationally-validated, non-animal test methods" as a possible priority area for OIE focus.

As for laboratory animal welfare in general, the unique benefit of OIE involvement was seen to be the scientific and policy credibility provided by an internationally recognised inter-governmental body dedicated to animal health and welfare issues and representing 176 members.

In this same discussion paper, the important role played by VICH and its relationship with the OIE was highlighted. The factors which influenced the establishment of VICH in 1996, under the auspices of the OIE, were emphasised i.e.

- The drive to reduce the number of animals used in regulatory testing by eliminating the need for duplication of tests in each VICH region.
- The International drive to harmonise regulatory standards and minimise their impact on trade.

Annex 36 (contd)**Discussion**

- Considerable research investment has been made in non-animal test methods over the last two decades, by both the private and public sectors, with a number of significant achievements.
- Validation bodies have been established in both Europe (ECVAM) and North America and the “European Partnership on Alternative Approaches to Animal Testing” is an important component of the EU animal welfare action plan.
- Individual Governments (eg. Canada in 2001), NGOs (RSPCA and UK 3Rs Centre) have taken a particular interest in this policy area, from both a scientific and regulatory perspective, and the subject continues to be an important programme item at World Congresses on Alternatives and Animal Use in the Life Sciences.
- Regulatory acceptance, however, continues to be perceived to be hampered by a conservative regulatory approach, with liability and litigation risks considered to be influencing attitudes of regulatory bodies and individual decision matters.
- A number of regulatory bodies have, however, taken a leadership position and confirmed formal policies promoting the use of validated non-animal tests.
- For transnational companies supplying a significant number of international markets, it is important that non-animal tests are acceptable in all markets, if changes to testing requirements are to be introduced.
- Selected relevant developments, since LAWAHG 3, include progress with EC acceptance of non-animal regulatory tests for shellfish biotoxin testing and the proposed EC establishment of a Reference Laboratory, at European level, to continue the work so far carried out by ECVAM.

The OIE LAWAHG has held valuable initial discussions with VICH on this issue but, to date, has had no contact with the human health equivalent, ICH.

Recommendations

The key decision for the OIE is whether it wishes to take an inter-governmental leadership position in encouraging regulatory acceptance of scientifically-validated, non-animal alternatives utilising its unique relationship with 176 Governments and the VICH.

It is proposed that the preferred strategic approach is to work through the existing relationship with VICH and to look at establishing a similar relationship with ICH depending on progress made with VICH.

It is recommended that:

- i) The OIE continues dialogue with VICH to identify opportunities for both organisations to encourage international regulatory acceptance of scientifically-validated, non-animal alternative test requirements in relation to veterinary product testing.
- ii) Depending on progress made with VICH, OIE initiates dialogue with ICH to identify opportunities for both organisations to encourage international regulatory acceptance of scientifically-validated, non-animal alternative test requirements in relation to medical product testing.
- iii) If there is support for the strategic approach proposed in i) and ii) a LAWAHG sub committee meet with VICH to formally advance this dialogue and identify specific opportunities and agree appropriate short and medium term actions and initiatives.
- iv) On completion of a draft action plan as outlined in iii), that this be discussed with selected regulatory authorities, private sector commercial organisations and animal welfare NGOs focused on the use of animals in regulatory testing, prior to finalisation.
- v) The final agreed action plan be submitted to the OIE Council for endorsement and consideration of resourcing implications.

Selected Background Publications

Title	Author
Animal Pain and Distress in Vaccine Testing in the United States, 2002	M L Stephens, G M Alvino, J B Branson
The ICLAS/CCAC International symposium on Regulatory Testing and Animal Welfare, 2004	Gilly Griffin, William S Stokes, Steven P Pakes, Clement Gauthier
Proceedings of the 6 th World Congress on Alternatives & Animal Use in the Life Sciences, 2008	Japanese Society for Alternatives to Animal Experiments (JSAAE)
Proceedings: Alternatives to Animal Testing: New Approaches in the Development and Control of Biologicals - Dubrovnik, Croatia, 23-24 April 2008	European Directorate for the Quality of Medicines & HealthCare
Immunotoxicology: opportunities for non-animal test development - Altern.Lab.Anim., 2009, 37, 4, 387-397, FRAME, England	Corsini, E.; Roggen, E.L.
Animal use in the chemical and product manufacturing sectors - can the downtrend continue? - Altern.Lab.Anim., 2009, 37, 6, 623-629, FRAME, England	Curren, R.
The future of toxicity testing - J.Toxicol.Environ.Health B Crit.Rev., 2010, 13, 2-4, 163-196, England	Andersen, M.E.; Al-Zoughool, M.; Croteau, M.; Westphal, M.; Krewski, D.
Lessons learned from alternative methods and their validation for a new toxicology in the 21st century – J. Toxicol.Environ.Health B Crit.Rev., 2010, 13, 2-4, 277-290, England	Hartung, T.
Working in partnership to advance the 3Rs in toxicity testing - Toxicology, 2010, 267, 1-3, 14-19, Elsevier Ireland Ltd, Ireland	Holmes, A.M.; Creton, S.; Chapman, K.
OECD Guidelines for the testing of chemicals	http://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals_chem_guide_pkg-en
International Workshop on Alternative Methods to Reduce, Refine, and Replace the Use of Animals in Vaccine Potency and Safety Testing: State of the Science and Future Direction.	http://iccvam.niehs.nih.gov/meetings/BiologicsWksp-2010/BiologicsWksp-present.htm

Annex 36 (contd)**Appendix 1****Guiding Principles**

1. Laboratories or companies performing regulatory testing have to follow rigid international protocols.
2. Every laboratory or company should have an animal care and use committee. It will play a key role in implementing the humane endpoints, best practices and public accountability.
3. Tests should only be accepted by the regulatory bodies if they are performed by laboratories that have full implementation of Good laboratory Animal Science Principles and Good Laboratory Practices.
4. The animals selected for a procedure should be of an appropriate species and quality required by the protocols and obtained from a known source.
5. The living conditions of animals should be appropriate for their species and contribute to their health and comfort.
6. Investigators and personnel performing the tests should be properly trained and experienced in the proper care, handling and use of the species being maintained. Provisions should be taken for their in service training, including the proper and humane care of laboratory animals.
7. Adequate veterinary care should be provided as indicated.
8. Proper use of animals, including the avoidance or minimisation of discomfort, distress and pain when consistent with sound scientific practices, is imperative. Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals.
9. Procedures with animals that may cause more than momentary or slight pain or distress should be performed with appropriate sedation, analgesia or anesthesia. Surgical or other painful procedures should not be performed on unanesthetised animals paralysed by chemical agents.
10. Animals that would otherwise suffer severe or chronic pain or distress that cannot be relieved should be painlessly killed at the end of the procedure or, if appropriate, during the procedure.
11. Mutual acceptance of test data can significantly reduce animal test requirements, and facilitate timely and ethical regulatory decisions.
12. If there is a need for deviations from the protocol these should be soundly justified to the pertinent authorities.

Appendix 2

Terms and Definitions

1. Animal test – any use of an animal for scientific purposes which may cause it pain, suffering, distress or lasting harm.
 - a. Note 1: the definition of an animal test excludes acts of recognised veterinary practice applied for the benefit of an animal or the group of animals of which it is part; recognised husbandry practices to manage or conserve the animal or the group of which it is part; marking by methods which cause no more than momentary pain or distress; and humane killing.
 - b. Note 2: The prevention of pain, suffering, distress or lasting harm by the effective use of anaesthesia or analgesia or other methods of rendering the animal insentient (eg. decerebration) does not place animal tests outside the scope of this definition. The administration of anaesthetics, analgesics or other methods of rendering the animal insentient are considered to constitute an integral part of the animal test
2. Procedural training (acclimatisation) – training and acclimatising animals to the interventions to be performed during an animal test, with a view to minimising stress to the animal when animal tests are conducted.
3. Purpose-bred animal – any animal purpose-bred for use in animal tests or for other experimental or scientific purposes.
4. Test animal – Any animal used in *in vivo* animal tests, or used to provide tissue for *ex vivo* or *in vitro* tests.
5. Validation – process by which the reliability and relevance of a test method is established for a particular purpose.