

Editorial Policy of the WC6 Proceedings

The “6th World Congress on Alternatives & Animal Use in the Life Sciences (WC6)” was held from August 21 through 25, 2007, in Tokyo, Japan. This special issue of the Alternatives to Animal Testing and Experimentation (AATEX) is published to serve as an archive of this conference by the Japanese Society for Alternatives to Animal Experiments (JSAAE).

The ad hoc committee, namely, Publication Committee for WC6 Proceedings (PubCom), was organized as the guest editorial board for this objective; it is comprised of 5 members—Shigenobu Hagino, Koichi Imai, Hidenobu Okumura, Yasuyuki Sakai, and Isao Yoshimura (chief). They established the following policy:

1. The maximum number of papers possible is included in the WC6 Proceedings. However, the manuscripts not listed in the table presented at the last meeting (on January 6, 2008) of PubCom are not included in the WC6 Proceedings.
2. The copyright transfer agreement provided by PubCom must be signed at least by the representative author. The exclusion of authors without their consent is not permitted.
3. Readability is an essential factor for a paper to be published in the WC6 Proceedings. Submission of the manuscript as a power point file is not acceptable, except in the case of plenary lectures. Abstracts and posters presented at the WC6 conference itself are also not included in the WC6 Proceedings.
4. The format of publication is completely under the control of PubCom.
5. Authors should be listed by their full names, with the family names appearing last, and only the first letter should be capitalized. Group name is not acceptable as the author.
6. Affiliations should be indicated in the simplest manner possible, and the corresponding author must be identified, with his/her surface mail address.
7. Three, four, or five keywords must be included.
8. Figures are printed in monochrome color, i.e., in white and black, except 4 pages of photo pictures of the conference.
9. All footnotes are moved to the last page of each paper.
10. Request for revision by PubCom must be duly addressed by the end of January 2008.
11. No reprints will be provided by PubCom because the copy of any paper can be reproduced from the appropriate web sites.
12. Only one copy of WC6 Proceedings will be sent to each participant of WC6 and member of JSAAE.



Isao Yoshimura
Chief, PubCom

Contents

Professor W.M.S. Russell (1925–2006): Doyen of the Three Rs	1
<i>Michael Balls</i> <i>FRAME, Russell & Burch House, UK</i>	
Three Rs in mutation research -- From <i>in vivo</i> to <i>in silico</i> evaluation --	9
<i>Makoto Hayashi</i> <i>National Institute of Health Sciences, Japan</i>	
Exploring new approaches to assess safety without animal testing.....	15
<i>Julia Fentem, Paul Carmichael, Gavin Maxwell, Camilla Pease, Fiona Reynolds,</i> <i>Guy Warner and Carl Westmoreland</i> <i>Unilever – Safety & Environmental Assurance Centre, UK</i>	
Alternative research and practice supported by international veterinary professionals	21
<i>Judy MacArthur Clark</i> <i>International Association of Colleges of Laboratory Animal Medicine, USA</i>	
The science of alternatives: 25 years and tomorrow.....	29
<i>Alan M. Goldberg</i> <i>The Johns Hopkins University, USA</i>	
A UK example of balanced inquiry into the ethics of animal experimentation.....	37
<i>Baroness Perry of Southwark</i> <i>Nuffield Council on Bioethics Working Party and University of Surrey, UK</i>	
Mission and accomplishments of ZEBET, the national centre for alternatives in Germany at the BfR (Federal Institute for Risk Assessment).....	41
<i>Horst Spielmann, Barbara Grune, Manfred Liebsch Andrea Seiler and Richard Vogel</i> <i>National Centre for Documentation and Evaluation of Alternative Methods</i> <i>to Animal Experiments, Germany</i>	
Standards for the rearing environment of laboratory animals in the United States	47
<i>Kathryn Bayne</i> <i>AAALAC International, USA</i>	
Standards of accommodation and care for animals used in scientific procedures in Europe	51
<i>David B. Anderson</i> <i>Animals (Scientific Procedures) Inspectorate, UK</i>	
The standards of the rearing environment for laboratory animals in Japan.....	57
<i>Hiroo Hachisu</i> <i>Nihon University, Japan</i>	
Animal rights in Islam	61
<i>Reza Gharebaghi¹, Mohammad Reza Vaez Mahdavi², Hasan Ghasemi²,</i> <i>Amir Dibaei³ and Fatemeh Heidary¹</i> <i>¹Middle East Breast Cancer Institute, ²Shahed University, Medical School,</i> <i>³Ahvaz University of Medical Sciences, Iran</i>	
An investigation in the use of forage grains for laboratory rats	65
<i>Michael Rowntree</i> <i>Covance Laboratories Ltd., UK</i>	
Collaboration between academia and industry with focus on improvement of the welfare of both animals and humans in laboratory animal facilities	69
<i>Jan Lund Ottesen¹, Lars Friis Mikkelsen¹, Thomas Bertelsen², Thomas Krohn³, Sten Velschow⁴,</i> <i>Jann Hau³, Henrik Møllegaard⁵, Nils Dragsted¹ and Axel Kornerup Hansen³</i> <i>¹Novo Nordisk A/S, ²LEO Pharma, ³University of Copenhagen, ⁴Lundbeck A/S,</i> <i>⁵Scanbur A/S, Denmark</i>	
A holistic approach to taking research animal suffering seriously	73
<i>Martin L. Stephens and Kathleen Conlee</i> <i>The Humane Society of the United States, USA</i>	

Fetal ‘awareness’ and ‘pain’: What precautions should be taken to safeguard fetal welfare during experiments?.....	79
<i>David James Mellor¹, Tamara Johanna Diesch¹, Alistair Jan Gunn² and Laura Benner²</i>	
<i>¹Massey University, ²University of Auckland, New Zealand</i>	
The development of a national guideline to promote the wellbeing of animals used for scientific purposes	85
<i>Elizabeth Grant, David Adams, Steve Atkinson, Simon Bain, Mary Bate, Lynda Bonning, Wendy Fahy, Denise Noonan and Margaret Rose</i>	
<i>National Health & Medical Research Council, Australia</i>	
Tramadol minimizes potential pain during post-oophorectomy in Wistar rats.....	91
<i>Maria Angelica Guzman-Silva, Carlos Eduardo Pollastri, Jose Augusto Soares Pantaleão, Ana Carolina Bergmann de Carvalho, Helene Nara Henriques, Natersia Rosa Camara, Juliana Tomaz Pacheco and Gilson Teles Boaventura</i>	
<i>Fluminense Federal University, Brazil</i>	
Does distress matter?	93
<i>Judy MacArthur Clark</i>	
<i>Institute for Laboratory Animal Research, The National Academies, USA</i>	
Innovative refinements to anaesthesia techniques can deliver pain research without pain	97
<i>Craig Brian Johnson¹, Jo Murrell², Troy John Gibson¹ and David James Mellor¹</i>	
<i>¹Massey University, ²University of Bristol, New Zealand</i>	
Why does carbon dioxide produce analgesia?.....	101
<i>Ken-ichi Otsuguro, Sumiko Yasutake, Yoshihiko Yamaji, Masaaki Ban, Toshio Ohta and Shigeo Ito</i>	
<i>Hokkaido University, Japan</i>	
Implementation of permanent group housing for cynomolgus macaques on a large scale for regulatory toxicology studies	107
<i>Janet L. Kelly</i>	
<i>Covance Laboratories Ltd., UK</i>	
Chimpanzees in research and testing worldwide: Overview, oversight and applicable laws.....	111
<i>Kathleen M. Conlee</i>	
<i>The Humane Society of the United States, USA</i>	
Chimpanzee experiments: Questionable contributions to biomedical progress	119
<i>Andrew Knight</i>	
<i>Animal Consultants International, UK</i>	
Systematic reviews of animal experiments demonstrate poor human utility	125
<i>Andrew Knight</i>	
<i>Animal Consultants International, UK</i>	
Promoting consideration of the ethical aspects of animal use and implementation of the 3Rs.....	131
<i>Barney T. Reed and Maggy Jennings</i>	
<i>RSPCA, UK</i>	
Effect of policy decisions on experimental animal use in the UK.....	137
<i>Derek J. Fry</i>	
<i>Animals Scientific Procedures Inspectorate, Home Office, UK</i>	
Genetically modified animals in the biomedical sciences: The challenge of rapid advances & ethical demands	141
<i>Margaret Rose¹, Elizabeth Grant² and David Adams²</i>	
<i>¹University of New South Wales, ²National Health & Medical Research Council, Australia</i>	
Pain-free animals: An acceptable refinement?.....	145
<i>Renee M. Gardner and Alan M. Goldberg</i>	
<i>Johns Hopkins Bloomberg School of Public Health, USA</i>	
Facilitation of an international approach for data sharing and acquisition in relation to genetically-engineered animals.....	151
<i>Gilly Griffin and Clément Gauthier</i>	
<i>Canadian Council on Animal Care, Canada</i>	
The institutional animal care committee: Keystone of international harmonization.....	157
<i>Clément Gauthier</i>	
<i>Canadian Council on Animal Care, Canada</i>	

A review of trends in animal use in the United States (1972 – 2006)	163
<i>Jodie Kulpa-Eddy¹, Margaret Snyder² and William Stokes¹</i>	
<i>¹ U.S. Department of Agriculture, ² U.S. Department of Health and Human Services, USA</i>	
Does regulation drive, manage or monitor change?	167
<i>Jon Richmond</i>	
<i>Home Office, UK</i>	
An analysis of reporting pain and distress recognition and alleviation in scientific journal publications.....	171
<i>Leah M. Gomez and Kathleen M. Conlee</i>	
<i>The Humane Society of the United States, USA</i>	
Japanese concept and government policy on animal welfare and animal experiments.....	179
<i>Katsuhiko Shoji</i>	
<i>Toyo University, Japan</i>	
Guidelines for proper conduct of animal experiments by the Science Council of Japan	183
<i>Hideaki Karaki</i>	
<i>Science Council of Japan, Japan</i>	
Research animals for scientific purposes in Thailand: Ethics & policies	189
<i>Pattamarat Kunjara and Pradon Chatikavanij</i>	
<i>The National Research Council of Thailand, Thailand</i>	
Public participation in decisions relating to the use of animals for scientific purposes: A review of 20 years experience in Australia.....	193
<i>Margaret Rose, Lynette Chave and Peter Johnson</i>	
<i>University of New South Wales, Australia</i>	
Public participation in informed decision-making on animal use in Canada	197
<i>Clément Gauthier and Gilly Griffin</i>	
<i>Canadian Council on Animal Care, Canada</i>	
AALAS resources and programs supporting the 3 R's and humane concepts in animal research	203
<i>Nicole E. Duffee and Ann T. Turner</i>	
<i>American Association for Laboratory Animal Science, USA</i>	
Is it possible to meet the learning objectives of undergraduate pharmacology classes with non-animal models?.....	207
<i>David Dewhurst</i>	
<i>University of Edinburgh, UK</i>	
Humane teaching methods prove efficacious within veterinary and other biomedical education.....	213
<i>Andrew Knight</i>	
<i>Animal Consultants International, UK</i>	
Role of simulator in surgical blood pressure	221
<i>Nimgulkar Chetan Chandrakant, Patil Savita Dattatray and Surana Sanjay</i>	
<i>R. C. Patel College of Pharmacy, India</i>	
Outreach, alternatives awareness and replacement in Russia.....	225
<i>Elena Maroueva¹ and Nick Jukes²</i>	
<i>¹ InterNICHE-Russia & VITA, Russia, ² InterNICHE, Leicester, England, England</i>	
Three Rs in the research and education system of Pakistan: Perspectives and possibilities	229
<i>Hafsa Zaneb and Christian Stanek</i>	
<i>Veterinary Medicine University, Austria</i>	
A prototype software to sensitize medical undergraduate students to animal research methodology.....	235
<i>Ramasamy Raveendran</i>	
<i>Jawaharlal Institute of Postgraduate Medical Education & Research, India</i>	
A new model for developing computer-based alternatives to using animals in tertiary education	239
<i>David Dewhurst, Stewart Cromar and Rachel Ellaway</i>	
<i>University of Edinburgh, UK</i>	

<i>BioSafaris: A rationale for educational software on human biology and health in pre-college as an alternative to dissection</i>	243
<i>Lynette A. Hart¹, Mary W. Wood¹, David Wiley², Bernd Hamann¹, Marco Molinaro¹, Stuart Meyers¹, Frazier T. Stevenson¹ and William A. Storm³</i>	
<i>¹ University of California, Davis, ² Stratovan Corporation,</i>	
<i>³ Davis Joint Unified School District, Davis, USA</i>	
From policy to practice: Illustrating the viability of full replacement.....	249
<i>Siri Martinsen¹ and Nick Jukes²</i>	
<i>¹ InterNICHE Norway, Norway, ² InterNICHE, Leicester, England, UK</i>	
Education and training system in Japanese research laboratories in a global pharmaceutical company	253
<i>Makoto Suzuki</i>	
<i>Ina Research Inc., Japan</i>	
Future alternatives in “3Rs”: Learning from history	257
<i>Tohru Inoue and Yukio Kodama</i>	
<i>National Institute of Health Sciences, Japan</i>	
The effect of the Middle East conflict on the use of animals in training, research and testing in Israel	261
<i>Tamir Lousky</i>	
<i>InterNICHE – The International Network for Humane Education, Israel</i>	
Ethically sourced animal cadavers and tissue: Considerations for education and training	265
<i>Siri Martinsen¹ and Nick Jukes²</i>	
<i>¹ InterNICHE Norway, Norway, ² InterNICHE, Leicester, England, England</i>	
Training the animal doctor: Caring as a clinical skill	269
<i>Siri Martinsen</i>	
<i>InterNICHE Norway, Norway</i>	
Guidelines for the development of student choice policies regarding dissection in colleges and universities: An ethnographic analysis of faculty and student concerns	273
<i>Laura Ducceschi¹, Lynette A. Hart² and Nicole Green¹</i>	
<i>¹ Animalearn, ² University of California, Davis, USA</i>	
Facilitating replacement through access to and training in alternatives	277
<i>Monika Perčič¹, Nick Jukes² and Elena Maroueva³</i>	
<i>¹ InterNICHE Alternatives Loan System, Ljutomer, Slovenia, Slovenia,</i>	
<i>² InterNICHE, Leicester, England, UK, ³ InterNICHE Russia & VITA, Russia</i>	
InterNICHE Humane Education Award: Assessing the international impact.....	281
<i>Nick Jukes¹ and Siri Martinsen²</i>	
<i>¹ InterNICHE, Leicester, England, UK, ² InterNICHE Norway, Norway</i>	
E-Learning – A new tool for the education of young scientists in the humane treatment of experimental animals: A contribution to the 3R	285
<i>Nicole Steinberg¹, Eckhard von Keutz², Jürgen Weiss³, Gerhard Heldmaier¹ and Cornelia Exner¹</i>	
<i>¹ University of Marburg, ² Bayer HealthCare AG, Wuppertal-Aprath,</i>	
<i>³ IBF University of Heidelberg, Germany</i>	
Three’s a crowd: The 1R of replacement for education and training.....	291
<i>Nick Jukes¹ and Siri Martinsen²</i>	
<i>¹ InterNICHE, Leicester, England, UK, ² InterNICHE Norway, Norway</i>	
CAAT and Altweb: Making 3Rs information and resources available around the world	295
<i>Carol J. Howard</i>	
<i>The Johns Hopkins Center for Alternatives to Animal Testing (CAAT), USA</i>	
ANZCCART and our strategies for sharing information.....	299
<i>Geoffrey W. Dandie</i>	
<i>ANZCCART, Australia</i>	
Selecting appropriate animal models and strains: Making the best use of research, information and outreach	303
<i>Mary W. Wood and Lynette A. Hart</i>	
<i>University of California, Davis, USA</i>	

Refinement in the literature: Searching for environmental enrichment.....	307
<i>Kristina M. Adams</i> <i>Animal Welfare Information Center, US Department of Agriculture, USA</i>	
Web 2.0 and alternatives	313
<i>Michael M. Hughes</i> <i>Johns Hopkins University Center for Alternatives to Animal Testing, USA</i>	
Japanese regulation of laboratory animal care with 3Rs	317
<i>Tsutomu M. Kurosawa</i> <i>Osaka University Medical School, Japan</i>	
Adopting alternative methods for regulatory testing in Canada.....	323
<i>Allison Guy, Clément Gauthier and Gilly Griffin</i> <i>Canadian Council on Animal Care, Canada</i>	
Multimedia software for demonstrating animal experiments in pharmacology	329
<i>Chandragouda R. Patil</i> <i>R. C. Patel College of Pharmacy, India</i>	
U.S. perspective on the “consideration of alternatives” regulatory requirement.....	333
<i>Jodie Kulpa-Eddy and Kristina Adams</i> <i>Animal Welfare Information Center, US Department of Agriculture, USA</i>	
Update on the Colipa research programme for development of <i>in vitro</i> alternative methods for eye irritation	337
<i>Pauline McNamee¹, Lieve Declercq², Ann De Smedt³, Bart De Wever⁴, Claudine Faller⁵, John Harbell⁶, Penny Jones⁷, Monique Marrec-Fairley⁸, Wolfgang Pape⁹, Uwe Pfannenbecker⁹, Klaus Schroeder¹⁰, Magalie Tailhardat¹¹, Christine Van den Berghe¹² and Freddy Van Goethem³</i> ¹ Procter & Gamble Company, UK, ² Estee-Lauder Companies, Belgium, ³ Johnson & Johnson Pharmaceutical Research & Development, Germany, ⁴ Phenion, Switzerland, ⁵ Procter & Gamble Cosmital, USA, ⁶ Mary Kay Inc., UK, ⁷ Unilever, Belgium, ⁸ COLIPA, Germany, ⁹ Beiersdorf, Germany, ¹⁰ Henkel, France, ¹¹ LVMH, France, ¹² L’Oreal, Belgium	
The use of the reconstructed Human Corneal Model (HCE) to assess <i>in vitro</i> eye irritancy of chemicals.....	343
<i>José Cotovio¹, Marie-Hélène Grandidier¹, Damien Lelièvre¹, Christelle Bremond³, Nicole Flamand¹, Sophie Loisel-Joubert², Aline Van Der Lee², Christophe Capallere³, Jean-Roch Meunier¹ and Jacques Leclaire¹</i> ¹ L’Oréal Research, ² L’Oréal Safety Evaluation, ³ SkinEthic Laboratories, France	
<i>In vitro</i> acute skin irritancy of chemicals using the validated EPISKIN model in a tiered strategy Results and performances with 184 cosmetic ingredients	351
<i>José Cotovio¹, Marie-Hélène Grandidier¹, Damien Lelièvre¹, Roland Roguet¹, Estelle Tinois-Tessoneaud² and Jacques Leclaire¹</i> ¹ L’Oréal Research, ² SkinEthic Laboratories, France	
Comparison of human skin irritation and photo-irritation patch test data with cellular <i>in vitro</i> assays and animal <i>in vivo</i> data	359
<i>Dagmar Jirova¹, Manfred Liebsch², David Basketter³, Erin Spiller⁴, Kristina Kejlova¹, Hana Bendova¹, Marie Marriott⁵ and Helena Kandarova⁴</i> ¹ National Institute of Public Health, Czech Republic, ² ZEBET, Federal Institute for Risk Assessment, Germany, ³ St Thomas’ Hospital, UK, ⁴ MatTek Corporation, USA, ⁵ Unilever Colworth Laboratory, UK	
BALB/c 3T3 cell transformation assays for the assessment of chemical carcinogenicity	367
<i>Ayako Sakai</i> <i>National Institute of Health Sciences, Japan</i>	
The COLIPA strategy for the development of <i>in vitro</i> alternatives: Skin sensitisation.....	375
<i>Pierre Aeby¹, Takao Ashikaga², Walter Diembeck³, Dietmar Eschrich⁴, Frank Gerberick⁵, Ian Kimber⁶, Monique Marrec-Fairley⁷, Gavin Maxwell⁸, Jean-Marc Ovigne⁹, Hitoshi Sakaguchi¹⁰, Magalie Tailhardat¹¹ and Silvia Teissier⁹</i> ¹ Procter & Gamble, Switzerland, ² Shiseido Research Centre, Japan, ³ Beiersdorf, Germany, ⁴ Phenion GMBH (Henkel), Germany, ⁵ Procter & Gamble, USA, ⁶ Syngenta, Central Toxicology Laboratory, UK, ⁷ COLIPA, Belgium, ⁸ Unilever, Safety and Environmental Assurance Centre, UK, ⁹ L’Oreal Recherche, France, ¹⁰ Kao Corporation, Japan, ¹¹ LVMH Recherche, UK	

Application of a systems biology approach for skin allergy risk assessment.....	381
<i>Gavin Maxwell and Cameron MacKay</i>	
<i>Unilever – Safety & Environmental Assurance Centre, UK</i>	
The EPISKIN Phototoxicity Assay (EPA): Development of an <i>in vitro</i> tiered strategy to predict phototoxic potential	389
<i>Damien Lelièvre¹, Pascale Justine¹, François Christiaens¹, Nicole Bonaventure¹, Julie Coutet¹, Laurent Marrot¹, Estelle Tinois-Tessonnaud² and José Cotovio¹</i>	
<i>¹ L'Oréal Research, ² SkinEthic Laboratories, France</i>	
<i>In vitro</i> cytotoxicity assessment of selected nanoparticles using human skin fibroblasts	397
<i>Fin Dechsakulthorn, Amanda Hayes, Shahnaz Bakand, Lucky Joeng and Chris Winder</i>	
<i>The University of New South Wales, Australia</i>	
Genotoxicity assays with Episkin [®] , a reconstructed skin model: Towards new tools for <i>in vitro</i> risk assessment of dermally applied compounds?	401
<i>Gladys Ouédraogo¹, Michelle Feltes¹, Linda Bourouf¹, Nicole Flamand¹, Estelle Tinois-Tessonnaud² and Jean-Roch Meunier¹</i>	
<i>¹ L'Oréal Safety Research Department, ² SkinEthic Laboratories, France</i>	
Percutaneous absorption test – A case of effectiveness evaluation of skin-whitening cosmetics	407
<i>Tooru Koike¹, Noriko Nakashima¹, Chinami Urata¹, Masaki Arashima¹, Hidenobu Okumura¹ and Akiyoshi Takada²</i>	
<i>¹ NOEVIR, Co. Ltd., ² Osaka University, Japan</i>	
Monocyte derived dendritic cells as a tool to predict skin sensitization: Limitations and opportunities	411
<i>Dietmar Eschrich¹, Ursula Engels¹, Julia Scheel² and Klausrudolf Schroeder¹</i>	
<i>¹ Phenion GmbH & Co.KG, ² Henkel KGaA, Corporate SHE and Product Safety/Human Safety Assessment, Germany</i>	
Study on the prediction of human lip irritation from cosmetics materials using HeLa-MTT assay	415
<i>Miyuki Morinaga, Kenta Shingaki, Tatsumi Mori and Koji Yanagihara</i>	
<i>NOEVIR Co., Ltd., Japan</i>	
Assessment of the <i>in vitro</i> skin irritation of chemicals using the Vitrolife-Skin [™] human skin model	417
<i>Noriyuki Morikawa, Tatsuya Kitagawa and Kenji Tomihata</i>	
<i>GUNZE Ltd., Japan</i>	
Validation of alternative endpoints for the LLNA: General considerations	425
<i>Silvia Casati</i>	
<i>ECVAM, IHCP, Joint Research Centre, European Commission, Italy</i>	
Validation studies on an alternative endpoint for the local lymph node assay (LLNA-DA): Importance of study management	429
<i>Takashi Omori¹, Yoshiaki Ikarashi², Yukiko Kanazawa³, Kenji Idehara⁴, Hajime Kojima², Takashi Sozu⁵, Kazunori Arima⁶, Hirohiko Goto⁷, Tomohiko Hanada⁸, Taketo Inoda⁹, Tadashi Kosaka¹⁰, Eiji Maki¹¹, Takashi Morimoto¹², Shinsuke Shinoda¹³, Naoki Shinoda¹⁴, Masahiro Takeyoshi¹⁵, Masashi Tanaka¹⁶, Mamoru Uratani¹⁷, Masahito Usami¹⁸, Atsushi Yamanaka¹⁹, Tomofumi Yoneda²⁰, Isao Yoshimura²¹ and Atsuko Yuasa²²</i>	
<i>¹ Kyoto University, ² National Institute of Health Sciences, ³ Food and Drug Safety Center, ⁴ Daicel Chemical Industries Ltd., ⁵ Osaka University, ⁶ Taisho Pharmaceutical Co. Ltd., ⁷ Otsuka Pharmaceutical Co. Ltd., ⁸ Nippon Shinyaku Co. Ltd., ⁹ Nakano Seiyaku Co. Ltd., ¹⁰ Institute of Environmental Toxicology, ¹¹ Biosafety Research Center, Foods, Drugs and Pesticides, ¹² Sumitomo Chemical Co. Ltd., ¹³ Drug Safety Testing Center Co. Ltd., ¹⁴ Santen Pharmaceutical Co. Ltd., ¹⁵ Chemicals Evaluation and Research Institute, ¹⁶ Meiji Seika Kaisha Ltd., ¹⁷ Ishihara Sangyo Kaisha Ltd., ¹⁸ Hoya Co. Ltd., ¹⁹ Pias Corporation, ²⁰ Toaeiyo Ltd., ²¹ Tokyo University of Science, ²² Fuji Film Co. Ltd., Japan</i>	
Alternative application route in the LLNA provides crucial environmental enrichment and broadens the usability of vehicles	433
<i>Ulla Festersen, Christine Rasmussen, Tanja M.R. Kjaer, Nanna K. Soni, Erwin L. Roggen and Ninna W. Berg</i>	
<i>Novozymes A/S, Denmark</i>	
<i>In vitro</i> hepatotoxicity testing in the early phase of drug discovery	437
<i>Ikuo Horii and Hiroshi Yamada</i>	
<i>Pfizer Global Research & Development, Pfizer Inc., Japan</i>	

Genetic polymorphism in drug metabolism and toxicity: Linking animal research and risk assessment in man.....	443
<i>Tetsuo Satoh</i>	
<i>Chiba University and HAB Research Institute, Japan</i>	
Renal drug transporters and nephrotoxicity.....	447
<i>Naohiko Anzai¹ and Hitoshi Endou^{1,2}</i>	
¹ <i>Kyorin University School of Medicine, ²J-Pharma Co. Ltd., Japan</i>	
Cisplatin-induced renal injury in LLC-PK ₁ cells.....	453
<i>Yoshiko Kawai¹ and Munekazu Gemba²</i>	
¹ <i>Osaka University of Pharmaceutical Sciences, ²Yokohama College of Pharmacy, Japan</i>	
Predictive <i>in vitro</i> cardiotoxicity and hepatotoxicity screening system using neonatal rat heart cells and rat hepatocytes.....	457
<i>Tomoaki Inoue, Kenji Tanaka, Masayuki Mishima and Kazuto Watanabe</i>	
<i>Chugai Pharmaceutical Co., Ltd., Japan</i>	
Toxicological and clinical computational analysis by the Informatics and Computational Safety Analysis Staff of the US FDA/CDER	463
<i>Daniel R. Benz, Edwin J. Matthews, Naomi L. Kruhlak, Anna A. Frid, Barbara L. Minnier and Joseph F. Contrera</i>	
<i>US Food and Drug Administration, USA</i>	
Evaluation of (Q)SAR models for the prediction of mutagenicity potential.....	469
<i>Stephanie Ringeissen, Reine Note, Catherine Dochez, Nicole Flamand, Gladys Ouedraogo-Arras and Jean-Roch Meunier</i>	
<i>L'Oréal Recherche, France</i>	
Internationally harmonized processes for test method evaluation, validation and regulatory acceptance: The role of OECD guidance document 34.....	475
<i>Leonard M. Schechtman</i>	
<i>Innovative Toxicology Consulting, LLC, USA</i>	
JaCVAM: An organization supporting the validation and peer review of new alternatives to animal testing	483
<i>Hajime Kojima</i>	
<i>National Institute of Health Sciences, Japan</i>	
A new signaling pathway of dioxin receptor ligands through targeted protein degradation	487
<i>Shigeaki Kato¹, Yoshiaki Fujii-Kuriyama² and Fumiaki Ohtake</i>	
¹ <i>ERATO, Japan Science and Technology Agency, University of Tokyo, ²University of Tokyo, ³University of Tsukuba, Japan</i>	
A strategy to explore the target receptor of endocrine disruptors: Estrogen-related receptor γ (ERR γ) as a genuine acceptor of Bisphenol A	495
<i>Ayami Matsushima and Yasuyuki Shimohigashi</i>	
<i>Kyushu University, Japan</i>	
What is better experimental design for <i>in vitro</i> comet assay to detect chemical genotoxicity?	499
<i>Yu F. Sasaki¹, Takanori Nakamura² and Satomi Kawaguchi^{1,3}</i>	
¹ <i>Hachinohe National College of Technology, ²Himeji Dokkyo University, ³Fuji Biomedix Co., Ltd., Japan</i>	
Comparative evaluation of cosmetic formulations with different alternative methods for eye irritation.....	505
<i>Andreas Heppenheimer¹, Albrecht Poth¹, Rolf Fautz² and Anne Fuchs²</i>	
¹ <i>RCC Cytotest Cell Research GmbH, ²KPSS - KAO Professional Salon Services GmbH, Germany</i>	
Preliminary study on neutral red uptake assay as an alternative method for eye irritation test.....	509
<i>Xingfen Yang¹, Wengai Zhang^{1,2}, Ying Yang², Xikun Xiong¹, Xiaoping Xie¹ and Xiaohua Tan¹</i>	
¹ <i>Center for Disease Control and Prevention of Guangdong Province, ²Sun Yat-sen University, China</i>	
Establishment and use of 3t3 NRU assay for assessment of phototoxic hazard of cosmetic products	515
<i>Ying Yanga¹, Xikun Xiong¹, Xinfen Yang¹, Junming Huan¹, Xiaohua Tan¹, Xiaoping Xie¹, Huisheng Zheng¹, Qing Li¹ and Xiwen He²</i>	
¹ <i>Center for Disease Control and Prevention of Guangdong Province, ²Center for Disease Control and Prevention of China, China</i>	
Bhas42 cell transformation assay as a predictor of carcinogenicity	519
<i>Albrecht Poth Andreas Heppenheimer and Susanne Bohnenberger</i>	
<i>RCC Cytotest Cells Research GmbH, Germany</i>	

ECVAM key area topical toxicity: Update on activities	523
<i>Valérie Zuang, Chantra Eskes, Claudius Griesinger and Thomas Hartung</i> <i>European Commission, Italy</i>	
Experiences in the development and utilization of an <i>in vitro</i> safety testing program for hair conditioners	529
<i>Pushpa Vavilikolanu¹, Catherine Lazaro¹, Greg Mun², Allison Hilberer², Matthew Hyder², Hans Raabe², Rodger Curren² and Gertrude-Emilia Costin²</i> <i>¹Alberto-Culver Company, ²Institute for In Vitro Sciences, Inc., USA</i>	
Protective effect of melatonin on spinal cord damage after gamma irradiation	535
<i>Sara Aghazadeh¹, Mahnaz Azarnia¹, Alireza Shirazi², Seied Rabie Mahdavi³ and Bagher Minaee Zangii¹</i> <i>¹Tehran University of Medical Sciences, ²Tarbiat Moalem University, ³Babol University of Medical Sciences, Iran</i>	
Does preclinical testing on insects help to predict human myelotoxic potentials?.....	539
<i>Josef Berger</i> <i>University of South Bohemia, Czech Republic</i>	
Evaluation of health risk due to the exposure to endosulfan in the environment.....	543
<i>Melissa Pui Ling Chan, Shinsuke Morisawa, Aki Nakayama and Minoru Yoneda</i> <i>Kyoto University, Japan</i>	
Responsiveness to painful stimuli in anaesthetised newborn and young animals of varying neurological maturity (wallaby joeys, rat pups and lambs).....	549
<i>Tamara J. Diesch, David J. Mellor, Craig B. Johnson and Roger G. Lentle</i> <i>Massey University, New Zealand</i>	
Predicting carcinogenicity in humans: The need to supplement animal-based toxicology	553
<i>Mara E. Long</i> <i>Johns Hopkins Bloomberg School of Public Health, Canada</i>	
Systemic testing by the dermal route can be precluded by new non-animal percutaneous absorption strategies	561
<i>Kristie Stoick¹, Ken Nitschke² and Chad Sandusky¹</i> <i>¹Physicians Committee for Responsible Medicine, ²The Dow Chemical Company, USA</i>	
The usage of <i>Daphnia magna</i> as alternative bioobject in ecotoxicology	565
<i>Valerii Tonkopii and Irina Iofina</i> <i>Institute of Limnology, Russia</i>	
Eco-toxicological effect of polycyclic musks for <i>C. elegans</i>	569
<i>Taiki Mori¹, Ayako Inokuchi¹, Moritoshi Nihira¹, Ryoko Yamamoto¹, Hiroshi Ishibashi¹, Shinya Kohra², Nobuaki Tominaga³ and Koji Arizono¹</i> <i>¹Prefectural University of Kumamoto, ²Nagasaki University, ⁴Ariake National College of Technology, Japan</i>	
Three Rs achievements in vaccinology.....	575
<i>Coenraad Hendriksen</i> <i>Netherlands Vaccine Institute and Utrecht University, The Netherlands</i>	
Alternatives to the LD ₅₀ assay for botulinum toxin potency testing: Strategies and progress towards refinement, reduction and replacement.....	581
<i>Dorothea Sesardic and Rose Gaines Das</i> <i>National Institute for Biological Standards and Control, UK</i>	
10 years of experience with alternative pyrogen tests (monocyte activation tests).....	587
<i>Ingo Spreitzer, Bettina Löschner, Christian K. Schneider, Kay-Martin Hanschmann and Thomas Montag</i> <i>Federal Agency for Sera and Vaccines, Germany</i>	
Alternative methods for animal tests in the quality control of biological products in China	591
<i>Zhengming He</i> <i>National Institute for the Control of Pharmaceutical and Biological Products, China</i>	
The importance of supplier qualification for vendors of materials used in <i>in vitro</i> assays.....	595
<i>Amanda K. Ulrey, Rodger D. Curren and Hans A. Raabe</i> <i>Institute for In Vitro Sciences, Inc., USA</i>	

Development of defined medium for mouse, monkey and human ES cell culture.....	601
<i>Miho Kusuda Furue¹, Jie Na³, Jamie P. Jackson³, Takamichi Miyazaki², Kei Takada², Hirofumi Suemori², Ryu-Ichiro Hata¹, Norio Nakatsuji², Tetsuji Okamoto⁴, J. Denry Sato⁵ and Peter W. Andrews³</i>	
<i>¹Kanagawa Dental College, Japan, ²Kyoto University, Japan, ³The University of Sheffield, UK, ⁴Hiroshima University, Japan, ⁵Mount Desert Island Biological Laboratory, USA</i>	
Chromatin remodelling, a novel strategy to expedite the hepatic differentiation of adult bone marrow stem cells <i>in vitro</i>	605
<i>Joery De Kock, Tamara Vanhaecke, Vera Rogiers and Sarah Snykers</i>	
<i>Vrije Universiteit Brussel, Belgium</i>	
Histone deacetylase inhibitors: Opening a new field of research in the development of alternative methods?	613
<i>Vera Rogiers, Mathieu Vinken, Sarah Snykers, Tom Henkens, Joanna Fraczek, Evelien De Rop, Joery De Kock, Tatyana Doktorova, Aneta Lukaszuk, Dirk Tourwé and Tamara Vanhaecke</i>	
<i>Vrije Universiteit Brussel, Belgium</i>	
Development of a disposable three-compartment micro-cell culture device for toxicokinetic study in humans and its preliminary evaluation.....	619
<i>Hidenari Nakayama, Hiroshi Kimura, Kikuo Komori, Teruo Fujii and Yasuyuki Sakai</i>	
<i>University of Tokyo, Japan</i>	
ToxCast™: Developing predictive signatures for chemical toxicity	623
<i>Robert J. Kavlock¹, David J. Dix¹, Keith A. Houck¹, Richard S. Judson², Matt T. Martin¹ and Ann M. Richard¹</i>	
<i>¹US Environmental Protection Agency, ²University of North Carolina, USA</i>	
Impact of systems toxicology on the 3 Rs	629
<i>James C. Fuscoe</i>	
<i>U.S. Food and Drug Administration, USA</i>	
Percellome toxicogenomics project and its possible contribution to 3R's	633
<i>Jun Kanno</i>	
<i>National Institute of Health Sciences, Japan</i>	
In vitro assays for evaluating the cellular responses to DNA damage induced by solar UV	637
<i>Tsukasa Matsunaga</i>	
<i>Kanazawa University, Japan</i>	
A quantitative <i>in vitro</i> assay to detect biological activity of endotoxin using rabbit peripheral blood	641
<i>Masaki Ochiai, Akihiko Yamamoto, Michiyo Kataoka, Hiromi Toyozumi, Yoshichika Arakawa and Yoshinobu Horiuchi</i>	
<i>National Institute of Infectious Diseases, Japan</i>	
A clinically relevant <i>in vitro</i> pyrogen test using a human cell line that have the similar responsiveness to various pyrogens to that of human peripheral blood cells (hPBC).....	647
<i>Akihiko Yamamoto, Masaki Ochiai, Kazunari Kamachi, Michiyo Kataoka, Hiromi Toyozumi, Yoshichika Arakawa and Yoshinobu Horiuchi</i>	
<i>National Institute of Infectious Diseases, Japan</i>	
Effects of experimental alloys containing indium for dental use <i>in vitro</i> embryotoxicity test	655
<i>Koichi Imai and Masaaki Nakamura</i>	
<i>Osaka Dental University, Japan</i>	
An advanced in vitro liver tissue model by combination of on-site oxygenation and double-layer coculture with fibroblasts.....	659
<i>Masaki Nishikawa, Nobuhiko Kojima, Takatoki Yamamoto, Teruo Fujii and Yasuyuki Sakai</i>	
<i>University of Tokyo, Japan</i>	
Liver cells culture on three-dimensional micropatterned polydimethylsiloxane surfaces.....	665
<i>Fanny Evenou, Teruo Fujii and Yasuyuki Sakai</i>	
<i>University of Tokyo, Japan</i>	
Development of the alternative method for renal drug excretion using <i>Xenopus</i> oocyte expression system combined with a high throughput method, OOCYTEXPRESS®	669
<i>Naoko Ohtsu¹, Jun Otomo², Naohiko Anzai³, Takeshi Sakata¹, Promsuk Jutabha¹, Shinichi Narikawa¹, Toshihito Kadota¹ and Hitoshi Endou^{1,3,4}</i>	
<i>¹Fuji Biomedix Co., Ltd., ²Hitachi, Ltd., ³Kyorin University, ⁴J-Pharma Co. Ltd., Japan</i>	

A higher throughput method to the Embryonic Stem cell Test (EST), to detect embryotoxicity in early development.....	673
<i>Annelieke K. Peters, Margino Steemans, Natalie Mesens, Erik Hansen, Geert R. Verheyen, Steven Spanhaak, Werner Coussement and Philippe Vanparys Johnson & Johnson Pharmaceutical Research & Development, Belgium</i>	
The possibility of the prediction of slimming by in vitro tests combination.....	679
<i>Muneo Tsukiyama¹, Yuko Ito¹, Noriko Nakashima¹, Chinami Urata¹, Masaki Arashima¹, Hidenobu Okumura¹ and Akiyoshi Takada² ¹NOEVIR, Co. Ltd., ²Osaka University, Japan</i>	
Establishment and characterization of a tracheal epithelial cell line RTEC11 from transgenic rats harboring temperature-sensitive simian virus 40 large T-antigen.....	685
<i>Takeshi Doi¹, Ichiro Takasaki¹, Ri-ichi Takahashi², Masatsugu Ueda², Yoshihisa Suzuki³, Masuo Obinata³ and Yoshiaki Tabuchi¹ ¹University of Toyama, ²The YS Institute, Inc., ³Tohoku University, Japan</i>	
Development of an effective three dimensional fabrication technique using inkjet technology for tissue model samples.....	689
<i>Chizuka Henmi¹, Makoto Nakamura^{1,2}, Yuichi Nishiyama¹, Kumiko Yamaguchi², Shuichi Mochizuki³, Koki Takiura⁴ and Hidemoto Nakagawa¹ ¹Kanagawa Academy of Science and Technology, ²Tokyo Medical and Dental University, ³Osaka Institute of Technology, ⁴Yamagata University, Japan</i>	
Histological study of pseudobranch in <i>Ctenopharyngodon idella</i>	693
<i>Gholamreza Hamidian and Naeem Alboghobeish Shahid Chamran University of Ahvaz, Iran</i>	
Initial study on the safety test using the planarian regeneration.....	697
<i>Sakiko Okumura and Yasuhiko Kobayashi Shiga-prefectural Yokaichi High School, Japan</i>	
HL-60 ATP assay for predicting rat oral toxicity study	699
<i>Yumiko Iwase and Naohisa Tsutsui Mitsubishi Tanabe Pharma Corporation, Japan</i>	
Thought before action - What do the public and others really want to know?.....	705
<i>Jon Richmond Home Office, UK</i>	
Severity assessment – The New Zealand experience and perspective.....	711
<i>A.C. David Bayvel, Linda A. Carsons and Kate E. Littin Ministry of Agriculture and Forestry, New Zealand</i>	
Categories of invasiveness – A precautionary approach.....	715
<i>Gilly Griffin, Maryse Dansereau and Clément Gauthier Canadian Council on Animal Care, Canada</i>	
Attitudes to severity assessment in Japan	721
<i>Takatoshi Kuhara Juntendo University School of Medicine, Japan</i>	
Animal welfare and ISO – the International Organisation for Standardization.....	723
<i>Jon Richmond Home Office, UK</i>	
The role of the World Organisation for Animal Health (OIE) in the development of international standards for laboratory animal welfare	727
<i>Sarah Kahn World Organisation for Animal Health, France</i>	
Setting global standards for animal welfare monitoring of external contractors.....	731
<i>Lars F. Mikkelsen, Helle N. Hansen, Lise Holst and Jan L. Ottesen Novo Nordisk A/S, Denmark</i>	
A global vision for laboratory animal medicine	735
<i>Judy MacArthur Clark International Association of Colleges of Laboratory Animal Medicine, USA</i>	

Practical consideration of 3Rs' reduction principle in a private sector CRO on Taiwan.....	739
<i>Hans Hsienchuan Chen, Chengnan Yang, Wenchi Jian and Sewfen Leu</i>	
<i>Greenseasons Biotech Co., Ltd., Taiwan</i>	
The past to present animal use and current animal protection law in Taiwan	743
<i>Hans Hsienchuan Chen</i>	
<i>BitotechPath Consulting, Ltd., Taiwan</i>	
Animal care and use programs: Global harmonization through alternatives.....	749
<i>Kathryn Bayne</i>	
<i>AAALAC International, USA</i>	
Necessity of world annual report and country's ranking in commitment to 3Rs; A novel proposition.....	753
<i>Fatemeh Heidary¹, Reza Gharebaghi¹, Mohammad Reza Vaez Mahdavi², Amir Dibaei³ and</i>	
<i>Hasan Ghasemi²</i>	
<i>¹Middle East Breast Cancer Institute, ²Shahed University, Medical School,</i>	
<i>³Ahvaz University of Medical Sciences, Iran</i>	
The 3 "R"'s approach to marine biotoxin testing in the UK.....	757
<i>Ngairé Dennison and David B. Anderson</i>	
<i>Animals (Scientific Procedures) Inspectorate, UK</i>	
Incentives and impediments to adopting alternative shellfish testing methods in Canada.....	763
<i>Allison Guy and Gilly Griffin</i>	
<i>Canadian Council on Animal Care, Canada</i>	
The European partnership for alternative approaches to animal testing.....	769
<i>Charles Laroche¹, Georgette Lalis² and Cornelis Brekelmans²</i>	
<i>¹Unilever, ²European Commission, Belgium</i>	
Implementation of the 3Rs in European regulation - activities of Working Group 4 of the European Partnership for Alternative Approaches to Animal Testing: I. Impact of liability issues and the precautionary principle, II. Evaluation of statistical reporting for measuring the uptake of 3Rs in regulatory testing	775
<i>Julia Scheel¹ and Cornelis Brekelmans²</i>	
<i>¹Henkel KGaA, Germany, ²European Commission, DG ENTR, Belgium</i>	
Overview of the test requirements in the area of food and feed safety.....	779
<i>Daniela Maurici¹, Susan Barlow², Diane Benford², Erik Dybing², Marlies Halder²,</i>	
<i>Susanna Louhimies², Marcelle Holloway², Antonio Lacerda², Alberto Mantovani², Otto Meyer²,</i>	
<i>Iona Pratt², David Morton², Willem Seinen², Horst Spielmann² and Pierre Le Neindre²</i>	
<i>¹EFSA, ²Working group of the EFSA's Scientific Committee on the Welfare of the</i>	
<i>Experimental Animals, Italy</i>	
Underreporting of the three Rs deployment that occurs during the planning of protocols that precedes their submission to animal ethics committees	785
<i>David J. Mellor¹, John C. Schofield² and Virginia M. Williams³</i>	
<i>¹Massey University, ²Otago University, ³Mt Admiral, New Zealand</i>	
Risk assessment in animal welfare – EFSA approach	789
<i>Christine Müller-Graf¹, Denise Candiani², Sara Barbieri², Oriol Ribó², Ana Afonso², Elisa Aiassa²,</i>	
<i>Per Have², Sandra Correia², Fabrizio De Massis², Thomasz Grudnik² and Jordi Serratosa²</i>	
<i>¹Federal Institute for Risk Assessment, Germany, ²European Food Safety Authority, Europe</i>	
The extended 1-generation study (OECD 415), as a replacement of the mammalian 2-generation study (OECD 416)	795
<i>Horst Spielmann and Richard Vogel</i>	
<i>National Centre for Documentation and Evaluation of Alternative Methods to Animal Experiments,</i>	
<i>Germany</i>	
Alternative testing – The intelligent way to REACH compliance	799
<i>Albrecht Poth and Martina Jaeger</i>	
<i>RCC Cytotest Cells Research GmbH, Germany</i>	
Legislation of animal use - Developments in Europe.....	805
<i>Bert van Zutphen</i>	
<i>Utrecht University, The Netherlands</i>	