Early Morning Sessions

MS1: 3R centers 1: Asian regulatory affairs in animal welfare and alternatives

The continuation of Asian activities of alternative research from WC6 to WC7

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Asian activities in alternatives to animal experimentation were fired up when the World Congress 6 (WC6) was planned to be held in Tokyo. In particular, the western colleagues in this field asked the Japanese Society for Alternatives to Animal Experiments (JSAAE), which was a host of WC6, to extend our activities to other Asian countries. Accordingly, JSAAE asked Korean and Chinese colleagues in this field to organize satellite meetings in their countries. Two satellite meetings were organized in Beijing and Seoul, and they were successfully attended by many participants from all over the world before WC6. WC6 itself was well attended with more than one thousand international participants in 2007, and these gatherings stimulated much research interest in alternatives to animal experimentation among biomedical scientists in Asian countries.

The success of WC6 was extended to academic information exchange among these countries. We of the JSAAE continue the mutual exchange of scientists among Asian countries and, in fact, several delegations were sent to attend the other societies' general meetings. The wave of Asian activities continues into WC7 and the JSAAE is organising the morning session "Asian regulatory affairs in animal welfare and alternatives".

The activities of alternative research should be extended to all countries in which animal experimentation is conducted, including many other Asian countries. Information on Asian alternatives activities will be shared among the international participants of WC7.

Accreditation of animal experiments by Japan Health Science Foundation

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Japanese animal protection law was revised in 2005 to include 3Rs principles of animal experiments. According to this, general principles of animal experiments were prepared and notified in 2006 separately by Ministry of Education, Culture, Sports, Science and Technology, Ministry of Health, Labor and Welfare (MHLW), and Ministry of Agriculture, Forestry and Fisheries. Main contents of these notifications were almost the same. All includes responsibility of director of the institutes, role of institutional committee for animal experiments, selection of scientifically valid methods and respect of 3Rs principles, appropriate facility and equipments, secure the safety of animal experiments, and culture and keeping of experimental animals.

On the other hands, needs of inspection of animal experiments by third party was not described in the MHLW's notification. However, JPMA companies, who are administered by MHLW, considered it necessary and asked Japan Health Science Foundation (HS) to play the role. HS started to construct the system in 2007 and organized "Center for Accreditation of Laboratory Animal Care and Use" in 2008. Purpose of the inspection is to evaluate the institute conducting animal experiments according to the general principles notified by MHLW. It examines by both document review and site visits. Our institute (NIHS) was the first accredited institute.

Two laws on laboratory animal welfare and use in Korea

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The Animal Protection Law (APL) of Korea was amended in December 2007. It includes two sections on laboratory animals. Section 13 described the principles of animal experiments, including 3R principles. Beside 3R, dogs that have worked for humans may not be used as laboratory animals. Section 14 describes an Institutional Animal Care & Use Committee. Over one third of the committee should be composed of persons who do not work at the corresponding animal experiment facility and do not have any relationship of gain and loss with the facilities. A veterinarian and a person recommended by an NGO on animal welfare should be included in the committee. The law was activated in February 2008. Now, about 600 animal facilities have set up IACUC and started inspection of proposals and animal facilities. The Animal Protection Law (APL) is led by the Korean Department of Agriculture.

The other law on laboratory animal use was adapted in 2008 by the Korean Food and Drug Administration (KFDA). The law on laboratory animal use indicates that animal facilities which provide testing of drugs, cosmetics, food and medical instruments should be enrolled in KFDA. KFDA should supervise and guide these animal facilities. The two laws seem to have some conflicts. According to the laws, many animal facilities must inform both the Department of Agriculture and KFDA of their activities.

Laboratory animal welfare and ethical review of animal experiments in Chinese regulations

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In 1988, Chinese State Council has issued "The Regulation for Administration of laboratory animals", and some provincial regulations of laboratory animals are issued in Beijing, Hubei, Yunnan and Heilongjiang. All these regulations pay more and more attention to the animal welfare and ethics on animal use as the issued time successively. The Ministry of Science and Technology has issued "The Guide of Well Treatment for laboratory animal". The guide consists of the requirements for hygiene, safety, watering, feeding, handling, breeding space, anesthesia, euthanasia, transportation and personnel training on animal use. The national standards for laboratory animals are issued and implemented since 1994. These national standards cover all aspects about animal breeding and use. In 2001, "Developing guiding principle during Tenth five years" issued by Ministry of Science and Technology indicate that to establish an animal welfare guarantee system which is agreement with international rules.

MS2: Industry activities 1

Building a 3R corporate culture at Johnson & Johnson

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With over 250 operating companies in 57 countries, Johnson & Johnson demonstrates its commitment to the 3Rs through a variety of internal and external endeavors. In 1992, a research group in the EU was established with the aim to develop and implement alternatives for animal testing in the area of pharmaceutical research. Several alternative models for eye irritation have been implemented and research is on-going for other domains of toxicological research such as embryotoxicity, vascular irritation, phospholipidosis testing, etc. To acknowledge the importance of research in the area of the 3Rs, the Johnson & Johnson Corporate Office of Science and Technology established an internal Annual 3Rs Award. Each of the awardees is recognized at a major company event to further emphasize the important work they have accomplished and to reinforce the commitment of the company's senior leadership to the 3Rs. In 2006, Johnson & Johnson established a post doctoral fellowship specifically targeting projects dedicated to advancing the 3Rs. The 2006 3Rs post-doc fellow presented the results from her research at the 6th World Congress on Alternatives & Animal Use in the Life Sciences. Externally Johnson & Johnson employees participate with several international organizations such as ECVAM, ICCVAM, COLIPA, EPAA, the OECD and numerous consortiums including the European Industry Initiative and IVTIP. Johson & Johnson maintains a leadership position with several non-profit organizations whose mission is targeted towards the advancement of the 3Rs. Specifically, Johnson & Johnson is a member of the Scientific Advisory Panels of both IIVS and CAAT.

Procter & Gamble's approach to the development of alternatives

M. Lafranconi

The Procter & Gamble Company, Miami Valley Innovation Center, Cincinnati, OH, USA

Procter & Gamble is committed to the eventual elimination of animal testing for evaluating the safety of consumer products. Our approach has three key elements: 1) Development of methods to replace animal-dependent tests and continue to refine, or reduce animal use until a replacement is developed, 2) Development or adaption of tools that maximize use of existing data, and 3) Participation in programs that foster acceptance. Our research efforts focus on gaining a mechanistic understanding of the toxicity and developing methods that target key events for early detection and optimal predictivity such as the Peptide Reactivity Assay. We have developed internal databases, systems, and developed or adapted computational methods, and risk assessment approaches, such as TTC, which enable us to more effectively utilize existing information. Finally, our strategic partnerships with academics, government, NGOs and others in industry accelerate development of methods and acceptance by the scientific community, the public, and regulators.

The *colipa* programme on alternatives

O. de Silva

Colipa Strategic Committee on Alternatives, Brussels, Belgium

The 7th Amendment prohibits the use of animal tests in the EU to meet the requirements of the Cosmetics Directive by introducing testing and marketing bans.

The cosmetics industry has a long standing and continuous commitment to the replacement of animal testing. It already eliminated animal testing for finished products back in the 1980s

and has contributed together with several partners and ECVAM to the development and validation of the replacement alternative methods that are available to date: phototoxicity, skin corrosion and skin irritation, percutaneous absorption.

The development of new alternative methods is a tremendous scientific challenge. Since 1992 ***colipa*** and its members are committed to making all possible efforts in order to achieve the best results in developing alternatives. Currently within ***colipa***, 4 project teams are working on four priority areas: eye irritation, genotoxicity/mutagenicity, skin sensitisation and systemic toxicity. They have the mission to coordinate all the efforts of the European cosmetics industry to ensure development and help acceptance of replacement alternative methods in these areas. ***colipa*** has also established a special Project Team on safety assessment approaches. This work is supported by all members of ***colipa*** and adds to the ongoing substantial efforts of individual companies.

Overall, safety assessment of our products draws on multiple factors: data banks, physico-chemical values, analytical chemistry, exposure, frequency, animal data, *in vitro* data, *in silico* data (mathematical modeling, computer predictions), structure activity, read-across, benchmarking, clinical studies, post-marketing surveillance… and it will be possible to continue business and innovation. However, in some rare cases we may lack the necessary information.

In view of 2013, ***colipa***'s goal is to deliver a first generation integrated testing strategy capable of providing skin allergy information, and research aimed at delivering second generation methods more predictive and more applicable by 2013. In addition, a joint collaboration with the European Commission on the funding of systemic toxicity research has been agreed.

Whilst industry will be able to deal with the 2009 deadline and still remain innovative, the 2013 deadline poses huge challenges.

MS3: Animal welfare associations

The Foundation Animalfree Research: 33 years of replacing animal experiments

S. Schindler

Animalfree Research, Zurich, Switzerland

It all started in 1976 with 5,000 Swiss Francs (3,300 Euro) in Zurich. The founders of the new organization, then called *Fonds für versuchstierfreie Forschung* (FFVFF) were deeply moved by reports on hair-raising cruelties towards experimental animals and decided to do something about it. Aware of the fact that animal experiments could not be completely abolished overnight and inspired by the concept of FRAME, they dedicated their foundation to the financing of alternative methods – pioneer work in the 1970s. From the first moment, the dialogue with the public as well as with scientists and politicians was considered pivotal. The FFVFF published ALTEX for the first time in 1984 and can look back on many successful projects, such as the meta-analysis by Prof. Gerhard Zbinden which, for the first time, demonstrated the low scientific value of the LD_{50} test and found worldwide recognition. In 2007, the name of the FFVFF was changed to Animalfree Research.

The American Society for Prevention of Cruelty to Animals (ASPCA) and 3R initiatives

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Founded in New York City in 1866, the ASPCA is the oldest humane organization in North America dedicated to animal welfare and protection. Currently, the ASPCA is recognized as a national animal welfare organization with both regional and national programs aimed at fighting animal cruelty, controlling pet overpopulation issues, preservation of population and species, and promoting the health and welfare of animals. The organization is wholly committed to effecting change through nonviolent approaches. It believes in achieving its vision of humane communities across the United States through education, advocacy, and other forms of intervention that support the beneficial relationship between people and animals. The society's policies are based on empirical evidence and are supported by scientific research that establishes animals capacity to feel pain and suffering. The ASPCA strongly supports the development and validation of alternative methods to the use of animals in biomedical research and testing. The organization believes that the 3Rs are fundamental and should be applied to the use of animals in all aspects of biomedical research.

For the last twenty years, the ASPCA has been supporting 3R initiatives by using their expertise in the use of animal alternatives in research and through educational means. These initiatives have included sponsorship, participation and presentations at the alternative world congresses and other forums; participation in the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) in the US; reviewing and approving organizational protocols promoting 3R concepts; publishing scientific information in peer-reviewed journals by using veterinary toxicology databases to characterize sensitivities, syndromes, and interspecies differences from different chemicals; providing toxicological data to pharmaceutical and government regulatory agencies without using traditional animal testing studies to help investigate product safety. The recently started alternative literature search services at the ASPCA will strengthen our 3R initiatives further. This service is aimed at helping industry meet animal welfare act guidelines by performing database searches for existing research and alternatives.

Eurogroup for Animals

K. Reid

Eurogroup for Animals, Brussels, Belgium

Eurogroup for Animals has been deeply committed to improving the way animals are treated and kept throughout the European Union. Since our creation in 1980 this includes protecting the millions of animals used in research every year. As a federation of NGOs, we speak for millions of Europeans who are concerned about animals. Our membership of 42 organisations stretching across the European Union makes us ideally placed to represent the views of animal welfare. The network we have created consisting of about 15 experts, facilitates the sharing of effective campaigning tools and ideas among our members. We work with legislators, experts and industry towards the introduction, implementation and enforcement of EU laws that will improve animal welfare and reduce animal suffering and whereby animal tests are replaced with alternative methods.

Key to Eurogroup's success has been its excellent communication and in-depth knowledge and experience of EU political processes. Through this we strive to influence legislation at an early stage to bring about key improvements at a very early stage. To do this we sit on more than ten advisory committees at five different Directorates General of the European Commission. We also work closely with the European Food Safety Authority (EFSA) and the European Centre for the Validation of Alternative Methods (ECVAM) through their advisory boards.

In our mission to ultimately replace all animal experiments with viable alternatives Eurogroup collaborates with the European Partnership on Alternative Approaches (EPAA) – a unique collaboration between the European Commission (including ECVAM) and major companies from seven industry. ECVAM has to this day validated 32 alternative testing methods and is currently looking at validating many more, which could prevent the suffering of thousands of animals each year. Eurogroup has 2 representatives in the ECVAM ESAC committee. We continue to express our grave concern over the Commission's decision to restructure the Centre as well as question the level of ECVAM's operational funding. We believe that increasing both funding to and the role of this important organisation is key to speeding up the development and use of alternatives. This is an excellent time, as EU policy makers are in the midst of revising the legislation on the protection of animals used for scientific purposes, the very legislation that brought about the creation of ECVAM.

We work with Members of the European Parliament (MEPs) to support the push for our welfare demands and we closely monitor the discussions in the various parliamentary committees and supply MEPs with facts and figures to ensure that the Parliament's reports include substantial improvements for the protection of animals and implementation of alternative meth-

ods. Furthermore, for nearly 25 years we have run the secretariat of the European Parliament's Intergroup on the Welfare and Conservation of Animals. This popular and well-established forum held its 250th meeting in January 2009. To further the cause of animals in Europe we also work hard to ensure that successive EU presidencies are informed of key welfare issues during their six month chairmanship of the Council of the EU.

Our mission to keep animal welfare firmly in the spotlight does not stop at Europe's borders. Through our membership of a number of coalitions, we work closely with international organisations such as the International Organisation for Animal Health (OIE) and the Organisation for Economic Co-Operation and Development (OECD) can also call on Eurogroup to offer expert advice through the International Council on Animal Protection (ICAPO) alliance.

The HSUS and the Three Rs

M. L. Stephens

The Humane Society of the United States, Gaithersburg, Maryland, USA

The Humane Society of the United States (HSUS) embraced the Three Rs approach of replacement, reduction and refinement shortly after its elaboration by Russell and Burch in 1959. In recent years, the HSUS's efforts in promoting alternative methods have been enhanced by the work of its sister organizations, the Humane Society International (HSI) and the Humane Society Legislative Fund (HSLF). Current projects in the area of toxicity/safety testing include coordinating a coalition of corporations and NGOs to promote 21st century testing methods; advocating for Three Rs-friendly provisions in the programs of national and international regulatory and standard-setting bodies; lobbying for funding of Three Rs-related programs; co-managing the AltTox website to provide information and an interactive platform to promote non-animal methods of testing; and pressuring Allergan to replace its use of the LD_{50} test in assessing the potency of Botox products. We are currently in negotiation with the European Union to coordinate a project ("AXLR8"), under the 7th Framework Programme, designed to facilitate the development of 21st century testing methods in Europe. In the area of biomedical research, we are encouraging universities to adopt refinement policies prohibiting the conduct of severe animal experiments, and we are lobbying for a ban on the use of dogs and cats rounded up by "Class B" animal dealers as well as a phase out of chimpanzees used in invasive research. In the area of animal use in education, we promote alternatives to dissection by supporting relevant legislation and school policies and by loaning out alternative materials to students and teachers. Cross-cutting efforts include suing the U.S. Department of Agriculture to secure more meaningful national statistics on animal use to better inform planning efforts on the Three Rs, and bestowing the Russell and Burch Awards to deserving Three Rs scientists.

Vereniging proefdiervrij (Dutch society for replacement of animal testing)

M. Zuidgeest

Proefdiervrij, The Dutch Society for the Replacement of Animal Testing, The Netherlands

In the Netherlands, each year some 600,000 animals are still used for various animal tests. Proefdiervrij is a non-profit organisation that works towards replacing all kinds of animal testing (in the Netherlands). Its focus is on the promotion of alternative research methods. Proefdiervrij seeks to peacefully raise awareness of the plight of laboratory animals by means of promotional activities. The organisation urges politicians, the scientific research community, and industries to stimulate and innovate by using alternative methods and replace animal testing altogether.

It can change, it must change

Naturally, research into life threatening diseases is necessary and Proefdiervrij supports that thought. But it should not be at the cost of hundreds of thousands of test animals. This is not only about medical research but also about tests for cleaning products and foods. There are alternatives for animal testing, which often produce even better results. For instance, testing for skin rashes can be done on artificially cultivated skin and toxicology tests can be performed in an imitation gastrointestinal tract.

Non animal methods

Despite the availability of non-animal methods, a lot of scientist still fall back on using live animals. A force of habit. Moreover, the same tests are repeated all over the world, time and time again. Proefdiervrij holds the view that more money and energy should be spent on developing new non-animal techniques, so that the suffering of animals can truly be brought to an end.

You can find more information on our website www.proefdiervrij.nl (in Dutch) or visit the (English) site of our colleagues www.eurogroupforanimals.org.

It's high time for animal free techniques

MS4: Educational activities

Establishment of dedicated chairs for alternative methods as strategy to promote the 3R

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The promotion of more 3R approaches classically builds on 4 major pillars. Industry develops and applies new methods, authorities and animal welfare groups are involved to some extent in method development and validation but also play a major role in the implementation of the methods and in creating legal and societal driving forces. Last but not least, academia contributes greatly to the design of new assay systems.

As academia is most transparent to the general public and associated with a large number of students, it has a special role in overcoming conceptual barriers to the use of 3R approaches. Such barriers, in contrast to technological and legal barriers, are frequently linked to a certain inertia or even resistance towards breaking traditions, to a trust issue with regards to new approaches, to misinformation on the benefits and advantages of classical animal experimentation as opposed to newer 3R approaches, and to psychological factors, such as the fear of a loss of academic freedom. One approach to strengthen the academic progress towards the development of 3R approaches is the introduction of university chairs dedicated to this topic. They add credibility to the discipline as a serious topic of modern science, influence student education early on, and show realistic career paths and options for gifted students who want to commit to this research field and may otherwise follow other interests. One difficult issue for the establishment of 3R chairs is that method development as a goal in itself is neither well accepted nor is it well-funded by scientific organizations. Also, the peer acceptance is relatively low, and this would be counterproductive to the major goal of enhanced scientific credibility and attraction of students.

The solution to this problem is relatively simple and has been demonstrated successfully by the Doerenkamp-Zbinden (DZ) Foundation, one of the major sponsors of 3R chairs in the world: The methods development approach needs to be coupled with a conceptual scientific question. For instance, the DZ chair in Erlangen couples the development of refinement methods on the basis of non-invasive imaging techniques with conceptual research on the pharmacology of analgesics, the DZ chair in Konstanz links *in vitro* method development with conceptual research on neurodegenerative conditions and the DZ-Naef chair in Geneva combines the development of test systems with non-sentient invertebrates, with basic cell biological and immunological questions. Such combinations allow the chairs to plug in to key technologies of highly dynamic basic research fields and to use them for the development of 3R methods. In general, medical, veterinary or engineering faculties are more open to method development as major goal of a chair. Therefore chairs with such an affiliation may fully dedicate to 3R method development and the implementation of and lobbying for new concepts of thinking in the field.

Accordingly, the DZ chair at Johns Hopkins University is a major driver for evidence-based toxicology and the DZ chair at Utrecht University is promoting the consideration of biokinetic aspects in the development of 3R methods and their application in risk assessment.

All these DZ chairs are anchored firmly in the academic curriculum and, based on a high reputation of the chairholders, have the best chances of attracting students to the field of 3R research and also to contribute to the education of journalists and the broad public for wider acceptance of the 3R principle.

CAAT's humane science policy, outreach & academic programs

B. N. Merrill

Johns Hopkins Center for Alternatives to Animal Testing (CAAT), Baltimore, USA

The Humane Science Policy and Outreach Program serves to educate US policy-makers and legislators on the need for alternatives to animals in testing, and to advocate for humane sciences in government research and regulations. This program focuses on individuals and institutions that make or implement policies influencing the use of humane sciences and alternatives. The goal is to create a legislative and policy culture that values the lives of animals and promotes the use of the 3Rs.

To bring about this goal, the policy and outreach program sponsors and participates in seminars, prepares articles, and works with members of the policy and legal communities to cultivate a greater understanding of the principles and applications of humane science. An important objective is to identify champions in the policy field to assist in implementing the National Academy of Sciences (NAS) report, Toxicity Testing and Assessment in the Twenty-first Century: A Vision and a Strategy.

CAAT's Academic Programs educate students and professionals in the research field about alternatives, helping them gain a better understanding of the 3Rs and humane science. A central component is CAAT's Humane Science and Toxicology Certificate Program, which has a six-course curriculum and is accessible to the business, legal and regulatory communities. It is anticipated to be available entirely on-line in 2010

The Three Rs in veterinary medical education

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The goal of veterinary medicine is to promote animal health and welfare. Therefore, the training of veterinary students aims at providing them with knowledge of physiological and pathological processes across the species, an understanding of different animal husbandry systems, clinical competencies such as the diagnosis and treatment of disease, the ability to reason in a scientific manner, a fundamental appreciation of business management, and the development of a professional attitude. The use of (healthy) animals in veterinary education is mainly directed towards learning (anatomy and physiology), observation of animal behaviour and the development of practical skills such as animal handling and surgical technique.

About 75 million vertebrates are used worldwide per year for experimental purposes. On average, about 2% for education and training. Legislation on the use of animals for experimentation includes the use of animals for educational purposes: it is only permitted if the objective cannot be achieved by the use of non-animal methods, competence of the staff involved has to be proven, and unnecessary pain and distress has to be avoided – following the Principle of Humane Experimental Technique, that is, the Three Rs of Russell and Burch (1959).

For veterinary education, a variety of replacement methods are available, such as:

- Audio-visual
- Models and simulators
- Multimedia computer simulation
- Ethically-sourced animal cadavers and tissues
- Clinical work with animal patients
- *In vitro* labs
- Non-invasive field studies

Especially the integration of veterinary students in clinical practice at an earlier stage of their study in addition to training them in virtual laboratories designed to improve their skills seems to represent a highly successful combination.

Whilst the humane use of farm and companion animals and a critical eye on the use of animals for education are hot topics in modern veterinary education, it does not however usually include training in the humane use of laboratory animals. Given the fact that veterinarians regularly use and have to assess the validity of the results of animal experiments (i.e. treatment methods, new pharmacological compounds), veterinary students should at least have an obligatory basic training in ethical aspects of the use of experimental animals and in the application of the three Rs.

MS5: 3R centers 2

The NC3Rs – supporting science and animal welfare

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The National Centre for the 3Rs (NC3Rs) was established by the Government in 2004 to provide a UK focus for driving advances which replace, reduce or refine the use of animals in research and testing. Working with scientists in universities and industry, research funding bodies and regulatory authorities, the Centre's goal is to use the 3Rs as a framework for supporting science and innovation and improving animal welfare. The NC3Rs is developing new approaches to addressing key areas of unmet medical need; exploiting emerging technologies such as tissue engineering and providing an environment for data sharing and discussion on the utility of model systems. The Centre is the UK's biggest funder of 3Rs research and has a number of schemes for supporting high quality research including a recently launched scheme for PhD studentships. This presentation will briefly describe the Centre's work and the resources it provides scientists. Further information can be found at www.nc3rs.org.uk

A proposal of establishing a Brazilian center for validation of alternative methods (BraCVAM)

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Many products on the Brazilian market are requested to be controlled by using animal testing. Some groups at official laboratories, universities and industries are studying alternative methods, but there is no improved mechanism for funding collaborative studies and there is no institution responsible for managing and coordinating these studies. Many validated alternatives need to be improved in Brazil, taking into account some country specificities. This includes that some methods must be validated for the specific kinds of products. The Oswaldo Cruz Foundation (FIOCRUZ) assembles all the conditions necessary to become the headquarters of the Brazilian Center for Validation of Alternative Methods (BraCVAM), since it is an internationally recognized scientific institution uniting a large number of scientific fields, including basic and applied research, drug and vaccine production, quality control, teaching, hospitals, etc. The multidisciplinary scientific infrastructure of FIOCRUZ could be used to establish a network in different fields of knowledge. INCQS has been participated in several Brazilian and International Congresses and has a group of about 20 professionals and students working on alternatives for replacing animals in skin, eye and mucous irritation, sensitization and pyrogen tests, as well as vaccine and anti-venom sera potency determination. During this period, a great amount of posters presentations, lectures, organization of meetings and roundtables, papers and post-graduation studies have been developed. The creation of BraCVAM would facilitate the development and validation of tests, not only in Brazil but also in South America and the Caribbean, working together with institutions developing alternative methods around the world.

A national center for animal alternatives in India: the Mahatma Gandhi-Doerenkamp centre for alternatives to animal use in life science education

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"*I abhor vivisection with my whole soul. All the scientific discoveries stained with innocent blood I count as of no consequence*" (Mahatma Gandhi, 1869-1948)

The Mahatma Gandhi – Doerenkamp Centre for Alternatives to Animal Use in Life Science Education will be established as a National Center for alternatives in India, at Bharathidasan University, Tiruchirappalli, Tamil Nadu. The Bharathidasan University is a renowned university under the University Grants Commission of the Government of India. The mandate of the center is to synergize the Gandhian Philosophy of "Ahimsa" or "Non-Violence" in the teaching/research of Life Sciences. For the first time in India, this Center will introduce a new socio-scientific concept of promoting the philosophy of "non-violence" in the teaching and research in Life Sciences. The center will be established with the generous financial support received from The Doerenkamp-Zbinden Foundation, Switzerland, and the establishment of the "Gandhi-Gruber-Doerenkamp Chair" for Alternatives in Biomedical Education. The Center is being established in knowledge that promoting humane science is an imperative scientific, legal, psycho-social, ecological and economic need of the hour. The Center will strive to create a strong positive presence of alternatives in India to the use of animals thereby promoting quality and excellence in Life Science education/research/testing by way of continuous training programs, an alternatives knowledge bank, library and a certificate/diploma/post-graduate diploma program in animal alternatives.

The Center will also bring together stakeholders in the 3Rs – academia, scientific community, industry, government and animal welfare personnel from national/international levels to raise the awareness/facilitate the exchange of information/ideas on alternatives to translate the vision of the 3Rs into policy and curricular changes in India as relevant to education and research. The Center will also help by way of funding research and development of environmentally friendly pedagogical tools and *in vitro* alternative methods for Life Science teaching and research. The twin approach will be to encourage the use of e-tools and help establish virtual learning centers for teaching, and to establish a state-of-the-art cell culture laboratory for training in non-animal methods of research and product testing. The Center will be essentially a service provider in respect of non-animal methods in learning, research and testing.

The Center is a fruitful culmination of a decade's work of People *for* Animals, Chennai, and I-CARE, Chennai, in promoting the concept of the 3R in India.

MS6: Associations

ecopa: realisations and future perspectives

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ecopa, the European Consensus Platform on 3R-Alternatives, is an International Not-For-Profit organisation, based in Belgium and complying with Belgian law. It is the quadripartite organization at the EU level promoting the 3Rs all over Europe. ***ecopa*** brings together National Consensus Platforms (NCPs) on alternative methods. Consensus means that the major parties concerned are represented, including animal welfare, industry, academia, and governmental institutes. ***ecopa*** actually counts 16 NCPs: 14 full members (Austria, Belgium, Czech Republic, Denmark, Finland, France, Germany, Hungary, Italy, Norway,

(the Netherlands), Spain, Sweden, Switzerland) and 2 associated members (Poland, Ireland). It is active through working groups. The fields of interest are concerned with Research, Policy, Education and Ethics.
ecopa is thus uniquely placed and has huge expertise to offer to the debate around scientific and politically-linked topics in the field of the 3Rs.
ecopa is in particular active in dissemination of 3R-information via its website: www.ecopa.eu and its newsletter: ecopa messenger. It organizes yearly workshops of general interest in the field of the 3Rs, expert workshops and 2 yearly eSI (ecopa Science Initiative) workshops bringing young scientists into contact with well established, more senior experts. ***ecopa*** is partner for dissemination of results in an important number of EU research projects on 3R-alternatives: Predictomics, ReProTect, Sens-it-iv, Carcinogenomics and Esnats. Dissemination is done via the website, newsletters, workshops and congresses. ***ecopa*** is also coordinator of the EU coordination action.
START-UP is concerned with the "Identification of bottlenecks/ strengths of 3Rs in different stages of drug development". As such ***ecopa*** stimulates the promotion, development and acceptance of 3R-alternatives. This is highly necessary since all parties concerned need to build up accurate knowledge in the field, understanding of the ethical, scientific, regulatory and economical concerns related to the switch from *in vivo* to *in vitro* testing, and above all realistic expectations.

ESTIV, a bridge between scientists working on alternative methods in Europe

G. E. R. Schoeters

European Society for Toxicology in Vitro, Belgium

The European Society for Toxicology *in Vitro*, ESTIV, connects people and information in the field of *in vitro* toxicology within Europe.

The field of toxicology is undergoing a big change as pressure mounts to reduce animal use while new technologies such as genomics, proteomics, and other cell-based molecular techniques have entered the field and offer new opportunities to develop and improve alternative tests.

The European Society for Toxicology *in Vitro* brings together, every two years, scientists that are committed to alternative tests. The ESTIV workshops (formerly INVITOX workshops) have recently expanded to congresses that are attended by more than 300 scientists from all over Europe. They cover a broad range of topics related to *in vitro* tests for different health endpoints, application of new technologies, needs from stakeholders. ESTIV encourages young scientists by awarding them for the best poster and best oral presentation. ESTIV seeks partnerships with alike organizations and supports and stimulates national scientific organisations that are active in *in vitro* toxicology by organizing joint initiatives. A major task of ESTIV is to advocate the value of the scientific progress made in refinement, reduction, replacement of animals for toxicology testing and as such act as the scientists' voice in the dialogue between different stakeholders.

Specific information on ESTIV is available at our web site www. estiv.org

CELLTOX – the Italian association for *in vitro* toxicology

I. De Angelis

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The Italian Association for *In Vitro* Toxicology (CELLTOX) was founded in 1991; the following aims are the mainstays of our association and are expressed in its statute:
- to promote the use of *in vitro* experimental models and alternative methodologies, in pharmacological and toxicological field;
- to investigate mechanisms of toxicity at cellular and molecular level, with special interest for cell culture models;
- to facilitate the exchanges of information and collaborations among research groups of different public and private institutions;
- to create a network of information about ethical and practical aspects of the reduction of animal use, spreading the 3R principles and philosophy in the scientific community.

The association has also been particularly active in favouring the dissemination of alternative methods in toxicology by organizing scientific events and courses. The education of young researchers is one of our main goals and it is also pursued by giving grants and fellowships to support their participation to scientific events on alternatives.

CELLTOX board, as well as its members, comes from several public and private institutions, allowing a fruitful sharing of knowledge and expertise between them.

CELLTOX has often worked in close collaboration with similar European Societies and the European Society for Toxicology *in Vitro* (ESTIV).

In these last years, the association web-site, www.celltox.it, is become an important point of reference for all Italian people that work in the area of *in vitro* toxicology.

MS7: Lessons learned from the validation and potential regulatory applicability of *in vitro* alternative pyrogen tests

Development, purpose and importance of *in vitro* pyrogenicity tests

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Pyrogenic, i.e. fever inducing, contaminations in pharmaceuticals cause adverse effects, therefore pyrogen exclusion is required for all parenteral drugs. The rabbit pyrogen test has been used for this purpose since 1942, but animal protection issues as well as the scientific problem that the human and rodent response is not always congruent motivated the development of *in vitro* alternative methods. The *Limulus* amebocyte lysate (LAL) specifically detects the prototypical pyrogen endotoxin; however, among other limitations, it does not detect other pyrogens.

The *in vitro* pyrogen test systems of the second generation detect mediators, i.e. interleukin-1β or interleukin-6, induced upon exposition of human immune cells, i.e. human whole blood, mononuclear cells or a monocytoid cell line, to pyrogens, thus reflecting the *in vivo* human response. These systems detect the entire spectrum of pyrogens relevant for humans with the respective sensitivity. Quantification may be performed by comparison with a standardized stimulus, e.g. *E. coli* endotoxin. Human blood required for some of these methods can be made available to laboratories without access to fresh blood by cryopreservation. The *in vitro* pyrogen test (IPT) based on human whole blood has been adapted to an air-collecting system for air quality assurance, to the detection of pyrogens on solid biomaterials, and can be combined with albumin-coated beads for accumulation and subsequent detection of pyrogens in the femtomolar range or in immunomodulatory or toxic drug preparations.

In vitro pyrogenicity tests – lessons learned from the European validation study and ESAC peer review

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Five *in vitro* pyrogenicity tests based on human blood cells (monocytes) have been validated within the framework of the EU-funded project "Human(e) Pyrogen Tests" and in a catch-up validation study coordinated by ECVAM. In March 2006, the ECVAM Scientific Advisory Committee approved their scientific validity. Recently, they had been adopted by the European Pharmacopoeia Commission and will be covered in the new General method 2.6.30 – Monocyte Activation Test (European Pharmacopoeia 6th edition). Following the peer review and recommendations of ICCVAM, the US Food and Drug Agency approved the methods in 2009.

The presentation will report on the various phases of and problems encountered during the validation process, summarise the outcome of the ESAC peer review process and the process of regulatory acceptance.

The monocyte activation test (MAT) for pyrogens in year zero of its regulatory acceptance

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The idea to exploit the human fever reaction for pyrogen detection was first described 25 years ago by Charles Dinarello. It took 15 years to develop and standardize such tests to enter validation and now another ten years until their regulatory acceptance by European Phramacopoeia and US FDA this year.

We have learned over these decades about the nature of pyrogens, the challenges of different products and the merits and limitations of different *in vitro* approaches. We have arrived at a situation where the traditional rabbit test is clearly outperformed by the novel assays for essentially any product assessed so far. The earlier partial replacement by the Limulus (or bacterial endotoxin) test has still some advantages with regard to price and duration, but its limitations with regard to species differences, limitations to Gram-negative endotoxins and multiple interferences by test substances are clearly overcome.

The agreement on a pharmacopoeial monograph is a milestone for the broad use of the novel tests. However, similar as in case for the Limulus assay further refinements, adaptations to test challenges and new uses will evolve. The presentation will take stock of the recent developments and discuss future prospects.

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Assuring safety without animal testing: Unilever's ongoing research programme to deliver novel ways to assure consumer safety

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Assuring consumer safety without the generation of new animal data is currently a considerable challenge. However, through the application of new technologies and the further development of risk-based approaches for safety assessment, we remain confident it is ultimately achievable. For many complex, multi-organ consumer safety endpoints, the development, evaluation and application of new, non-animal approaches is hampered by a lack of biological understanding of the underlying mechanistic processes involved. The enormity of this scientific challenge should not be under-estimated. To tackle this challenge a substantial research programme was initiated by Unilever in 2004 to critically evaluate the feasibility of a new conceptual approach based upon the following key components: 1. Developing new risk assessment approaches. 2. Developing new biological (*in vitro*) and computer-based (*in silico*) predictive models. 3. Evaluating the applicability of new technologies for generating data that can be interpreted for risk-based safety assessment (e.g. "omics", informatics, mathematical modelling). Our research efforts are focussed in the priority areas of skin allergy, cancer and general toxicity (including inhaled toxicity). In all of these areas, a long-term investment is essential to increase the scientific understanding of the underlying biology and molecular mechanisms that we believe will ultimately form a sound basis for novel risk assessment approaches. Our research programme in these priority areas consists of in-house research as well as Unilever-sponsored academic research, involvement with EU-funded projects (e.g. Sens-it-iv, Carcinogenomics), participation in cross-industry collaborative research (e.g. Colipa, EPAA) and ongoing involvement with other scientific initiatives on non-animal approaches to risk assessment (e.g. UK NC3Rs, US "Human Toxicology Project" consortium).

Providing solutions for industry, regulators and the animal protection community

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Current scientific, political and ethical concerns about the use of animals in safety testing are causing increased attention to *in vitro* (non-animal) methods. This interest is not limited to industry toxicologists, but also includes other stakeholders, e.g. regulators and the animal protection community. All three of these constituencies need to have reliable information on the availability and performance characteristics of *in vitro* methods, and, in addition, industry must be able to have a source which can conduct these tests on their products. The Institute for *In Vitro* Sciences (IIVS) – a non-profit organization – was created to fulfil these needs. The approach that IIVS uses to meet the above-mentioned needs is to operate a high quality laboratory facility that conducts *in vitro* safety and efficacy testing for industrial and government clients worldwide. Knowledge of the performance of various test methods and protocols gained from having this unique hands-on familiarity is then shared with others through education and outreach programs. IIVS strives to obtain experience with all types of *in vitro* models, especially those that may commercially compete with one another, so that unbiased information about the performance of the various systems is available. This is especially useful for international researchers who may only be able to conveniently purchase from a supplier in close geographic proximity. The overall goal is to accelerate the use and acceptance of *in vitro* methods through the sharing of practical information. Thus all stakeholders in the *in vitro* field benefit from our experience.

The science strategy of the European centre for ecotoxicology and toxicology of chemicals, ECETOC

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ECETOC was established in 1978 as a scientific, non-profit, organisation. It has 51 member companies with a broad range of scientific expertise and experience in their respective external fora, including regulatory circuits. Most of these companies offer their senior scientific staff to work together, often with input from non-industry experts, on selected scientific topics. The strategic themes covered by ECETOC will be presented with examples of work programmes that have been running during the past year. One of the strategic themes is Intelligent Testing Strategies (ITS). ECETOC's work on topics such as fish testing and the 1-generation reproduction study will be reviewed, together with the oversight of several projects monitored by ECETOC which fall under the ITS theme.

The economics of animal testing

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How do animal testing-based regulatory and economic measures interplay? Which role do European legislations and regulatory entities such as those of the European Commission play? How does globalization impact on animal testing? Is there harmonization of regulation or do differences prevail? If an economic approach is attempted does this mean that industries, the consumer and animals will be better off?

This thesis also investigates the role and networking of several different industries e.g. cosmetic and chemical industries, and looks deeper into how these are connected through animal testing in the validation of alternatives for consumer product safety. The economic implications of animal testing are colossal with sales value of regulated products in Europe alone touching 1.7 trillion € per year (5.6 t€ world-wide). Within this context alone the reader should be able to grasp the sheer enormity and massive effects on manpower, investments and animal numbers related to animal testing. Indeed the classical toxicology of chemical substances on animals costs 620 m€ in the EU (2-2.5 b€ world-wide), directly employs 15,000 people (world-wide 73,000) and involves about 60,000 experimenters (300,000 world-wide) and in terms of animals 23.3% of the 12.1 million animals used in the EU 2005 were for regulatory tests and 31% for industrial R&D!

For brevity reasons but also because of the limited availability of reliable data resources, the analysis discussed here focuses on Europe, but where possible and necessary, a global perspective is also taken, since the effects of globalization cannot be ignored.

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CAAT: a 3Rs center for the 21st century

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The Johns Hopkins Center for Alternatives to Animal Testing (CAAT), founded in 1981, is one of the oldest of the 3Rs Centers. For 28 years, CAAT's innovative programs have served to promote the creation, development, validation, and use of alternatives to animals in research, product safety testing, and education.

CAAT also is, in many ways, one of the newest of the 3Rs Centers, with a new director – former Head of ECVAM Thomas Hartung – and an ever-expanding array of new programs and projects.

This session will offer an overview of CAAT's diverse activities and resources, from our long-standing research grants program, workshops and symposia series, and awards (two CAAT awards will be presented at WC7) to such developments as a Transatlantic Think Tank of Toxicology (t4); a union of Altweb with the journal ALTEX (now all in English), a new website devoted to 3Rs Centers, a variety of policy and outreach programs, implementation of the report, Toxicity Testing and Assessment in the Twenty-first Century: A Vision and a Strategy, and more.

ANZCCART's publication strategy: maintain, update and expand

G. Dandie

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The Australian and New Zealand Council for the Care of Animals in Research and Teaching (ANZCCART) is a not-for-profit organization charged with the responsibility of maintaining an informed and balanced public debate about the scientific use of animals as well as offering well researched, up to date advice to anyone wanting information. This is a role we have now been fulfilling for 22 years.

ANZCCART publishes high quality resource material for use by researchers, teachers and particularly Animal Ethics Committee (AEC) members across Australia and New Zealand. One example of this has been our series of Fact Sheets, which have been published progressively over the past 16 years. Of course times, ideals and attitudes change and during those 16 years, we have also seen two major revisions of the Australian Code of Practice for the Care and Use of Animals for Scientific Purposes (The Code), with yet another revision currently underway. All of these factors have highlighted the need to institute a programme of regularly assessing the relevance of the material we publish and ensuring that it at least meets if not exceeds current international "best practice" standards.

We have traditionally employed a range of methods to disseminate information and have largely concentrated our efforts in the areas of research and tertiary teaching. While these sectors remain essential target areas, it has become increasingly clear that we also need to expand our area of expertise and influence to include the use of animals in both primary and secondary education. The use of animals in schools is also covered by The Code but has not traditionally received the same level of support as the tertiary sector in all regions.

The challenge for ANZCCART as well as many of our related organizations around the World is to achieve more, without real hope of additional personnel or genuine increases in our funding base. We propose that the answer lies in the strength of collaboration and formation of strategic partnerships and this is a path ANZCCART has actively begun to explore.

The new Three Rs program at the Canadian Council on Animal Care

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For a number of years, the Canadian Council on Animal Care (CCAC) has been viewed as the Canadian Centre for the Three Rs by other like-minded organizations. In 2008 CCAC formally launched its Three Rs Program, providing the opportunity to outline, substantiate and better focus the role of the CCAC in the promotion and implementation of the Three Rs in Canada. The Three Rs Program is fully integrated within the CCAC, including appropriate links with the other three programs: Assessments; Guidelines; and Education, Training and Communication.

The Three Rs Program has already begun to establish a theoretical basis for its work and to prioritize its activities. The focuses of the program are: promoting the Three Rs through communication of the CCAC's ethics of animal experimentation, the maintenance of an up-to-date Three Rs microsite to make new Three Rs information and tools available to investigators, and the consolidation of CCAC's role as Canada's national centre for the Three Rs; and supporting the implementation of the Three Rs in all areas relating to the use of animals in science covered by the CCAC Program.