Theme IV – Communication, Dissemination and Data Sharing

Coordinators
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Session IV-1: Information requirements on project proposals

Co-chairs
David Anderson, Pentlands Management Systems, UK
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Session IV-1: Oral presentations

IV-1-322

Animal ethics approval and monitoring process in an Australian institution

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Animal based research in Australia requires approval by an institutional Animal Ethics Committee (AEC) and must demonstrate adherence to the principles of the Australian Code (2013) and relevant Commonwealth, State and Territory legislation, polices and guidelines.

The Code details the ethical principles and decision-making framework to guide all involved with the care and use of animals for scientific purposes; an obligation to respect animals throughout their involvement in any project underpins the Code. To ensure appropriate evaluation of project proposals, the Code specifies criteria for categories of AEC membership including scientists, veterinarians, community and animal welfare members.

A duty of care and reciprocal responsibilities of investigators and AECs to ensure ethical acceptability throughout the lifetime of the project encompass all aspects of the planning, review approval and conduct of a project (Rose and Grant, 2013). Applications to the AEC must set out the case that a proposed project is ethically acceptable not only justifying the proposed use of animals but also weighing evidence of benefits and potential impact on animal wellbeing. Alternatives must be applied at all steps of animal care and use.

This presentation will outline the approval process and continuing assessments of an animal ethics application by an Australian institution.

References

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IV-1-483

Information requirements for project proposals under EU Directive 2010/63/EU

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In September 2013, the National Competent Authorities for the implementation of Directive 2010/63/EU on the protection of animals used for scientific purposes endorsed recommendations prepared by an Expert Working Group convened by the European Commission to develop guidance on Project Evaluation. This document contains advice and guidance on the information which should be included in a project proposal to facilitate subsequent evaluation by competent authorities. Applications which contain all the necessary and appropriate information are likely to be processed more quickly. The provision of correct, complete, current and relevant information is a prerequisite.

The guidance provides details of the issues which need to be addressed, offers suggestions on how these can be addressed and gives examples of the common faults in provision of information.

The key requirements are information on the scientific objectives and the expected benefits, the estimated harm to the animals, confirmation that the Three Rs have been rigorously applied, and information which relates to the likelihood of success.

IV-1-494 *

Public trust in animal research practices

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Research institutions often respond to criticisms of animal use by increasing the level of secrecy around how animals are used, including access to information about the types of animals used and the specifics of the procedures they are exposed to; however, this lack of openness may futher undermine the public's trust. The objective of this study was to assess whether people's willing to support the use of animals in research varies depending on the openness of the university governance system in place. Participants (n=279) took part in an online survey where they were presented with four different options for the governance of animal research at universities: a) status quo (no information shared), b) some information made publicly available, c) detailed information made available for public comment, and d) detailed information made available for both public comment, plus animal facility inspections. Results indicate that participants were progressively more willing to support animal research under systems that have higher levels of openness, and that have opportunities for public feedback. These results suggest that research institutions may benefit

from developing mechanisms for better sharing of information and for constructive dialogue regarding animal-based research.

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IV-1-789

Requirements on project proposals in Singapore

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In Singapore, all research institutions using animals must be licensed under the Agri-Food and Veterinary Authority (AVA) and comply to the "Animals and Birds Act (Chapter 7) Animals and Birds (Care and Use of Animals for Scientific Purposes) Rules 2004". The project proposals for animal studies must be reviewed by the local IACUC in accordance to the requirements stated in "Guidelines on the Care and Use of Animals for Scientific Purposes" developed by the National Advisory Committee for Laboratory Animal Research (NACLAR) in 2004.

In general, written project proposals must be submitted on proposed projects or significant changes in on-going projects. All proposals must contain sufficient information to justify the proposed use of animals and compliance with the 3Rs Principles including the rationale for involving animals, the species and numbers of animals to be used, and that the activities do not unnecessarily duplicate previous experiments. The project proposal must give a complete description of procedures designed to assure that discomfort, distress or pain to the animals will be limited to that which is unavoidable for the conduct of scientifically valuable research. Further, humane end-points, including a description of any euthanasia method to be used, must be described and justified.

References

Animals and Birds Act (Chapter 7). Animals and Birds (Care and Use of Animals for Scientific Purposes) Rules 2004, Ministry for National Development, Singapore 2004.

Guidelines on the Care and Use of Animals for Scientific Purposes, National Advisory Committee for Laboratory Animal Research (NACLAR), Singapore 2004.

Session IV-2: Scientific reporting standards (*in vivo* and *in vitro*)

Co-chairs

Mardas Daneshian, University of Konstanz, Germany

Merel Ritskes-Hoitinga, Radboud University, The Netherlands

Session IV-2: Oral presentations

IV-2-540

Classifying editorial policies on animal use in science: the EXEMPLAR scale

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Along with external regulation of animal use (e.g., legislation), self-regulation by the scientific community also impacts researchers' attitudes and practices regarding animal experimentation. One example is journals' editorial policies (EP) on animal welfare. Researchers' drive to publish can motivate compliance with EP, particularly for journals of high impact factor (IF). The latter, however, often demand less details on how studies are carried out (Hooijmans et al., 2010). To overcome the shortcomings found on a previously available scoring system (Osborne et al., 2009), the EXEMPLAR (Excellence in Editorial Mandatory PoLicies on Animal Research) scale was developed. Scoring is divided into four categories (4 points each, maximum 16 points): A) Regulatory Compliance; B) Quality of research and reporting of results; C) Animal Welfare and Ethics and D) Criteria for the exclusion of papers. An analysis of journals publishing papers on murine tuberculosis (n=49) and diabetes (n=29), revealed remarkably low scores (mean=3.56, Median=3). Typically, category A scored higher than all other categories, which were overwhelmingly neglected. This suggests journals' main concern is regulatory compliance, and displacement of their responsibilities for animal welfare/ethics to institutions. No linear relationship between IF and EXEMPLAR score was found. Higher scoring journals (>8 points) and the highest mean were found in journals with average IF (2,000<IF<4,000).

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IV-2-586

Animal studies: more than a modern sacrifice ritual?

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Currently, one of the main factors for evaluating the performance of scientists is the number of publications in high impact factor journals. This has led to a situation in which editorial boards of journals have gained a decisive power on how science is reported. It appears that many essential details are not reported, not even the two basic starting points of good scientific practice, namely randomisation and blinding, as is demonstrated again and again when performing systematic reviews. Moreover, a lack of correlation between the impact factor of a journal, the number of citations and the quality score of the publication has been reported. SYRCLE (http://www.SYRCLE.nl) is dedicated towards education and performing systematic reviews of animal studies to create more awareness on scientific quality when planning,

executing and reporting animal studies. Besides insufficient reporting, also the quality of planning and execution is in great need of improvement. In addition, it is critical that negative results and other raw data are made available always. The current situation is unacceptable for scientific, ethical and societal reasons. It also raises the question whether animal studies in science are regarded as more than a modern sacrifice ritual?

IV-2-677

Research reporting standards, scientific validity, animal welfare and the 3Rs

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Scientific journals are instrumental in the communication of knowledge around the world and play a key role in disseminating information on animal welfare, the three Rs (replacement, reduction and refinement) and good scientific practices. When reporting research, critical information includes experimental design and analysis, housing and care arrangements, experimental procedures, pain management, humane end-points and euthanasia methods. These details are crucial to the development of more humane science, but are also vital to enable an assessment of whether results are reliable, reproducible and scientifically valid.

This presentation will provide an overview of the analysis and output of a recent ICLAS working group on harmonisation of animal research reporting standards. This will include discussion of data from published studies of journal publication policies (Osborne et al., 2009, 2010) and existing efforts to raise research reporting standards (Hooijmans et al., 2010; Kilkenny et al., 2010; ILAR, 2011). By improving the reporting of animal research, the validity of the research will become easier to assess, whilst also promoting animal welfare and implementation of the 3Rs. This in turn can help facilitate an informed discussion of the ethical issues that are integral to the use of animals in research.

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IV-2-750

The ARRIVE guidelines: improving the reporting of *in vivo* research

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The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) is leading an initiative to improve the design and reporting of animal research. The ARRIVE (Animal Research: Reporting of *In Vivo* Experiments) guidelines (Kilkenny et al., 2010; http://www.nc3rs.org.uk/ARRIVE) were developed in consultation with scientists, statisticians, journal editors and research funders with the aim to maximise information published and minimise unnecessary animal use. The guidelines consist of a checklist of 20 items, which researchers can use when designing and reporting scientific experiments to ensure animal studies are robust, transparent and reproducible. Over 350 journals, major research funders, research intensive universities and learned societies endorse the guidelines; the recent translation of the guidelines into popular languages has contributed to their widespread international adoption. The guidelines are now available as a pocket-sized reference – last year, over 3,500 copies were distributed to researchers in 24 countries.

Following on from the ARRIVE guidelines, the NC3Rs is developing an online tool – the Experimental Design Assistant (EDA) – to guide researchers through the design of their experiments and improve the internal validity of animal studies. Through a graphical representation of the experiment, the EDA also provides a tool to improve transparency of design and analysis.

Reference

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IV-2-904

Quality standards for publications dealing with *in vitro* test systems

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Every study is different and needs to be presented in a different way. But, there is a broad interest in more transparency and clarity of published data. Moreover, publications should provide sufficient information to repeat experiments described in the literature. However, Each and every issue of toxicological journals still contains publications dealing with *in vitro* methods, but that lack essential information. These publications are slowing the progress of *in vitro* toxicology, not necessarily because there is a problem with their quality and the relevance of their science as such, but simply because it is difficult, and sometimes even impossible, to understand what was really done in the experiments and what was the outcome. Therefore, the Center for Alternatives to Animal Testing – Europe (CAAT-Europe) started a project to define a set of criteria, which should be met as quality standards for publications dealing with *in vitro* test systems in order to ensure sufficient and thus responsible information. This project involves over 70 co-authors working on different aspects of *in vitro* data, such as minimum requirements on descriptive information on biological and non-biological tools, methods and techniques, data processing approaches, statistics and data presentation as well as on the wealth and richness of information regarding the message of the publication. The list of criteria compiled here is thought to provide some support and guidance and poses as a plea for a code of good practice, guided by common sense.

Session IV-2: Poster presentation

IV-2-111

Study on the scientific validity of animal experiments in Switzerland

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Accumulating evidence indicates that poor experimental design and conduct may be widespread in animal experiments (Kilkenny et al., 2009), thereby contributing to poor reproducibility and translational failure (Van der Worp et al., 2010). Journal editors, researchers, and research funders therefore call for improvements, with more rigorous reporting guidelines (e.g., ARRIVE guidelines) being a first step (Howells et al., 2014; MacCallum, 2010; Kilkenny et al., 2010). An important question, however, is whether funders and licensing authorities have sufficient information on experimental design and conduct to decide whether a planned study is worthwhile both economically and ethically. In an attempt to assess this systematically we are currently screening all application forms submitted for approval of animal experiments in Switzerland in 2008, 2010, and 2012 (n=1600). The forms are screened for key indicators of internal validity (e.g., randomization, blinding, sample size calculation) and external validity (systematic variation of study population), and the data will be compared with data reported in publications resulting from these experiments to determine how well the application forms predict the scientific validity of the published reports. The expected results should allow us to identify problems underlying poor experimental design and conduct, and facilitate the implementation of new strategies to effectively prevent them.

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MacCallum, C. J. (2010). *PLoS Biol 8*, e1000413.
Van der Worp, H. B. et al. (2010). *PLoS Med 7*, e1000245.

Session IV-3: Retrospective analysis / non-technical summaries (2010/63)

Co-chairs
Barbara Grune, ZEBET BfR, Germany
Stephen Ryder, Home Office, UK
Moderator
Ursula G. Sauer, EUSAAT, Germany

Session IV-3: Oral presentations

IV-3-283

Establishing a web-based IT system for publishing non-technical project summaries in Germany

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Based on the EU Laboratory Animal Directive2010/63/EU the public has the right of access to information concerning projects using live animals in the European Union (EU, 2010). In order to fulfil this legal mandate the so-called non-technical project summaries are published by the European Member States. Non-technical project summaries provide information on the objectives of the projects, predicted harm and benefits, the number and types of animals to be used, a demonstration of compliance with the requirement of replacement, reduction and refinement. The German Animal Welfare Law and the new German Regulation on the implementation of Directive 2010/63/EU give the German Federal Institute for Risk Assessment the responsibility for publishing non-technical summaries on the Internet (Federal government of Germany, 2013a,b). The Federal Institute for Risk Assessment is currently establishing a web-based IT system for publishing non-technical project summaries in closed cooperation with the competent authorities of the German federal states. The IT solution should cover the key workflows between applicants (scientists), competent authorities at the state level and the Federal Institute for Risk Assessment as well as it should allow user-friendly information retrievals.

References

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Federal government of Germany (2013a). Drittes Gesetz zur Änderung des Tierschutzgesetzes vom 4. Juli 2013. BGBl. I Nr. 36, S. 2182-2196.
Federal government of Germany (2013b). Verordnung zur Umsetzung der Richtlinie 2010/63/EU des Europäischen Parlaments und des Rates vom 22. September 2010 zum Schutz der für wissenschaftliche Zwecke verwendeten Tiere. BGBl. I Nr. 47, S. 3125-3145.

IV-3-292

Requirements for non-technical summaries and retrospective assessment under Directive 2010/63/EU

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Non-technical summaries: To improve transparency and availability of information on the use of animals in scientific procedures, all Member States shall publish non-technical summaries (NTS) of authorised projects as described in Article 43 of the Directive. A consensus on the approach to publication has been agreed by Member States with a significant number already publishing in the agreed common framework. The NTS should include information on the objectives and expected benefits, the numbers and species projected, the expected harms and fate of the animals, and how the Three Rs have been addressed.The information should be presented in a format understandable by the general public – and an example was prepared to help scientists meet this need.

Retrospective assessment: Article 39 of the Directive describes the requirements for Retrospective Assessment (RA). Retrospective assessment is considered a powerful tool to facilitate critical review of the use of animals in scientific procedures, to identify future Three R improvements and, where published, to inform future studies and to enhance transparency to public. In September 2013, the Member States endorsed recommendations prepared by an Expert Working Group convened by the European Commission to develop guidance on Retrospective Assessment.

IV-3-382

Annual statistical reports and actual severity

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Directive 2010/63EU changes how statistics on animal use will be reported, including, for the first time at EU level, information on the impact of scientific procedures on animals. This is in addition to information on the purposes for which animals are used in science within the European Community.

While providing greater transparency and opportunities for targeting of 3Rs initiatives, the assessment of actual severity creates difficulties; it is not a wholly objective process. Without accurate and consistent classification of actual severity across the EU there is a risk that the quality of the data presented will be compromised. The intended improvements in communication and transparency may not be fully achieved

The criteria set out in Annex 8 of the Directive relate predominantly to *prospective* classification of *techniques* and provide little guidance on how *actual* severity of *entire procedures* should be assessed.

Additional guidance on severity assessment has been provided for UK users (http://www.gov.uk/research-and-testing-using-animals#annual-returns), but areas of difficulty remain, in particular in the severity of breeding of genetically altered animals; the assessment of the severity of animals found dead; and in the differences between procedural and non-procedural harms.

Some examples of these challenging areas will be presented and discussed.

IV-3-453

Experience with publication of non technical summaries

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The Directive 2010/63/EU calls for publication of the non-technical project summaries of authorised projects and any updates thereto.

This regulation opens for questions of, i.e., practicality, safety, academic ownership, intellectual property and economical matters.

The Danish authorities have on its website for ten years published both non technical and the technical parts of all applications for a license to perform animal experimentation.

Experience and problems with this procedure will be presented and discussed.

IV-3-766

Making numbers count: 3R gains from animal statistics

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Statistics can be a powerful tool in gaining 3R benefits for animals used for scientific purposes. To make this happen you need to collect correct and relevant data as well as successfully disseminate the results.

Statistics in this field has been collected for over two decades in the EU. Since research areas are continuously developing and the understanding of the 3Rs has grown, the demands for the statistics need to follow this evolution.

Directive 2010/63/EU on the protection of animals used for scientific purposes states more detailed demands for the statistics than before. Actual severity, origin and generation of non-human primates, and an increased spectrum of diseases and disorders are among the new data to be collected.

With actual severity for each individual noted we will know what severities the animals have been exposed to in which areas and be able to direct 3R efforts to the most urgent ones.

Reporting will be done yearly on a newly designed Microsoft Excel-sheet. It has built-in validating systems enhancing the correctness of the submitted data. The data will be stored and analyzed in an EU database in which the public will have access to reports facilitating the dissemination of data.

Session IV-3: Poster presentation

IV-3-334 *

Public openness in laboratory research: a survey study

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The objectives of this study were to model a system that makes animal protocols available for public comment, and identify key factors that affect public acceptance of animal research. Participants (n=247) completed an online survey where five different research scenarios were presented: a) Parkinson's Disease with chimpanzees, b) organ transplant research with pigs, c) smoking research with mice, d) cancer research with zebrafish, and e) chronic pain research with mice. Participants were asked "Are you willing to support this use of animals in research?" They could choose "yes," "neutral," or "no." Participants were also asked to provide a reason for their choice. Willingness to support the proposed use of animals varied with scenario. The proposal to use mice for smoking research received the lowest level of support (26% of participants voted "yes"). Reasons provided for not supporting this research were framed around a belief that science is well informed on the negative effects of smoking, and that the research is therefore unnecessary. This study illustrates one way in which research protocols could be open to public scrutiny and comment, providing institutions a better sense of how their practices meet public expectations, and which practices are the most contentious.

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Session IV-4: Information systems and databases

Co-chairs
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Session IV-4: Oral presentations

IV-4-189

Development of the new Korean guidance on the Three Rs search: adaptations and use of the European Commission's search guide

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In Korea, investigators planning to use animals for scientific purposes must complete an animal use protocol and submit it to an Institutional Animal Care and Use Committee (IACUC) for approval prior to commencement of the study. The animal use protocol outlines how the Three Rs (*Replacement*, *Reduction* and *Refinement*) will be implemented in the proposed animal-based procedures after searching for the most up-to-date information on the Three Rs. Based on our national survey of the Korean IACUCs and investigators in 2012, 25% of the respondents were not aware of how or where to find the Three Rs alternatives. We consider that the promotion and protection of animal welfare is one of the core competencies of well educated investigators and other personnel involved in uses of animals. This paper details the development of the new Korean guidance on efficiently and effectively finding information on the Three Rs based on the EURL ECVAM Search Guide of the European Commission. This guide sets out a step-by-step search strategy which provides detailed instructions based on their roles, i.e., investigator or IACUC, and a loose-leaf publication which is suitable for regular updating.

IV-4-297

Considering alternatives: searching for the 3Rs

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Types and sources of information continue to multiply at a phenomenal rate. While daunting and some times exhausting, mastering the unregulated disordered world of information, and managing the diverse results and outcomes, is achievable. Successful navigation requires a basic understanding of scholarly communication applied to a well-planned and thoughtfully considered search inquiry. Additionally, a clear understanding of the 3Rs and how they are practically reflected in a search is required in order to also address alternatives and produc-

tively consider the many alternatives-related information resources.

Effective searching for 3Rs information, specifically, has been researched, results have been published, and guides have been created; notable examples are the NC3Rs ARRIVE Guidelines, the systematic review work of SYRCLE at Radboud University Medical Center in the Netherlands, and the EURL ECVAM Search Guide recently published by Roi and Grune (2013). The question is how laboratory scientists and principal investigators make use of the research in order to comply with regulations and to find useful 3Rs information that may affect their research design. As significant obstacles to scientific inquiry and information acquisition, time, access and expertise are the primary concerns to be addressed.

Reference

Roi, A. J. and Grune, B. (2013). *The ECVAM Search Guide: Good Search Practice on Animal Alternatives*. Luxembourg: Publications Office of the European Union.

IV-4-524

Promotion of the use and development of alternatives by the European Commission: the EURL ECVAM databases

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Ready access to comprehensive information on (non-animal) methods is a prerequisite for their use within decision making processes by regulators for safety assessments or any end-users. To satisfy this need, the European Union Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM) of the European Commission's Joint Research Centre (EC-JRC) is managing public dissemination platforms (EC, 1991) providing peer-reviewed information on suitable and adequately described experimental and *in silico* methods in the field of biomedical sciences and toxicology, such as, the:

i. DB-ALM (DataBase service on ALternative Methods) providing information on well over 250 mainly experimental *in vitro* methods, at all stages of development, validation and regulatory acceptance used for research or regulatory purposes (http://ecvam-dbalm.jrc.ec.europa.eu/).
ii. QSAR model database providing structured information on 70 *in silico* models for physicochemical, environmental and human health effects (http://qsardb.jrc.it/qmrf/)
iii. TSAR (Tracking System on Alternative testing methods towards Regulatory acceptance) monitoring the method's progress from proposal for validation until its adoption into the regulatory frameworks (e.g., EU, OECD) (http://tsar.jrc.ec.europa.eu/).

Moreover, additional ongoing projects refer to the EURL ECVAM Search Guide (http://bookshop.europa.eu/en/the-eurl-ecvam-search-guide-pbLBN124391/) and improvements to the DB-ALM and QSAR models databases for easier access. "Non-stop" online demonstrations will be given at the JRC booth during the congress.

Reference

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IV-4-689

Sources of information needed to comply with requirements of Directive 2010/63//EU on animal welfare in the field of biomedical sciences in Lithuania – a researcher's point of view

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Planning investigations in life sciences, researchers have the main task to find the best experimental model which can enhance the experimental design and diminish data variance. Directive 2010/63//EU and best scientific practices, moreover, require consideration of the Three Rs when experiments involve animal use. Having a precise knowledge and, furthermore, access to relevant information resources is a prerequisite to achieve this as a basis for the permission to be granted by Lithuanian Ethics Committee on the Use of Laboratory Animals at State Food and Veterinary Service. However, the only information source suggested by the authorities is the link to EURL ECVAM webpage on their local internet site. The approach generally used by scientists was mainly the search of PubMed® database for available bibliographical data on similar investigations. Recent publication of EURL ECVAM search guide was a long expected breakthrough in information retrieval. Further expectations of researchers would be the availability of thematic reviews including basic research topics in evaluated databases. Problems and needs for accessing relevant information to comply with sound scientific practice and demands for animal welfare will be presented from the perspective of a researcher active in biomedical sciences in Lithuania.

IV-4-831

Single database versus multi-database searches for alternatives: a comparative review

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The US Animal Welfare Act requires that investigators consider 3Rs alternatives when proposing to use painful or distressful procedures involving animals. One method of examining potential alternatives is a comprehensive literature search. Often, only one database is consulted despite recommendations that variation in subject coverage and sources indexed requires searching more than one. For this project, we asked whether a single database might perform reasonably close to multiple databases at returning seminal articles for a particular 3Rs question, and if so, which singular database(s) would perform best. We conducted a comparative evaluation of common citation databases including PubMed, Scopus, Google Scholar, and a proprietary multi-database system. A "gold standard" collection of pertinent articles was

established for each question by identifying references used in recently published review articles and guidance documents. After identifying a relevant 3Rs question (for example, eye irritation testing), we conducted simple keyword searches in each database and evaluated the search results against references identified in the "gold standard" collection. Each database was analyzed for sensitivity and specificity to test whether it and the gold standard collection were correlated. Preliminary results show little agreement between references in gold standard collections and those from single database searches.

Session IV-4: Poster presentations

IV-4-035

The status of a new database construction for the safety results of Korean alternative researches

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During the cosmetic development, animal experiments have been used to confirm safety. However, recently the banning of animal test in cosmetics is on progress, and thus various alternative methods to replace animal tests are currently under development and/or being validated in the world.

In Korea, in Nov 2009, the KFDA established the Korean Center for the Validation of Alternative Methods (KoCVAM) that can undertake the developing and validation of alternative methods to animal testing. KoCVAM enables the institutionalization of animal alternative tests by building cooperative system that verifies and reviews alternative methods, and develops internationally certified standards for domestic animal alternative tests.

In developing new animal alternative tests, the research data related to the test substance are important. Specifically, in case of the safety management of cosmetic materials in Korea, the sharing of the safety information is currently missing. It is thus imperative to build a database of safety data, and toxicity mechanism and pathways as *in silico* method, so we would like to introduce the status of a new database construction for the safety results during Korean alternative researches. This DB will give more information to establish new alternative researches, and to conduct safety evaluation of cosmetic materials.

IV-4-459

Monitoring and evaluation of developments in animal use and 3R-alternatives

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Over the last years the annual numbers of laboratory animal use in the Netherlands remained stable. Annually approximately 600,000 animals are used for animal experiments and testing. Does this mean that not much was done to reduce these numbers or to develop 3R-methods? No. These numbers do not say much about the development and application of 3R-alternatives, or about the value of animal experiments.

There is a political and societal need for more insight into 3R developments and the effectiveness of policy measures. In 2013, the Netherlands Knowledge Centre on Alternatives to animal use (NKCA) published a report that proposes an integrated approach for data storage, monitoring and evaluation of laboratory animal use and 3R-alternatives in the Netherlands.

Developments in the field of the 3Rs could be monitored by using a set of indicators that give information on specific subjects within the broad 3R spectrum, such as the implemented 3R-methods in research institutes; animal use per procedure/test/substance; welfare (objectively measured); substitution by evolutionary less complex organisms; publications about the use of 3R-methods; effects of Codes of Practice; adaptations of guidelines; increased awareness/understanding. Experts will have an important role in explaining the stories behind the numbers and figures.

IV-4-476

Use of ASPCA Animal Poison Control Center's toxicology database for characterizing toxicity of human medications in pets

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The ASPCA Animal Poison Control Center (APCC) maintains a state of the art, fully relational and searchable database containing information on more than two million animal exposure cases. In 2013, approximately 20% of the 180,000 cases received by the APCC involved pets exposed to human medications. The APCC database has been used for characterizing minimum and lethal toxic doses of several human medications, onset time, duration of clinical effects, species sensitivity, new syndromes, trends, better treatment options, and other useful clinical information by using retrospective or prospective approaches. For example, APCC data has shown that pamidronate, a bisphosphonate, is a useful adjunct treatment for treating hypercalcemia from ingestion of calcipotriene in dogs. Similarly, high mortality rate associated with acute 5-flurouracil ingestion, isoniazid-induced seizures at low doses, serotonin syndrome from 5-hydroxytryptophan ingestion and its treatment with cyproheptadine in dogs also came from this database. These aforementioned syndromes and treatment options are now well recognized and are great examples of the benefits of leveraging clinical data, in place of laboratory animal studies, to gain critical and valid medical knowledge. These examples also show the significance of finding alternatives to animals in research highlighting the principles of the 3Rs (reduction, replacement, refinement).

IV-4-607

3R Guide: a new database of 3R resources

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There is a bewilderingly large number of websites listing databases, information centres, guidelines and regulatory policies which may be of relevance to researchers attempting to implement the 3Rs of Russell & Burch. The majority of these lists merely give links to the resource's website, leaving it up to the reader to try and assess the relative importance of the individual items. We are very aware of this problem, having spent nearly 20 years building such a website (http://oslovet.norecopa.no), which now consists of approx. 7,000 pages. Many of the resources on this site were identified by a collaborative effort between the Norwegian Reference Centre for Alternatives and AWIC to locate global resources.

The information gathered is being converted on the oslovet website into a "database of databases", known as 3R Guide. The resource will function as a fully searchable, English-language tool for researchers, project leaders, animal welfare bodies and others who need to identify relevant resources as quickly as possible.

The oslovet website aims to be a "one-stop-shop" for those needing help to find direct links to global 3R-resources.

IV-4-686

The EURL ECVAM Search Guide – promoting global standards for searching 3Rs information

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Encouraged by the success of the publication of the EURL ECVAM Search Guide, the European Commission's Joint Research Centre has published an entirely revised second edition in August 2013 (http://bookshop.europa.eu/en/the-eurl-ecvam-search-guide-pbLBN124391/). After its first publication the impact of the Guide included:

- its promotion by EU Member States implementing provisions of the EU Directive 2010/63/EU
- inclusion of the Guide in the 2012 June/July Top 10 (4th position) of the most downloaded publications by the European Union's Bookshop
- use of the Guide within laboratory animal science training courses in Europe, Asia and South America

use of the Guide to produce a Korean Guidance on Three Rs searches
The Guide is aimed at untrained database users and provides examples of search procedures, suggested search terms and user guidance. It includes descriptions of relevant sources of information and thesauri. A check list is moreover offered (the seven golden steps) to allow for searches in a structured way and to document them – a fundamental step in preparing a research project in biomedical sciences and toxicology. In this way, the Guide contributes to a standardised approach for information retrieval that ensures systematic, unbiased and comprehensive searches, as well as it improves transparency.

IV-4-915

An optimized hypothermic storage medium capable to maintain histology and functions of skin tissue and allow epidermal stem cell isolation

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The human skin models have become indispensable for the cosmetic industry. The full thickness skin as an organotypic *in vitro* model represents a valuable tool: 1) in toxicology for assaying the effects of dermatological and cosmetic products, 2) in the study of skin inflammatory process.

In our last study we saw that after hypothermic storage during 5 days at +4°C, we found some resistant cells after this extreme storage and we hypothised that they are epidermal stem cells (ESC).

For characterized ESC, we used following methods: HES staining to check the integrity of junction line at epidermal-dermal interface, specific staining with p63, ki67 and keratin 19 to study the presence of ESC and keratinocyte proliferation and clonogenicity assay to check the ability of a single cell to grow into a colony.

After long storage of skin in our new storage medium, we observed the presence of proliferative cells in epidermis and the high clonogenicity potential of cells.

We demonstrated that our new cold storage medium allows stored skin to maintain self-renewal, clonal growth and cell differentiation of cells.

Session IV-5: Intellectual property, data sharing and data ownership

Co-chairs
Derek Knight, ECHA, Finland
Harald Schlatter, Procter & Gamble, Germany

Session IV-5: Oral presentations

IV-5-317

P&G's approach to data sharing for the Seurat-1 COSMOS project

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Collation and curation of historical unpublished toxicity data is vital for the development of databases to serve computational predictions of toxicology. Procter & Gamble has put in place a robust data sharing platform to aid efforts aimed at replacing repeated dose systemic toxicity testing in Human Safety assessment of cosmetic ingredients and has shared a number of data (totaling 96 studies) with the Seurat-1 COSMOS project. Consideration is given to the challenges encountered and the efforts to overcome them that has paved the way for P&G's approach to data sharing.

IV-5-534

Shared toxicity data: adding value to predictive models

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There has been a long-term goal to develop databases of toxicological information, and progress is being made ranging from solutions such as DSSTox to eChemPortal. Such databases are required to allow for modelling, develop alternative tests and to interpret data. Data sharing brings many benefits including increased knowledge and domains of chemical space. It is also very much in keeping with the ethos of 21st Century Toxicology as we move towards the development of pathways for toxicology and analysis of molecular biology information. In order to progress database building and data sharing, a number of obstacles need to be overcome. There has been, and still remains, resistance from industry to release high quality toxicity data even for historical or failed products and ingredients. Technological solutions are also required to capture the data that go beyond the traditional viewpoint for datasets to searchable and mineable relational databases. The eToX IMI and COSMOS EU Projects have provided solutions to using industry data and the development of a database structure. This has allowed for novel modelling approaches to be implemented.

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IV-5-669

Data sharing and joint submission as tools for avoiding unnecessary testing for registration under the REACH Regulation

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The obligation to share data applies to any registrant under REACH Regulation irrespective of the phase-in or non-phase-in status of their substance. The analysis of the registration dossiers provides statistical insights as to how registrants have met their obligations to share data. The first ECHA Article 117(3) report from 2011 concluded that the joint submission of information worked well in general as shown by the proportion of total registrations submitted jointly. Further insights will be gained from the second Article 117(3) report due in June 2014.

References

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IV-5-893

Data sharing of alternative evidence in replacement research and safety assessment supported by OpenTox and ToxBank

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Data sharing is a key ingredient for advancing alternatives development and application, but its successful implementation involves a complex mixture of scientific, technical, social, legal, quality and business issues. We discuss here the potential of OpenTox in providing open standards and services for data sharing for both federated and

local solutions. Within OpenTox security approaches for authorisation and authentication for component resources were implemented and the use case for the creation of validated predictive models based on a combination of public and private data was demonstrated.

ToxBank created an infrastructure supporting SEURAT-1 at different levels of data sharing: local, partnership, consortium, cluster, and international collaborations and resources (e.g., Tox21, TG-GATEs). Particular attention was given to the processes of data sharing to support in a quality-based controlled and evolving manner different contexts. Protocols linked to datasets emerging from laboratories are provided an accelerated pathway to validation situations. Careful consideration is given to both IP protection and Open Access goals for datasets.

We will discuss a security, privacy and IP review of our resources and others providing some recommendations for the healthy development of secure open, mixed and private big data toxicology clouds for the scientific community.