News

EU: Impact assessment of 2013 marketing ban for animal-tested cosmetics

The European Commission is compiling an impact assessment on the final marketing ban of cosmetics tested on animals scheduled for March 2013. Stakeholders were sent a questionnaire to be returned by March 25, 2011.

The Directive foresees that in case alternatives to animal testing in relation to the endpoints repeated-dose toxicity (includes tests requiring a repeated dosing such as skin sensitization and carcinogenicity testing), reproductive toxicity and toxicokinetics will not be developed and validated by the 2013 implementation date foreseen in the Directive, the Commission shall inform the European Parliament and the Council and put forward a legislative proposal. According to current knowledge (see Adler et al., 2011 and Hartung et al., this issue), alternatives to animal testing for the concerned complex endpoints will not be available by 2013. Based on this, the EC must now consider whether to put forward a proposal. The current options considered in this context are to:

- postpone the deadline (sub-options are also considered, such as postponing for certain endpoints only),
- maintain the deadline irrespective of availability of alternatives (thus not to make a proposal), or
- maintain the mechanism according to which the marketing ban applies once an alternative method has been validated and adopted at Community level with due regard to the development of validation within the OECD, but without a cut-off date.

The questionnaire asked for assessment of:

- existing data on the cosmetics market and the industry
- impacts on animal welfare/environmental impacts
- impacts on consumers
- impacts on competitiveness of cosmetic and cosmetic ingredients manufacturers
- impacts on small and medium sized enterprises (SME's)
- impacts on employment
- impacts on trade

The Commission has published the questionnaire and the separate answers from the Competent Authorities of 15 Member States, from industry, NGO's and other parties (http://ec.europa.eu/consumers/sectors/cosmetics/documents/animal-testing/stakeholders_consultation_en.htm) though no final document on the impact assessment is currently available. The answers are very varied in their level of detail and their assessment of the situation. While all animal welfare associations argue to maintain the 2013 deadline, the Member States mostly formulate no clear recommendations. Where one of the options is supported this is most often the third option, i.e. reverting to banning the animal tests once alternative tests have been validated and adopted at EU level.

Reference

Adler, S., Basketter, D., Creton, S., et al. (2011). Alternative (non-animal) methods for cosmetics testing: current status and future prospects – 2010. *Arch. Toxicol. 85*, 367-485.

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EU: ECHA reports on animal use for REACH

The European Chemicals Agency (ECHA) has published its first report on how companies are providing information on the properties of their substances for REACH (Regulation 1907/2006 on the Registration, Evaluation, Authorisation and Restriction of Chemicals) purposes. The report analyses how many new animal experiments have been conducted and how options to waive new animal tests are being used based on about 25,000 registration dossiers submitted by February 28, 2011.

The REACH regulation requires companies to submit information dossiers for each chemical substance manufactured in or imported to the EU at or above one ton per year. The type of information required depends on the volume of handled chemical. The goal is to ensure a high level of protection of human health and the environment.

Companies can avoid performing new animal tests by sharing existing data and submitting dossiers together with other companies (as substance information exchange fora – SIEFs), by using alternative tests (grouping and read-across, weight of evidence, *in vitro* studies and QSAR) to generate the required information or when exposure of humans and the environment will be low. For substances at or above 100 tons per year, testing proposals for long-term hazards (e.g. carcinogenicity, reproductive toxicity) must be approved by ECHA.

The report finds that registrants made full use of options to avoid animal testing; they mainly used the option to share existing animal studies but also the option to predict the properties of substances by read-across (comparing one substance with a similar substance for which test data are available). 1849 new animal studies were conducted since REACH entered into force; however 107 of these appear to have been conducted without approval of the testing proposal by ECHA. 711 proposals for new vertebrate animal studies were made, which is fewer than anticipated by the European Commission. However, the report states that justifications provided by the registrants for waiving new animal experiments are often insufficient to fulfill requirements and that full compliance checks will result in the requirement of new animal tests if the justifications cannot be improved.

The full report is available at: http://echa.europa.eu/doc/117reports/alternatives_test_animals_2011_en.pdf

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GER: BMBF calls for applications on alternatives

The Federal Ministry for Education and Research (BMBF) of Germany has published new guidelines on applications for 3Rs projects. These may be projects dealing with research, development and validation of alternative methods that promise significant contributions in regulatory testing, applied or basic research, including in the areas of education and of production, storage or propagation of materials, products or organisms. Complementary studies, workshops and other 3Rs relevant measures can also be supported as can German participation in international cooperative projects and method-specific regulatory contributions.

Proposals may be for individual or cooperative studies; German universities and technical universities, research institutions (each up to 100% of project costs) and industry (up to 50% of project costs) can apply. Project outlines structured according to a template must be submitted by March 15 of each year, starting 2012; detailed project proposals will be invited based on review of the outlines before the final decision is made.

For more detailed information see:
http://www.bmbf.de/de/16595.php
Project submission via:
https://www.pt-it.de/ptoutline/application/alternativ

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Press release of June 17, 2011
BMBF, Germany

GER: Prize for simulation of inflamed colon tissue model

The Prize for "Research on Replacement and Alternatives to Animal Experiments of the Federal State of Rhineland-Palatinate" was awarded to Dr Claus-Michael Lehr, Dr Eva Maria Collnot and Fransisca Leonard, Helmholtz Center for Infection Research (HZI) and Saarland University, Saarbrücken, Germany on June 30, 2011.

The group established a three-dimensional coculture of enterocytes, monocytes and dendritic cells to model inflamed intestinal mucosa *in vitro*. The controlled inflammation developed in this model simulates chronic inflammatory processes in diseases such as Crohn's Disease and colitis.

The prize of € 20,000 was awarded by Minister for the Environment Ulrike Höfken in Mainz, Germany.

Press release
Ministry for Environment, Agriculture, Food, Viniculture and Forestry
Rhineland-Palatinate, Germany
June 30, 2011

GER: Update on the internet platform InVitroJobs

InVitroJobs is a bilingual information platform for scientists, students, authorities and the general public, and pursues the goal of closing existing information gaps and overcoming obstacles to communication. So far, some 130 groups from ten different nations are represented in the working group list. The response from researchers is positive. Since the platform's launch in May 2009, there has been a continuous increase in the number of visits to the site, amounting to 100,000 page impressions so far.

In addition to the job board with up-to-date job offers, a list of working groups that use animal-free testing methods or are involved in developing such methods is regularly updated. These methods include *in vitro*, *in silico* methods, as well as imaging procedures or the use of voluntary study participants when investigating questions for which animal tests have traditionally been used. The data are supplemented with information on funding programs and awards. The list of working groups has now had several functions added, such as searches for research teams according to categories or keywords that can be found via search engines on the internet.

The new category "Working Group – A Portrait" presents working groups in detail. In an interview interested groups can describe their experiences in project development to inclusion in European or international test specifications, as well as provide an outlook on the future. The information is featured online for four to six weeks and can be downloaded as a pdf. In guest articles, scientists developing or implementing methods can give short-term reports on insights or news, or can open a discussion forum.

To date more than 220 job offers have been published with confirmation by the advertisers that applications were submitted in response to the publication on InVitroJobs. With 54%, the most visitors are from Germany, followed by the United States, Switzerland, Austria and Japan. However, there are also visitors from Eastern European countries, Egypt, Saudi Arabia, Iran, China, Brazil or Colombia. Visitors are mostly interested in offers of paid jobs, followed by interest in the researchers on the working groups list. Often, a job search is immediately followed by visits to pages featuring the researchers or internet searches for known researchers or test methods. News and information on funding programs are also often looked up. The platform is seen by researchers as a useful information hub and as an opportunity to gain publicity according to direct user feedback. A survey of working group representatives is planned for the future.

The increasing number of visitors to the website and feedback show that InVitroJobs is a viable tool for providing useful information to scientists, jobseekers, authorities and interested members of the public, and for transporting the topic of replacement methods for animal testing. We intend to expand the platform's contents and to broaden the spectrum of the working groups according to the status of research developments.

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GER: Two prizes for animalfree cancer research

The society "Doctors Against Animal Experiments Germany" awarded research prizes for 2011 to Dr Maret Bauer of the Department of Gynecology and Midwifery, Schleswig-Holstein University Hospital in Kiel, Germany and to Dr Irinia Nazarenko and Dr Stefan Giselbrecht of the Karlsruhe Institute of Technology (KIT), Karlsruhe, Germany.

Dr Bauer won the prize for her three-dimensional cell culture model that allows breast cancer research without animal experiments or use of animal materials. This research focuses on the contribution of stromal fibroblasts to the growth and metastasis of tumors. Primary stromal fibroblasts and tumor cells from necessary operations on cancer patients are grown on a 3D matrix to study and manipulate their interactions.

Dr Nazarenko and Dr Giselbrecht study the development of metastases by culturing human tumor cells and stem cells on microstructured biochips, modeling bone marrow and breast cancer in an interdisciplinary project of the BioInterfaces program. These models aim to develop new therapeutic strategies in tumor nanotechnology.

The prize money of € 10,000 comes from a donation specified for this purpose and has been awarded annually since 2006. The research projects use no animals or animal materials, also not as cell culture medium additives or antibodies. The prizes were awarded at the prize winners' institutes on July 26 and August 10, respectively.

Press releases
Doctors Against Animal Experiments Germany
July 27 and August 9, 2011

INT: InterNICHE outreach: Mexico, Portugal, Russia, Iran

A major focus on alternatives in medicine and veterinary medicine, particularly in clinical skills and surgical training, is underway with InterNICHE outreach visits in Mexico, Portugal, Russia and Iran.

In Mexico, a highly successful seminar on alternatives featuring a detailed demonstration of the Pulsating Organ Perfusion (POP) trainer was held within the surgery department of a major medical faculty. Co-organized by Sofia Ponce, InterNICHE National Contact for Mexico, and the head of surgery, the April 1 event was attended by heads of department and senior and junior teachers from medical and veterinary medical surgery. There was major progress in openness towards and acceptance of innovative and humane learning tools, particularly concerning their pedagogical advantages over conventional animal experimentation. A similar event may soon be held in the veterinary faculty, followed by national-level training in specific medical procedures using the device. A visit to another medical faculty involved the donation through the InterNICHE Humane Education Award of the Biopac Student Lab, a self-experimentation apparatus used for physiology practical classes that uses consenting students as the experimental animals. The annual use of over 30 dogs in severe experiments has now been ended. The faculty is exploring the roles of motivation, sensitization and alternatives in addressing effective skills acquisition for the future doctor, and is actively supporting students' own initiatives in the field of alternatives.

In conjunction with VITA, Russia's animal rights group, InterNICHE had a booth and Nick Jukes gave a presentation to delegates at the 17th Moscow International Veterinary Congress held April 16-18. The continuing collaboration between the organizers and InterNICHE/VITA is built on the common ground between veterinarians and animal protection organizations, and acknowledges the support given by the latter to veterinarians over the ketamine scandal in Russia.

In Portugal on April 29, InterNICHE National Contact for Norway, Siri Martinsen, addressed the National Seminar on Veterinary Teaching at Portuguese Veterinary Faculties, organized by the Portuguese Veterinary Chamber. With a focus on the diversity and quality of alternative tools and approaches available, Siri explored how care is an essential clinical skill that must be situated at the heart of any effective education and training program of a professional standard.

The first outreach work for humane education and alternatives within Iran is currently underway. Nick Jukes was an invited speaker at the 3rd International Symposium of Veterinary Surgery and 9th Iranian Symposium of Veterinary Surgery, Anesthesia and Radiology, held April 25-28 on Kish Island. Organized by the Iranian Veterinary Surgery Association (IVSA), Nick gave a presentation and workshop, and hosted a Multimedia Exhibition with support from InterNICHE National Contact Sepehr Shafiezadeh, supportive teachers, and

the new Iranian Anti-Vivisection Association (IAVA). Following a very positive response from teachers at the congress, particularly to the clear potential to enhance the quality of training in clinical skills and surgery with alternatives like the mannekin Critical Care Jerry and the POP trainer, plans were made for visits to universities across the country. Return visits for training in open surgery and laparoscopy, using perfused organs and cadavers, may also be organized.

Such events and future plans illustrate the success of collaboration between InterNICHE and teachers when focusing on the dual objectives of enhanced training and replacement of animal experiments. They also reflect a productive dynamic between international-level co-ordination on the one hand and the decentralized network of InterNICHE National Contacts and alternatives resources on the other.

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SUI: ALTEX impact factor rises to 4.4

At the end of June 2011, Thomson Reuters announced the Journal Citation Reports® for 2010 on the ISI Web of Knowledge℠ website. ALTEX came in with an Impact Factor of 4.429 ahead of *ATLA*, *Animal Welfare* and numerous larger toxicological journals.

The Impact Factor relates the number of articles and reviews published in the previous two years (in this case 2009 and 2010) to the number of citations of those articles during the same time.

The ALTEX staff and the board of ALTEX Edition are very pleased with this result and are confident that the stream of high quality of articles being submitted as well as the widespread interest in the developments in the field will continue to keep the Impact Factor of ALTEX at a high level.

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SUI: ALTEX Prize 2011 for Philipp Kuegler et al.

The ALTEX prize 2011 goes to the t[4] review *Markers of murine embryonic and neural stem cells, neurons and astrocytes: reference points for developmental neurotoxicity testing* by Philipp B. Kuegler, Bastian Zimmer, Tanja Waldmann, Birte Baudis, Sten Ilmjärv, Jürgen Hescheler, Phil Gaughwin, Patrik Brundin, William Mundy, Anna K. Bal-Price, André Schrattenholz, Karl-Heinz Krause, Christoph van Thriel, Mahendra S. Rao, Suzanne Kadereit and Marcel Leist. It is a truly international effort with authors from Germany, USA, Sweden, Switzerland, Singapore, and Estonia.

About 50 years ago, the thalidomide disaster and later the Minamata poisoning and the issue of lead additives in gasoline attracted increasing public attention to the issue of the hazards of chemical compounds on the development of the fetal neural system. However, to this day, data on the developmental neurotoxicity potential of industrial compounds, let alone mixtures of these compounds, are scarce and their relevance to the human situation is unclear. The technology of embryonic stem cells, or induced pluripotent cells for that matter, is one of the most dynamic and promising technologies in toxicity testing, with a huge potential for the development of *in vitro* methods. The review takes a first step to systematically evaluate the possibilities and challenges of this approach with regard to developmental neurotoxicity, and provides a basis for characterizing cell markers of differentiating and maturing cell populations and subpopulations at different stages of development, then goes on to suggest approaches for identifying toxicants. This review provides a most comprehensive and detailed overview of this field, and a broad understanding of the possibilities and issues around testing for developmental neurotoxicity.

Stefanie Schindler
President of ALTEX Edition

The ALTEX editorial staff and the scientific advisory board annually choose the best main article of the previous year. The prize money is CHF 2,000.

SUI: DZF Prize 2011 for Sonja Jeram

Sonja Jeram, National Institute of Public Health, Slovenia, was awarded the Doerenkamp-Zbinden Prize 2011 on August 25 at the 8th World Conference on Animal Use and Alternatives in Montreal, in acknowledgment of her outstanding work in the promotion of alternatives to animal testing in ecotoxicology, especially in recognition of her contribution to acute fish toxicity. With last year's acceptance by the OECD of the respective guidance document describing the Threshold Approach for Acute Fish Toxicity Testing (GD 126), a major reduction in fish use is expected.

Sonja Jeram attained her PhD in Biology at the University of Ljubljana, Slovenia, in 1990. After working at the National Institute of Biology for 8 years she established a laboratory at the National Institute of Public Health to control pollution of industrial waste water in 1997. This led to interests in hazard and risk assessment of chemical substances and the establishment of the Slovenian Society of Toxicology in 2000, where she became secretary general. She developed a new testing strategy to reduce the use of fish in acute ecotoxicity testing of new chemical substances notified in the European Union in collaboration with the European Centre for Validation of Alternative Methods (ECVAM). She is currently working in the field of environmental noise and health.

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The DZ Foundation (DZF) awards a yearly prize of CHF 25,000 for distinguished services to animal protection in science. Single persons, teams, as well as institutions can be suggested for the prize. Suggestions can be made by the members of the Foundation Board and Scientific Advisory Committee (SAC) of the DZF. Direct applications are not possible. For more information and a list of previous laureates go to www.doerenkamp-zbinden.org

SUI: New title and format for ALTEXethik

ALTEXethik will from now on be published in book format under the title TIERethik. It will be available in bookshops as well as by subscription. The board of ALTEX decided as much at its last meeting. This change shall expand the scope to encompass the full spectrum of the human-animal relationship, which is currently a hot topic in numerous scientific disciplines.

While philosophy has worked intensively on animal ethics since the 1970s and the biological sciences are increasingly questioning our treatment of animals, sociologists, historians and cultural scientists among others are now discovering this field.

TIERethik will be the first German language medium for this "animal turn" and will be open for all disciplines that deal with the human-animal relationship in a critical manner. TIERethik will have a focus theme for every issue and shall appear twice in 2012.

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UK: Call for grant applications on animal welfare measures and assessment

The NC3Rs and BBSRC call for expressions of interest for funding of research in the field of measures and assessment of animal welfare, as applied to laboratory animals, livestock species and companion animals. Applications could focus on:

- Pain assessment in animals
- The development of validated behavioral, physiological, and cognitive indicators of welfare
- The development of validated measures of affective states in animals
- The development of accurate welfare measurement tools that can be used under lab and/or field conditions
- The development of novel methods for the assessment of cumulative suffering and severity

Expressions of interest including research aims, project summary and approximate cost (max. one page) must be submitted by October 14, 2011, 4 p.m. Full applications will be invited for January (BBSRC) or February (NC3Rs).

For further information go to:
http://www.nc3rs.org.uk/page.asp?id=1551

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UK: New book on cost benefit analysis of animal experiments

In *The Costs and Benefits of Animal Experiments*, bioethicist and veterinarian Andrew Knight presents scientific research, analysis and experience to provide evidence-based answers to a key question: is animal experimentation ethically justifiable? By using meta-analyses of large numbers of animal experiments selected randomly – the "gold standard" when assessing biomedical research – and analyzing over 500 scientific publications, Knight is able to offer insights into the contributions of animal experimentation to human healthcare, and the extent to which laboratory animals suffer. He provides evidence-based estimations of laboratory animal use globally and in major world regions, and reviews the types of procedures animals are subjected to and their level of invasiveness. Knight concludes with an overview of key regulations governing animal experimentation within Europe and North America, and proposes a set of policy reforms to facilitate increased implementation of alternative research and testing strategies.

Adapted from press release
Palgrave Macmillan
Publishers Ltd
Hampshire, UK
May 27, 2011

UK: Non-human primate experiments reviewed

The major funders of invasive research on non-human primates in the UK, i.e. the Biotechnology and Biological Sciences Research Council, the Medical Research Council and the Welcome Trust, have commissioned an independent panel chaired by Patrick Bateson to prepare a *Review of Research Using Non-Human Primates*. This review scrutinized the scientific importance, the probability of medical and public benefit, and the likelihood of animal suffering in all invasive NHP research projects funded by these organizations from 1997 to 2006.

The panel found that much of the funded research was justifiable but stated that it could not find a clear scientific, medical or social benefit for about 9% of projects. It further stated that there was seldom evidence of direct medical benefit in contrast to the public statements of funding bodies and grant applicants and recommended that claims of the medical benefit of NHP research should not be overstated or generalized. It severely criticized the eight researchers (11%) that declined to participate in the review or could not be contacted and stated that recipients of public or charitable funding should be held accountable on issues of public interest.

The panel recommended that grant applicants should provide evidence of interest in and use by the medical and biopharmaceutical sectors when promising human health benefits of planned research. It also noted the disproportionate failure to publish negative results, and asserted that researchers have a moral obligation to publish results – even if negative – in order to prevent work being repeated unnecessarily.

The full list of recommendations and the responses of the three funding bodies can be found at http://www.bbsrc.ac.uk/web/FILES/Reviews/review-research-using-nhps-response.pdf. A detailed animal welfare and ethical critique of the review is available at www.animalexperiments.info/news.html.

Andrew Knight

USA: FDA approves cell-based assay for BOTOX® and BOTOX® Cosmetic

On June 24 California-based Allergan, Inc. announced that the US Food and Drug Administration (FDA) has approved a cell-based assay for stability and potency testing of BOTOX® (onabotulinumtoxinA) and BOTOX® Cosmetic. The new assay will be implemented immediately for release of product for the United States. Allergan estimated that this assay could reduce animal use for testing of these products by 95% over the next three years as it hopes that regulatory agencies in other countries will approve the new assay quickly. The assay is currently specifically applicable to Allergan's products. Allergan stated in a press release that it is discussing how to license the assay to other companies but did not disclose the principle of the assay.

BOTOX® is derived from *Clostridium botulinum* and has 21 approved medical uses. BOTOX® Cosmetic, which is marketed for aesthetic use, has the same formulation as BOTOX® and undergoes the same potency and stability tests for each batch produced. The active ingredient, Botulinum neurotoxin A blocks the release of neurotransmitters from nerves. Its application results in a localized and temporary reduction in the overacting muscle or gland. According to Allergan, owing to its high potency, less than one gram per year is required to supply the whole world. Until now the mouse LD_{50} potency assay has been required by regulatory agencies around the world for testing final product containing Botulinum neurotoxin A for release.

See also Bitz, S. (2010). The botulinum neurotoxin LD_{50} test – problems and solutions. *ALTEX 27*, 114-116 and comments on this article in *ALTEX 28*, 60-63.

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USA: EPA contracts companies to screen chemicals

The U.S. Environmental Protection Agency's (EPA) ToxCast chemical screening program has awarded contracts to four United States-based companies to test up to 10,000 chemicals for potential toxicity to people and the environment. ToxCast is designed to determine how chemical exposures affect human health. When fully implemented, ToxCast will be able to screen thousands of chemicals in fast, cost-effective tests.

The four companies will initially screen up to 1,000 chemicals currently in the ToxCast program using innovative technologies such as stem cell toxicity tests. These new technologies can quickly determine the potential for a chemical to cause harm to the human body. Screening results from the new technologies will be combined with data already being generated by the other 500 rapid chemical tests used by EPA's ToxCast program.

The chemicals ToxCast is now screening are found in industrial and consumer products, food additives and drugs. ToxCast's goal is to reduce EPA's reliance on slow and expensive animal toxicity tests, enabling the agency to screen chemicals more quickly and to predict and identify potential risks to Americans.

EPA scientific studies using ToxCast have already been published in peer-reviewed science journals, and demonstrate the ability of ToxCast to predict a chemical's potential to cause several diseases.

The four companies awarded the contracts have offices throughout the country and plan to hire new scientific staff to help with the project. The companies are Vala Sciences, Cee Tox, CellzDirect and BioReliance. Two of the companies, Vala Sciences and BioReliance are small businesses based in San Diego, CA and Kalamazoo, MI. All four companies plan to hire new employees as a result of these contracts.

More information on ToxCast: http://epa.gov/ncct/toxcast/
More information on ToxCast database: http://actor.epa.gov/actor/faces/ToxCastDB/Home.jsp

U.S. Environmental Protection Agency Weekly Digest Bulletin Press release on August 4, 2011