

Five human-blood-based, non-animal tests for pyrogenicity were endorsed by the European Scientific Advisory Committee (ESAC) in March of this year. What effort has been made to ensure they are brought into full use throughout the European Union? Would the Commission confirm that as of March 2006, no animal tests should be undertaken in the EU for the detection and quantification of pyrogenicity mediated by Gram-negative endotoxins because the non-animal methods provide full replacement tests as concluded by the ESAC?

In addition, would the Commission confirm that these non-animal methods must be recognised and accepted by EU regulatory agencies without the need for any further regulatory steps in order to ensure compliance with Directive 86/609/EEC⁽¹⁾ regarding the protection of animals used for experimental and other purposes? Furthermore, would the Commissioner also estimate the number of animals who will be saved annually through use of the new non-animal methods?

Given the excellent performance of the new non-animal tests, would the Commission propose ways in which the EU might promote use of these tests in third countries, including the US, China and Japan, in line with the commitment made in the Commission's 'Communication to the European Parliament and Council on a Community Action Plan on the Protection and Welfare of Animals 2006-2010' to promote high animal welfare standards in the EU and internationally? Specifically, in order to hasten the acceptance of the non-animal methods internationally, would the Commission consider preparing formal submissions of the validation data to the US Pharmacopoeia and other pharmacopeias?

[\(1\)](#) OJ L 358, 18.12.1986, p. 1.

20 December 2006 Answer given by Mr Verheugen on behalf of the Commission

According to Article 7 Paragraph 2 of Council Directive 86/609/EEC of 24 November [P-5002/2006](#) 1986 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes⁽¹⁾, an experiment shall not be performed if another scientifically satisfactory method of obtaining the result sought, not entailing the use of an animal, is reasonably and practicably available.

It belongs in the first place to national authorities in charge of implementing this directive and Community law relating to specific product categories such as cosmetic products, to ensure a correct implementation of this provision at national level.

The Commission agrees that agencies set up under Community law are also bound to implement the provisions of Council Directive 86/609/EEC. For instance, in the pharmaceutical sector, both the safety guidelines and the quality tests, especially included in the European Pharmacopoeia, provide for a number of alternative tests not requiring the use of animals. The European Centre for the Validation of Alternative Methods (ECVAM) of the Directorate General Joint Research Centre (DG JRC) works closely with these agencies, e.g. regularly commenting on Pharmacopoeia monographs. ECVAM is steering the process of validation of alternative methods, which are submitted to the relevant agencies after formal validation. Current work on the replacement, reduction or refinement of animal tests takes place also at the level of the scientific committees of the European Medicines Agency. The same approach is taken by the European Pharmacopoeia. Similarly, the European Chemicals Bureau (ECB) at the JRC is carrying out Computational Toxicology (including quantitative structure-activity relationships (QSARs)), to promote the development, validation and implementation of computational models and estimation approaches that are useful for regulatory purposes. The European Food Safety Authority's Scientific Committee has set up a working group on experimental animal welfare that had its first meeting in November 2006.

In that context, the Commission expects relevant agencies or assimilated institutes, such as the European Pharmacopoeia, to consider also the appropriateness for regulatory compliance of the non-animal test for pyrogenicity.

Animal numbers for pyrogen testing in Europe are estimated at about 200 000 animals per year. Since the new methods provide for a replacement of the rabbit test, the Commission expects that this number of animals can be saved through the progressive adoption of the non-animal tests for pyrogenicity.

Validation of non-animal tests must be distinguished from their legal acceptance with a view to establishing regulatory compliance. Different procedures may have to be followed for legal acceptance, involving different actors. In specific cases, this may involve regulatory change, such as for the Crop Protection Directive⁽²⁾ whilst in other cases, such as pharmaceutical products, technical guidance would be sufficient. Whether or not non-animal tests can effectively be used for regulatory compliance is an assessment that in the end belongs to authorities or agencies in charge of implementation of Community law. It is therefore essential to have authorities involved in the process of validation of test methods in order to ensure that validated tests do indeed meet regulatory needs. It is noteworthy that the ECVAM pyrogen test validation study sponsored by Directorate-General for Research (DG RTD) in the fifth framework programme (FP5) did include European Pharmacopoeia as observer as well as four national control authorities as participating laboratories. The validated methods have been submitted to the European Pharmacopoeia, where an expert group has been formed in order to develop general provisions, and which will consider whether the validated methods will be included in these provisions.

While making all possible efforts, the Commission therefore cannot guarantee that as of March 2006 all animal tests for pyrogenicity will have been replaced.

The Commission promotes the use of alternative approaches to animal tests also internationally using different platforms. The acceptance of alternative approaches has been raised in bilateral regulatory dialogues with major trading partners and in international organisations, such as OECD. Similarly, the Commission has invited at sectoral level the ICH⁽³⁾ and VICH⁽⁴⁾ to examine guidance in order to streamline harmonisation of testing requirements following the 3 R principles⁽⁵⁾. More particularly regarding the novel pyrogen tests, ECVAM has submitted the respective dossiers to its US counterpart Interagency Coordinating Committee on the Validation of the Validation of Alternative Methods (ICCVAM), where the public peer-review process shall be completed by May 2007. A submission to the Japanese Centre for the Validation of Alternative Methods (JaCVAM) is under discussion.

In this context, the Commission draws the Honourable Member's attention to the European Partnership for Alternative Approaches (EPAA) to Animal Testing. The EPAA is an unprecedented collaboration between the Commission and major companies from seven industry sectors. The partners have committed to pooling knowledge, research and resources to accelerate the development, validation and acceptance of alternative approaches, and have agreed on an initial five-year action programme, precisely addressing the concerns raised in this question. EPAA will publish yearly implementation reports. The Honourable Member is invited to consult the following website: (http://ec.europa.eu/enterprise/epaa/index_en.htm)

(1) OJ L 358, 18.12.1986.

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(2) Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market, OJ L 230, 19.8.1991.

(3) Internal Conference on Harmonisation of the Technical Requirements for the Registration of Medicinal Products for Human Use.

(4) Internal Conference on Harmonisation of the Technical Requirements for the Registration of Medicinal Products for Veterinary Use.

(5) 3 R principles = Replacement, Reduction, Refinement.

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