1 Research Ethics

Many countries have legislation regulating research on humans and animals, as well as on how to handle information from humans participating in a study. In addition, there are guidelines for universities, industry and funding bodies (see Chapter 5). Legislation and guidelines are, however, not always enough to ensure a good scientific practice, as even the clearest guidelines and laws need to be interpreted by those working within their framework. The individual researcher or research group still has to discuss and decide how to implement the ethical values underlying legislation and guidelines in their everyday work. In this chapter we outline the most important discussions within the area of research ethics as they relate to core issues in animal-based research.

1.1 Challenges in the Research Process: The Need for Research Integrity

Research integrity (also known as responsible conduct of research) is relevant to research performed in all scientific disciplines, as its focus is on ethical issues evoked in and by research as such. Hence, depending on the discipline, somewhat different issues are at stake. For example, in anthropology, medicine, psychology and sociology, issues related to involving or using informants are frequent, whereas research ethical issues in history or geography rather concern how to use documents and research material in a correct way; across all disciplines, research making statistical analyses needs to be concerned with relevance, reliability and validity. Independent of disciplines, a number of areas and issues are relevant to consider in order to ensure good research practice: research planning and conduct; data management; publication and communication; authorship management;

collaboration practices; and conflicts of interest (see e.g. Danish Code of Conduct for Research Integrity [Ministry of Higher Education and Science, 2014]).

Scientific misconduct and questionable conduct of research can occur within in all these spheres. Examples of misconduct are fabrication of data (creating data 'out of thin air'), falsification of data (inclusion or exclusion of data to falsely underpin a certain result) and plagiarism (using own or someone else's text or material without accurate reference). Examples of questionable conduct of research are accepting or granting undeserved authorships, using inappropriate methodologies and failing to acknowledge contributions from others. Due to time and resource limits, verification of research, i.e. repetition, might not always be done, whereby false results are spread. Further, dishonesty in relation to funding bodies and publishing the same study in several contexts reveal lack of professionalism and poor research ethics (ESF, 2011).

There are many reasons for researchers to adhere to responsible conduct of science. For one thing there are problems related to one's own consciousness but there are also issues related to the failure of being a reliable researcher and colleague. Promotion of unfair competition implies cheating upon society which listens to and depends on research in many areas to inform political decisions. If legislation and policies are built on false results, people may be harmed, and if research proves to be unreliable, trust in research decreases, which may lead to less support from both private and public funding bodies (VR, 2011). For all these reasons, if revealed at some point, research based on false results must be retracted (e.g. by publishing a correction in a journal). See Table 1.1 for an overview of examples of scientific misconduct and questionable conduct of research taken from the world of animal research.

1.2 ETHICAL AWARENESS IN DESIGN OF ANIMAL RESEARCH

A central part of responsible conduct of research is how experiments are designed. When designing a study with animals, scientists are

Table 1.1 *Different phases of research and examples of type of misconduct in animal research*

Phase of research	Example of kind of misconduct	Practical example from research with animals
Research setup and design	Not complying with the rules for authorization of animal experiments Lack of implementation of guidelines	Non-compliance with the animal experiment license was found in a published paper; the experiment reported tumour growth beyond what was approved for that experiment. This lead to a published correction and apology by the authors (Nature, 2015; Raj *et al.*, 2015).[a]
Handling of research material	Insufficient responsibility for material Fabrication or falsification of data Plagiarism (misleading use of material, ideas, designs, methods etc.) Lack of implementation of guidelines	Fabrication of data, exemplified by a classical case in 1974 in transplantation immunology: William T. Summerlin fabricated changes in skin colours of mice by painting them with a permanent marker as an evidence of successful transplantation.
Research collaboration incl. authorship	Lack of responsibility for research process, lack of contribution Plagiarism (wrongful appropriation of texts) Order of authors, false or gift authorship, excluded from authorship in spite of substantial contribution	A paper on social stress and pain perception in mice was found to have plagiarized 17 sources. This lead to retraction of the paper (PLoS One, 2016; RetractionWatch, 2016).[b]

(*continued*)

Table 1.1 *(continued)*

Phase of research	Example of kind of misconduct	Practical example from research with animals
Publishing results	Limitation of 'relevant' results and manipulated results Dishonesty about a person's contribution	A paper on nutritional supplementation methods in sheep production was withdrawn due to complaints about the data presented and the attributions of authorship (RetractionWatch, 2015; Sweeny *et al.*, 2015).[c]

[a] http://www.nature.com/news/protection-priority-1.18354 Correction and excuse by authors: L. Raj *et al. Nature* http://dx.doi.org/10.1038/nature15370; 2015

[b] http://retractionwatch.com/2016/05/31/plos-one-paper-plagiarized-from-17-articles-yes-17/#more-40553. The retraction note: http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0156567

[c] http://retractionwatch.com/2015/08/11/sheep-study-pulled-for-issues-with-the-validity-of-data-and-attribution-of-authorship/#more-30416. The retraction note: http://www.sciencedirect.com/science/article/pii/S1090023315002555

Source: Original table by Röcklinsberg, Gjerris and Olsson.

mainly motivated by the research question they want to address. They are hopefully well acquainted with the present state of the art of methodologies in the field and the questions for which an answer is necessary to move the field forward. The overall plan of research will probably have been presented in an application for funding and its scientific merit evaluated by other scientists. Presently, nearly all scientific research in academia takes place within funded projects which have undergone this kind of scientific evaluation.

In industry, decisions to go ahead with animal experiments will be based on an internal scientific discussion and economic evaluation. For the other main area of animal experiments, the so-called

regulatory testing, it is the legal requirements for testing new substances and devices which provide the reason for using animals. Such testing uses strictly defined protocols which are applicable across a range of substances, because all testing basically attempts to answer the same question: is this substance or device likely to be safe to use in the way that it is intended? In contrast, research is much more variable and highly dependent on the field in which it is conducted and on the questions to be asked.

It takes more than scientific excellence to plan and run a good research project with animals. Different skills are needed and represented by different groups of personnel. Selecting an appropriate animal model for the research question requires knowledge about the biological differences between different animal species in different respects. To design the experiment properly requires understanding of experimental design from both the biological and statistical perspectives. These are competences of the responsible scientist, but other personnel (animal caretakers, technicians, attending veterinarians, research students) also need to be competent in the tasks they have to carry out in the study. In the Directive 2010/63/EU four main tasks in animal-based research are pinpointed and connected to a range of requirements to be fulfilled in mandatory education of these groups (see Table 1.2). In addition, the experiments need to be done in appropriate facilities to produce reliable results.

1.3 RELATION BETWEEN RESEARCH ETHICS, ANIMAL ETHICS AND ANIMAL WELFARE

Well-conducted research may correspond with sincere ethical considerations regarding research ethics. From an ethical point of view, it is, however, not merely a question of conducting research in a good way to get the best results, but also of considering the ethical issues related to the animals themselves. Whereas the main responsibility for how studies are designed and executed lies with the researcher, there are also instituted mechanisms to ensure that animal research

Table 1.2 *Proposal of the topics in which different types of personnel must be competent, according to a European Commission expert working group on training*

Topic	Function according to Directive 2010/63/EU Article 23			
	(a) carrying out procedures on animals	(b) designing procedures and projects	(c) taking care of animals; or	(d) killing animals
National legislation	•	•	•	•
Ethics, animal welfare and the 3Rs	•	•	•	•
Basic and appropriate biology	• ○	•	• ○	• ○
Animal care, health and management	•	•	•	•
Recognition of pain, suffering and distress	•	•	•	•
Humane methods of killing	•	•	•	• ○
Minimally invasive procedures	• ○	•		
Design of procedures and projects		•		

• theoretical competence ○ practical skills

Source: EWG, 2014.

complies with basic expectations of society. There is of course a variety of views on how or even if animals can be used in research, and different ethical theories give support to different positions. For example, if one shares a radical animal rights view, all medical research for the sake of humans will be unjustifiable, whereas other positions allow for use of animals but with different limitations or constraints regarding impairment of animal welfare (see Chapter 2 for more detailed discussion). A kind of a compromise position underpins legislation saying that animal research is acceptable only when there are no alternative methods to achieve the objective; when animal suffering and animal numbers are minimized; and when the harms caused to animals are justified by the expected benefit of the research. In most countries, one important mechanism to ensure compliance is to require that projects involving use of animals are reviewed before they can start. Usually this review is carried out by a group of people with different backgrounds – often called an Animal Ethics Committee or an Animal Care and Use Committee.

This, however, raises further questions, specifically regarding the definition of harm, as there is no general agreement on what constitutes a harm. Also, 'minimized animal numbers' needs to be explored in relation to statistical parameters to justify the use of them in the first place. It is the task of both researcher and ethical committee to balance potential benefits to humans and possible welfare impairments for the animals. Such a balancing process requires acquaintance not only with research procedures and practices but also with different parameters and measurements relevant in welfare assessment, as well as familiarity with considerations of animal and research ethics. Each decision by an animal ethics committee can thus be seen as a meeting point for issues of animal ethics, research ethics, animal welfare and research design (see Figure 1.1).

Another example of the interdependence of these fields concerns how to handle risks in animal research. The consequences of some procedures on animals are difficult to predict. Parameters to consider are whether the risks are large or small, whether they occur

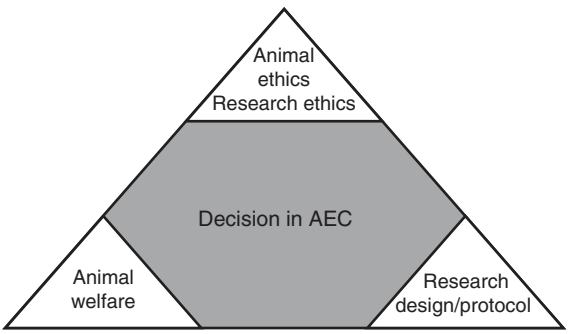

FIGURE 1.1 Three distinct fields of research, each contributing with necessary perspectives on research procedures, here exemplified with the different aspects contributing to a decision of an Animal Ethics Committee (AEC). They are also interdependent, as a decision in any of the disciplines influences what issues are evoked or questions posed in the others, and hence also the outcome of what is deemed ethically justifiable.

Source: Original figure by Röcklinsberg, Gjerris and Olsson.

frequently or seldom, are direct or indirect, as well as easy or difficult to detect. The best approach then is to consider such procedures through a risk assessment, in which one considers the potential harmful consequences, the likelihood that they will occur and measures to be taken not to cause more harm than necessary. The creation of a new line of genetically modified animals is a good example of a procedure with a welfare risk until the phenotype of the animals has been characterized and its effect on their welfare is known (Turgeon and Meloche, 2009).

Experiments using stressed or otherwise impaired animals will in most procedures produce results different from the ones using animals that are better off. Moreover, from a research ethics point of view, if the animal welfare status is not known at the outset, it is difficult to evaluate whether the welfare status influences the results, and thus the results will be difficult to interpret. Further, if complications are not known, e.g. a mouse is infected with a contagious disease without clinical symptoms, this might have an unnoticed impact on the animal. In such instances, researchers will not only evaluate results based on insufficient knowledge, but the ethical evaluation

will be flawed as well. Unpredictable or unknown changes in animal welfare might cause unpredictable or unknown effects on the animal and influence results without the researcher's knowledge.

To put it more positively, sincere research ethical considerations will help with choosing a relevant research question, finding the most suitable methodology and producing trustworthy interpretation of results. In animal-based research, research ethical considerations include awareness of the importance of good animal housing and handling for accurate and relevant results. Reliable research results thus are dependent on both well-handled animals and researchers' personal engagement in research ethical dimensions of their work.

1.4 ETHICAL REASONING IN ANIMAL ETHICS COMMITTEES

Given that ethical reasoning is beneficial for the research community, for the animals and for research as such, and hence important, how then is ethics understood by researchers and committee members? There are only a few studies describing this. According to a German study by Kolar and Ruhdel (2007) Animal Ethics Committee (AEC) members had disparate experiences of how an ethical evaluation was performed. The majority performed their own ethical evaluation (42 of 52), whereas fewer relied on the applicants' statements if comprehensive (10 of 52), and 3 out of 52 referred to the ethics discussions in the committee and another 3 found ethical considerations were entirely lacking in the committee work. This latter group consisted of animal welfare representatives.

In a study by Ideland (2009) on ethical reasoning in animal ethics committees in Sweden, informants expressed different views on what the term 'ethics' meant for them in their committee work. Furthermore, when asked for whose sake they were doing this, three clearly different reasons were presented. The answer of the scientists was 'for the sake of science', lay persons from political parties (although not representing such) answered 'for the case of patients' and lay persons from animal welfare organizations said 'for the sake

of animals'. These different views were not found to be explicitly discussed during committee meetings, nor was there an effort to reach a common view. Rather, Ideland could, in line with other studies (e.g. Sengupta and Lo, 2003; Tjärnström, 2013) see an established hierarchy in the committee, where scientists' statements and perspectives set the agenda.

> Even if the scientific experts are not in the majority, they have power over the agenda. Observations from the committee meetings show that the priority of interpretation belongs – exclusively – to scientific ideals. There is no room for ethical questions about research purposes and animal suffering in this context. (Ideland, 2009, p. 260)

One obvious explanation for the predominance of scientific ideals is that the entire activity lies within their arena. Another is the traditional perception among scientifically trained persons of science as objective and ethics as subjective. The believed value neutrality of science is widely disputed, however (Rollin, 2006; see also Chapter 2), and the discipline of ethics strives for solid coherent argumentation as the basis for justification of a position, and thereby can be seen as intersubjective. An ethical evaluation of a research application builds on considering relevant facts and an ethical evaluation of these facts (e.g. considering welfare definition and justification of minimum welfare levels) but also taking general issues of human responsibility for humans and animals into account. In this latter aspect emotions and empathy have a role to play.

Interesting enough, scientists and lay persons' perception seem to differ when it comes to the role of emotions and empathy. According to recent studies of Swedish AECs (Tjärnström, 2013), lay persons decide to exclude emotions from the discussion for tactical reasons. Scientists, who have the leading role during meetings, instead argue that in order to ensure rationality and objectivity in the decisions, emotions should be excluded. Taking research on ethical discernments in animal ethics into account, one could, however,