News

IN: Call for papers/chapters

Proposed edited manual entitled "Potential alternatives to dissection and experimentation in life science (Zoology) curriculum and biomedical research: a practical manual for Indian universities and colleges" (Sharma BK et al., eds.)

Dear Authors,
the above manual is being planned with an aim to introduce alternatives in life science curriculum and basic biomedical research in Indian colleges and Universities with the sole aim to put a stoppage to cruelty against animals & animal abuse and promote conservation of our faunal biodiversity. The manual will be an integral part of the forthcoming workshop to be organized by the editor during July 13-15, 2009. The workshop *Potential Alternatives to Dissection and Experimentation in Life Science (Zoology) Curriculum and Biomedical Research* is likely to be sponsored by the University Grants Commission (UGC) and the Department of Science and Technology (DST), Govt. of India. UGC is the premier educational body in India responsible for the overall running of higher education system while DST is the apex scientific agency, funding for laboratory infrastructure development and research projects in all branches of science.

I treat it as my proud privilege and cordially invite you to send your valuable contributions as paper (s)/ chapter (s) on any of the following themes/topics. I expect to have your confirmation as early as possible to enable us to finalize the contents of this important publication. Please email me your consent at any of the following email ids. The format and other details will be sent upon hearing from you.

Themes:
Psychological impact of dissection and animal killing on the growing minds of young students
Common dissection exercises and replacement alternatives with reference to life science curricula;
Alternatives to exercises on the study of anatomy/dissection skills (from invertebrates to proto-chordates and fishes to mammals)
Alternatives to experiments involving use of animals (physiology, biochemistry and cell biology, histology and pathology, embryology and developmental biology etc.)
Alternatives to the study of museum specimens, permanent preparations of external body parts/internal organs, microscopic slides, osteology
Emerging alternatives in life science education and biomedical research
Stem cell technology and mammalian cell lines as potential source of cells in life science education and biomedical research
Non-animal alternatives to the use of mice in monoclonal antibody production and animal cruelty issues in the production of fetal calf serum (fcs) - the rationale and reasons to replace with serum free media
Miscellaneous issues

I am looking forward to hear from you.

Warm regards.
Sincerely,

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- Member, Board of Studies in Zoology, University of Rajasthan, Jaipur, India (Since July 2001)
- Elected Member, Committee of Courses in Investigative Biotechnology, University of Rajasthan, Jaipur, India (Academic Sessions 2001-03)
- Commonwealth Academic Staff Fellow, University College London (UCL), UK (2003- 04)
- INSA-DFG Visiting Fellow, University of Heidelberg, Germany (2006-07)
- Royal Society International Incoming Fellow, University of Nottingham, UK (2007-08)

News

CH: Even Great Apes are not safe

The action group *Schweizer Tierversuchsgegner* (Swiss Opponents of Animal Experiments) is petitioning for a ban on experiments on apes in Switzerland. The subject of experiments on primates was also discussed in Swiss parliament in connection with the Graf Initiative 06.464, "*Verbot von mittel- und schwerbelastenden Tierversuchen an Primaten* (Ban of experiments on primates causing medium and severe suffering)". The Commission for Science and Education of the Swiss National Assembly as well as the National Assembly itself did not act on the initiative and decided that experiments on Great Apes and experiments on other primates that cause severe suffering will not be banned in Switzerland. The National Assembly took this decision on the 20th of December 2007 after voting 103:68. The justification for this decision was that the provisions of the Animal Protection Law were sufficient to ensure the protection of the dignity of these animals. Experiments on primates and Great Apes are only authorised after a rigorous balancing of interests and in awareness of the heavy responsibility towards the animals. It was also mentioned in the justification that a total ban on experiments on Great Apes could curtail research too severely. The discussion of the ape experiments has had repercussions in Swiss academia, as the Commission for Animal Experiments of the Canton Zurich, invoking the current animal protection laws, denied two applications for experiments on primates on ethical grounds in early 2007. The Commission for Science and Education also discussed the concept of an animal's dignity on occasion of the council on the Animal Protection Law. It remains an undefined legal term, and it must be decided on a case by case basis whether or not an experiment is consistent with protecting an animal's dignity. In the area of animal protection, this decision has explicitly been assigned to the commissions. Thus, the Council of States decided to recognise the petition but not to act on it on the 2nd of October 2008.

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"At a cost of billions of dollars, most of the 85 AIDS vaccines created to date have been tested in hundreds of chimpanzees who endured decades of experiments and laboratory confinement. Almost all of these vaccines protected chimpanzees from HIV infection, but none has worked in humans. Claims of the continued importance of chimpanzee use are therefore misleading. For the millions of people at risk of AIDS, as well as the chimpanzees, we must move toward more humane and scientifically superior methods."

Jarrod Bailey, Ph.D.
Science Director for Project R&R: Release and Restitution for Chimpanzees in U.S. Laboratories

EU: ESAC endorses validity of the Local Lymph Node Assay

The ECVAM Scientific Advisory Committee (ESAC) has endorsed the scientific validity of the harmonised ECVAM performance standards for the Local Lymph Node Assay (LLNA) at its 29th meeting held in November 2008.

The LLNA is a scientifically validated and regulatory accepted method for assessing the skin sensitisation potential of chemicals. Both the European Centre for the Validation of Alternative Methods (ECVAM) and the US Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) have developed performance standards for the LLNA that can be used to assess with a reduced set of reference substances the accuracy and reliability of modified versions of the LLNA, as long as these versions are mechanistically and functionally similar to the validated test.

ECVAM and ICCVAM have now harmonised their respective performance standards with regard to the three main elements, namely: the essential test method components, the minimum list of reference chemicals and the accuracy and reliability values. These harmonised performance standards can now be used by national and international validation organisations to assess the validity of non-radioactive variations of the LLNA. The availability of non-radioactive versions of the standard test will broaden its use and will therefore contribute to further reducing and refining animal use for skin sensitisation safety assessment.

The harmonisation of the Performance Standards for the LLNA represents a significant accomplishment of the international collaboration in the field of alternative methods.

ECVAM Website

EU: ESAC accepts two further *in vitro* skin irritation tests

After the successful validation of two *in vitro* models for the study of skin irritation last year, the ECVAM Scientific Advisory Committee (ESAC) has endorsed the scientific validity of two further *in vitro* skin irritation tests on its 29th meeting held in November 2008. Both tests are based on reconstructed human epiderms and measure or predict the same biological or toxic effect as the fully validated and accepted reference method.

Any test method submitted to or validated by ECVAM must be reviewed and endorsed by its Scientific Advisory Committee before they can be used within the regulatory framework.

The *SkinEthic RHE model*, a similar/me-too method has been submitted to ECVAM as a non-ECVAM coordinated catch-up study. The test was confirmed by ECVAM as sufficiently similar with regard its structural and functional characteristics in reference to the Performance Standards and the test method was admitted as a *non-ECVAM coordinated catch-up validation study*.

The EpiDerm SIT model, a modification of the previously validated EpiDerm method, has been submitted to ECVAM as a non-ECVAM coordinated update validation study. The main modification performed is the prolongation of the exposure time to the test substances from 15 to 60 minutes, while all other essential model parameters remained unchanged. The test method was admitted as a *non-ECVAM coordinated update validation study*.

ECVAM Website

EU: Animal testing alternative methods website

The European Commission has launched today a new website, the "Tracking System for Alternative test methods Review Validation and Approval (TSAR)", designed to track the development of new alternative test methods which should replace, reduce and refine current animal testing.

TSAR is a tool to provide a transparent view on the status of alternative methods as they progress from purely scientific protocols submitted for pre-validation to being actively used in a regulatory context.

This tracking system intends to cover all steps, from the initial submission for pre-validation until final adoption by inclusion in the EU legislation and/or related Guidance Documents, when appropriate. It is worth mentioning that not all alternative methods will or need to be included in the test methods regulation (TMR, Commission Regulation (EC) No 440/2008 of 30 May 2008), as this regulation only contains relevant methods for the assessment of properties of chemicals that fall directly under its remit (see below some links to relevant legislation that contains data requirements). In addition to TMR, a number of methods are used on a day to day basis in a regulatory context through other product related guidance, as part of intelligent testing strategies or as pre-screening methods. Regardless of the way of implementation, they all contribute to the replacement, reduction and refinement of the use of animals in scientific procedures.

The process of validation and regulatory approval has been broken down into a number of steps. Although this is a continuous process that may, sometimes, also involve some iterations, for practical reasons it has been broken down in two parts: Review/validation and regulatory approval.

However, currently, the system only contains information tracking specific alternative methods in terms of the regulatory approval part from the stage "Validation statement" onwards. The remaining parts of the TSAR web site dealing with the other stages in the process of validation and regulatory approval are under construction and it is foreseen that they will be added in the near future. Some other utilities as site searching capabilities will also be added in future.

http://tsar.jrc.ec.europa.eu/

EU: Inventory on "Who's Who in the field of alternative methods" now online

This inventory of persons and their institutions active in the field of animal alternatives includes:

- The collection of contact details and related information coming from the survey launched *via* the ECVAM website and known as: "Who's who in the field of alternative methods".
- Contact details of scientists using/developing specific *in vitro* techniques that are available as *INVITTOX* protocols.

For new submissions and/or corrections on "Persons & Institutions", please contact ECVAM at:
dbalm-contact@jrc.it

To use the inventory of persons and their institutions go to
http://ecvam-dbalm.jrc.ec.europa.eu/
and continue with "IN VITRO METHODS SEARCH" and continue with Persons & Institutions (Who's who). You have to register to get valid login access codes.

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EU: Scientific Committee opinion on the need for non-human primates

On 13 January 2009 the Scientific Committee on Health and Environmental Risks (SCHER) adopted an opinion on the need for non-human primates (NHPs) in biomedical research, production and testing of products and devices. The opinion covers the major areas of research in which NHPs are used[1]. The scope of the opinion is confined to the scientific aspects and does not consider the ethical, economic, cultural and social aspects of NHPs use. The opinion was requested from Directorate General on Environment in the framework of the revision of the Directive 86/609/EEC[2] on the protection of animals used for experimental and scientific purposes.

SCHER recognizes that there are promising developments towards the replacement of NHP in biomedical research. A number of alternative methods (either in vitro or using other animal species) have been developed and implemented over the last decade. However, based on the available scientific evidence, SCHER concludes that at present, for many areas of biomedical research, there are no valid alternatives which would allow for a discontinuation in the use of NHP. Moreover, a specific timetable for the complete replacement of NHP use is difficult to predict. Based on the available science, the total replacement of NHP in many areas of use, either by other animal species or by non-animal methods, is unlikely to be achieved in the foreseeable future.

SCHER recommends advancing the "Three Rs[3]" concept in the use of NHPs in research. Other SCHER recommendations include; developing validated alternative methods to the use of NHPs; investments and activities encouraging the use of other non-primate species or genetically modified rodents where possible; developing the use of new accessible technologies in order to refine experimental procedures on NHPs (e.g. non-invasive procedures such as imaging and biocompatible implants). Finally, the Committee recommends the development of accessible and comprehensive databases and collaborative users' networks (e.g. on data sharing, tissue sharing, alternative to animal models).

The SCHER opinion can be found at: http://ec.europa.eu/health/ph_risk/committees/04_scher/scher_opinions_en.htm#8

[1] Notably, the safety assessment of pharmaceuticals, infectious diseases, neuroscience research, xenotransplantation

[2] OJLSSS, 18.12.1986

[3] Three Rs: Reduction (use of fewer animals), Replacement (alternative methods that replace animal testing) and Refinement (methods which cause least harm to the animals)

D: Hessian prize for animal protection/ research goes to Beate Kraemer/Paul Ehrlich Institute in Langen

Beate Kraemer, a biologist and researcher at the Paul Ehrlich Institute in Germany, has successfully established an alternative test to the animal rabies vaccine assay. This alternative method requires the use of 12 laboratory mice which is, in comparison with the previous standard use of 120 mice per rabies vaccine test, a very significant improvement of the testing efficacy and animal welfare. Although the test still includes the use of a certain number of laboratory mice, they are spared any pain or suffering. Kraemer's outstanding work was awarded with the Hessian prize for animal protection/research on December 5th 2008. Additionally, Beate Kraemer has managed to promote the use of the test not only in Germany but also in other countries.

The advantages of the test are numerous. By employing this test at the Paul Ehrlich Institute in the period from January 2007 until December 2008, the number of mice used for this application was reduced from 13,064 to 1,302. Because the number of animals is significantly reduced and the remaining test animals are spared from experiencing the progressive phases of rabies disease, this method successfully fulfils two of the 3R goals (refinement and reduction). In the meantime, the test and its results have been accepted by all European testing laboratories ("Official Medicines Control Laboratories – OMCL").

The Hessian prize for animal protection/research in the amount of 15,000 EUR is awarded by the federal government of Hesse, Germany. By awarding this prize, the government wants to participate directly in the reduction of the number of experimental animals in research and education as well as in the production of biomedical products. As the results gained using the alternative method clearly correlated with the results provided by the standard test procedure, it is to be expected and hoped that this alternative will become widely used and will significantly reduce the number of animals used for testing rabies vaccines.

GK

D: Announcement of the prize for animal protection in research 2009

28th prize for research on the development of methods with the aim of reducing and replacing animal experiments, published on the 17th of November 2008.

The German Federal Ministry of Food, Agriculture and Consumer Protection aims to stimulate research into developing new methods to reduce or replace animal experiments in the development, assessment and control of chemical and plant materials, especially in the area of pharmaceuticals, food additives and consumer articles by awarding a research prize of up to 15,000 Euro.

The prize is awarded for scientific progress that has contributed to the development of pharmacological-toxicological assays, e.g. for the testing of acute, subchronic or chronic toxicity, mutagenicity, cancerogenicity and reproductive toxicity as well as the pharmacologic effects of substances.

Applicants are requested to submit eight copies of accepted or printed scientific articles in English or German, published less than two years ago by the 31st of March 2009 to the

Bundesministerium für Ernährung,
Landwirtschaft und Verbraucherschutz
Referat 321 -
Rochusstraße 1
D-53123 Bonn
Germany

Later applications will not be considered. Posters and abstracts are not accepted. If numerous documents are submitted, an additional summary of their contents is requested. An explanation of the relevance of the work for animal protection, specifically which animal experiment is to be replaced or reduced and an estimation of how many animals could be spared, is required. The submitted documents will not be returned. The decision is made by an independent committee; the prize may be shared. Documents that have already been awarded an animal protection prize or have been submitted previously are to be marked as such.

USA: ACToR – new chemical database of the US-EPA

ACToR (Aggregated Computational Toxicology Resource) is a new chemical database that centralises access to toxicity data on a large number of environmental chemicals. The ACToR database and software applications were developed by the U.S. Environmental Protection Agency's (EPA) National Center for Computational Toxicology (NCCT).

The free, publicly-accessible ACToR database provides a portal for information on chemicals collected from over 200 sources. Chemical structure and toxicity information have been compiled for each chemical from various EPA databases, other U.S. government databases (PubChem, National Institutes of Health, Department of Agriculture, and Food and Drug Administration), and other national and international sources. Data of the EPA ToxCast chemical screening and prioritization programme will also be available through ACToR.

The ease of access to data compiled from many different sources by ACToR is expected to be welcomed by regulatory and industry scientists who use chemical toxicity data. Judson et al. (2008) described the following key uses of ACToR: a) derivation of training and validation data sets for chemical screening and prioritisation efforts; b) a unique resource for researchers developing computational models linking chemical structure with *in vitro* and *in vivo* assays; and c) a valuable resource for EPA and other regulatory agency reviewers who are examining new chemicals submitted for marketing approval. One important application of ACToR has been a survey of the toxicity data that is available on key environmental chemicals. In a recently published paper (Judson et al., 2008), the extent of publicly available toxicity information on approximately 10,000 substances including industrial chemicals, pesticide ingredients, and air and water pollutants was analysed. Key findings were that, while acute hazard data is available for 59% of the surveyed chemicals, detailed testing information is much more limited for carcinogenicity (26%), developmental toxicity (29%) and reproductive toxicity (11%). The EPA ToxCast screening and prioritization programme is designed to address this toxicity data gap.

Chemical structure, physico-chemical values, *in vitro* assay data and *in vivo* toxicology data are the primary types of data in ACToR. This structure-searchable database is expected to facilitate studies of structure-function relationships and serve an important role in the advancement of computational toxicology.

References

Judson, R., Richard, A., Dix, D. et al. (2008). ACToR – Aggregated Computational Toxicology Resource. *Toxicol. Appl. Pharmacol. 233*, 7-13.

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USA: CAAT 25th anniversary and Center of Excellence

On the website of the Center for Alternatives to Animal Testing (CAAT) http://caat.jhsph.edu/media/documentary.htm a documentary can be downloaded in three parts: 25 years of humane science.

This documentary, produced for CAAT's 25th Anniversary Symposium, examines the work of the center in promoting the 3Rs, from its beginnings in 1981 to current issues and future developments in alternatives.

The Center for Alternatives to Animal Testing is an academic center affiliated with the Division of Toxicological Sciences in the Department of Environmental Health Sciences of the Johns Hopkins University Bloomberg School of Public Health.

In July 2008, CAAT became part of the American Consortium on European Studies (ACES), an EU Center of Excellence based at the Johns Hopkins School of Advanced International Studies (SAIS). CAAT's role will be to establish a Humane Sciences and *in vitro* Alternatives component to this Center.

ACES is one of eleven EU Centers of Excellence in the United States. The consortium was created in 2001 to advance academic and public understanding of the European Union and to improve US-EU relations. It seeks to strengthen education and research opportunities and to create new synergies among scholars, students, policymakers and the private sector, representatives of governmental and non-governmental organizations, and the media. In addition to SAIS, the Consortium includes American University, George Mason University, George Washington University, and Georgetown University.

Through ACES, CAAT will serve as an information gateway, working to establish programs that provide reciprocity in communication between the EU and the US in the area of alternatives and the humane sciences. As part of this EU Center of Excellence, CAAT will coordinate EU-related humane sciences and alternatives activities in the United States, share US progress with our European counterparts, and foster a greater understanding and awareness of alternatives and the respective regulatory requirements of the EU and the US.

Center for Alternatives to
Animal Testing
caat@jhsph.edu

USA: Rodger Curren receives Cave Award

Rodger D. Curren, Ph.D., President of the Institute for In Vitro Sciences, Inc., has received the William and Eleanor Cave Award for achievements in advancing alternatives to the use of animals in research and testing.

The award was presented on October 23, 2008 by the Alternatives Research & Development Foundation (ARDF) at its 15th Anniversary celebration held in conjunction with the Spotlight on Ingredients 2008 Alternatives Forum in Philadelphia.

ARDF president Sue Leary presented the award, which includes an honorarium of five thousand dollars, commending "Rodger Curren's vision, leadership, and commitment in advancing alternatives methods". In the evening's program, the organization highlighted Rodger's "scientific acumen, ethics, integrity and esprit de corps" which have made him "an international leader in the alternatives arena".

The Cave Award is named for the couple who together led the American Anti-Vivisection Society for many years, and who decided in 1978 to dedicate resources of the Society to alternatives research. Their commitment to non-animal research led to the establishment of the Alternatives Research & Development Foundation (ARDF).

Past recipients of the award have been from testing and basic research fields, as well as education, and have included: Dr. Ruy Tchao of Philadelphia's University of the Sciences, who was part of the team that developed one of the first alternatives for the controversial Draize rabbit eye irritancy test; Dr. Leon Bruner of Proctor and Gamble who has conducted validation studies of a number of product test alternatives, as well as John Sheasgreen, President of MatTek Corporation, that manufactures alternative test systems for industry, and Dr. George Russell, professor of biology at Adelphi University who developed innovative teaching alternatives for college level biology classes, including methods that students can use to study their own metabolism and physiology.

The mission of the Alternatives Research and Development Foundation is to fund and promote the development, validation and adoption of non-animal methods in biomedical research, product testing and education. For more information, contact ARDF at sleary@ardf-online.org.

www.ardf-online.org

USA: ICCVAM sees no complete replacement for the rabbit pyrogen test

ICCVAM has evaluated the validation status of five *in vitro* test methods proposed for assessing the potential pyrogenicity (i.e., ability to induce fever) of pharmaceuticals and other products, as potential replacements for the rabbit pyrogen test (RPT). ICCVAM recommends that, although none of these test methods can be considered a complete replacement for the RPT for the detection of Gram-negative endotoxin, they can be considered for use to detect Gram-negative endotoxin in human parenteral drugs on a case-by-case basis, subject to validation for each specific product to demonstrate equivalence to the RPT, in accordance with applicable U.S. Federal regulations. When used in this manner, these methods should be able to reduce the number of animals used for pyrogenicity testing.

ICCVAM's evaluation of the validation status of the *in vitro* pyrogen test methods, as well as ICCVAM's recommendations for current uses and limitations for each test method and recommendations for standardized protocols, future studies, and performance standards are included in the *ICCVAM Test Method Evaluation Report: Validation Status of Five In Vitro Test Methods Proposed for Assessing Potential Pyrogenicity of Pharmaceuticals and Other Products* (NIH Publication Number 08-6392).

See the complete report on http://iccvam.niehs.nih.gov/methods/pyrogen/pyr_tmer.htm

NICEATM-ICCVAM

ALTEX comments this news in the editorial of this issue