A Matter of Importance: Considering Benefit in Animal Ethics Review

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Summary

Animal-based research presents an ethical dilemma between harms (to animals) and benefits (mainly to humans). According to Directive 2010/63/EU, project evaluation should include "a harm-benefit analysis of the project, to assess whether the harm to the animals in terms of suffering, pain and distress is justified by the expected outcome". By defining benefit and its assessment very generally, legislation opens for a variety of interpretations. In this paper, we review different approaches, consider potential disagreements and highlight the need for a wider discussion of the role of the harm-benefit analysis in ethics review.

Keywords: Benefit, harm-benefit, scientific relevance, societal relevance, animal research

1 Introduction

Animal-based research presents an ethical dilemma: if it is pursued, animals may be caused to suffer; if it is not, important biomedical benefits may be lost. Although minority views range from total opposition to total endorsement, the majority view seems to be that it is acceptable to use animals in experiments if the experiments in question are likely to deliver benefits that cannot be obtained with a non-animal method, if the harm caused to animals is kept to a minimum and if the benefit outweighs the harm. This view is reflected in the recently revised European legislation which highlights the relevance of research with animals, the need to ultimately abolish it and the importance of ensuring that such research is only carried out when appropriately justified.

When animal ethics or animal care and use committees[1] address the ethical dilemma, this usually involves balancing harm and benefits. The fundamentally revised and expanded European legislation (Directive 2010/63/EU, see EU, 2010), protecting animals used in research, now covers review and authorization procedures, aspects that the previous Directive (86/609/EEC, see EEC, 1986) left to the individual member states to organize. The need to evaluate benefit and to weigh it against harm is made clear in the recitals (the part of the legislative text that provides the background justification for the norms introduced by the legislation): "It is also essential, both on moral and scientific grounds, to ensure that each use of an animal is carefully evaluated as to the scientific or educational validity, usefulness and relevance of the expected result of that use. The likely harm to the animal should be balanced against the expected benefits of the project" (Recital 39).

In this paper, we will discuss what benefit assessment and harm-benefit weighing mean in the context of animal research. We will consider guidelines for ethics committees and discuss different notions of benefit in the light of existing literature. The background for this analysis is the changing European legislation, but the applied perspective is international, as the questions are similar across the countries in which there is wide use of animals in research. This is work in progress and we do not claim providing a complete analysis of the topic or coverage of the literature.

2 What are committees asked to evaluate?

In Directive 2010/63/EU, it is Article 38 which establishes in what the project evaluation shall consist. Regarding benefit evaluation and harm-benefit weighing, this procedure must cover

> *"(a) an evaluation of the objectives of the project, the predicted scientific benefits or educational value*
> *(…)*

[1] The term "animal ethics committee" is predominant in Europe (although it is not used in Directive 2010/63/EU) and Australia/NZ, whereas "animal care and use committees" is the term used in North America.

(d) a harm-benefit analysis of the project, to assess whether the harm to the animals in terms of suffering, pain and distress is justified by the expected outcome taking into account ethical considerations, and may ultimately benefit human beings, animals or the environment;"

At the time of the conference at which this paper was first presented (March 2013), more detailed guidelines as to how to carry out this procedure were not available on the European level (however, see below for subsequently published guidelines). For comparison, we therefore consulted the guidelines for Canadian and US research with animals. Canada and the USA have a long tradition of well-established systems for regulating animal research, with uniform national standards within each country. They also provide written guidelines to support the committees reviewing animal research protocols (OLAW, 2002; CCAC, 1997). However, as regards how to evaluate benefit or how to weigh it against harm, these documents contain little information beyond the general wording also expressed in the European Directive.

The same type of very general information is given to scientists in documents informing them about the ethics review process and how to prepare material for application. Regarding the evaluation for research funded within the European Framework Program (FP7), the booklet *Ethics for researchers* asks researchers to "*explain why the anticipated benefits justify the use of animals and why methods avoiding the use of living animals cannot be used*" (EC, 2013).

Later in 2013, a set of guidelines[2] was made available on the European Commission website, aimed to provide "*guidance and principles for P(roject)E(valuation) and R(etrospective) A(ssessment) in line with Articles 38 and 39 of the Directive to assist all those involved in the preparation, evaluation and assessment of projects*" (Expert Working Group (EWG) for Project Evaluation (PE) and Retrospective Assessment (RA), 2013). These guidelines include a list of benefits to be considered together with a few reflections on these. Briefly, evaluators are advised to consider the following: for basic research, the soundness of hypotheses, links to a tangible strategic role and dissemination of results; for applied health research, the number of individuals affected and the improvement successful research could lead to; and for safety assessment product and food safety. Key considerations are defined so as to consider immediate and longer term benefits, as well as the wider impact.

The document further acknowledges that "*there may be differing priorities among Member States resulting in differing weights being allocated to benefits*". It is recognized that "*(w)eighing of non-comparable, sometimes abstract benefits arising from different types of research programmes is very difficult to perform objectively*" and that "*since there is no common agreement, it is not possible to place the benefits from the use of animals in research projects objectively in a simple hierarchical order to assist in the harm-benefit assessment of individual projects*."

3 What is to be understood as benefit and how to evaluate it?

As the previous section demonstrates, official documents provide little guidance on how to evaluate benefit or how to weigh it. By defining benefit and its assessment very generally, legislation opens for a variety of interpretations. In order to weigh benefit against harm, one must find a way to estimate benefit. And a fundamental condition for being able to estimate benefit is to determine what it means to say that an experiment will deliver benefit.

One way of tearing apart the different issues at stake could be to describe benefit in terms of scientific versus societal relevance[3]. The scientific community already has mechanisms in place for evaluating scientific relevance: this is what the peer-review process is expected to estimate when analyzing applications for funding and manuscripts for publication. Access to competitive funding and publication in highly valued journals are measures of high scientific relevance and quality. Societal relevance is more difficult to pinpoint, at least within existing evaluation systems (see Erno-Kjolhede and Hansson, 2011, for a review), because it involves a much wider range of issues and there is no agreement on how to evaluate or rank them. Treatment and prevention of diseases is relevant, but so are economic growth, education, environmental protection and redistributive justice.

A related distinction is between applied and basic research, which introduces the question of how *immediate* the benefit will be. Although this is probably not his intention, Peter Singer indirectly makes a normative statement on animal use in applied versus basic research when writing "*...If a single experiment could cure a major disease, that experiment would be justifiable. But in actual life the benefits are always much, much more remote, and more often than not they are nonexistent...*" (Singer, 1975).

Another related aspect is the purpose of the research. The public takes the research purpose into account when forming their opinion about animal research. Those who want to influence

[2] This document is part of the guidance documents aimed to assist Member States in implementing Directive 2010/63/EU. They are produced by Expert Working Groups, usually during two-day meetings in Brussels, subsequently endorsed by National Competent Authorities and made publicly available at the European Commission website. These documents do not impose additional obligations beyond those laid out in the Directive.

[3] This distinction is coherent with the science sociology discussion around modes of knowledge production (for a review, see Hessels, L. K. and van Lente, H., 2008) to give a background to this question. Briefly, science sociologists describe a transition from Mode 1 (in which knowledge is produced and valued for its own sake) to Mode 2 (in which knowledge is produced to address a specific problem) knowledge production. In Mode 1, academic researchers determine which questions are relevant to investigate and their research is driven primarily by the motivation of increasing knowledge. In Mode 2, issues to be addressed by research are determined by external problems and research motivated by practical goals.

the public opinion are well aware of this and describe animal use in terms of medical relevance ("*to learn more about health problems, and to assure the safety of new medical treatments*", "*to develop drugs and medical procedures to treat diseases*") if they are appealing to public support (New Jersey Association for Biomedical Research[4]) and in terms of "*cruel chemical, drug, food and cosmetic tests, biology lessons, medical training exercises, and curiosity-driven medical experiments*" (People for the Ethical Treatment of Animals[5]) when appealing to opposition. Systematically varying different factors in a recent study of the attitude of the Danish population, Lund and co-workers (Lund et al., 2012) demonstrated that support for research with animals drops as the purpose of research moves from cancer and cardiovascular diseases (just under 70% approval) through migraine (60%) and obesity (50%) to cosmetics testing (35%)[6].

A distinctly different aspect is the technical quality of the proposed research. This includes considerations such as good experimental design, correct sample sizes and appropriate control treatments. As opposed to questions of societal relevance and research purpose, technical quality can be assessed relatively objectively using agreed standards in scientific research.

4 Animal ethics review relies mainly on standard measures of scientific potential and quality

The absence of concrete guidance on how to evaluate benefit in the guidelines for ethics review reflect the state of the arts regarding knowledge and discussion of benefit and harm in animal experimentation. Of the two elements in the harm-benefit assessment, the question of harm (or more precisely, how to reduce it) has been central to research and teaching in laboratory animal science worldwide over the last couple of decades.

It would, of course, not be fair to say that these activities which are aimed to develop knowledge and increase associated technical skills exclusively focus on harm reduction. When they address issues such as experimental design and laboratory animal biology, the primary objective is that improved practice in these domains will increase the validity of the results and thus the quality of the research – improvements which ultimately will enhance the benefit.

Indeed, animal ethics review, as described by members of committees across Europe, mainly considers standard measures of scientific potential and quality. In order to assess the potential benefit of the proposed project, members of the FELASA working group on ethics review (Smith et al., 2005) recommend that committees ask how original, timely and realistic the objectives are, if there is replication of previous work and how the proposed work relates to other work in the field. In order to assess the likelihood of achieving the potential benefits, committees are recommended to consider the validity of the experimental design, the competence of researchers, the appropriateness and quality of facilities and the way the results will be communicated.

It is obvious that a poorly designed experiment that cannot give a reliable answer to the questions it poses will not be beneficial; it may indeed even be harmful if it produces misleading results. But the technical quality is only one of many aspects of benefit. Asking what it means for an experiment to be beneficial requires opening of a complex discussion involving the various notions of benefit outlined above. The discussion becomes even more complex when we move from estimating benefit to weighing this estimated benefit against the predicted animal harm.

There is some reluctance within ethics committees in taking on this discussion, sometimes even in handling the benefit evaluation and weighing: "*a small but significant number of respondents suggest that their ethical evaluations do not include consideration of the balance of likely benefit over harms of the studies*" (FELASA, 2005) and "*Whether IACUCs should review animal research protocols for scientific merit is not addressed in the federal regulations, resulting in ongoing confusion on the subject*." (Mann and Prentice, 2004).

But it is a discussion that cannot be avoided if we are to respect the intention of the law "*to ensure that each use of an animal is carefully evaluated as to the scientific or educational validity, usefulness and relevance of the expected result of that use. The likely harm to the animal should be balanced against the expected benefits of the project*" (EU, 2010).

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[5] http://www.peta.org/issues/animals-used-for-experimentation/animals-used-experimentation-factsheets/animal-experiments-overview/

[6] It should be noted that cosmetics testing is no longer allowed in the European Union, whereas the remaining four cases fit into the legitimate purpose of benefiting human health.

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