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Comments on Thompson: Research ethics for animal biotechnology

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Rules and principles of ‘animal care and use’ committees

In these comments I will compare the functioning of DEC's (dierexperimentencommissies¹) in The Netherlands, with the functioning of Animal Care and Use Committees (IACUC) in the United States as described by Paul Thompson². Several aspects of the functioning of IACUCs in the Netherlands appear to be more or less similar to Thompson's description of the situation in the United States, but there also seem to be differences. As in the US, institutions in The Netherlands are required to constitute an internal DEC that will review and approve protocols. A DEC advises the licence holder on whether the protocol is acceptable from an ethical point of view. Contrary to the situation in the US, a governmental department ('veterinaire inspectie') is responsible for inspecting whether animal experiments are performed under licence, and whether animals used for research in the institution are in fact being used as indicated. This department also enacts rules concerning proper treatment of the animals. In my experience, an external governmental organization that sets certain rules and that controls whether rules and procedures are being followed contributes to the proper functioning of DEC's because different roles are divided in this way. This provides the possibility of a more co-operative and open interaction between a DEC and researchers in the process of producing a protocol³.

Besides governmental laws there may be some locally set rules or guidelines, which have been developed by precedents for similar cases. Examples of such rules are: "in decapitating animals anaesthesia should be used", "anaesthesia with an ether pot is not allowed", "solitary housing of rats should be avoided", "in applying this model for multiple sclerosis, measures should be taken for proper urinating of the animals". As can be seen, those rules aim at diminishing the amount of suffering. Usually these requirements lead to an adaptation of the proposal. Local guidelines and rules are not often laid down in an explicit code. The main reason for this may be that an explicit code often raises the impression that proposals are evaluated by a set of rigid rules, which as a consequence puts the burden of proof against procedures at the side of the committee.

Another class of local rules or guidelines consists of ethical principles that may lead to disapproval of an animal experiment, e.g., "animal experiments with a purely scientific aim are not allowed when causing major suffering", or "experiments with primates are not allowed at this university". With regard to very delicate issues, such as the use of primates, the board of a university can take the decision to lay down an

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explicit rule. If not, those ethical principles play a role in the deliberation of a DEC, but may very well be overruled when stronger interests are at stake, such as ‘important’ scientific understanding, scientific reputation or Nobel prizes. Therefore, such principles do not function as ethical principles that judge what animal experiments are to be rejected irrespective of any interests.

Hence, like in the US ethical evaluation is not based on consistency with basic principles or norms with regard to the intrinsic value of an animal. From my point of view, a decision that (certain) animal experiments are no longer accepted, which is based on an ethical principle that is related to the intrinsic value of animals, should be a governmental decision and cannot be taken by a local animal-care and use committee. As long as society has not democratically decided to reject (certain) animal experiments principally, it would be unjustified for local DEC’s to take such decisions. As a consequence, decisions of DEC’s are utilitarian because they have to weigh different interests: besides care for animals, also interests of patients, researchers, ‘science’, university, consumers and companies have a part in the ethical considerations. But I agree with Thompson that this should not be thought of as involving a classical cost–benefit style of justification. Nevertheless, it is important to recognize the sketched practice as legitimate in order to understand that principle ethical difficulties with animal experiments will not be ‘solved’ by setting up animal use and care committees. In conclusion, decisions of DEC’s are not guided by general ethical principles concerning the intrinsic value of animals, since such principles would disapprove of (a certain class of) animal experiments irrespective of any other interests. On the contrary, decisions of DEC’s involve a utilitarian approach where interests of both animals and people are taken into account.

What should also worry us, and here I also agree with Thompson, is that nothing in this procedural approach itself guarantees that the right ethical questions regarding animal use are being considered. In my view, this problem occurs at two different levels. First, how a DEC is doing its job is not externally examined⁴. Thus, different DEC’s may uphold different standards. To a certain extent the nature of the approval reflects the culture and values of the institution, as Thompson puts it, but, as I see it, also those of ‘society’. This brings me to the second level at which we should worry about whether the right ethical questions are considered. As I already pointed out, since DEC’s are held responsible for the ethical assessment of animal experiments, confusion may arise about who should decide on ethical principles concerning the intrinsic value of animals. As I stated earlier, principle decisions concerning the prohibition of (certain) animal experiments – i.e. legislation in which primacy is being given to the intrinsic value of animals instead of utilitarian arguments – ought to be taken democratically at a governmental level, not at the level of DEC’s at particular institutions. This latter point is often disregarded in critiques on the functioning of ethical committees. I will get back to this point below.

The role of ethical expertise

A consequence of this utilitarian approach by DEC’s is that in most cases proposed animal experiments are approved when animal suffering is reduced ‘as much as reasonably possible’. For, proposed animal experiments usually aim at ‘accepted’ interests. Diminishing the amount of animal suffering helps to balance the interests of different parties, and thus meets utilitarian requirements. As a consequence, many discussions in the committee deal with rather technical or scientific questions concerning details of how animal welfare in the experimental set-up can be improved

and how the amount of animals used can be reduced. According to Thompson judging animal welfare also involves an ethical decision because such judgments presuppose ideas about how to interpret ‘animal welfare’. In his view, this would require specific ethical expertise in the committee. Although this may be the case at the level of methodology in animal-welfare research, in my view this cannot be a topic for an animal-care and use committee. My disagreement with Thompson on this point may have to do with the fact that in The Netherlands veterinary and animal-welfare expertise is represented by a specialist in service of the institutions, who advises both DEC and researchers. Usually, the committee accepts his or her assessment of animal suffering. Therefore, assessment of animal welfare in an experimental set-up is a technical or scientific – and not an ethical – question in the context of the committee.

One could ask, as Thompson did, why ethical expertise is required in animal-care and use committees. The committee’s major goal appears to be meeting the aims of reduction, replacement and refinement (‘the three R’s’), and weighing the interests of different parties involved. This is an ethically set goal, but approaching this goal does not seem to require specific ethical expertise. Here, I assume that specific ‘ethical expertise’ is only required when deciding on whether a certain new ethical principles is at stake. Aiming at the reduction of animal suffering and weighing interests of different parties, requires a discussion between prudent people endowed with specific scientific expertise, practical intelligence and *common morality*, not specific *ethical expertise*. Nevertheless, ethical problems concerning fundamental issues may be at stake every once in a while, and ethical expertise may be required to recognize these issues and direct the discussion to a specific ethical level. Examples are whether animal experiments on smoking or drugs addiction are ethically justifiable, or how to deal with research paid by an industry that is commercially dependent of the results, or how to judge the new research possibilities that are generated by using transgenic or knock-out animals. And also the issue raised by Thompson about whether animal welfare should be reduced to the prevention of stress and pain occasionally comes up in discussions of the committee. Despite the importance of these ethical issues, they often cannot productively be dealt with within the context of the committee or institution. For in most cases, as soon as scientific and/or societal significance is recognized, ethical principles concerning the intrinsic value of animals appear to be too weak to ‘outweigh’ these interests. In such cases a strong implicit argument seems to be that rejecting a protocol for ethical principles concerning the intrinsic value of animals would be unfair because such a decision will put a researcher or a research group at a disadvantage in its community⁵. In my view, these problematic issues can – and should – only be productively discussed at the public or governmental level. Possibly, those members of the committee endowed with specific ethical expertise, could take the responsibility to bring those ethical issues to the level of the public debate. These debates may finally lead to new laws, such as the law that animal experiments for cosmetic products are prohibited.

The use of transgenic and knock-out animals

In order to discuss problems of animal welfare concerning the use of transgenic and cloned animals in experiments, Thompson makes use of insight about the use of such animals in agriculture. In my view this approach is of minor value because several problems apparently relevant to biotechnology in agriculture are not relevant to animal experiments and, on the other hand, important problems in animal experiments are overlooked. Before pointing out specific problems in animal

experiments, I will explain in what respect the use of biotechnology differs in the two fields.

Firstly, contrary to agriculture where transgenic animals are used, so-called 'knock-out' animals are often used in animal experiments. Transgenic animals carry a foreign gene, for instance a transgenic cow that produces a certain pharmaceutical product in her milk. In knock-out animals one or more genes are 'knocked-out' in order to inhibit or destroy certain physiological functions. Knock-out animals are used to study the role of those genes in physiological processes. Secondly, Thompson discusses the problems of animal welfare that may arise as a consequence of manipulation of embryos and in-vitro fertilization. As far as I know, this technique is not used in breeding knock-out or transgenic animals (mostly mice) for experiments.

Beside ethical problems with genetic modification of animals as such, several ethical problems that may not be relevant to agriculture do occur however in applying biotechnology to experimental animals. (1) Changing the animal's DNA can have various effects on the animal's functioning. Usually those effects cannot be predicted. Therefore, in animal experiments consequences to animal welfare should be assessed for each specific case. As I already stressed, this assessment is largely dependent of the expertise of animal-welfare specialists. (2) A specific problem with the breeding of knock-out animals is the number of 'surplus' animals, i.e. animals that do not have the right genotype. From Mendelian calculations one can understand why, in order to produce one pure knock-out, at least 12 animals are wasted, and in order to produce a double knock-out, this number increases exponentially. Since homozygotic knock-out animals are often infertile after several generations, one can imagine that enormous numbers of surplus animals are a consequence of experiments with 'knock-out' animals. (3) The production of knock-out animals seems to provide scientists with almost infinite possibilities to do research. This may easily lead to a significant increase of animal experiments. (4) From a methodological point of view one may doubt whether results with knock-out animals can always be translated to human diseases. As we know by now the genetic make-up often appears to be very adaptive and is able to compensate for imperfections. Moreover, in different people a particular disease may be caused by different combinations of several genes. Therefore, one can doubt whether experiments with knock-out animals will usually lead to the sophisticated results biotechnology seems to promise.

Taking these problems together it becomes obvious that possibilities of biotechnology in animal experiments burden us with new and serious ethical problems, which to some extent are different to problems of biotechnology in agriculture. Therefore, the suggestions of Thompson for a proper approach of these problems by IACUCs seem to be of limited value. In my view, the assessment of animal experiments with transgenic or knock-out animals does not in principal differ from other assessments⁶. For reasons I have already pointed out, new ethical problems concerning the use of transgenic or knock-out animals should be recognized by DEC members but cannot be properly dealt with by the committee. Again, those ethical problems should be treated in public and governmental debates. There, members of animal-care and use committees can contribute from their specific expertise.

From these examples that help to illustrate how DECs actually function, it becomes obvious that DECs have a delicate role in the dynamics between animal experimentation, public opinion and legislation. For some it may be disappointing that animal-care and use committees do not act as moral crusaders in expelling animal experiments. I have tried to make clear that applying ethical principles that overrule utilitarian considerations is unjustified if those ethical principles are not accepted by

Parliament. In other words, institutions such as a DEC should only overrule utilitarian considerations by ethical principles if such ethical principles are enacted in laws. Nevertheless, members of animal-care and use committees could play an important role in showing the dilemmas and possible ethical viewpoints, which may lead to new laws that are shaped by those principles.

¹ In the Netherlands the abbreviation DEC stands for animal experimentation committee, not for animal ethics committee

² Comments on this paper are based on my experience as the chairman of a Dutch Animal Care and Use Committee of the Free University in Amsterdam for the last six years

³ In this context it should be recognized that many researchers genuinely care about their animals. Often the societal relevance of their research is required by themselves too. These researchers appreciate input of the DEC in meeting the three R's (reduction of animal use, refinement to reduce animal suffering, replacement of animal experiments by other methods)

⁴ In The Netherlands a long-running debate on the public accountability of DEC's concerns this issue

⁵ Exceptions are proposals where it is generally accepted that the societal benefit is in no proportion to sincere suffering of the animals. However, due to self-censorship of researchers and subsidizing institutions, these situations appear to be very rare

⁶ Even the argument that the amount of suffering caused by the genetic transformation cannot be predicted properly does not differ in principle from difficulties in predicting the suffering caused by other treatments