

Chapter 4

Animal concerns : principles

- 4.1 For many people, the principal ethical problem raised by xenotransplantation will concern the relationship between human beings and other animals. As described in Chapter 3, xenotransplantation is currently at the research stage. The research involves the use of animals to provide transplant material and also to act as experimental recipients of transplants. Should xenotransplantation develop into a successful clinical procedure it will involve the breeding and killing of animals on a large scale in order to provide organs and tissue for transplantation. In addition, the use of transgenic pigs for xenotransplantation raises questions about the genetic modification of animals to provide organs and tissue.
- 4.2 The Working Party was charged with examining the ethical issues raised by the use of animals specifically for xenografting. As a first step, the arguments for and against the use of animals for medical purposes **in general** were reviewed. These arguments are summarised briefly in the first part of the chapter. The chapter then goes on to consider whether, even if the use of animals for medical purposes in general is held to be ethically acceptable, there are particular concerns about their use for xenografting. Two issues are discussed:
- ▶ the ethical acceptability of the use, respectively, of primates, and of animals other than primates, to supply transplant material;
 - ▶ the ethical issues raised by the use of genetically modified animals to provide organs for xenotransplantation.

The use of animals for medical purposes

- 4.3 Many would endorse the view that animals have interests, particularly in the avoidance of suffering, that should be respected, but that in certain limited circumstances those interests may be outweighed by the interests of human beings provided that everything possible is done to minimise distress to the animals. In considering the ethical concerns about the use of animals for xenotransplantation, it was found necessary to explore this view in more detail. For others hold the opinion that all use of animals by human beings for medical purposes is wrong, no matter how great the benefits. The view that there should be an absolute prohibition on the use of animals for medical purposes is a minority position within UK society. It meets an equally conscientiously held view that, in certain circumstances, it is

permissible, and perhaps even required, to use animals for human benefit. But justice will not have been done to the importance and complexity of the issues involved if the arguments for and against the use of animals for medical purposes are not reviewed.

- 4.4 The essence of the problem is that, if animals are to be used for medical purposes in ways that would not be considered ethically acceptable if applied to human beings, then there must be some basis for drawing the distinction between animals and human beings. If there are no convincing reasons to ascribe to animals a lower moral status than that ascribed to human beings, then the use of animals for medical purposes would be hard to justify. In recent years, the argument has been gaining ground that animals should be accorded a higher moral status than has been admitted hitherto. Two distinct philosophical approaches may be used to support this shift in opinion. The first approach starts from the position that the interests of animals, particularly in avoiding suffering, should be taken into account when judging whether it is acceptable to use them for medical purposes that benefit human beings. The second approach argues that animals, like human beings, have rights that must be respected when considering their use for such purposes.

The balance of animal suffering and human benefit

- 4.5 It is now widely recognised that many animals, and certainly the mammals that would be used for xenografts, are susceptible to pain and suffering. Some argue that there is no logical reason to distinguish morally the pain and suffering felt by animals from that felt by human beings. Suffering is suffering wherever and to whoever it is caused. It would be wrong to weigh animal suffering less heavily than human suffering, just as it would be wrong to weigh the suffering of one human being less heavily than another.¹ This is a utilitarian argument which holds that ethically acceptable actions are those which increase the benefit, or reduce the harm, to as many individuals as possible. When judging the acceptability of the use of animals for xenotransplantation, or for any other medical purpose, a decision must be made about whether the pain and suffering caused to the animals is justified by the potential benefit to the human being.
- 4.6 In some cases, such as the use of animals for testing cosmetic products used for beauty treatments, there is widespread agreement that the benefit to human beings is trivial and does not warrant the suffering involved. But in other cases, weighing the pain and suffering to animals against the benefit to human beings is not easy. Different people will give different weight to the harms and the benefits and so will come to differing conclusions about the acceptability of using animals for a particular purpose. Despite these difficulties, however, judgements have to be made and the Working

¹ Singer P (1995) **Animal Liberation** Second edition. London: Pimlico.

Party accepts the principle that in some cases, the saving of human life or of significantly enhancing its quality may justify a certain amount of animal suffering, provided this is kept to a minimum.

Animal rights

- 4.7 According to the alternative, rights-based approach, if animals share with human beings some or all of those characteristics that, in the case of human beings, would lead us to assert that they have certain rights, then those rights should be ascribed to the animals as well.² The ascription of rights, whether to human beings or animals, rests on the principle that the lives of individuals have an inherent value. Such individuals should be treated as ends in themselves rather than merely as means to the happiness or well-being of others. The British Union for the Abolition of Vivisection wrote in their submission: “*The use of healthy animals as a source of ‘spare parts’ for humans represents a fundamental denial of the inherent value of those animals’ lives.*”
- 4.8 According to this view, there are fundamental moral constraints on what can be done to those who have rights. Such constraints should not be overridden, no matter how great the benefit accruing to others from so doing. The right to life, for example, dictates that a rights holder, human being or animal, should not be killed, however painlessly, even if countless others could potentially benefit thereby. Similarly, restrictions on the ways in which human beings may be used in medical research should extend to animal rights holders as well. Some argue that any use of animals for medical purposes is a violation of their basic rights, and as such, that it should not be countenanced. Thus, Animal Aid wrote in their submission: “*Animals have value in their own right and do not exist to be harmfully exploited by man.*” The issue of rights, however, remains controversial and is even more so in the case of animal rights. Moreover, it is not necessary to endorse the notion of animal rights in order to conclude that animals should be granted protection against certain procedures.

Self-awareness and personhood

- 4.9 Whether the argument is framed in terms of the interests or the rights of animals, the crucial point is the extent to which animals share the features supposed to be important to human interests and rights. The feature to which most importance has generally been attached is that of self-awareness.³ This may be described as the

² Regan T (1983) **The Case for Animal Rights**. London: Routledge & Kegan Paul.

³ Reviewed in Smith J A and Boyd K M eds. (1991) **Lives in the Balance : The ethics of using animals in biomedical research**. The report of a Working Party of the Institute of Medical Ethics. Oxford: Oxford University Press. In particular pp 319-23.

consciousness an individual has of his or her own condition and experiences. To be self-aware requires a high degree of intelligence, the capacity to make comparisons and judgements, and a language with which to articulate them. Self-awareness allows individuals to plan, to make choices and to engage in complex social relationships. Most significantly, for the purposes of this discussion, it has been argued that suffering and death are uniquely painful to a self-aware being who not only senses pain but can also perceive the damage being done to his or her self and future.

- 4.10 Individuals that possess these characteristics, founded in self-awareness, may be regarded as persons. Until recently, the moral status of personhood has been supposed to be the unique prerogative of human beings. On these grounds the human being is often regarded as more than a ‘mere animal’, and the human condition as fundamentally superior to that of animals. In Christian thought, human beings “*have unique significance and value because only they are made in the image of God. (Genesis 1:27)*”⁴ In this view, animals would not merit the same moral consideration as human beings, and animal interests would weigh less heavily than human interests. While great weight would be placed on the reduction of animal suffering as an end in itself, the painless killing of animals for the purposes of saving human life or improving its quality would be considered acceptable.
- 4.11 Recent research into the mental life and intelligence of non-human animals has, however, led to claims that the features qualifying human beings for personhood are also present, to varying degrees, in other species.^{5, 6} There is evidence that some animals, notably the higher primates, have much in common with human beings, including self-awareness, complex social relationships and many of the other characteristics that have often been supposed to make human beings unique.⁷ If that is so, then these animals should be accorded the same moral status as human beings.
- 4.12 On the other hand, certain human individuals, whether due to congenital defects, accident or disease, lack the features such as self-awareness and intelligence that are generally taken as criteria for personhood. Thus, the boundaries of personhood and of the human species do not exactly coincide, but rather overlap. Some non-human animals might be considered persons and some human beings might not be considered persons.

⁴ Submission to the Working Party from the Christian Medical Fellowship.

⁵ Singer P (1995) **Animal Liberation** Second edition. London: Pimlico.

⁶ Regan T (1983) **The Case for Animal Rights**. London: Routledge & Kegan Paul.

⁷ Parker S and Gibson K eds. (1990) “**Language” and intelligence in monkeys and apes**. Cambridge: Cambridge University Press.

Speciesism and the moral community

- 4.13 According to this argument, the capacities of human beings and some non-human animals, such as higher primates, may overlap to such an extent that there is no basis for a distinction of treatment. To deny this implication, it is argued, is simply to draw a distinction on the ground that one individual is of the human species and another is of a non-human species. Such speciesism, some have claimed, is no more acceptable than racism or sexism.⁸ Stephen Clark wrote in his submission: “*Till the eighteenth century every civilised society kept human slaves. Those of us who have tried to absorb the implication of Darwinian theory (that species are not natural kinds) suspect that our descendants will be just as critical of our casual contempt for those we know to be our cousins.*” For those who wish to press the charge of speciesism there are two further implications. One is that non-human animals whose capacities match those of human beings should be included within the moral community. A second implication is that it would not be appropriate to include within the moral community human beings whose capacities do not qualify them for personhood. It has been argued, for example, that anencephalic babies, suffering from a fatal neurological condition in which the cerebral hemispheres of the brain are absent, are not persons. Some would regard it as acceptable to use such babies to provide organs for transplantation.⁹ It is even argued that to use animals that qualify as persons for medical purposes, rather than human beings that do not, is morally unacceptable.¹⁰
- 4.14 This second implication leads many to caution against the use of animals as sources of organs for transplantation, since to do so is to embark upon a ‘slippery slope’.¹¹ Once the use of animals is sanctioned, it is argued, then there can be no principled objections, for example, to the procurement of organs from anencephalic human babies. For many people, the idea that **any** human being could be used in such a way is deeply abhorrent. Similar sentiments underlie the protection, extended to all human beings, from uncontrolled use in medical research, and the prohibition on using organs from human beings except under conditions of consent. It can be argued that vulnerable individuals, such as anencephalic babies, are more deserving of protection not less so.¹² These sentiments are too strong to be easily cast aside.
- 4.15 Thus the notion of speciesism has to be treated with some caution. Our natural emotional response to, and concern for, members of our own species is clearly built deeply into our nature and it is not clear that the option of responding to members

⁸ Singer P (1995) **Animal Liberation** Second edition. London: Pimlico.

⁹ British Medical Association’s Ethics, Science and Information Division (1993) **Medical Ethics Today: Its practice and philosophy**. London: BMJ Publishing Group. p 27.

¹⁰ Frey R G (1987) Animal Parts, Human Wholes : On the use of animals as a source of organs for human transplants. **Biomedical Ethics Reviews**, pp 89-107.

¹¹ A point made by Meg Stacey in her submission to the Working Party.

¹² A point made by Jeremy Caddick in his submission to the Working Party.

of other species, with the same concern in every case, is open to us. We should consider therefore what our treatment of non-human animals should be in its own terms, rather than in terms of consistency with our treatment of human beings.

Relationships

- 4.16 Arguably the moral status of human beings depends not only on their individual capacities but also on the histories of their relationships with others. Thus, although an anencephalic baby might be considered to lack the capacities or potentials necessary for personhood, it is nevertheless bound to particular human parents and, through them, to a wider set of people, in deep networks of emotion and attachment. These relationships with parents and others would draw it into the moral community. In general, then, human beings cannot be understood or treated as though each were an isolated, self-contained entity, whose rights and responsibilities, or well-being and suffering, could be assessed independently of his or her involvement with others.
- 4.17 This argument could apply, moreover, not only to relationships among human beings but also to relationships between human beings and animals. In this context it is important to distinguish between **relationship** and **relatedness**. It might be expected that the non-human animals most likely to have the capacities necessary for personhood, and therefore to be eligible for inclusion within the moral community, would be individuals of species most closely related to humankind – above all, higher primates such as chimpanzees and baboons. In practice, however, we may be more ready to include familiar, domestic animals than unfamiliar primates, even though the latter are much closer to human beings in a biological sense. This is because the personhood of the animal is seen to derive from its involvement with human beings (most obvious in the case of pets), rather than from its underlying genetic relatedness to human beings. When relationships are taken into account, pet dogs or cats, or indeed farm animals such as pigs, may well seem more person-like than baboons or chimpanzees. This is reflected in the special legal protection extended to dogs, cats and horses, as well as primates, in the UK.¹³
- 4.18 Animals may also form relationships among themselves. Just as in assessing the well-being or suffering of human beings it is necessary to take into account their relationships with others, the same may be true in the case of animals as well. A chimpanzee mother suffers grief at the loss of her offspring: to harm her offspring causes harm to the mother. If animals are to be killed to provide organs for transplantation, or otherwise used for medical purposes, and if these animals form social relationships with one another, then the pain and suffering caused to others by the harm done to an individual animal cannot be disregarded.

¹³ Animal (Scientific Procedures) Act 1986 : Section 10.

Attitudes to nature

- 4.19 Arguments for and against the use of animals for medical purposes also have to be placed in the context of differing views about the relationship of human beings to nature in general. Those who favour using animals in medicine have been accused by their opponents of adopting a wholly instrumental attitude towards nature, and of failing to recognise that human beings are part of the natural world and have responsibilities for it. The Genetics Forum wrote in their submission: *“The use of animals as sources of cells, tissues and organs for humans causes us much concern. It encourages the concept of animals as ‘pharm’ factories and reinforces the ethos that they merely exist in order to satisfy human needs.”*
- 4.20 As an alternative, critics advocate a concept of stewardship, according to which human beings should not seek to dominate nature but should instead stand in a relationship of care and concern for its continued flourishing. Another, not incompatible, view is that human beings should see themselves not as separate from nature but as a small part of a larger world.¹⁴ For some people, these views would be compatible with the limited use of animals in medical procedures where the benefit was clear, demonstrable and large. For others, these views might entail a direct prohibition on the use of animals for medical purposes. The argument might turn, in part, upon scale. Thus, it might be held that the limited use of animals in current medical procedures does not abuse the human relationship with nature. But procedures involving the use of animals on a large scale, such as xenotransplantation if it were successful, would be unacceptable.
- 4.21 Another element of this argument might depend on a distinction between customary and new practices. New uses of animals might be objectionable in the way that existing uses, provided that they are not cruel, are not. In their submission to the Working Party, the Farmers’ Forum (a discussion group of Christian farmers) expressed an objection to rearing animals solely for the purposes of xenotransplantation. For some, a completely new use of animals, such as for xenografting, might be unacceptable, whereas if that use developed from, and was continuous with, an established use of animals, then it might be more acceptable. It is important not simply to be prejudiced against innovation, however, and some would question the ethical acceptability of established practices involving animals, such as eating meat. The Church of Scotland pointed out in their submission: *“There is also a ‘naturalness’ argument here. It is a basic fact of life that everyone has to eat to live. We may debate whether eating animals by humans is acceptable, but it is clearly ‘natural’ in the sense that many animals are also carnivores. It is not ‘natural’ to use an animal as spare parts. It is human artifice. That is not to say it is wrong, but it is not the same as eating an animal.”*¹⁵

¹⁴ Goodin R E (1992) **Green Political Theory**. Cambridge: Polity Press.

¹⁵ Submission to the Working Party from the Working Group on Genetic Engineering in Non-human Life Forms of the Society, Religion & Technology Project of the Church of Scotland.

- 4.22 How far should public policy be based on concerns about the underlying attitudes that the development of a particular technology is thought to reveal? If human beings have not got their relationship with the rest of nature right, and if there is continual unjustifiable exploitation of other species for human use, then it would be wrong to allow the development of a new technology that increased this exploitation. Innovation may be undertaken for a variety of motives, however, and it is not easy to determine, from people's actions, what their attitudes are. But there is undoubted force in the moral argument that rests upon the question: what sort of people do our social and technical practices reveal us to be? If we do not like what we see when we look honestly in the mirror, then there is cause for thought at least.

Conscientious objections to the use of animals for medical purposes

- 4.23 Some people may oppose the use of animals for medical purposes because of particular religious or metaphysical views. For example, the Jain Academy wrote that "*Jains are against all animal experimentation and use of animal cells, tissues and organs, as it is against all the principles of reverence for life and non-violence.*" Where convictions of this kind rest upon metaphysical assumptions that are not widely shared, they cannot easily be made the basis of public policy. People's opinions about the use of animals for medical purposes, whether or not articulated in the name of a religious faith, are highly diverse, as the submissions received by the Working Party reveal. The Medical Ethics Group of the Reform Synagogues of Great Britain wrote in their submission: "*Yet whereas we are expected to do everything possible to prevent [animal] suffering there is no doubt that our duty to human beings outweighs that to animals*".
- 4.24 A more specific issue is raised by the proposed use of pigs for xenotransplantation. Would the use of animals regarded as ritually unclean be ethically acceptable? The Chairman of the Sharia Council has explained that under Islamic law, while eating pigs is forbidden, other uses can be assumed to be permitted.¹⁶ Indeed, even eating pigs is permitted if this is necessary to save life. Similarly, the Reform Synagogues of Great Britain indicated in their submission to the Working Party that the mainstream Jewish authorities would accept the use of pigs in order to save life. Thus, xenotransplantation of pig organs and tissue, as a life-preserving treatment, would be acceptable. Nevertheless, some people viewing pigs as unclean may have objections to their use for xenotransplantation. The Union of Muslim Organisations of UK and Eire wrote in their submission that xenografts "*might be allowed provided the animal used is not a pig or other prohibited animal*". Thus, there may be, quite legitimately, a range of positions with regard to xenotransplantation even within one

¹⁶ Zaki Badawi explains the Islamic position. **The Guardian**, 25 August 1995.

religion. These diverse opinions highlight the importance of taking account of different attitudes towards xenotransplantation. This issue is discussed further in Chapter 7 (paragraph 7.27 - 7.33).

The use of animals for medical purposes: conclusions

4.25 The ethical issues raised by the use of animals in medical research are complicated and, in this chapter, the arguments are briefly reviewed. The issues have been discussed at length in the book **Lives in the Balance: The ethics of using animals in biomedical research**¹⁷ produced by a Working Party of the Institute of Medical Ethics. That Working Party produced the following statement:

“The Working Party contains a variety of views on the moral status of animals but is prepared to accept for the present that biomedical research using animal subjects is justified as an undesirable but unavoidable necessity. This working agreement extends to the following points:

- 1 *In the absence of any scientifically and morally acceptable alternative, some use of animals in biomedical research can be justified as necessary to safeguard and improve the health and alleviate the suffering of human beings and animals.*
- 2 *The benefits, in turn, depend on the advancement of fundamental scientific knowledge but even when no therapeutic or other practical benefit can yet be derived from it, any significant advance in scientific knowledge is a good, and **may** serve as a justification for using animals to that end.*
- 3 *However, not every projected improvement to human health or addition to scientific knowledge is sufficiently significant to justify every use of animals. Some uses of animals may have adverse effects too serious to justify them at all, while in other cases the adverse effects may be considered disproportionately serious in relation to the significance of the results gained.*
- 4 *In the latter case especially, both the potential benefits of a particular research project and the likelihood of the project achieving those benefits need to be assessed carefully before they, in turn, are weighed against the likely adverse effects to the animals.”*

¹⁷ Smith J A and Boyd K M eds. (1991) **Lives in the Balance : The ethics of using animals in biomedical research.** The Report of a Working Party of the Institute of Medical Ethics. Oxford: Oxford University Press. pp 310-11.

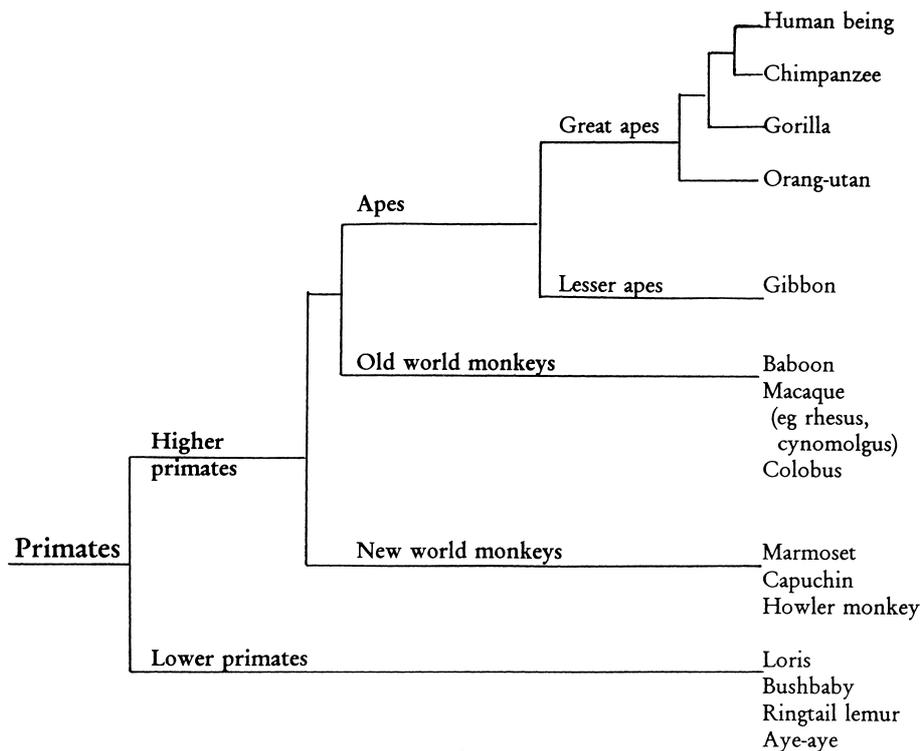
- 4.26 All members of the present Working Party are prepared to accept the statement of the Institute of Medical Ethics Working Party, though they differ in the detailed interpretation of the judgements implied in them. Another Committee, which examined the ethical implications of emerging technologies in the breeding of farm animals, reached similar conclusions, stating that the use of animals is permissible providing that use is humane, but that “*harms of a certain degree and kind ought under no circumstances to be inflicted on an animal.*”¹⁸ Of paramount importance is the need to keep to a minimum any suffering or pain experienced by the animals. This is discussed at length in Chapter 5. It is also important to keep the number of animals used to a minimum, and to find alternatives to the use of animals where possible.
- 4.27 For those who do not accept the use of animals for medical purposes, xenotransplantation will, in principle, be unacceptable. The Working Party does not take this view and considers that some use of animals for xenotransplantation can be justified in principle. There are specific issues, however, that need further consideration. In what follows the particular ethical implications of the use of primates for xenotransplantation are considered. Attention has focused on the pig as an alternative to the use of primates for xenotransplantation (paragraph 3.4). In the final part of this chapter the ethical issues associated with the use of pigs for xenotransplantation are discussed, including those issues arising from their genetic modification for this purpose (paragraphs 4.42 - 4.54).

Concerns about the use of primates for xenotransplantation

- 4.28 Because of the genetic closeness of higher primates to human beings, their organs and tissue are likely to offer a good chance of success for xenotransplantation (paragraphs 3.18 - 3.20). With a suitable immunosuppressant drug regime, it may become possible to transplant primate organs and tissues reliably and effectively. If xenotransplantation using primate organs and tissue subsequently became widespread, this would represent a significant and new way of using primates. Currently, in the UK, the use of primates is very strictly controlled with only very small numbers being used for research purposes (paragraphs 4.37). Thus, to breed primates on a large scale would be contrary to currently accepted practice in the UK. As such, the ethical issues raised by the use of primates for xenotransplantation require exploring in some detail.
- 4.29 The very reason that makes primates appear to be well suited for transplantation, namely their evolutionary relatedness to human beings, also leads many people to think that it would be wrong to use them for this purpose. A simplified diagram showing the evolutionary relationships between different primate species is shown in Figure 4.1.

¹⁸ Banner M (Chairman) (1995) **Report of the Committee to Consider the Ethical Implications of Emerging Technologies in the Breeding of Farm Animals**. London: HMSO. p 1.

Figure 4.1 The evolutionary relationships between primate species¹⁹



The characteristics, for example, of intelligence and complex social interactions, of these closely related higher primates appear to be so like those of human beings that using members of those species as sources for xenotransplantation might well be seen as ethically unacceptable. Many have argued that the same concern should be extended to higher primates as is extended to human beings. The question then is how far this concern should extend. The close evolutionary relationship of higher primates with human beings suggests that they will share the capacity for self-awareness to the highest degree, and there is good scientific evidence that this is the case. Some would argue, however, that any ethical reservations about using higher primates for xenotransplantation should apply much more broadly. Many non-primate species, possibly including pigs, display comparable capacities of intelligence and sociality, albeit in forms that less closely resemble the human and thus appeal less strongly to human moral sensibility. To limit reservations to those species closest to human beings, in this view, is to be swayed by sentimental anthropomorphism.

¹⁹ Adapted from Byrne R (1995) **The Thinking Ape : evolutionary origins of intelligence**. Oxford: Oxford University Press.

- 4.30 Contrary to both the above positions, there is a view that, notwithstanding the features that primates (or other species) share with human beings, it would still be wrong not to save a human life even if the price of so doing was the life of a primate. According to this position, human life has the greater value, and therefore the primate's life can be legitimately sacrificed.
- 4.31 It is difficult to know what sort of argument would resolve this disagreement of value. For the question is whether there is sufficient likeness between human beings and other primates for the same constraints to be imposed upon the use of primates as are imposed upon human beings. This question of likeness is not amenable to empirical resolution, but is one of fundamental moral judgement. The difficulty of resolving the issue is reflected in the diversity of opinions that people hold on the matter. Some consider that there is sufficient difference between the moral value of human life and the value of higher primate life to make the use of the latter acceptable in certain circumstances. Yet many who take this view would nevertheless argue that higher primates should be used only in very restricted and carefully controlled circumstances and only if, for example, the use of pigs for xenotransplantation turned out not to be possible. Others argue that the resemblance between human beings and species like chimpanzees and baboons is too close to justify the use of such primates as a source of material for xenotransplantation. Yet many of these people would accept that no clear boundary separates animals whose use is acceptable from those whose use is not acceptable. This dilemma concerning the moral distinction between human beings and primates is extremely difficult to resolve. In addition to this fundamental judgement of value, however, there are a number of other considerations that contribute to determining the ethical acceptability of using primates to provide organs for xenotransplantation. These are discussed below.

Welfare

- 4.32 The similarities in behaviour between human beings and other primates may not lead to a consensus about their relative moral status. But they undoubtedly highlight the importance of welfare considerations in the use of primates for xenotransplantation. The routine breeding and maintenance of animals free from infectious organisms might require birth by Caesarean section, rearing in isolation, and repeated monitoring to assess levels of infection (paragraphs 5.18 - 5.22). The intelligent and social nature of primates would make such conditions particularly severe for them.

Conservation

- 4.33 In the case of chimpanzees, which are an endangered species, strong conservationist concerns suggest that their use for xenotransplantation should be forbidden. While chimpanzees have been used to provide organs for xenotransplantation in the past, there is now an international consensus within the xenotransplantation community that the use of chimpanzees for providing organs is unacceptable on conservation grounds alone.
- 4.34 Conservation concerns do not currently apply to baboons, which are not endangered at present, and which are, in fact, regarded as a pest in many parts of the world. Might baboons become endangered if they were to be used as a source of organs for xenotransplantation? Capture of wild baboons for use as a source of organs is unlikely because of the need to ensure that the animals used for xenotransplantation are free of disease (Chapter 6). Like all primates, however, baboons breed slowly, with breeding females producing a maximum of one offspring every 15 months.²⁰ Because of this slow rate of reproduction, the current colonies of baboons would probably not be able to provide sufficient numbers with which to establish breeding colonies of disease-free baboons to supply organs for xenotransplantation. It would be necessary to capture wild baboons to augment these breeding colonies.
- 4.35 In contrast to chimpanzees, baboons are relatively easy to catch and transport. They also adapt well to captivity and breeding colonies are not difficult to establish. With the unmet demand for organs for transplantation in the US alone estimated to be 100,000 every year,²¹ however, establishing breeding colonies of baboons to provide organs for transplantation would require the capture of large numbers of animals. Hence, although baboons are abundant at present, their use to provide organs for xenotransplantation might have a significant effect on their numbers. It should also be borne in mind that deforestation is destroying the natural habitat of all primates. Baboons, being tough and adaptable, can survive in other habitats, but large-scale capture for xenotransplantation would be one more pressure. Moreover, it is possible that, if xenotransplantation involving baboons were seen to be successful, there would be renewed interest in attempts to use chimpanzees for xenotransplantation. This might lead to increased pressure on the endangered chimpanzee population.

²⁰ Whitney R A and Wickings E J (1987) Macaques and other old world simians, Chapter 40 of **The UFAW Handbook on the Care and Management of Laboratory Animals** Sixth Edition. UK: Longman Scientific & Technical.

²¹ From the belly of the beast. **The Economist**, 21 October 1995, pp 137-9.

Safety

- 4.36 The safety of the use of primate organs and tissue for xenotransplantation must also be considered. A risk associated with the transplantation of animal organs or tissue into human beings is that infectious organisms will also be transmitted into the human population, leading to the emergence of new diseases. Because of the biological similarity between human beings and other primates, the risk that infectious organisms from a primate will be able to infect and cause disease in human beings is greater than the risk of disease transmission from, say, pigs to human beings. There is evidence that infectious organisms do, indeed, pass from primates to human beings and cause disease.²² This suggests that a cautious attitude should be adopted to xenotransplantation involving primates (paragraphs 6.10 - 6.12).

The use of primates for xenotransplantation: conclusions

- 4.37 Serious ethical concerns are raised by the possible use of primates for xenotransplantation. The sophisticated capacities of primates suggest that any harm suffered by them should be given great weight. This position is reflected in the principles underlying current practice in the UK. Wherever possible, primates used for medical purposes must be purpose-bred.²³ Very few licences allowing primate use are awarded: only 29 in 1994. The use of wild-caught primates for medical purposes requires “*exceptional and specific justification*”.²⁴ **The Working Party endorses the special protection afforded to higher primates used for medical and scientific purposes.**
- 4.38 The Working Party would accept the use of very small numbers of primates **as recipients of organs** for research during the development of xenotransplantation using non-primate animals as sources of organs. In this case, the harm caused by using a small number of primates for research into xenotransplantation, while undesirable, can be justified by the potential benefits if xenotransplantation were to become a successful procedure.
- 4.39 The routine use of higher primates to supply organs for xenotransplantation on a scale sufficient to meet the organ shortage would represent a new use of primates in the UK. In contrast to the use of primates for research purposes, this would entail the use of relatively large numbers of animals, not for a short period during the development of a procedure, but for the long term. As discussed above, in addition to the special weight given to the harm suffered by primates, additional concerns

²² Allan J S (1995) Xenotransplantation at a crossroads: Prevention versus progress. **Nature Medicine**, 2: 18-21.

²³ Animals (Scientific Procedures) Act 1986: Section 7.

²⁴ **Report of the Animal Procedures Committee for 1994** (1995) London: HMSO Cm 2996, p 7.

must be taken into account. The potential risk of extinction, even to species like the baboon that are not currently endangered, must be taken seriously. Xenotransplantation using primate organs or tissue may pose particular risks of disease transmission.

4.40 Given the ethical concerns raised by the use of primates for xenotransplantation, attention has turned to developing the pig as an alternative source of organs and tissue. As discussed below, in the view of the Working Party, the use of pigs for xenotransplantation raises fewer ethical concerns. To develop the use of primates for xenotransplantation, when there is an ethically acceptable alternative, would not be justifiable. **The Working Party recommends that non-primate species should be regarded as the source animals of choice for xenotransplantation.** However, possibilities for alleviating the organ shortage which do not involve the use of animals, such as increased donation of human organs and the development of artificial organs and tissue, should be actively pursued.

4.41 The Working Party would like to draw attention to a longer-term issue. It is possible that, after a number of years of research, it would be found that the use of pigs could not deliver effective, reliable and safe organs and tissue for transplantation. Would it then be ethically acceptable to use primate organs and tissue for xenotransplantation? The members of the Working Party were agreed that the use of primates would be ethically **unacceptable** if **any** of the following conditions obtained:

- ▶ improving the supply of human organs and tissue and the use of alternatives, such as mechanical organs and tissue replacement, could meet the organ shortage;
- ▶ the use of higher primates would result in them becoming an endangered species;
- ▶ concerns about the possible transmission of disease from higher primates to human beings could not be met; or
- ▶ the welfare of the animals could not be maintained to a high standard.

These conditions would rule out all use of chimpanzees on conservation grounds. When considering the hypothetical situation in which the conditions might be satisfied for a species such as the baboon, the members of the Working Party found that their opinions did not coincide on what would be the correct course. Some felt that the use of primates to supply organs for xenotransplantation would never be acceptable. Other members of the Working Party felt that, should these circumstances come to prevail, it would be appropriate to reconsider the use of higher primates to supply organs for xenotransplantation. This division of opinion may reflect an ethical dilemma that is currently unresolved for many people.

The use of pigs for xenotransplantation

- 4.42 The main alternative to using primates for xenotransplantation is to use pigs (paragraph 3.4). Thus, the moral justification for using pigs to provide organs for xenotransplantation must be considered. When considering the use of primates for xenotransplantation, the capacities they share with human beings, notably their self-awareness, led to ethical concerns about their use for xenotransplantation. While unquestionably intelligent and sociable animals,²⁵ there is less evidence that pigs share capacities with human beings to the extent that primates do. As such, the adverse effects suffered by the pigs used to supply organs for xenotransplantation would not outweigh the potential benefits to human beings. In the UK, the breeding of pigs for human use is well established. It is difficult to see how, in a society in which the breeding of pigs for food and clothing is accepted, their use for life-saving medical procedures such as xenotransplantation could be unacceptable. **The Working Party concluded that the use of pigs for the routine supply of organs for xenotransplantation was ethically acceptable.**
- 4.43 In order for it to be ethically acceptable to use pigs for xenotransplantation it will be necessary to ensure that the conditions in which they are bred and reared are of the highest possible standard from the point of view of welfare, and that any pain and suffering is kept to a minimum. Animal welfare issues are discussed in Chapter 5.
- 4.44 If pigs are to be used for xenotransplantation, they are likely to have been modified so that they contain genetic material of human origin (paragraphs 3.24 - 3.32). The next section discusses the ethical concerns that may arise from the use of transgenic animals for xenografting.

The use of transgenic animals for xenotransplantation

- 4.45 The essence of transgenesis is that a gene from one species is incorporated into another. The transferred gene enables the transgenic animal to produce a particular protein. The transgenic pigs bred for xenotransplantation contain a human gene which produces a complement regulating protein. This reduces the immune response to transplanted organs (paragraphs 3.24 - 3.29). It is around the transfer of genetic material that ethical concerns turn. One UK study, of schoolchildren aged 14 - 16, found that they were particularly concerned about genetic modification of farm animals.²⁶ Some see the production of transgenic animals as an unnatural act that attempts to change the nature of animals and violates species boundaries. According to this view, genes have a particular significance because they contain the information

²⁵ Singer P (1995) **Animal Liberation** Second edition. London: Pimlico. pp 119-29.

²⁶ Lock R and Miles C (1993) Biotechnology and genetic engineering: students' knowledge and attitudes. **Journal of Biological Education**, 27, 267-72.

that determines the essence of any one species. To move genes around is to destroy the integrity of species as natural kinds, and to create unnatural hybrids. Within the Judaeo-Christian tradition human beings are seen as being created in the image of God which leads, for some, to a specific objection to experimentation using God-like human genes.²⁷ For others such “*‘mutilation’ of the human body*” would be sanctioned in the interests of saving life.²⁸ A number of arguments, however, suggest that the production of transgenic animals need not be viewed as a drastic or unnatural procedure. The issues have been thoroughly examined by two committees set up by the Ministry of Agriculture, Fish and Food.^{29, 30}

- 4.46 First, species boundaries are not, in fact, inviolate, but change as evolution occurs. Some regard transgenic techniques as no more than an extension of traditional breeding techniques that artificially produce new animal breeds.³¹ There is also evidence that, at a low level, the transfer of genetic material from one species to another occurs naturally. For example, genetic material may be transferred between different types of bacteria. Some would question whether there is any significant qualitative difference between this type of event and the transfer of genetic material from human beings into pigs.
- 4.47 Second, it can be questioned whether genes of human origin represent particular elements of essential humanity. It is only in combination with all the other genes that make up the human genome that a particular gene contributes to the specification of features characteristic of the human species. Considered in isolation, therefore, there is nothing specifically human about a gene that has been obtained from a human source. Similarly, genes obtained from an animal species do not have to be seen as representing a particular element of that animal. If this view is adopted, the transfer of a gene from one species to another is far less significant. In addition, because of the technology involved, the genetic material actually transferred to a transgenic animal is almost certain to be a copy of the gene rather than the original gene that was obtained from the organism.³²
- 4.48 In addition, many transgenic animals are modified on a very small scale and in a very specific way. Consider the production of transgenic pigs to supply organs for xenotransplantation. At present, it is unlikely that more than one or two genes of

²⁷ A view set out by R. Gill in his submission to the Working Party.

²⁸ Submission of the Reform Synagogues of Great Britain.

²⁹ Polkinghorne J (Chairman) (1993) **Report of the Committee on the Ethics of Genetic Modification and Food Use**. London: HMSO.

³⁰ Banner M (Chairman) (1995) **Report of the Committee to Consider the Ethical Implications of Emerging Technologies in the Breeding of Farm Animals**. London: HMSO.

³¹ A point made in the submission from the Church in Wales.

³² Polkinghorne J (Chairman) (1993) **Report of the Committee on the Ethics of Genetic Modification and Food Use**. London: HMSO, pp 5-6.

human origin will be incorporated into transgenic pigs. Since the pig genome probably contains in the order of 50,000 - 100,000 genes, this is proportionately a very small change.³³ In addition, the human genes contain information that will make only a very minor and specific alteration to the surface antigens of the pig's cells (paragraph 3.25). The physical appearance and characteristics of the pig will not change in any measurable sense. Will the nature of the pig change in any way that is ethically important? For the reasons set out above, the Working Party does not consider that the introduction of very small numbers of human genes into transgenic pigs makes the pigs in any sense human or creates a hybrid species. Similar conclusions were reached by both the Polkinghorne and the Banner Committees. Inserting small quantities of genetic material of human origin was not thought to make an animal in any sense human. The Banner Committee concluded that procedures that failed "*to respect the natural characteristics, dignity and worth of animals*" would be objectionable.³⁴ While this might rule out the use of transgenesis to produce pigs with altered behaviour, for example reduced sentience, the Banner Committee considered the production of transgenic pigs for xenotransplantation acceptable. The Polkinghorne Committee reported that, for many people, whether genetic modification is acceptable would depend on whether it was intended to preserve or enhance human life.³⁵ By this criterion the production of transgenic pigs to provide organs for xenotransplantation would be acceptable.

- 4.49 In the light of the arguments discussed above, **the Working Party concluded that the use of transgenic pigs that have been genetically modified to reduce the human immune response to pig organs was ethically acceptable.** As with any use of animals for medical purposes, it is important that the welfare of transgenic animals is not unacceptably compromised. This is of particular concern in the context of transgenesis because some of the transgenic animals produced to date have suffered from ill effects. One example is the introduction of growth genes into pigs in order to make them grow faster for food production. The animals suffered from a variety of conditions such as arthritis, ulcers and diabetes.³⁶ There is no evidence to date that the welfare of transgenic pigs developed for xenotransplantation is adversely affected.³⁷ It is important, however, to be vigilant in assessing the effects of transgenesis on animal welfare. Monitoring the welfare of transgenic pigs for xenotransplantation is discussed in Chapter 5 (paragraphs 5.9 - 5.17).

³³ Polkinghorne J (Chairman) (1993) **Report of the Committee on the Ethics of Genetic Modification and Food Use.** London: HMSO, p 9.

³⁴ Banner M (Chairman) (1995) **Report of the Committee to Consider the Ethical Implications of Emerging Technologies in the Breeding of Farm Animals.** London: HMSO, p 1.

³⁵ Polkinghorne J (Chairman) (1993) **Report of the Committee on the Ethics of Genetic Modification and Food Use.** London: HMSO, p 9.

³⁶ Reiss M and Straughan R (1996) **Improving Nature? The science and ethics of genetic engineering.** Cambridge: Cambridge University Press.

³⁷ Cozzi E and White D J G (1995) The generation of transgenic pigs as potential organ donors for humans. **Nature Medicine**, 1:964-6.

- 4.50 Considerable concern about transgenic organisms has turned on the potential risks to the environment should they escape or be released. Some organisms, such as micro-organisms, are not easily contained. Other organisms may have advantages over their unmodified counterparts: for example, transgenic salmon have been produced that grow much faster than unmodified salmon. Initially, at least, transgenic pigs produced for xenotransplantation are likely to be few in number, commercially valuable, relatively easily contained, and with no growth advantage over unmodified pigs. This means that they are unlikely to be made commercially available on the general agricultural market, to escape, or to cause problems if they do escape. Should xenotransplantation become more widespread, it is possible that surpluses of transgenic pigs may arise, and at this point, whether or not they should be made available on the general agricultural market may become an issue.
- 4.51 The production of transgenic animals is regulated by the Animals (Scientific Procedures) Act 1986 (paragraphs 5.2 - 5.4). To date, relatively few strains of transgenic farm animals have been produced, and none of them have been released from the control of the Act. Were any transgenic animals to be released from control of the Act, a regulatory framework is in place to control the release of genetically modified organisms into the environment. The Advisory Committee on Genetic Modification and the Advisory Committee on Releases to the Environment would advise on such matters. The Genetically Modified Organisms (Deliberate Release) Regulations 1992 and 1993 would require that consent is obtained from the Department of the Environment before transgenic animals were made available or sold, and the Health and Safety Executive would require notification.³⁸
- 4.52 The most likely purpose of making surplus transgenic pigs available on the general agricultural market would be their sale for food. The Polkinghorne Committee concluded that it was acceptable that surplus transgenic animals produced for medical purposes should be used as food rather than discarded needlessly.³⁹ Both the Advisory Committee on Novel Foods and Processes, and the Food Advisory Committee would advise on the use for food of transgenic pigs produced for xenotransplantation. Should the food use of transgenic pigs or other farm animals be approved, labelling would be required to allow consumers to exercise choice about whether they eat food from genetically modified animals.
- 4.53 Should their organs and tissue be effective for xenotransplantation, applications may be made to patent transgenic pig strains. There has been much discussion about whether patenting transgenic animals is ethical, and whether it is legal under current patent law.⁴⁰ In Europe, patent law is governed by the European Patent

³⁸ Health & Safety (Genetic Manipulation) Regulations (1978).

³⁹ Polkinghorne J (Chairman) (1993) **Report of the Committee on the Ethics of Genetic Modification and Food Use**. London: HMSO, p 15.

⁴⁰ Is this the work of man or nature? **Independent**, 20 November 1995.

Convention and patents are granted by the European Patent Office. In 1992, the European Patent Office granted a patent for the Harvard Oncomouse, a transgenic mouse strain that has been genetically modified so that it has a predisposition to cancer. The decision provoked widespread protests from animal welfare and environmentalist groups and the European Patent Office has heard evidence relating to 17 different appeals against the patent.⁴¹ The verdict on the appeals is still awaited. At the same time, the European Commission is trying to clarify the situation with a directive that would allow patents on genetically altered animals and plants.⁴² The directive has been submitted to the Council of Ministers and the European Parliament for their approval, but a similar directive has previously been rejected by the Parliament.

- 4.54 A detailed discussion of the ethics of patenting transgenic animals lies outside the scope of this report. The issues have been examined in some detail in a previous report of the Nuffield Council on Bioethics, and elsewhere.^{43,44} Proposals to patent transgenic pigs produced for xenotransplantation would increase the debate about the morality and legality of patenting transgenic animals. This adds force to the recommendation of the Nuffield Council in their previous report “*that the Government joins with other member states of the European Patent Convention (EPC) in adopting a protocol to the EPC which would set out in some detail the criteria to be used by national courts when applying the immorality exclusion to patents in the area of human and animal tissue.*”⁴³

⁴¹ Oncomouse hearing ends up in confusion (1995) **Nature**, 378:427.

⁴² European proposal reopens debate over patenting of human genes (1995) **Nature**, 378:765.

⁴³ Nuffield Council on Bioethics (1995) Patent Issues, Chapter 11 in **Human Tissue : Ethical and Legal Issues**.

⁴⁴ National Academies Policy Advisory Group (1995) **Intellectual Property & the Academic Community**.