Theme VII – Ethics

Coordinators
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Session VII-1: Ethical and normative aspects of human-based approaches

Co-chairs
Brett Cochrane, Dr Hadwen Trust, UK
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Session VII-1: Oral presentations

VII-1-100

Creating safe spaces for ethical reflection by animal researchers

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Aim/Objective: Those who work in animal research, whether inside the animal house or laboratory, confront ethical challenges. How they respond affects not only these people and their co-workers, but the animals they interact with and the quality of research undertaken. (AALAS; Birke et al., 2007) Our work aims to assist researchers address these ethical issues in a safe and supportive environment.
Methods: Our methods are philosophical and sociological. In this paper we systematically identify the ethical issues confronting those who work with research animals, examine and critique existing attempts to tackle these issues, and articulate features essential to successfully addressing such challenges.
Results: From our research we develop an approach which emphasizes creating "safe spaces" in which researchers can reflect on and discuss the ethical issues they encounter as part of their work. For such an approach to be successful, it needs to be supported at several institutional levels and to be integrated into workplace and professional culture.
Conclusion: It is important for humans and the animals in their care that ethical issues raised by animal researchers be identified, discussed and addressed. The approach we develop in this paper outlines mechanisms to achieve this end.

References

AALAS – American Association for Laboratory Animal Science. Cost of Caring: Human emotions in the care of laboratory animals. http://www.aalas.org/pdf/06-00006.pdf (accessed 22.04.2013).

Birke, L., Arluke, A. and Michael, M. (2007). *The Sacrifice: How scientific experiments transform animals and people*. Purdue University Press, West Lafayette, Indiana.

VII-1-312

The used of animals in research or alternative methods – pros and cons

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The arguments which are used today in support of and against the use of animals in research are essentially the same as they were more than 100 years ago, the period when serious scientifically-based research began in the world. The history of the controversy over animal research is long and has taken place with either particular interest or indifference to the medical discoveries which are used to illustrate that without animal experiments the treatment would be ineffective or could not be used at all. The concept of alternatives comes from a publication in 1959 which recommended. Scientists look for replacements to animals – REPLACE. Reduce their numbers – REDUCE. Relieve their pain, stress and discomfort – REFINE. Legislative bodies and the majority of the public have accepted the alternative term, including many company scientists, the academic sphere until now has resisted and has preferred to pay more attention to reducing the pain, stress and discomfort of animals during research. Both, experiments on animals and alternative methods have a place in the research and later practical application in therapeutic use.

VII-1-474

Use of fresh functional human tissue as a highly predictive alternative to animal research

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High clinical attrition rates, particularly during phase II trials, have been partly attributed to an over-reliance on animal models. To address this problem, fresh human tissue is increasingly being used as a physiologically representative model; however, is it feasible that functional human tissue models can contribute significantly to

the 3Rs? Numerous public and private operations collect and distribute fixed and frozen human tissues, but these are not useful for pharmacodynamic (PD) or pharmacokinetic (PK) studies, which are essential to better predict drug safety, efficacy and absorption. For PK and PD studies, fresh, functional human tissue is emerging as the "gold-standard" preclinical test system. A review of surgical and transplant procedures illustrates that most tissues suitable for research are simply discarded, but if made available for research, could make a significant contribution to the prediction of clinical efficacy and the 3Rs. Moreover, for human functional tissue assays to become routine, persuasive evidence is required to demonstrate the greater predictive value of human tissue over animal models, thereby increasing demand in the pharmaceutical industry. Current initiatives by regulators, which are exploring the potential for human tissues to be used in safety pharmacology, are likely to accelerate the collection of such evidence.

VII-1-629

Practical and ethical issues with using stem cells in research

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In a five and a half-year multidisciplinary collaboration of leading European researchers in alternative testing, as well as representatives from regulatory bodies, the pharmaceutical industry and ethical advisors have developed a battery of toxicity tests using ESC lines. Throughout the project duration, ethical issues associated with the work undertaken in ESNATS have been monitored. In particular, amongst others, the ESNATS partner in charge of ethical issues, Edinethics Ltd., wrote public ethical guidelines on the use of hESC for toxicity testing. Edinethics also created a "Democs Card Game". This Card Game aims at engaging lay publics on the issues of the use of hESCs and their derivatives to test potential new medicines for toxic side-effects, as an alternative to testing them on animals. A hard copy of the game has been distributed to all ESNATS partners as well as EC DG Research, the European Group on Ethics, and the Environment, Public Health and Food Safety of the European Parliament, and the European Medicines Agency. The primary purpose of the game is to get the public to play the game and think about the issues at stake. But it also produces qualitative and semi-quantitative information, which can be analysed.

Session VII-2: Ethics of using animals

Co-chairs
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Session VII-2: Oral presentations

VII-2-053

Openness, transparency and public engagement on the use of animals in research and testing – recent developments

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Across many countries there is an increasing expectation that organisations, in both the public and private sectors, should be proactively open (and honest) about their activities, policies, standards and wider impacts on society.

Since the last World Congress we have seen a number of developments aimed at supporting greater "openness" – some dictated by legislation and some established voluntarily by sections of the animal research community. Initiatives often seek to "inform the public" of, and influence confidence in, the standards to which science – specifically animal research – is done, and the systems of regulating animal experiments.

This presentation will review recent activities related to openness, transparency and public engagement from those involved in the use and regulation of animal experiments, along with other stakeholders involved in the wider debate. It will also consider recent polls and surveys which provide a current insight into public opinion. Finally, it will highlight examples of good practice on openness and opportunities for future contributions from the range of stakeholders towards progress in this area.

VII-2-122

Why animal suffering matters

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How we treat animals arouses strong emotions. Many people are repulsed by photographs of cruelty to animals and respond passionately to how we make animals suffer for food, commerce, and sport. But is this, as some argue, a purely emotional issue? Are there really no rational grounds for opposing our current treatment of animals?

The paper considers how animals have been traditionally defined as naturally slaves, non-rational beings, linguistically deficient, not moral agents, soulless, and devoid of the divine image. But, if true, these differences should require more, not less, moral solicitude since it fol-

lows that animals cannot give or withhold their consent, cannot represent or vocalize their own interests, are morally innocent or blameless, and are vulnerable and relatively defenceless. These considerations provide the objective, rational basis for regarding both animals and children (especially infants) as special cases.

VII-2-151

A system for retrospective assessment of cumulative severity to identify targeted refinements

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The EU Directive requires retrospective reporting of actual severity at the end of procedures (Animal Procedures Committee, 2013), but continuous assessment of actual severity is recommended (http://bit.ly/U3BwGV). Ethical justification of procedures is balanced between harm to animals and benefit to society from knowledge gained. Levels of harm and cumulative severity are affected by how work is conducted in the context of application of the 3Rs, this includes elements of contingent and direct suffering. Implementation of the refinement loop (Lloyd et al., 2008) can reduce cumulative severity but assessment of welfare depends on measurement of interrelated parameters which vary according to species, the environment and procedure. Currently there are few tools to assess cumulative severity or even to recognise its existence. Assessment methods are required and the system presented develops a matrix (Honess and Wolfensohn, 2010) applied retrospectively using data collected as an intrinsic part of studies. It provides opportunities to identify key events which impact on welfare, and explain to lay observers how the harms may be justified by the research. The analysis shows thorough retrospective review enables continual assessment of the harm:benefit balance at ethical review, and how on-going refinements can be targeted at the specific elements that will improve the animals' welfare and quality of life.

References

Animal Procedures Committee (2013). Review of the assessment of cumulative severity and lifetime experience in non-human primates used in neuroscience research. Report of the Primate Subcommittee of the Animal Procedures Committee

Honess, P. and Wolfensohn, S. (2010). *Altern Lab Anim 38*, 205-212.

Lloyd, M.H., Foden, B.W. and Wolfensohn, S.E. (2008). *Lab Anim 42*, 284-293

VII-2-185

Openness and accountability of animal research: results of an expert forum

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In November 2013, a group of international experts in animal research policy (n=11) gathered in Vancouver, Canada to discuss openness and accountability of animal research. The primary objective was to bring together participants from various jurisdictions (United States, Sweden, Australia, New Zealand, Germany, Canada, and the United Kingdom) to share practices regarding the governance of laboratory animal use with emphasis on the governance process followed, methods of community engagement, and the balance of openness *versus* confidentiality. During the forum participants came to consensus on the need for: a) evidence-based metrics for evaluation and quality assurance to allow a "virtuous feedback" system for animal research, b) increased public access to information together with opportunities for stakeholder dialogue about animal research, c) a greater diversity of views to be represented on decision-making committees, d) a standardized, robust ethical decision-making process that incorporates some sort of societal input, and e) a declaration on transparency to promote increased openness of animal research.

VII-2-621

Analysis of the ethical review process of projects to be funded under the European Union's Horizon 2020 Framework Programme

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In 2012 and 2013, the European animal welfare community carried out a study on the ethical review of projects involving non-human primates funded under the European Union's 7th Research Framework Programme (Sauer et al., 2013).

The study also determined how project proposals are assessed from an ethical point of view, and considered whether any changes are required to the ethical review process for the next research framework programme, *Horizon 2020*, taking into account relevant requirements of Directive 2010/63/EU. It illustrated some common problems with the process of Ethical Review so a follow-on study was initiated.

Horizon 2020 started in 2014. This presentation will follow on from work carried out in the original study, looking at what changes there are regarding the process of ethical review under Horizon 2020 and what recommendations have been taken up in relation to the use of any animal for scientific procedures. It will consider what benefits, if any, there may be in improving the transparency and the accountability of animal use, how it acts as a driver for take up of the 3Rs and whether the requirements of Directive 2010/63/EU relating to the use of these animals are properly addressed.

Reference

Sauer, U., Phillips, B., Reid, K. et al. (2013). *Altern Lab Anim 41*, 271-306.

VII-2-076

Virtue ethics: an ethical approach for non-clinical drug development?

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Aims: For A. MacIntyre (2007), today's ethics are characterized by fragments of morality and by disagreement. This is also true for the conflicting ethical standpoints concerning animal use in non-clinical

drug development. This presentation shows how virtue ethics may complement ethical decision-making in non-clinical development.
Approach: Aristotelian and Thomistic virtue theory are applied to studies in non-human primates (NHPs) to highlight the need for awareness of the intrinsic relationship between virtues and a first person's perspective in assessing a concrete situation. Proposals for safety studies in NHPs are used to illustrate the reductionism of moral status concepts which focus on single virtues.
Results: Ethical justification requires compassion to prevent suffering, justice to reflect respect for the animal's intrinsic value (e.g., social rank) and the trust between NHP and trainer, and temperance and integrity for the harm-benefit analysis. The monitoring virtue prudence provides the basis for dynamic animal welfare and integration of the good of the animal and the human patient.
Conclusion: Virtue ethics outline a holistic approach for animal ethics committees, which, coupled with the 3Rs and basic principles, will obviate check-the-box ethics.

Reference

MacIntyre, A. (2007). After virtue. A study in moral theory. Notre Dame: University of Notre Dame Press.

VII-2-090

A patient tail

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Aim/Objective: We propose a new means of Refining nonhuman animal use in research by re-construing animals as patients.
Methods: Following Russow (1999), we argue philosophical reasoning can facilitate progress in debates about animal research. We therefore propose a thought experiment in which two cancer sufferers are compared: one a human patient in a clinical trial of a new medicine; the other an "oncomouse" used in testing that same product. Specifically, we compare differences in – ethical review, recruitment, consent, research methods, endpoints and outcomes.
Results: Significant differences in the experience of these cancer sufferers are identified, highlighting important ethical considerations. In response, we propose construing animals like "oncomouse" as akin to human patients in clinical trials. This approach assuages many ethical objections to animal research and arguably delivers data more relevant to human medicine. It does however have limitations which we identify and discuss.
Conclusion: Given regulatory norms and the societal value accorded scientific knowledge, animal experimentation will continue into the foreseeable future. What we propose is a Refinement in animal use which can deliver ethical and epistemological benefits to humans and animals, and contribute to work on the implications of using "humanized" animals in translational biomedical research (Davies, 2012).

References

Davies, G. (2012). *Body & Society 18*, 125-155.
Russow, L.-M. (1999). *ILAR J 40*, 15-21.

VII-2-149

Animal rights and ethics in research: is it possible a non-speciest approach?

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The term *speciesism* denotes a different assign of values or rights to beings, depending on their affiliation to certain species. A discrimination that construct a hierarchical relationship between species, creating an uneven allocation of rights and prerogatives. In an anthropocentric speciesism point of view the human beings are on the top of a *moral status pyramided*. Therefore, the principle of equal consideration shall be applied only to human beings, reducing the nonhuman animals as objects.

The Human Rights construction derives from the notion that man as beings endowed with moral rationality has something that sets it apart from other species, and that something allows us to interact with nature and other animals in a relationship of domination.

Following this logic, it is intended here to confront this speciesist perspective on scientific research and raise the question: is possible/feasible a non-speciesist approach in scientific research? In other words, the current state of art of scientific research allows an ethical approach that takes into account the moral *status* of nonhuman animals and the interests of the entire biotic community? This issue will be discussed by analyzing the potential of applying animal rights principles in scientific research.

VII-2-184

Openness and accountability of animal research: a focus group study with local stakeholders at a Canadian university

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The University of British Columbia (UBC) has recently been subject to complaints over the lack of publicly available information about animal-based research at the university. The local nature of the debate provided an opportunity to use UBC as a case study to explore people's views on openness and accountability of animal research. Four homogeneous focus groups were conducted with UBC researchers (n=7), local animal advocates (n=8), UBC students (n=6), and UBC animal care staff (n=6). The facilitated conversations addressed one overarching question: "How can universities be better held accountable for their various animal research practices?" Within this question participants explored the concepts of openness, democratic decision-making and public engagement. Participants expressed a desire for greater openness of animal research. Publicly accessible lay summaries and annual UBC open houses were two of the suggested methods to increase openness. Most participants also welcomed bi-directional dialogue about animal research, rather than simply being provided information. That diverse stakeholders all expressed a desire for greater openness suggests that policy makers should now prioritize efforts to develop mechanisms for better sharing of information and for constructive dialogue about university-based animal research.

VII-2-230

Trends in animal use at US research facilities

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Minimizing the use of animals in experiments is universally recognized by scientists, governments, and advocates as an ethical cornerstone of animal research. Yet, despite growing public opposition to animal experimentation, mounting evidence that animal studies often do not translate to humans, and the development of new research technologies, a number of countries – including Canada, Australia, Israel, the United Kingdom, and Germany – have reported increased animal use in recent years. In the United States (US) – the world's single largest user of animals in experiments – a lack of readily available data on the species most commonly used in laboratories (i.e., mice, rats, and fish) have limited such analyses. Using information included in reports submitted to the government by the top 25 institutional recipients of National Institutes of Health research funds, this study analyzes their use of all vertebrate animals over a 15-year period ending in 2012. Despite institutional commitments and government policies to reduce animal experimentation, these data show the use of animals at these US facilities grew by 71% during this time period – driven primarily by increases in the use of mice, mirroring the increases in animal use seen globally.

VII-2-402

1R is the new 3Rs

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Replacement of animal experiments is one of the 3Rs, but this does not always result in complete substitution of animal use. It has become accepted by many in the research community that some aspects of animal use can be classed as "alternatives". In particular, the use of species thought to either not experience pain or to have lower levels of sentience (e.g., invertebrates, fish), of animal parts (including tissues, embryos, serums) or of data from previous animal experiments. Some species are exempt from legislation designed to protect animals used in research, either entirely or for early parts of their lives, leading to accepted use despite the potential to experience pain and suffering. These methods are entrenched by regulatory bodies, making it more difficult to reach a time when no animal use will exist in research. Individual "replacements" are explored with discussion of the benefits and problems of their use. If animal testing is both scientifically and ethically invalid then the continued use of any animal or animal part should not be accepted. It is argued that replacement should mean the total elimination of animals and animal parts and that focus should be moved from 3Rs to a true 1R.

VII-2-413

The curious language of animal research and how it jeopardizes the public trust

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The public trust is an essential element of the continued use of animals in biomedical research. Currently, the public largely supports the use of animals in research, but only when assured that (1) the use of animals is necessary and that (2) the animals are treated humanely. The scientific community has proclaimed both. However, the meaning, value, and truthfulness of these assertions – and with this, the credibility of researchers – are wholly dependent upon the way in which the key terms, in particular, "necessary" and "humane," are defined. Furthermore, "necessary" can only have meaning when the definition specifies "necessary *for what*"? Other provocative terms used in the context of animal care, such as "cruel" and "undue suffering," also have definitions relevant to animal research and public support. This issue is not an argument for or against the morality of using animals in research; rather, the concern is whether the scientific community, when discussing animal research publicly, is using standard dictionary definitions for the most important terms. If not, the question of honesty arises, and being that the credibility of researchers and the public's trust in the scientific research community is at stake, clearly the issue must be directly confronted.

VII-2-414

Life after research: the psychological well-being of animals following release from the laboratory

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Recent years have seen increasing consideration for alternatives to the routine euthanasia of research subjects at the conclusion of all studies (Anon, 2003). As a result, a small but growing percentage of animals used for research are eventually released to live out their lives outside the laboratory (Carbone et al., 2003). In these cases, the notion of laboratory animal welfare extends well beyond the period of time the animal serves as an experimental subject.

While the ideal for many of the companion animals released from the laboratory is to live out their remaining years with a loving family[1], some companion animals and all noncompanion animals (such as farm animals and chimpanzees) live out their lives in animal sanctuaries (Noon, 1999). The foremost concern for all of these animals is how well their lives fare after release from the laboratory, that is, their quality of life, psychological well-being, and enjoyment of life.

This talk will present a comprehensive view of the well-being of animals formerly used in research, including the peer-reviewed published reports as well as individual cases of the one-time laboratory animals now living in sanctuaries.

References

Anon (2003). *Lab Anim 32*, 7.

Carbone, L., Guanzini, L. and McDonald, C. (2003). *Lab Anim 32*, 37-41.

Noon, C. (1999). *J Appl Anim Welf Sci 2*, 141-146.

VII-2-616

Animal experimentation: transparency and public concerns

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The public is scarcely informed about what transpires in animal research, and is rarely engaged in decision making. Some justify this state of affairs by describing the public at large as emotive and lacking experience-based expertise. Some researchers claim to be able to represent society at large, and to possess the relevant knowledge for decision-making with regard to science (Marks, 2013). Ethical concerns of the public often appear to be downplayed when making decisions about research priorities and projects. The purpose of this paper is to show how interested publics can gain access to relevant information so they are suitably educated in order to participate in decision making, and articulate their ethical concerns. In the first part of the paper I will give some insight into why the number of animals used in experiments continues to rise internationally, despite the integration of 3Rs Principle (Russell and Burch, 1959) into most applicable legislation (Directive 2010/63/EU) worldwide. The second part will identify methods of obtaining information pertaining to animal experimentation in seven countries including Germany, the UK and the US. The third part will analyse a questionnaire concerning transparency and ways of public engagement in animal research which was recently conducted with members of the interested public.

References

Marks, N. (2013) *International Journal of Deliberative Mechanisms in Science 2*, 33-61.

Russell, W. M. S. and Burch, R. L. (1959). *The Principles of Humane Experimental Technique*. London, UK: Methuen. Reprinted by UFAW, 1992.

VII-2-628

Emerging trends in alternative to animal experimentations

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Biomedical research and toxicological studies involving animal models have served the human race very well. However, these experiments are highly animal intensive. Therefore, toward reducing the animal cruelty, Russell and Burch (1959) put forth the principle of the Three Rs (Reduction, Refinement and Replacement), with the idea that alternatives to animals would play a vital role in reducing the numbers of animals used, as well as the level of their suffering during experimentation. Since then, research has come a long way in finding alternatives for various aspects of toxicological testing. However, animal models could not be replaced completely by non-animal research models. Despite this, several alternative research models, such as *in vitro* (cell culture), *in vivo* (lower vertebrates and invertebrates) and *in silico* (computational modeling) systems, are being employed by scientists and researchers to limit the numbers of animals used in experiments. Although the use of animals cannot be completely avoided, the initiative toward developing faster, cheaper and more-accurate methods is essential to ensure that the innumerable chemicals present in the environment can be evaluated. The development of alternative animal models and the subsequent interrogation of models, methods and data from all platforms, to better predict public health outcomes.

Reference

Russell, W. M. S. and Burch, R. L. (1959). *The Principles of Humane Experimental Technique*. London, UK: Methuen.

VII-2-794

Attitudes on animal use shown by scientists at workshops in Taiwan

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Taiwan law covers the use of animals in science and requires least pain and minimal numbers and ethical committee supervision. However, Taiwan has a cultural background very different from that in the UK, and it was of interest to assess attitudes to the use of animals in science by those involved in animal experiments and how that might change after a two day course on ethics, animal welfare and the 3Rs. A questionnaire presented 20 statements with an ethical content and asked for responses on a five-point scale, from strongly disagree to strongly agree. This was given to attendees at the beginning and end of each of two workshops run jointly by the RSPCA International and Taiwan's National Laboratory Animal Centre. These workshops did not discuss specifically the statements used in the questionnaire. On some statements the initial responses were similar to those that might be expected in the UK, differed little between the 66 respondents, and did not change much. Other responses were variable, and in some, such as the routine use of single housing, there was a marked shift in attitude over the course of the workshops. This presentation will review the responses and what they indicate.

VII-2-911

The harm-benefit analysis within the evaluation of animal experimentation projects. How to assess criteria like species, number of animals or death of animals?

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The Directive 2010/63/EU requires a harm-benefit analysis as a part of the project evaluation by the competent authority, which has to take ethical considerations into account. In Austria, the Animal Experimentation Act 2012 (TVG 2012) transposes this requirement into national law. As a specific feature, the TVG 2012 demands that applicants have to fill in a catalogue of criteria to objectify and standardize the harm-benefit analysis. We are developing this Austrian Catalogue of Criteria (ACC), which has to be used within the authorization process.

The ACC consists of different categories, including specific questions to the applicant. The answers are assessed, counted as factors in the harm-benefit analysis and reviewed considering the facts and justifications the applicant has to provide.

However, some criteria cannot be assessed easily. Given that the project has been planned accurately and the 3 Rs have been taken into account, the following questions still arise: Should the species play a role in the harm-benefit assessment? If yes, according to which criteria should the species be assessed? Is the number of animals relevant? If yes, what are high and low numbers? Should the death of animals count on the harm side in the context of Austrian legislation?

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VII-2-948

Using minipigs in pre-clinical studies in Russia

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In Europe, minipigs are widely used as an animal model in toxicology studies (Foster et al., 2010). The minipig presents a favourable profile as a non-rodent toxicology model, in terms of the similarity to man and also in terms of applicability to different study types. Minipig studies may better reflect human drug-induced toxicities than studies performed in traditional non-rodent toxicology models. It would be of particular value to gain a better vision of the potential utility of the minipig as a model for the safety testing of new biologics, where the minipig could potentially replace the use of non-human primates and dogs in the testing of some new products (Bode et al., 2010).

In Russia, mainly rodents are used for pre-clinical studies. Only a few organizations use minipig for biomedical research. Our organization (http://www.nc3rs.org.uk) adhere to the principles of 3Rs (Russell and Burch, 1959) and Directive 2010/63/EU. To improve the work in accordance with the principles of 3Rs 2 years ago we started breeding minipig as an alternative to rodents.

Minipig use in biomedical research will reduce the number of experimental animals. Using minipig for pre-clinical studies will improve the safety of drugs and will protect volunteers in phase 1 clinical trials.

References

Bode, G., Clausing, P., Gervais, F. et al. (2010). *J Pharmacol Toxicol Meth 62*, 196-220.

Foster, R., Ancan, P., Fredholm, M. et al. (2010). *J Pharmacol Toxicol Meth 62*, 236-242.

Session VII-3a: Ethical evaluation

Co-chairs
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Session VII-3a: Oral presentations

VII-3a-104

Update from the AALAS-FELASA WG on harm-benefit analysis

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Aims/Objectives: Define the concept of harm-benefit analysis (HBA). Recommend how it can be implemented.
Methods: Literature review included papers from 1986 to 2013. References on cost/risk benefit from clinical trials were also included. A workshop on harm-benefit analysis where participants were introduced to one method of HBA was organized.
Results: Several approaches to HBA were identified including algorithms, graphic presentations and generic processes. All existing processes have been criticized. The definition of harm is based on a several factors influencing animal welfare. The 5 freedoms were suggested as a basis for harm assessment. Severity categories for harm are also defined. Subjective opinions cause problematic bias. To limit bias different modulating factors which aggravate and mitigate are defined for the HBA. Benefit domains include benefits for humans, animals, environment, knowledge and education. It was questioned if economic benefits alone can justify animal use. A similar approach to limit bias was applied to harm analysis. Examples of the working groups approach illustrations are included.
Conclusion: Several approaches to HBA are presented in the literature. The WG proposes a practical methodology to address HB analysis. Independent of method HBA must be systematic, transparent and verifiable. Further work-shops and training sessions are scheduled.

VII-3a-558

Harm-benefit analysis of animal experimentation: lack of conceptual clarity and underlying moral disagreement

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Harm-benefit analysis is now a required key element of the legal framework regarding animal experimentation in Europe and elsewhere. Despite its wide adaptation, however, there is a huge lack of clarity concerning what is meant by it; and there seem to be some genuine underlying ethical disagreements. We will highlight key challenges and discuss to what extent agreement can be reached over how to evaluate animal research.

Firstly, there is lack of clarity and potential disagreement over what to include in the benefit analysis and on how to evaluate benefits. One approach includes evaluating societal contribution (Bateson, 1986), whereas another focuses more narrowly on knowledge gain in relation to other work in the field (Smith et al., 2007). Including research purpose in the analysis will reveal disagreements about how to value different purposes. For example, some will attribute a lower value to obesity than to cancer research as a justification for using animals (Lund et al., 2012).

Secondly, the idea of weighing harms against benefits lends itself to different interpretations, in turn linked to ethical disagreements. The controversy over the non-renewal of Swiss neuroscience project licences because the "expected benefits to society were not sufficient to justify the burden to the animals" (Buchen et al., 2008) illustrates this tension.

References

Bateson, P. (1986). *New Scientist 1986*, 30-32.
Buchen, L. et al. (2008). *Scientific American*, Sept. 2008.
Lund, T. B. et al. (2012). *Painful dilemmas: A study of the way the public's assessment of animal research balances costs to animals against human benefits*. Public Understanding of Science.
Smith, J. A. et al. (2007). *Lab Anim 41*, 143-160.

VII-3a-649

Harm:benefit analysis – if no projects fail the test has the system itself failed?

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The conduct of an animal experiment in Europe is now only permitted following a positive harm:benefit analysis (HBA). However, HBA is new for many countries and is only done in a rudimentary sense by others. Using graphical representation of principles and real examples, we explore the animal protection view of some key theoretical issues relevant to the HBA and ask the question-if the system fails to reject any projects does this mean the system itself has failed?

Questions for discussion include, is the purpose of a HBA to apply the 3Rs or to evaluate an application after these have been applied? At what stage does the question of whether there is a better way (the "alternatives test") need to be considered? Is the extent of harm being measured on the same level as the extent of benefit, i.e., at the level of the experiment? If quantification of harms and benefits is impossible, what is the best way to ensure the "right" answer? What is the value of single experts over committees? How do you ensure good representation of views in committees and does this matter? If regulators fail to reject projects what does this say about the process itself?

VII-3a-783

Is the concept of euthanasia (a good death) for laboratory animals a myth?

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It is sometimes argued that death is not detrimental to animal welfare (Webster, 1994); indeed animals are often killed to end suffering. Whilst it may be theoretically true that an animal's death per se does not impact upon its welfare, in the case of laboratory animals dying almost always negatively impacts welfare because the "euthanasia" process usually causes suffering.

In the case of rats and mice, which comprise >80% of laboratory animals used, almost every attempt to assess whether they suffer during killing procedures has concluded that they probably do. Using evidence from my own experiments, and the work of others I will argue that dying should be considered as a harm in the harm-benefit analysis of experiments which result in death. For instance; carbon dioxide exposure likely causes fear and distress before death occurs, anaesthetics used for overdoses cause aversion and physical methods such as cervical dislocation may cause pain before consciousness is lost and have high failure rates.

Thus, there is a need for an ongoing search for more humane killing techniques as well as improved understanding of the welfare impacts of killing to allow selection of the most humane methods and ethical evaluation of the harms caused.

Reference

Webster, J. (1994). *Animal welfare: A cool eye towards Eden*. Oxford, UK: Blackwell Publishing.

VII-3a-884

Ethical analysis and an endpoint matrix: opening up the harm and benefit calculus

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The development of decision-support tools to conduct ethical analysis and encourage reflexivity in animal research is not new. Tools such as The Ethical Matrix (Mepham, 1996) have been applied to support decision-making by scientists as they face ethical dilemmas when working with animals (e.g., Webster et al, 2010; England and Millar, 2008). However, Directive 2010/63/EU challenges individuals and institutions to apply and develop tools. Some have been proposed to structure procedures for balancing potential benefits against harm to experimental animals (Lindl et al. 2012) and in the form of an Endpoint Matrix to support decision-making when defining humane endpoints (Ashall and Millar, 2014). These are attempts to open up the harm/benefit calculus.

Further work to develop tools to conduct a harm/benefit calculus within individual animal experiments and across programmes is needed. New concepts such as Responsible Research and Innovation (RRI) are increasingly embedded with EU funding programmes. However do such concepts have meaning in this context, can they be translated into practice and support sound ethical decision-making? Do new governance concepts, such as RRI, distract and diminish the

application of established approaches or the development of specific frameworks, such the Endpoint Matrix. These issues will be discussed in this paper.

References

Ashall, V. and Millar, K. (2014). *ALTEX 31*, 209-213.
England, G. and Millar, K. (2008). *Reproduction in Domestic Animals 43, Suppl. 2*, 165–171.
Lindl, T., Gross, U., Ruhdel, I. et al. (2012). *ALTEX 29*, 219–228.
Mepham, B. (1996). *Ethical analysis of food biotechnologies: An evaluative framework*. In Food Ethics (ed. B. Mepham), pp. 101–119. London, UK: Routledge.
Webster, J., Bollen, P., Grimm, H. and Jennings, M. (2010). *J Pharmacol Toxicol Meth 62*, 160–166.

Session VII-3b: Ethical evaluation

Co-chairs

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Session VII-3b: Oral presentations

VII-3b-226

Ethical evaluation process: international approaches, issues and assessment

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Ethical evaluation of animal use is mandated in many geopolitical areas. Processes are based on institutional and/or government bodies. Such ethical oversight range from institutional committees, such as the American IACUC model to competent authorities at the country level. Differences exist also on functions, composition and authority of evaluation bodies. However, regardless of the differences in implementing procedures (engineering standards), the ethical principles and the desired outcome of the processes (performance standards) are similar.

AAALAC International categorized the findings (mandatory items and suggestions for improvement) identified during 671 site visits across the globe related to the ethical review process since 2011. Most frequent issues relate to Protocol Review Considerations (i.e., inadequate description of procedures), followed by Policies (more often categorized as a mandatory item). Other issues belong to categories such as Committee Composition and Participation; Oversight of Activities; Program Review and Facility Inspections; and Protocol Review Process.

Regardless of the existing process, the assessment of the ethical review efficacy should be based on the outcome: the actual implementation of the 3Rs and a culture of care at the institutional level. This performance based assessment can be performed internally by institutional committees and externally by competent authorities and independent specialized bodies.

VII-3b-274

Dignity of the animal: weighing of interests in the context of the Swiss animal welfare act

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The Swiss Animal Welfare Act (SR 455, 2008) protects the dignity of animals. In the context of the act, the term "dignity of the animal" implies values beyond the mere wellbeing but is not considered an absolute asset. Therefore, respect for dignity does not preclude the imposing of strain on animals. However, potential strain must be justified by overriding interests. The relative importance of strain vs. interests is assessed by the "weighing of interests". Because the animal welfare act does not provide detailed instructions, a study group of the Federal Food Safety and Veterinary Office has devised a model procedure to ensure that "weighing of interests" is carried out correctly and uniformly (FFSVO, 2014). The model, which will be presented at the congress, provides an interpretation of the terms "strain" and "overriding interest" and leads users through the procedure in seven stages. It helps determine whether interventions are permissible in vertebrates, cephalopods and decapods, especially in the context of animal experiments, where weighing of interests is explicitly requested for each experiment. As condition precedent to the justification of animal experiments, any strain inflicted on animals must be limited to the indispensable minimum.

Reference

FFSVO – Federal Food Safety and Veterinary Office (2014). Dignity of the animal: guide to the 'weighing of interests'. http://www.blv.admin.ch/themen/tierschutz/05459/index.html?lang=de

VII-3b-306

Project evaluation under Directive 2010/63/EU

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The Directive requires that all projects are subjected to a project evaluation and sets out in detail the elements to be considered, and the type of expertise which should be considered when conducting such an evaluation. The evaluation requires that a harm – benefit analysis forms part of the process, to assess whether the harm to the animals is justified by the expected outcomes, taking account of ethical considerations. 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. These included guidance on the conduct of the harm-benefit assessment, and highlighted the importance of training for those involved in Project Evaluation. Further work is planned to provide illustrative examples.

VII-3b-752

Ethics within legal limits? Considering ethical aspects in harm-benefit analyses against the background of legal frameworks

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According to the EU directive 2010/63 on the protection of animals used for scientific purposes, not only the application of 3Rs, but also the harm-benefit analysis is part of to the project evaluation. Here, ethical considerations have to be taken into account. For all member states the question arises how to implement "ethical considerations" within the project assessment on the basis of the directive and with regard to the relevant national legal frameworks. What is meant by "taking ethical considerations into account" and should their content be identified with "legal requirements" or go beyond legal requirements? If so, how can these aspects be integrated into the harm-benefit analysis and can they play a decisive role?

A research project is currently carried out at the Messerli Research Institute in Vienna to develop a applicable methodology for the harm-benefit analysis that aims to accomplish the task and deals with the related problems. In my presentation, results and possible solutions of the mentioned problem will be presented.

VII-3b-845

The Austrian catalogue of criteria to objectify the harm-benefit analysis within the evaluation of projects using living animals

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According to the Directive 2010/63/EU (Article 38 (2) d) a comprehensive project evaluation comprising a harm-benefit analysis, taking into account ethical considerations, has to be carried out in Austria. As an outstanding feature, the Austrian Animal Experimentation Act (TVG 2012, which has come into force on January 2013) demands that the applicant of a project has to fill in a catalogue of criteria. As a part of the application for project authorisation the catalogue has to be submitted to the respective competent authority.

Within a project at the Messerli Research Institute, we are developing the Austrian Catalogue of Criteria (ACC). This project is funded by the Austrian Federal Ministry of Science, Research and Economy (BMWFW). The ACC has to be published not later than by the end of 2015 and to be used within the authorization process six month after publication.

The catalogue is based on scientific criteria in order to objectify and standardize the harm-benefit analysis. To provide a feasible methodology several methodological approaches have been integrated, amongst others a scoring and weighing procedure. The methodological structure of the ACC will be presented.

References

EU (2010). Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the Protection of Animals Used for Scientific Purposes. 20.10.2010, *Off J European Union L 276*, 33-96.

TVG (2012). (Austrian) Animal Experimentation Act 2012, Federal Law on Experiments on Live Animals, BGBI. I Nr.114/2012, Art.1.

Session VII-3: Poster presentations

VII-3-032

Ethical and legal perspectives on alternatives

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Directive 2010/63/EU on the protection of animals used for scientific purposes requires that animal experiments should not be performed when an alternative method exists. Although the concept of alternatives is understood to refer to the 3Rs of reduction, refinement and replacement, the Directive has not succeeded in achieving meaningful reduction in the numbers of animals used for experiments. Indeed, in some areas, there has been a marked increase in animal use, particularly in basic research. One of the major obstacles with regard to the wider use of alternatives is the lack of a legal definition of what constitutes an "alternative method". The term is open to different interpretations and may have confused and misled the general public. In the example of a brain study whose stated aim is to benefit human patients, the researchers could argue that there is no alternative to the live monkey experiment, while those opposed to animal experiments would argue that non invasive human data would be more relevant to human medicine. Therefore, a legal examination of what constitutes a scientifically satisfactory alternative method would be helpful to scrutinize animal studies, particularly in the field of basic research, for the sake of transparency and public accountability.

VII-3-055

Environmental impacts of animal research and testing

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The laudable trend among individuals, companies, and governments to decrease one's environmental footprint has yet to fully address the significant impact of animal research and testing on the environment. The use and disposal of millions of animals globally from research and testing, and the associated use of chemicals and supplies, contributes to pollution as well as adverse impacts on biodiversity and public health. Environmental and human health hazards related to animal use occur as a result of the generation of chemical and biological wastes, energy usage, atmospheric release of incinerator gases and particulates, deposition of soil contaminants, and potential entry of waste and toxins into groundwater and drinking water (Taylor et al., 2008; Cubitt and Sharp, 2011; Office of Laboratory Animal Welfare, 2002; National Research Council, 2011; Chen et al., 2004). Investigations into these contributors to environmental harm will be presented. The environmental implications of animal use is another and to-date underaddressed reason for industries, government agencies, and other stakeholders to monitor and consider the need for and benefits of replacing animal use with increasingly available, non-animal alternatives that have fewer negative impacts. Science, human and animal well-being, and environmental sustainability together offer a cogent argument for accelerated development, validation, and use of non-animal research and testing methods.

References

Chen, S.-J., Hung, M.-C., Huang, K.-L. and Hwang, W.-I. (2004). *Chemosphere 55*, 1197-1205.

Cubitt, S. and Sharp, G. (2011). *Animal Technology and Welfare*, Aug. 2011.

National Research Council (2011). Prudent practices in the laboratory: Handling and management of chemical hazards. http://www.nap.edu/openbook.php?record_id=12654

Office of Laboratory Animal Welfare (2002). Institutional Animal Care and Use Committee Guidebook. National Institutes of Health. http://grants.nih.gov/grants/olaw/guidebook.pdf

Taylor, K., Gordon, N., Langley, G. and Higgins, W. (2008). *Altern Lab Anim 36*, 327-342.

VII-3-138

Analysis of animal experimentation oversight committee membership at US institutions

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In response to growing public concerns about the welfare of animals in laboratories stemming from high-profile exposés of abuse at research facilities, United States (U.S) authorities mandated the institutional animal care and use committee (IACUC) system to review, approve, and oversee vertebrate animal use and ensure compliance with federal regulations and guidelines. While minimum IACUC membership requirements set forth by federal bodies reflect equal representation of all interests – animal researchers, institutions, animals, and the public – there is no requirement in the US to maintain a balance between these interests. This study analyzed the overall membership of IACUCs at leading US research institutions. We found that these committees are comprised predominantly of animal researchers (62.5 percent); veterinarians, most of whom are involved in animal experimentation (17.1 percent); nonscientists (10.1 percent), and unaffiliated members (9.6 percent). This overwhelming presence of animal research and institutional interests dilutes input from the few IACUC members representing animal welfare and the general public, contributes to previously documented committee bias in favor of approving animal experiments, and reduces the overall objectivity and effectiveness of the oversight system.

VII-3-139

Great ape disgrace: how the US laboratory oversight system failed chimpanzees

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The US remains the last industrialized country to conduct invasive biomedical experiments on chimpanzees. In recent years, significant public opposition has prompted a reappraisal of the scientific need for the controversial practice. In 2011, the Institute of Medicine released a landmark report concluding that "most current biomedical research use of chimpanzees is not necessary." A subsequent report by the US National Institutes of Health (NIH) further determined that "research involving chimpanzees has rarely accelerated new discoveries or the advancement of human health for infectious diseases..." As a result, NIH cut funding for most of its invasive chimpanzee experiments, established new oversight mechanisms specific to chimpanzee use, and made plans to retire most federally owned chimpanzees in laboratories to sanctuaries. Until that point, NIH had widely funded, conducted, and advocated for experiments on chimpanzees. The findings of both IOM and NIH reports raise the question of how and why NIH was continuing to approve, conduct, and fund experiments on chimpanzees that were ultimately deemed "unnecessary." By examining the approved applications for several of these now-defunct projects, we discuss how the scientific review and animal welfare oversight systems failed and ways to improve these systems for all animals going forward.

VII-3-403

Germany: animal welfare representative legal action and its effects on animal experimenting

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In Germany, the decision as to whether the legal requirements for authorising animal experiments is more or less dependent on a subjective assessment, but the decisions made by applicants and authorities are by no means based on generally accepted scientific precepts. This statement especially applies to questions regarding available alternatives, the benefits and ethical justifiability of the animal experiment. For this reason, PARG has campaigned for the introduction of legal action and court examination of compliance with applicable animal protection legislation. To date, only those experimenting on animals could file law suits before administrative courts challenging animal welfare requirements deemed too stringent. No one could apply for a court examination of insufficient animal welfare requirements. Five of Germany's 16 federal states have passed laws providing for representative legal action. Five more state parliaments are currently debating their introduction. In the states with animal welfare representative legal action, animal welfare organisations can be accredited by the state governments. The responsible authority forwards applications to them. In four weeks they can submit objections to the authority. If the authority does not take these objections into account, the accredited organisation can file legal action against the approved animal experiment at the administrative court.

VII-3-726

German animal welfare act in breach with Directive 2010/63/EU

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The German Federal Administrative Court recently announced an order (finalized on January 20, 2014) on the neurobiological experiments on primate brains of Prof. Kreiter at the University of Bremen. With this order, a preceding court decision by the Higher Administrative Court of Bremen was established as final and absolute and the last glimmer of hope to end the suffering of the primates in Bremen was extinguished. The court decision had claimed the experiments to be ethically justified. The Federal Administrative Court upheld the court decision and issued the order on the grounds that due to the phrasing of both the former and the current German Animal Welfare Act, authorities had no entitlement to assess the ethical justification of an experiment, but were obliged to approve an application if all formalities were complied with. The impact the order will have on the authorization of animal experiments and testing in Germany caused an outrage in the animal welfare community.

VII-3-844

The "benefits" standard: how can it better protect animals?

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Biomedical or toxicological experimentation on animals is usually accepted on the basis of its assumed or anticipated benefits to human health. When ethical justification of a study is required or requested, reviewers (and the general public) can usually be satisfied by a presentation of the costs (or harms) and benefits, comparing the moral weight of the study's benefits to humans against the likely harms to the animal subjects. Because it is a consensus approach, underlying assumptions about the nature and moral status of humans and other animals are rarely questioned or challenged.

This presentation will briefly review those assumptions in order to show how the "benefits-to-humans" standard for animal experimentation will ultimately fail to protect animals without a more flexible interpretation of harms. Past efforts to refine harm assessment will be reviewed; new, practical approaches to such assessment will be explored; and ways to make our public communications about the ethics of animal research more exacting, educational, and enlightening will be discussed.

Session VII-4: Distress evaluation

Co-chairs
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Session VII-4: Oral presentations

VII-4-059

Norecopa: using a national consensus-platform to promote the 3Rs

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Differences in the perception of stakeholders regarding the harm and benefit of animal experiments led to an initiative in the late 1990s to increase dialogue and thereby identify areas where there was common ground. This resulted in the establishment of *ecopa* (European Consensus-Platform for Alternatives), an umbrella organisation which promotes the 3Rs by bringing together regulators, academia, industry and animal welfare organisations. *Ecopa* encourages the existence of national consensus platforms which do the same, among those the Norwegian organisation Norecopa (http://www.norecopa.no).

A consensus platform can identify and address issues of national relevance to the 3Rs. The extensive use of fish in Norwegian research has led Norecopa to focus on welfare issues and severity classification for these species, but it has also arranged international consensus meetings on the care and use of wildlife and agricultural animals in research. Consensus statements from these meetings and Norecopa's own guidelines for research act as useful checklists when planning activities to further advance the 3Rs.

National Consensus Platforms have access to resources and opinions from a wide range of sources. These platforms can generate 3R-tools which are relevant worldwide to welfare assessment, severity classification and project evaluation. Examples of these will be presented.

VII-4-140

Distress evaluation in experiments using rodents

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There is a rise in concern among scientists on different techniques to be employed in assessment of stress and pain assessment after animal experimentation. Assessment of stress severity itself may add on or interact with course and planning of animal experimentation apart from adding on to the stress levels to which the animals are already exposed to. Ethological tests like nest building scores in mice and testing for anhedonia in rats may be employed with high effectiveness to measure stress levels whereas faecal corticosteroid scores are proven for its minimal disturbance caused to the animals to draw the severity of stress in colonies. The elevated plus maze and open field tests for anxeity can also be employed in severity of stress assessment but in-depth study points towards the added stress in rodents measured after such behavioural tests. This presentation describes with the aid of many previous works on how effectively behavioural tests can be used to assess the severity of stress in rats and mice. This also discusses in detail the adverse consequences of employing certain tests in stress measurements post-experimentation. The work also describes about developing a stress score in rats after a severe interventional procedure.

VII-4-308

Severity assessment under directive 2010/63/EU – a continuous process

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Directive 2010/63/EU requires that a prospective assessment is made on the severity of each procedure in a project and that a severity classification is assigned to each procedure.

For annual statistical reporting, the actual severity of the pain, suffering, distress or lasting harm experienced by the animal must be reported. In addition, the actual severity of any previous procedures will be a key consideration in determining whether or not an animal can be reused in further procedures.

The consideration of severity within a procedure should therefore be a continuous process beginning with initial study design, through the study-specific day-to-day monitoring of animals during the project, to the "actual" severity assessment upon completion of the study, which provides opportunities to identify further refinements for future studies.

By approaching in this manner, there are many opportunities to ensure that the Three Rs are considered and implemented throughout, benefiting both science and welfare, and, by inclusion of the actual suffering experienced by the animal, should provide greater transparency and understanding of the impact of scientific procedures on animal welfare.

To assist researchers, a number of worked examples of the severity process have been prepared.

VII-4-556

Assessing welfare – why and how

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Assessing the welfare of animals used in scientific procedures is important for several reasons. First, a good system for observing and monitoring animals, and recording observations, is necessary in order effectively to recognise signs of pain or distress. Any suffering that is detected can then be alleviated in good time, which benefits animal welfare. Second, unrelieved pain or distress leads to physiological and behavioural responses that can negatively affect data, so good welfare

assessment benefits the science. Finally, assessment records are the basis for retrospective reporting of actual severity, a legal requirement under Directive 2010/63/EU.

A robust protocol for assessing the welfare of animals day-to-day should include specific behavioural and physiological indicators for each species and procedure, to help judge the level and nature of any pain or distress – or whether welfare was good. Consistency in observations and judgements should be promoted by taking a "team approach", including input from staff with a range of expertise and priorities, coupled with adequate training in animal biology and behaviour and in the assessment protocol itself.

This presentation will set out available guidance on assessing laboratory animal welfare, from the European Commission and other bodies, including examples and recommendations for good practice.

VII-4-635

The case for refinement: making prospective and retrospective assessment of the severity of procedures count for animal welfare in biomedical research

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Scientists conducting animal experiments work under a social licence, which warrants its scientific and ethical justification, and a commitment to the 3Rs. To uphold these standards, a set of external (legislation), internal (community-centred) and mixed (ethical appraisal) regulatory systems are commonly in place. However, animal experiments often fail to yield valid results, due to methodological errors and/or unaccounted biases (Perrin, 2014; Macleod, 2011). Also, many studies still allow animals reaching severe end-stages or death, even when ethically approved (Franco et al., 2012; Franco and Olsson, 2012). The regulatory framework set by the 63/2010/EU directive can help improve the relevance of protocol appraisal, through mandatory prospective and retrospective assessment of the severity of procedures. These provide an opportunity for a community-centred, case-by-case, reflection on the welfare impact of experiments and on how it can be alleviated. While prospective assessment calls upon scientists to consider all potential sources of animal suffering and means to address them, retrospective assessment allows for an evidence-based reappraisal of the impact of experimental procedures and refinement measures. This presentation will stress the necessity to make such data available to inform subsequent studies, as it can allow to more accurately predict adverse outcomes; develop early, scientifically sound humane endpoints; improve prospective severity assessment; and identify opportunities for refinement.

References

Franco, N. H. and Olsson, I. A. S. (2012). *Altern Laboratory Anim 40*, 271-83.

Franco, N. H., Correia-Neves, M. and Olsson, I. A. S. (2012). *PloS One 7*, e47723.

Macleod, M. (2011). *Nature 477*, 511.

Perrin, S. (2014). *Nature 507*, 423-5.

Session VII-4: Poster presentations

VII-4-410

Emotional pain: why it can matter more to animals than physical pain

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The last two decades have seen remarkable advances in the understanding, methodology, and ethics of pain control in laboratory animals. However, the prioritization of physical pain has ascribed to other forms of distress and suffering – specifically, emotional pain – considerably less importance. Recent research in neuroanatomy and neurophysiology has indicated that the view of unpleasant emotional states as a form of pain has strong empirical support (Eisenberger, 2012). Current evidence suggests that in the course of brain evolution, the brain systems that underlie specific types of emotional pain developed by co-opting brain circuits that mediate the affective component of physical pain (Panksepp et al., 1997) and that in present day mammals physical and social pain rely on the same neurobiological substrates (Kross et al., 2011). Separation distress and loneliness, for example, are now known to be regulated largely by endogenous opioids (Benton et al., 1988). More generally, and importantly, current evidence demonstrates that emotional sufferings in animals and humans often weigh more heavily in decision-making, i.e., matter more to the individual, than physical sufferings (Anil et al., 2005).

This talk will present the current knowledge regarding emotional pain and suffering; clarify the essential distinctions between emotion, stress, and distress; and explain the importance of these issues for laboratory animal care.

References

Anil, L., Anil, S. S. and Deen, J. (2005). *J Appl Anim Welf Sci 8*, 261-278.

Benton, D. and Brain, P. F. (1988). In R. J. Rodgers and S. J. Cooper (eds.), *Endorphins, Opiates and Behavioural Processes* (217-235). Chichester: John Wiley & Sons.

Eisenberger, N. I. (2012). *Nat Rev Neurosci 13*, 421-434.

Kross, E., Berman, M. G., Mischel, W. et al. (2011). *Proc Natl Acad Sci U S A 108*, 156270-156275.

Panksepp, J., Nelson, E. and Bekkedal, M. (1997). *Ann NY Acad Sci 807*, 78-100.

VII-4-412

The complexity of animal well-being: advances in our understanding of quality of life, welfare, and happiness – and why it matters in animal research

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For the objective of maximizing animal well-being, the near-exclusive emphasis on the alleviation of suffering (also commonly viewed as minimizing stress) is an incomplete approach, and attention to promoting positive mental states is recently recognized as also impor-

tant (Boissy et al., 2007). However, this well-being issue is relatively simple when compared to the much more complex questions that arise when the various well-being constructs – quality of life, welfare, psychological well-being, and happiness – are applied to animals. Current research is revealing the relevant similarities – and crucial differences – in these constructs between animals and humans (Weiss et al., 2011), with compelling evidence in nonhuman primates and other species for (1) the coexistence of short-term, momentary affective states (e.g., transient happy feelings) and long-term, relatively stable mood states (e.g., global happiness or subjective well-being) (Weiss et al., 2006), (2) correlations between long-term well-being and personality traits (Weiss et al., 2002), and (3) the health benefits of positive dispositions (Glickman et al., 1997).

This talk will present the current understanding of quality of life, well-being, welfare, and happiness in animals; the evidence for long-term affective states and their relationship with animal personality; how these states in animals compare with those in humans; the beneficial health effects of positive mental states; and recent advances in evaluating well-being states.

References

Boissy, A., Manteuffel, G., Jensen, M. B. et al. (2007). *Physiol Behav 92*, 375-397.

Glickman, L. T., Glickman, N. W., Schellenberg, D. B. et al. (1997). *J Amer Anim Hosp Assoc 33*, 197-204.

Weiss, A., King, J. and Enns, R. M. (2002). *J Pers Soc Psychol 83*, 1141-1149.

Weiss, A., King, J. E., and Perkins, L. (2006). *J Pers Soc Psychol 90*, 501-511.

Weiss, A., Adams, M. J., Widdig, A. and Gerald, M. S. (2011). *J Comp Psychol 125*, 72-83.

Session VII-5: Benefit evaluation

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Session VII-5: Oral presentations

VII-5-087

An analysis of the use of dogs in predicting human toxicology and drug safety

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Dogs remain the main non-rodent species in preclinical drug development. Despite the current dearth of new drug approvals and meagre pipelines, this continues, with little supportive evidence of its value or necessity. To estimate the evidential weight provided by canine data to the probability that a new drug may be toxic to humans, we have calculated Likelihood Ratios (LRs) for an extensive dataset of 2,366 drugs with both animal and human data, including tissue-level effects and Medical Dictionary for Regulatory Activities (MedDRA) Level 1-4 biomedical observations. The resulting LRs show that the absence of toxicity in dogs provides virtually no evidence that adverse drug reactions (ADRs) will also be absent in humans. While the LRs suggest that the presence of toxic effects in dogs can provide considerable evidential weight for a risk of potential ADRs in humans, this is highly inconsistent, varying by over two orders of magnitude for different classes of compounds and their effects. Our results therefore have important implications for the value of the dog in predicting human toxicity, and suggest that alternative methods are urgently required.

VII-5-243

Lack of clinical results: are animal experiments still ethically acceptable?

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The ethical acceptability of animal experiments is to a great extend dependent on the anticipated (health) benefits for Humans. After decades of performing animal experiments, it is useful to do retrospective research into the extent in which animal research has archived these benefits. The results until now show that only a small percentage of data from animal research reaches the clinic, which constitutes a threat for the ethical acceptability of animal research. There seems to be two reasons for this. First the methodological quality of the experiments is often too low. Second there is an intrinsic conflict between the reductionist character of preclinical research and the complex nature of clinical treatment. For example working with young, healthy, inbred animals of one gender may produce interesting scientific results which, however, have little relevance for the patients of different (genetic) background, age, gender, etc. Ways must be found to include the complexity of the patient into the research, instead of "reducing it out".

In the scientific field these problems have been recognized and ways to address them have been figured out, but in a scattered and not systematic way. In order not to lose credibility, action of the scientific community is needed.

VII-5-337

Added value of research synthesis in laboratory animal science

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To fully implement the principles of humane science, it is essential to ensure that animal studies are of the highest possible relevance and quality. Methodology and reporting of animal studies is currently inadequate and improvements are urgently needed (Anon, 2014). Research synthesis may be helpful to improve this situation. Recently, systematic reviews of animal studies, as a methodological approach of synthesis of evidence, were introduced within laboratory animal science. For example, in 2011 the Montréal Declaration on the synthesis of evidence to advance the 3Rs principles in science was adopted at the 8th World congress on Alternatives (Leenaar et al., 2012). The potential benefits of systematic reviews of animal studies are: stimulating better science, leading to better informed ethical review, helping to achieve the Three Rs, and improving translational transparency to inform clinical trials. The number of systematic reviews of preclinical animal studies (Ritskes-Hoitinga et al., 2014) is growing. Education and training is already available and needs further development and widespread distribution worldwide, just as tools and guidelines need to be developed further (Van Luijk et al., 2014). An overview of activities on systematic reviews of animal studies within laboratory animal science, the current state of affairs and what is needed for further progress will be presented.

References

Anon (2014). *The Lancet 383*, 156-185.

Leenaars, M., Ritskes-Hoitinga, M., Griffin, G. and Ormandy, E. (2012). *ALTEX Proc 1*, 35-38.

Ritskes-Hoitinga, M., Leenaars, M., Avey, M. T. et al. (2014). *Cochrane Database Syst Rev 3*, ED000078.

Van Luijk J., Bakker, B., Rovers, M. et al. (2014). *PLoS ONE 9*, e89981.

VII-5-417

Does interpretation of the principle of reduction by ethics committees lead to underpowered studies?

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When animal use in science cannot be replaced, there is an ethical imperative to use the minimum number of animals consistent with the study's objectives. Determining the right number of animals should be the shared goal of investigators and animal ethics committees. However, this is not easy: if too many animals are used, then their lives and other resources are wasted; and if too few animals are used, then results may lead to a type II error. It has been suggested that few animal ethics committees ask for an increase in numbers when the proposed experiments are underpowered, with the implication that a narrow interpretation of "Reduction" is trumping optimal experimental design. We wanted to assess how the principle of Reduction is interpreted and sample size calculations evaluated by Canadian animal care committees (ACCs). We surveyed all ACCs in Canada to determine: 1) if ACCs utilize *a priori* sample size calculations when evaluating proposed experiments; 2) how ACCs interpret Reduction; and 3) if other considerations (e.g., costs) are included in the evaluations. We will discuss whether the results show that ACCs' interpretation of Reduction is indeed discouraging optimal experimental design.

VII-5-653

Why considerations of rigour should be central to the ethical review of experiments using animals

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Research regulators are now quite good at ensuring that adequate attention is given, in the design of experiments, to the principles of refinement and replacement. Attention to reduction, combined with limited resources, mean that in many fields experiments are too small reliably to detect biologically important effects.

The focus on regulation from the perspective of the experimental animal has led to a failure to consider another, fundamentally important consideration. It simply cannot be ethical to conduct animal experiments which are at such high risk of bias that their results are of little value.

In a random sample from PubMed 20% of *in vivo* studies reported randomisation, 3% reported the blinded assessment of outcome, and none reported a sample size calculation. 68% of *in vivo* studies from 5 leading UK universities in 2009-10 did not report any of 4 measures to reduce the risk of bias and only one reported all 4 (Nagel et al., 2011).

Considerations of the ethical status of experiments using animals cannot have legitimacy unless they consider the scientific rigour of those experiments; and that, at least for research which is published, the available evidence suggests that this is either not being done at all or not being done well.

Reference

Nagel, S., Papadakis, M., Chen, R. et al. (2011). *J Cereb Blood Flow Metab 31*, 132-143.

VII-5-866

A structured approach for using preclinical studies to assess risk/benefit in trials and animal studies

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Moral evaluation of risk/benefit in animal studies of new drugs and early phase human trials requires assessing the clinical promise of a candidate intervention using preclinical evidence. Yet there is little to guide ethics committees or investigators making these assessments. In what follows, we draw on published guidelines for preclinical study design to develop a structured process for assessing the clinical promise of new interventions. In the first step, reviewers gather all relevant

preclinical studies, assess the magnitude of treatment effects, and determine clinical promise in light of various threats to valid clinical inference. In the second step, reviewers adjust assessments of clinical promise from preclinical studies by examining how other agents in the same reference class- and supported by similar evidence- have fared in clinical development. Assessments of clinical promise can then be fed into moral evaluation of risk and benefit in early phase trials and animal studies. Though our approach has limitations, it offers a systematic and transparent method for assessing risk/benefit for studies involving novel interventions.

Session VII-5: Poster presentation

VII-5-307

Benefit evaluation within project evaluation under directive 2010/63/EU

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The Directive requires that all projects are subjected to a project evaluation, which includes that a harm-benefit analysis forms part of the process, to assess whether the harm to the animals is justified by the expected outcomes.

In September 2013, the National Competent Authorities for the implementation of Directive 2010/63/EU endorsed recommendations prepared by an Expert Working Group convened by the European Commission to develop guidance on Project Evaluation.

The recommendations include guidance on the assessment of benefits, both direct and indirect. Issues to consider include, for example – What will be the benefits of the work? Who will benefit from the work? How will they benefit – impact? When will the benefits be achieved?

The weighing of non-comparable, sometimes abstract benefits arising from different types of research programmes is very difficult to perform objectively.

The "importance" of work is a subjective judgement changing with time and place depending on a number of variables such as culture, environment, economic situation, acquired knowledge, emerging unsolved scientific problems and ethical values.

His emphasises the need for a unique, case-by-case evaluation of the importance and magnitude of benefits for each proposed project.