Norecopa
c/o Norwegian Veterinary Institute
P.O. Box 750 Sentrum
0106 Oslo

www.norecopa.no

Harmonisation of the Care and Use of Agricultural Animals in Research

Gardermoen, Norway, 26 – 28 September 2112

A consensus document from the participants

1. Introduction

An international consensus meeting was held in September 2012 at Gardermoen, Norway, to discuss the care and use of agricultural animals in research. A total of 47 participants attended the meeting from Norway (17), the UK (14), Germany (4), Denmark (2), Switzerland (2), the USA (2), Belgium (1), Canada (1), France (1), Italy (1), Sweden (1) and The Netherlands (1). These represented government/regulators (14), academia/research (24), industry (7) and animal welfare organisations (2).

The meeting was organised by Norway's Consensus-Platform for Replacement, Reduction and Refinement of Animal Experiments, Norecopa (http://www.norecopa.no). It was the third in a series of consensus meetings arranged by Norecopa (http://www.norecopa.no/sider/tekst.asp?side=21).

The specific aims of the meeting were:

- to provide a forum for dialogue between stakeholders (regulators, industry, researchers, animal technologists and care staff, veterinarians and animal welfarists)
- to increase focus on "the 3Rs" *(Replacement, Reduction, Refinement)* of Russell & Burch (http://altweb.jhsph.edu/publications/humane_exp/het-toc.htm)
- to further harmonise best practice in the care and use of terrestrial agricultural animal species when used in research projects on the farm, in the laboratory or on 'model' farms (i.e. farms created specifically for research/teaching purposes)
- to prepare for implementation of Directive 2010/63/EU
- to identify tasks for Norecopa and other organisations to work on in this area.

This document summarises the participants' views on research, testing, teaching and training involving agricultural animals and the potential for further implementation of the 3Rs in these areas. It is a consensus document that has been circulated to all participants for approval. Specifically, the document summarises:

1. *The participants' perception of the current status of the use of agricultural animals as regards implementation of the 3Rs, expressed in terms of strengths and opportunities.*
2. *Tasks identified by the participants that still remain to be undertaken by those involved in or concerned with such work.*

Agricultural animals are used in:

1. Teaching and training
2. Agricultural studies (where the animals are the target species)
    a. on model farms
    b. on commercial farms
3. Biomedicine
    a. where human disease is the research target
    b. veterinary research for the animals' benefit
    c. fundamental (basic biology) research
    d. toxicology and pharmacodynamic/kinetic studies, safety and efficacy evaluation
4. The production of biologicals

The scientific, animal welfare and ethical issues vary between these areas but the animal's basic requirements are the same. These requirements are best summed up by the concept of the Five Freedoms (http://www.fawc.org.uk/freedoms.htm):

1. Freedom from Hunger and Thirst - by ready access to fresh water and a diet to maintain full health and vigour.

2. Freedom from Discomfort - by providing an appropriate environment including shelter and a comfortable resting area.

3. Freedom from Pain, Injury or Disease - by prevention or rapid diagnosis and treatment.

4. Freedom to Express Normal Behaviour - by providing sufficient space, proper facilities and company of the animal's own kind.

5. Freedom from Fear and Distress - by ensuring conditions and treatment which avoid mental suffering.

2. Strengths of the use of agricultural animals

1. Applied research using agricultural animals can provide direct health and/or welfare benefits for the species on which it is being performed, unlike research using one species as a 'model' for another.
2. There may be acceptance in some sectors of society for research on these species, for example to secure sustainable food production, food safety, animal health and welfare (e.g. agricultural animal behaviour, welfare assessment, welfare indicators, anaesthesia and analgesia) or for the protection of the environment.
3. Agricultural animals are considered by some to be useful models in some areas of biomedical research.
4. Research can be conducted at model farms, where staff training can be tailored to the specific animal use and it is easier to standardise research conditions than on commercial farms. In some circumstances, pilot studies at model farms can be used to refine research objectives and protocols in the field. It is, however, often necessary to repeat research under commercial conditions to assess whether or how new treatments or care practices will work.
5. Standards for animals used in research may help to raise standards on farms, e.g. with respect to better environmental enrichment, better recognition of clinical signs or more humane methods of slaughter.
6. Animals may be able to be rehomed or returned to their original environment under appropriate circumstances, which may boost staff morale.

3. Challenges in the use of agricultural animals

1. In contrast to 'conventional' laboratory animals, there are relatively few fora for exchanging information and views about welfare and the Three Rs with respect to agricultural animal use in research and testing. Advances in knowledge may also be delayed because of competition between institutions or the length of the publication process.
2. Research guidelines and requirements from local ethical committees may be different from guidelines and codes of practice for the farming industry, which can vary considerably between countries, companies and organisations.
3. The large variety of research areas in which agricultural animals are used, and the different types of facility in which they are kept, makes standardisation difficult. Some

guidelines focus on performance standards (e.g. 'animals should be able to rest comfortably'), while others are more geared to engineering standards (e.g. minimum enclosure sizes). It is accepted that standards should be evidence-based, but the various bodies producing guidelines may choose different literature and interpret it in different ways, which can result in widely differing standards.

4. Different standards, e.g. for environmental enrichment, health monitoring or the use of protective clothing, may be applied when research animals are used in the laboratory and on the farm. Variability in results may also occur because of differences in animal health standards or inconsistent application of environmental enrichment (N.B. enrichment is mandatory under European Commission Directive 2010/63/EU unless there is scientific justification otherwise).
5. There may be a tradition for lower standards when using agricultural animals in research. For example, there may be greater acceptance of death or morbidity as an endpoint, lower standards of housing, hygiene, husbandry and care, and less questioning of the necessity and justification for each project.
6. Commercially available "enrichment" devices may not have been properly evaluated with respect to how much animals want them or benefit from their use.
7. The use of analgesics in agricultural animals is still clouded by incomplete understanding of the physiology of pain perception and expression in all species. This can result in avoidable suffering, for example post-surgery.
8. The use of agricultural animals in teaching and training can cause pain, suffering and distress, even if the purpose is apparently innocuous e.g. for practical demonstrations. There may be a danger of overuse of individual animals if only a few animals are available, or if the drive to reduce numbers is given priority over the individual animal's experience.
9. There is public concern about the welfare of farmed animals, such that some sectors of the public may be opposed to agricultural animal research that is perceived as merely a means of improving productivity. There may also be controversy over the use of agricultural animals to create 'models' of human diseases, if it is perceived that they are used with the assumption that using 'food' animals will be more acceptable to the public than using 'companion' animals, for example.
10. There can be significant physiological and psychological differences between breeds, strains and crossbreds, which should be considered at the project design stage when

research animals are being selected. The individual animal's experiences or memories of earlier procedures should also be considered.

11. Animals may need to be transported relatively long distances, as there are few specialist breeders of agricultural animals for research and specific breeds or lines may be required.
12. Implementing the principle of reduction can be problematic in large field trials, for example feeding studies in which hundreds or thousands of animals are fed diets of differing composition. Provided that adverse treatment effects are not expected, it may be necessary to accept that numbers cannot be reduced in certain circumstances. Where reduction is applied, the minimum number of experimental subjects required for statistical significance may be less than the optimal social group size for the species and breed.
13. Refinement can cost money and staff resources.
14. There is a risk of zoonoses and physical injury when using agricultural animals, particularly when students and others with less awareness of the potential dangers are exposed to them.
15. On-farm research programmes run the risk of being confounded or even ended by disease outbreaks, and restrictions or treatment programmes imposed as a result of these.

4. General opportunities for further implementation of the 3Rs within the use of agricultural animals

1. There is considerable scope for all stakeholders to work together and improve the implementation of the 3Rs when agricultural animals are used in research, testing and teaching, and also to encourage questioning of the necessity and justification for their use. The concept of striving for positive welfare and a good quality of life for agricultural animals is also very important and increasingly recognised in both the farm and experimental setting.
2. It is essential to be honest, open and transparent about the purpose of agricultural animal projects and the reasons for choosing each species, with respect to scientific validity and translatability.
3. Greater awareness should be raised of the animal welfare and scientific benefits of applying the 3Rs. This includes ensuring that the definition and meaning of the 3Rs

are properly defined and understood by all[1]. Greater emphasis on the 3Rs should be included in applications for research involving agricultural animal species.

4. The challenge of ensuring more effective relief of suffering for agricultural animals can be addressed by measures including research into behavioural and physiological indicators of suffering, implementation of better systems for the recognition and assessment of suffering and adequate out-of-hours surveillance. Increased liaison between laboratory animal veterinarians and farm animal veterinarians working in the field would also help to ensure better recognition and alleviation of suffering.
5. Legal restrictions on drug use in agricultural animals should be carefully measured against the welfare implications to the animal. Such restrictions are based on the need to protect the food chain and the lack of data on drug combinations. In situations in which the animal is not to enter the food chain, the selection of anaesthetics and analgesics should be based entirely on optimizing the animal's welfare.
6. The numbers of animals required for regulatory purposes (e.g. vaccine development and testing) should be reassessed based on good science and advanced statistical methods. Harmonisation of regulatory guidelines between different areas of the world should be a priority.
7. Animal welfare can be improved by considering the lifetime experiences of individual animals, rather than thinking at a 'population' level as can be the norm in a farm situation.
8. Recent advances in behavioural research and monitoring techniques suggest that there is great potential to evaluate both positive and negative welfare indicators in agricultural animals.
9. Building a good relationship between researchers and farmers will help to ensure that the scientific method is properly applied in field studies.

[1] For example, 'refinement' is often taken to mean 'refining experiments to obtain better data'; 'replacement' to be substituting one animal species with another that will supposedly suffer less; and 'reduction' to mean using the minimum number of animals possible, to the detriment of statistical significance. None of these is correct. The following is a concise description of the 3Rs (http://www.rspca.org.uk/sciencegroup/researchanimals/implementing3rs/-/article/RAD_ImplementingThe3Rs):
Replacement - methods which avoid or replace the use of animals.
Reduction - minimising the numbers of animals used - for example by improving the experimental design and statistical analysis used in a study.
Refinement - improving experimental procedures, and other factors affecting animals such as their housing and care, to reduce suffering and improve welfare throughout the animals' lives.

5. Specific tasks for those involved in the use of agricultural animals

1. The establishment of an exchange network for animal technologists and researchers to encourage best practice and to promote continued dialogue, similar to those that already exist in traditional laboratory animal environments. Data, protocols (e.g. anaesthesia techniques), tissue and even animals could be shared (where appropriate) to promote the 3Rs.
2. Commitment and collaboration between all stakeholders should be fostered to research, understand and meet the requirements necessary to promote good welfare of agricultural animal species used in research and testing. For example, regular meetings of relevant experts should be held to exchange information and discuss issues relating to the necessity and justification of agricultural animal use, harm-benefit assessments and the application of the 3Rs. Results of applied agricultural research should be fed back to the farming community, and to regulators producing guidelines on animal care and use. Farmers and their organisations should be involved as stakeholders in research. They should be kept informed and their experience utilised.
3. Options in the research environment for publishing refined experimental protocols, as well as sharing negative results, should be used more widely, to minimise the continued use of suboptimal procedures. Scientific papers reporting the outcome of experiments should provide detailed information on housing, husbandry and procedures, highlighting the 3Rs including environmental enrichment. Including this information will also facilitate comparison with the predicted result in the original project application, when retrospective evaluation is performed.
4. The Five Freedoms (http://www.fawc.org.uk/freedoms.htm) should be more frequently referred to and followed in research using agricultural animals.
5. In many procedures such as vaccine studies, researchers should develop methods that can lead to replacement of some animal use with *in vitro* studies, reductions in the numbers of animals used in studies that must be performed *in vivo*, refinement of administration methods and improved implementation of humane endpoints. Where tests are conducted to fulfil regulatory requirements, they should also communicate their results to the bodies that require the data.
6. New techniques such as the use of telemetry or imaging should be considered as possibilities for refinement and reduction, but these should be used in such a way that

pain, suffering or distress is minimised and the harms to the individual are properly recognised and given due weighting.

7. Existing guidelines on capture, blood sampling, marking for identification, anaesthesia, analgesia, administration of substances and humane killing should be used and further developed. These must be carefully reviewed before use, since they can have different bases, approaches and areas of focus. The ones most relevant to the institution and research which is planned can then be selected. This means that specialists with knowledge of the guidelines must be available, or external ones must be consulted. Where scientific data is lacking or insufficient, practices which have been used successfully and are believed to be humane should be employed.
8. Species-specific guidelines should be produced for the detection of emotional states and any suffering (e.g. by recognition of facial expressions), as well as how to utilise this knowledge to alleviate pain or distress. There should be more focus on positive emotions, anticipation, cognitive enrichment, rewards and opportunities for playing, not just on the absence of signs of discomfort, pain or distress.
9. Guidelines on good practice for housing, husbandry and care in biocontainment systems should be developed if existing guidelines cannot be found. Input should come from all stakeholders including regulators, researchers, relevant industries (e.g. telemetry device manufacturers), veterinarians, animal technologists and care staff, and welfare organisations.
10. More anaesthetic protocols should be developed, with increased use of pre-emptive analgesia, partial intravenous anaesthesia, and more incorporation of analgesics rather than just general anaesthetics so as to prevent central nervous system 'wind up' and chronic hyperalgesia. Local anaesthetics can be refined to reduce pain on injection, but this may be in conflict with legislation on drug use. The precautionary principle with respect to the capacity to experience pain, suffering and distress should be applied where knowledge is lacking, accepting that agricultural animal species share many of the physiological characteristics seen in humans.
11. More widespread use should be made of science- and behaviour-based welfare indicators and monitoring systems that already exist, and work should be done to refine and implement these better as well as to develop and promote better indicators and protocols for their use. Scoresheets could be used more extensively, as a flexible tool to assist the expert judgement of care staff. More examples of different types of sheets for recording observations should be developed.

12. AAALAC International's template for a program description (which is available free of charge, http://www.aaalac.org) should be used more widely as a checklist for harmonising animal research, regardless of whether or not an institution aims for accreditation.
13. It is essential to have in place a sound decision-making process with respect to whether studies should be undertaken according to 'farm' conditions or 'laboratory' conditions. There are scientific, animal welfare, practical and ethical factors that ought to be considered in each case. In general, animal welfare should be paramount unless there is scientific justification otherwise. For example, relatively intensive space allowances may be considered to be justified in welfare studies evaluating the effects of inadequate space. Legislation on research performed on the farm may require the same space allowances as in the laboratory. If 'farm' conditions are deemed to be necessary and justifiable, these should comply with the relevant legislation or codes of practice for farmed animals. Implementing refinement on a farm where research is conducted may be constrained by legal requirements relating to food safety, environmental standards and occupational health and safety.
14. More research should be conducted on the welfare implications of using agricultural animals in research, testing and teaching. For example, relatively little has been done to evaluate good practice for housing, husbandry and care, or the stress of capture, handling or transport, the effects of telemetry devices, stress associated with the use of animals in practical demonstrations for students, the aversiveness of anaesthetic agents, or recovery from surgical procedures. As a matter of principle, such research should be done using animals undergoing painful or distressing procedures that would have been conducted in any case, so as not to cause additional harm to animals for the purpose of welfare research.
15. Increased handling, habituation and training of animals before procedures such as administration of substances or blood sampling, and/or rewarding them afterwards if appropriate, may lower the severity level of a procedure. This does not have to mean training animals to perform complex tasks – it could just be a matter of walking cattle through a crush a few times. Positive Reinforcement Training should always be used and unwanted behaviour should be ignored without 'punishment'. Naming the animals and relating to them as individuals may also be perceived as positive by the caretakers.
16. Behaviourists should use preference, motivational and cognitive bias tests to evaluate optimal housing conditions and environmental enrichment.

17. Refinement should always be applied, for example in the form of humane transport and restraint, adequate anaesthesia and analgesia, optimal housing, husbandry and care, within any scientific constraints. It is necessary to involve researchers, animal technologists and care staff, veterinarians and those responsible for animal house management when planning refinement, to ensure that it will be practical, feasible, beneficial and accepted by all.
18. Indwelling catheters and similar less invasive techniques should be considered and used wherever animals will benefit, for example when high sampling frequencies are planned.
19. All use of animals in teaching and training should be subjected to ethical review and there may be a requirement for project authorisation in some legislations if pain, suffering, distress or lasting harm may occur. Replacements such as models, surveillance systems and non-invasive techniques should be used wherever possible. The overuse of individual animals, for example for rectal examinations, should be avoided. Replacements and refinements within teaching, such as the Haptic Cow (http://www.live.ac.uk/html/projects_haptic_01.html) should be encouraged and used wherever possible.
20. The use of enrichment should be harmonised by implementing a defined programme. Enrichment items and other husbandry refinement protocols should be carefully observed and evaluated on a case by case basis, with respect to their effects on animal welfare and the scientific data. Increasing animal numbers to allow for greater variation due to enrichment may be the right thing to do, if the suffering of individual animals is reduced and/or quality of life improved.
21. Where reduction is applied, the minimum number of experimental subjects required for statistical significance may be less than the optimal social group size for the species and breed. It may be possible to overcome this by housing animals in the most appropriate group size, with a mix of experimental animals and 'buddies'.
22. More use should be made of farms with a good health status, animal welfare standards and stockmanship for applied research that requires 'field' conditions.
23. Education in ethics should begin in schools and continue in veterinary schools, agricultural colleges and farming organisations.
24. Sufficient training courses that are specifically designed for agricultural animal researchers should be developed and made available, with input from those with expertise in training, researchers, veterinarians, regulators, animal technologists and care staff.

Visiting other facilities can help to educate staff and exchange ideas and information, as long as visitors are shown examples of best practice.

25. Training of staff caring for or using agricultural species should include the natural history and behaviour of the study species, with emphasis on interpreting behaviour, fulfilling behavioural requirements and recognising indicators of both good welfare and suffering.
26. Humane endpoints and early scientific endpoints should always be implemented and resources on these tools should be consulted. A website such as http://www.humane-endpoints.info, but which is more related to these topics on agricultural animals, should be developed.
27. If possible, animals should be humanely killed on site rather than transported to a slaughterhouse. If animal transport is unavoidable, all journeys should be in accordance with best practice and stress kept to a minimum.
28. More funding should be made available to improve the quality of agricultural animal research, including studies designed to implement the 3Rs in research, testing and teaching using agricultural animals.

6. Tasks for Norecopa and similar advisory organisations

These organisations should:

1. promote the concept of positive animal welfare and a good quality of life for agricultural animals.
2. arrange regular further meetings on 3Rs topics where all stakeholders are represented.
3. provide a forum for discussion of the improvement of all aspects of agricultural animal use in research, testing and teaching, including consideration of necessity, justification, ethical issues, good practice guidelines and implementation of the 3Rs.
4. collect, review and stimulate the production of species-specific guidelines, checklists, behaviour and welfare assessment schemes and protocols for agricultural animal research, recommending those that represent best practice for all of the above issues.
5. encourage the production of templates for the non-technical summaries that will be mandatory when the new EU directive 2010/63/EU is implemented.
6. communicate and liaise with national animal research authorities, research councils, regulators and relevant international bodies on all of the issues mentioned in this document.

7. promote discussions between regulators and the vaccine industry to replace, reduce and refine the number of animals used for vaccine development and testing.
8. seek consensus and then issue position statements based upon scientific evidence on controversial or central aspects of the care and use of agricultural animal species in research.
9. inform the general public about research and testing involving agricultural animals, to enhance openness and the understanding of research, and to increase focus on agricultural animal welfare in society.