

Chapter 10

Conclusions and recommendations

- 10.1 There is considerable interest in the transplantation of animal organs or tissue as a means of reducing the shortage of human organs and tissue for transplantation. Transplantation is an important and successful procedure in modern health care. It provides significant benefits to patients, both extending life expectancy and improving quality of life (Chapter 1). Debate continues about how to reduce the gap between the demand for transplantation and the shortage of human organs and tissue (Chapter 2). The benefits of preventive measures to improve health and prevent the diseases requiring treatment by transplantation are likely to be long-term ones (paragraphs 2.2 - 2.3). Some of the suggested measures for increasing the supply of human organs, such as changing the consent requirements, are not without ethical and practical difficulties (paragraphs 2.4 - 2.10). Even radically innovative measures to increase rates of human organ donation are likely to be insufficient to bridge the gap between supply and demand. The gap is, if anything, likely to widen, not least because improvements in surgical and medical techniques will permit a larger range of patients to be treated by transplantation.
- 10.2 Thus, there is interest in alternative ways of meeting the organ shortage. Mechanical devices, notably battery-powered hearts, have made great advances in recent years, and may be expected to develop further (paragraphs 2.11 - 2.21). They are prone to problems, however, associated with increased risks of infection and of blood clotting. Mechanical devices are also unlikely to be able to take the place of some human organs, such as the liver, which has sophisticated biochemical functions. Tissue engineering techniques, in which living cells are used to produce replacement organs and tissue, are promising, but still in the early stages of development (paragraphs 2.22 - 2.31). Skin can now be replaced by tissue engineering, but the development of bioengineered heart valves, much less functioning organs, is a more distant prospect.
- 10.3 Xenotransplantation of animal organs and tissues is an alternative option for reducing the shortage of human organs and tissue for transplantation. The strong immune response to animal organs or tissue, however, means that transplant rejection is a major problem and, to date, xenotransplantation involving human recipients has not been successful (Table 3.1). An exception is the routine transplantation of pig heart valves. These can be treated so they do not cause such a strong immune response. Two main strategies have been used to try and prevent xenograft rejection. In the US, attempts have been made to use organs and tissue from primates, such as baboons, for xenotransplantation. Since, biologically speaking, primates are closely related to human beings, the immune response to a primate xenograft is not that

much stronger than the response to a poorly matched human transplant. In December 1995, an AIDS sufferer from the US received a transplant of baboon bone marrow in the hope that this would restore the function of his bone marrow (paragraphs 3.18 - 3.21).

- 10.4 Ethical concerns about the use of primates for xenotransplantation have led to attempts to develop non-primates as sources of organs and tissue. Attention has focused in particular on pigs, since their organs are comparable in size to human ones, and they breed rapidly and could thus be used to supply transplant material on a large scale. Since pigs are less closely related to human beings than primates, the immune response to pig xenografts is rapid and severe. Attempts are being made to modify pigs genetically so that their organs do not cause such a strong immune response when transplanted into human beings (paragraphs 3.24 - 3.32). Hearts from these transgenic pigs last longer than unmodified organs when they are transplanted into monkeys. The UK company Imutran Ltd has announced its intention to start transplanting hearts from transgenic pigs into human recipients in 1996. In the US, Parkinson's sufferers have undergone xenotransplantation of fetal neural tissue from unmodified pigs in an attempt to treat their condition (paragraph 3.35).

Ethical concerns

- 10.5 Given the recent developments in overcoming the problems associated with xenotransplantation, the moves by some to initiate clinical trials, and the amount of interest that has been aroused in the subject, an examination of the ethical issues that arise from xenotransplantation is timely. The following principal ethical concerns arising from xenotransplantation were identified by the Working Party and have been discussed in the body of the report:
- 1 Is using animals to provide organs and tissue for transplantation into human beings acceptable? Are there special concerns about the use of higher primates, or of genetically modified animals (Chapter 4)?
 - 2 If some use of animals for xenotransplantation is considered ethically acceptable, how can the welfare of the animals be adequately protected (Chapter 5)?
 - 3 Xenotransplantation raises the possibility that infectious diseases of animals will be transmitted into the human population. How can this risk be assessed and managed (Chapter 6)?
 - 4 When should clinical trials of xenotransplantation start and how can the welfare and interests of early patients be protected (Chapter 7)?

- 5 How should the introduction and provision of xenotransplantation, should it develop into a successful clinical treatment, be managed? What are the implications for the financing of the health service if xenotransplantation is successful (Chapter 8)?
 - 6 What attitudes will people have to xenotransplantation and how will individual recipients adjust to receiving a xenograft? What will be the effect of developments in xenotransplantation on the willingness of human beings to donate their organs (Chapter 9)?
- 10.6 These issues were discussed in the body of the report. The conclusions are summarised below. A series of recommendations is offered to demonstrate how the conclusions should be implemented in practice. The interests at stake and the potential consequences are so great that there is a need for regulation and control of xenotransplantation at a national level. The Working Party recommends an Advisory Committee on Xenotransplantation is established to perform these functions (paragraphs 6.38 - 6.41).

Animal concerns: principles

- 10.7 Current thinking about the use of animals for medical purposes has been reviewed in Chapter 4. One line of thought holds that when judging whether it is acceptable to use animals for medical purposes, it is necessary to consider whether the pain and suffering of the animals is justified by the potential benefit to human beings (paragraphs 4.5 - 4.6). Another line of thought suggests that animals, like human beings, have rights that must be respected when considering their use for such purposes (paragraphs 4.7 - 4.8). 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 (paragraph 4.9). 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. 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.
- 10.8 The Working Party accepted that some use of animals for medical purposes is “*an undesirable but unavoidable necessity*” and that “*in the absence of any scientifically and morally acceptable alternative, some use of animals . . . can be justified as necessary to safeguard and improve the health and alleviate the suffering of human beings*”. Not every benefit to human beings will justify the use of animals and, in some cases, the adverse effects on the animals will be so serious as to preclude their use. This conclusion

drew on the position set out by the Institute of Medical Ethics towards biomedical research using animals (paragraphs 4.25 - 4.27).

The use of primates for xenotransplantation

- 10.9 Even if some use of animals for medical purposes can be justified in principle, their use for xenotransplantation raises specific issues that need further consideration. Particular concerns are raised by the use of primates, such as baboons (paragraphs 4.28 - 4.41). The high degree of evolutionary relatedness between human beings and primates both suggests that xenotransplantation of primate organs and tissue might be successful and also raises questions about whether it is ethical to use primates in ways that it is not considered acceptable to use human beings. Certainly, any harm suffered by primates should be given great weight. This position is reflected in the principles underlying current practice in the UK. **The Working Party endorses the special protection afforded to primates used for medical and scientific purposes.**
- 10.10 The Working Party would accept the use of very small numbers of primates as **recipients of organs** during research to develop xenotransplantation of organs and tissue from non-primates. In this case, using a small number of primates for research, while undesirable, can be justified by the potential benefits if xenotransplantation were to become a successful procedure (paragraph 4.38).
- 10.11 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 addition to the special weight given to the harm suffered by primates, other concerns must be taken into account. The endangered status of chimpanzees rules out their use for xenotransplantation. The potential risk of extinction, even to a species like the baboon that is not currently endangered, must be taken seriously. Xenotransplantation using primate organs or tissue may pose particular risks of disease transmission (paragraphs 4.33 - 4.35 and 6.10 - 6.12).
- 10.12 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 (paragraph 4.40).

10.13 The Working Party considered the possibility that, after a number of years of research, it might be found that pig organs and tissue could not be used for xenotransplantation. 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 the use of alternative methods of organs replacement 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, some members of the Working Party 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 (paragraph 4.41).

The use of pigs for xenotransplantation

10.14 While the pig is an animal of sufficient intelligence and sociability to make welfare considerations paramount, there is less evidence that it shares 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. It is also 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 (paragraph 4.42).**

10.15 If pigs are used for xenotransplantation they are likely to have been genetically modified so the human immune response to the pig organs and tissue is reduced. The production of transgenic pigs for xenotransplantation is likely to involve the transfer of a gene or a few genes of human origin. This is a very small and specific change.

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 the characteristics of the human species. Thus, inserting these genes into a transgenic pig would not destroy the integrity of either species. Species boundaries, in any case, are not inviolable but change through a number of other processes. **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** (paragraphs 4.45 - 4.49). Monitoring the welfare of transgenic animals is discussed below (paragraphs 10.18 - 10.23).

- 10.16 Should xenotransplantation become widespread, it is possible that surpluses of transgenic pigs may arise, raising the question whether they should be made available on the general agricultural market and used for food. Regulatory mechanisms are in place to examine the acceptability of any proposal to release transgenic animals into the environment or to allow them to enter the food chain (paragraphs 4.50 - 4.52).
- 10.17 Should the organs and tissue of transgenic pigs be effective for xenotransplantation, applications may be made to patent the pig strains. A detailed discussion of the ethics of patenting transgenic animals lay outside the scope of this report. The issues have been examined in some detail in a previous report of the Nuffield Council on Bioethics, **Human Tissue : Ethical and Legal Issues**, and elsewhere. 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 that 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*” (paragraphs 4.53 - 4.54).

Animal concerns: practice

- 10.18 In the UK, animals used for scientific purposes are protected by the Animals (Scientific Procedures) Act 1986 (the 1986 Act). Before the use of animals is permitted, the likely adverse effects on the animals must be weighed against the benefits likely to accrue from their use. The Home Office Inspectorate grants licences, in consultation where necessary with the Animal Procedures Committee. The use of animals for xenotransplantation raises questions about their breeding, especially if they are genetically modified, the welfare implications of producing animals free from infectious organisms, and their slaughter. **The Working Party recommends that the convention by which the Animal Procedures Committee advises on project licences in difficult areas should extend to applications for the use of animals for xenotransplantation.** When weighing

the harm and the benefits of the use of animals for xenotransplantation, the ethical issues discussed in Chapter 4 should be taken into account (paragraphs 5.2 - 5.5).

- 10.19 Xenotransplantation research may require the use of limited numbers of primates as xenograft recipients. Primates are afforded special protection by the 1986 Act. Project applications involving primates are examined by the Animal Procedures Committee and the Home Office sets standards for the care and welfare of primates involved in research. The Working Party recommended that non-primate species should be regarded as the source animals of choice for xenotransplantation. What follows, therefore, refers to the welfare implications of the use of non-primate animals, notably transgenic pigs, to supply organs and tissue for xenotransplantation (paragraphs 5.6 - 5.8).
- 10.20 The breeding of transgenic animals is under the control of the 1986 Act. Transgenic animals can, in principle, be released from the control of the 1986 Act if there is no significant effect on the animals' welfare after two generations. If they are released, welfare concerns would be covered by the less demanding standards regulating agricultural practice and animal husbandry (paragraphs 5.9 - 5.17).
- 10.21 Animals used to provide organs and tissue will need to be free, as far as possible, from infectious organisms in order to reduce the risk that xenotransplantation will lead to the transmission of diseases into the human population. Repeated testing of animals and other procedures may adversely affect animal welfare. **The Working Party recommends that, when decisions are made about the acceptability of using animals for xenotransplantation, particular attention is paid to reducing the adverse effects associated with the need to produce animals free from infectious organisms** (paragraphs 5.18 - 5.22).
- 10.22 Removal of organs or tissue from anaesthetised animals will come under the control of the 1986 Act. It is possible, however, that killing animals and removing their organs without the use of an anaesthetic would not come under the control of the 1986 Act. It would be possible, in principle, to remove non-vital organs, or tissues that regenerate, sequentially from animals. This could well result in an increase in animal suffering. The Home Office has stated that the provisions of the 1986 Act regarding re-use of animals would preclude the sequential removal of organs or tissue. **The Working Party recommends that the Animals (Scientific Procedures) Act should continue to be interpreted as prohibiting sequential removal from animals of tissues or organs for transplantation** (paragraphs 5.23 - 5.26).
- 10.23 Important welfare implications are raised by the breeding of transgenic animals; producing animals free from infectious organisms; and removing organs and tissue from animals for xenotransplantation. There is some uncertainty about whether, in practice, all these aspects would be covered by the 1986 Act. In view of the important welfare implications raised by xenotransplantation, **the Working Party**

recommends that the Home Office should require that all animals used for xenotransplantation are protected under the Animals (Scientific Procedures) Act 1986. Any reputable company producing animals in order to supply organs and tissue for xenotransplantation would, in any case, wish to be licensed under the 1986 Act in order to reassure the public that their activities were meeting the highest standards of animal welfare. **The Working Party recommends that the standards set by the 1986 Act become the minimum for the industry** (paragraph 5.27).

Transmission of infectious diseases

- 10.24 Xenotransplantation of animal organs and tissue carries with it the potential risk that diseases will be transmitted from animals to xenograft recipients and to the wider human population (Chapter 6). It is difficult to assess this risk, since it is impossible to predict whether infectious organisms that are harmless in their animal host will cause disease in human xenograft recipients or whether the disease will spread into the wider human population. There are certain to be infectious organisms of both primates and pigs that are currently unknown, and some of these might cause disease in human beings. There is evidence that infectious organisms of primates, notably viruses, can pass into the human population and cause disease. This supports the recommendation that non-primate species should be regarded as the source animals of choice for xenotransplantation. The possible risk of disease transmission from pigs, however, also requires careful consideration (paragraphs 6.10 - 6.12).
- 10.25 It is not possible to predict or quantify the risk that xenotransplantation will result in the emergence of new human diseases. But in the worst case, the consequences could be far-reaching and difficult to control. The principle of precaution requires that action is taken to avoid risks **in advance** of certainty about their nature. It suggests that the burden of proof should lie with those developing the technology to demonstrate that it will not cause serious harm. **The Working Party concluded that the risks associated with possible transmission of infectious diseases as a consequence of xenotransplantation have not been adequately dealt with. It would not be ethical therefore to begin clinical trials of xenotransplantation involving human beings.** In order to address the risks of disease transmission associated with xenotransplantation, the Working Party suggests that the measures set out below should be taken (paragraphs 6.20 - 6.23).
- 10.26 Stringent efforts should be made to assemble as much information as possible about the risks of disease transmission **before** further xenotransplantation goes ahead. This would involve reviewing existing research and undertaking new research where necessary on the infectious organisms of primates and pigs and the possibility of transmission of disease to human beings. Reliable and accurate methods for identifying potentially dangerous infectious organisms in both source animals and

human recipients should be in place before clinical xenotransplantation trials are undertaken (paragraphs 6.24 - 6.26).

- 10.27 Xenotransplantation should use only source animals reared in conditions in which all known infectious organisms are monitored and controlled. It is ethically unacceptable to use source organs from animals that are known to be infected with infectious organisms (pathogens) which can be eliminated. **The Working Party recommends that a code of practice should be drawn up specifying which organisms should be excluded from specified-pathogen free animals. Xenotransplantation teams should be required to exclude from source animals all the pathogens listed in the code of practice.** Mechanisms should be in place to allow the list of organisms to be updated in the light of experience. The code of practice should recommend the diagnostic tests to be performed by accredited test centres. There is currently no regulatory mechanism that would cover the safety and quality of animal organs and tissue. **The Working Party recommends that a regulatory framework is devised to control the safety and quality of animal organs and tissue for xenotransplantation** (paragraphs 6.27 - 6.32).
- 10.28 There should be thorough monitoring of early recipients, with regular testing for signs and symptoms of disease. **The Working Party recommends that standards and mechanisms for monitoring xenograft recipients and for the action to be taken in case of disease transmission should be in place before human trials begin. It should be a requirement of clinical trials that the need for monitoring is explained to the patient and that it is made clear that consent to the operation also implies consent to subsequent monitoring** (paragraphs 6.33 - 6.36).
- 10.29 In order to facilitate the recording and analysis of information concerning possible disease transmission, **the Working Party recommends that xenotransplantation teams should be required to record all information concerning individual xenograft recipients in a xenotransplantation register maintained by an independent body.** Suitably anonymised data should be reviewed for evidence of the possible emergence of new diseases. Since, initially, xenograft recipients are likely to be few, and to be spread across several countries, international co-operation should take place to enable effective review of all the available evidence (paragraph 6.37).
- 10.30 There should be a commitment to suspend, amend or, if necessary, discontinue xenotransplantation procedures at any signs that new infectious diseases are emerging (paragraph 6.23).

Advisory Committee on Xenotransplantation

10.31 Implementing the precautions outlined above will require an expert and authoritative body that is independent of the research teams at work on xenotransplantation. In view of the seriousness of the issues and of the public concerns about the technique, **the Working Party recommends that the Department of Health should establish an Advisory Committee on Xenotransplantation.** The proposed Advisory Committee on Xenotransplantation should combine the necessary scientific and medical expertise to examine early protocols with broader expertise to ensure that the Committee keeps in mind the wide range of issues raised by xenotransplantation. It should be open and accountable. There would be a need for close liaison between the proposed Advisory Committee and the Animal Procedures Committee (paragraphs 6.38 - 6.41).

Early patients

10.32 Xenotransplants should be offered to human patients only when results using animal recipients suggest that these operations will have a reasonable chance of success. There is currently little consensus within the transplantation community, both in the UK and in the US, as to whether the current data using animal recipients justifies progressing to clinical trials. **The Working Party recommends that no xenotransplantation trials involving human recipients should proceed until the proposed Advisory Committee on Xenotransplantation is in place and has approved the trials** (paragraphs 7.2 - 7.8). The restriction of xenotransplantation to a small number of centres would allow effective control of the risks associated with the potential transmission of infectious diseases and careful protection of early patients (paragraph 7.34).

10.33 Local Research Ethics Committees (LRECs) review, and must approve, all proposals for research involving human participants. All proposals for clinical trials of xenotransplantation will require LREC approval, in addition to the approval of the proposed Advisory Committee on Xenotransplantation (paragraph 7.9).

10.34 Even when the results from animal experiments suggest that xenotransplantation involving human recipients is justifiable, the early clinical trials will involve unknown and unpredictable risks. The question then becomes how best to protect early patients' welfare and interests. It is of the utmost importance that potential patients give free and properly informed consent to participation in the first xenotransplantation trials. **The Working Party recommends that the consent of patients to participation in xenotransplantation trials is sought by appropriately trained professionals who are independent of the xenotransplantation team. The information given to prospective recipients should include an estimation of likely success, attendant risks and subsequent quality of life** (paragraphs 7.14 - 7.18).

- Patients consenting to xenotransplantation should be informed that post-operative monitoring for infectious organisms is an integral part of the procedure, and that their consent to the operation includes consent to this monitoring (paragraph 10.28).
- 10.35 Teams conducting experimental trials on patients are under a scientific and ethical obligation to research and report the subsequent quality of life of recipients. **The Working Party recommends that no protocol to conduct a trial should be accepted unless it contains a commitment to a robust description and assessment of the patient's pre-operative and post-operative quality of life.** Quality of life information should be included in any scientific publication (paragraphs 7.19 - 7.21).
- 10.36 Special issues arise in the case of children. Xenotransplantation has been proposed as a method of reducing the especially acute shortage of organs for babies and children. Early clinical trials of xenotransplantation will be a form of therapeutic research. Therapeutic research must offer some prospect of genuine benefit for the patient, but it involves greater uncertainties than treatment, and therefore greater caution must be exercised. The British Paediatric Association and the Medical Research Council have advised that therapeutic research should not involve children if it could equally well be performed with adults. It would be difficult to justify the involvement of children in major and risky xenotransplantation trials before some of the uncertainties have been eliminated in trials involving adults. **The Working Party recommends that the first xenotransplantation trials involve adults rather than children** (paragraphs 7.22 - 7.23).
- 10.37 The special protection afforded children needs to be balanced with the importance of not withholding potentially beneficial treatment, even if that benefit is offered in the context of therapeutic research. If the first adult trials are successful, and there is greater certainty about the benefits, there would be stronger arguments for offering xenotransplantation to children. The question of consent then becomes important. Children between 16 and 18 may be considered capable of consenting on their own behalf to participate in therapeutic research, although a higher level of maturity would probably be required than that needed for consent to medical treatment. Given the complexity of the ethics and law in this area, a cautious approach would be to obtain the consent of the person with parental responsibility before a child under 18 participates in a major procedure like xenotransplantation. The agreement of any child to participation in therapeutic research such as xenotransplantation should always be obtained (paragraph 7.24).
- 10.38 Similar issues arise for adults who are considered incapable of consenting to participation in therapeutic research because they are mentally incapacitated. The law would appear to be that incapacitated adults may be involved in therapeutic research if this is in their best interests. It would be difficult to justify the involvement of incapacitated adults in the first xenotransplantation trials before some of the major uncertainties have been eliminated in trials involving adults who are capable of

weighing the benefits and risks on their own behalf. **The Working Party recommends that the first xenotransplantation trials should not involve adults incapable of consenting to participation on their own behalf** (paragraph 7.25).

- 10.39 The Medical Research Council has recommended that the participation of incapacitated adults in therapeutic research may be justified if, in addition to evidence that the procedure will benefit the individual, it relates to their incapacitating condition and the relevant knowledge could not be gained by research in adults able to consent. One situation in which this might justify xenotransplantation trials involving the mentally incapacitated is the proposed transplantation of pig fetal neural tissue to treat people suffering from Huntington's disease, a neurodegenerative disorder which affects mental capacity. Such trials should only take place, however, if there is evidence to support progressing from animal research to human trials and to indicate that the procedure will benefit the individuals involved (paragraph 7.26).
- 10.40 Public policy must be able to take account of different attitudes to xenotransplantation. Some people may wish to refuse xenotransplantation as a form of treatment. If refusing a xenograft reduced a person's priority for a human transplant, consent to xenotransplantation would certainly not be freely given. **The Working Party recommends that, at any stage in the development of xenotransplantation, patients who, for whatever reasons, refuse xenografts should remain entitled to consideration for human organs on the same basis as before their refusal** (paragraphs 7.27 - 7.30).
- 10.41 What should happen to someone who has accepted a xenograft, but for whom a human organ or tissue at some later date might offer better prospects? In the early stages of development, xenografts are unlikely to be as successful as human transplants, and it is possible that they will only work for a fairly short period of time. **The Working Party recommends that xenograft recipients should remain entitled to consideration for human organ transplantation on the same basis of clinical need as before xenotransplantation.** The Working Party recognises that an implication of this position is that the demand for human organs may not decline, and may even increase, in the early years of xenotransplantation, since xenograft recipients may remain on the waiting list for human organs whereas without a xenograft they might not have survived (paragraph 7.31).

Effects on the health care system

- 10.42 What are the implications for the NHS, should xenotransplantation move beyond the experimental stage and become a routine surgical procedure? It is likely that the major cost implications of xenotransplantation would arise from the larger number of transplants that would be possible. Should xenotransplantation develop into a successful procedure, decisions about its provision would have to be made within the context of wider debate about resource allocation within the NHS (paragraphs 8.1 - 8.13).

- 10.43 There are good reasons for introducing new and potentially expensive specialist services in a controlled way. Restricting xenotransplantation to designated centres for the foreseeable future would ensure adequate monitoring of its cost and effectiveness. Already in existence is the Supra Regional Services Advisory Group which is responsible for the introduction and provision of specialist services. **The Working Party recommends that, if xenotransplantation becomes a treatment of choice, the introduction of the treatment into the NHS should be overseen by the Supra Regional Services Advisory Group** (paragraphs 8.14 - 8.17).

Personal and social effects of xenotransplantation

- 10.44 Attitudes to xenotransplantation will vary. Some may view it as part of a quest to prolong life, in pursuit of which goal, human beings are prepared to abuse their relationship with other animals. Others may regard it as offering a way of providing organs and tissue for transplantation that is preferable to some of the measures proposed for increasing the supply of human organs. There is a need for transparency and openness in the activities of researchers and policy-makers involved in xenotransplantation, and of full debate about its acceptability (paragraphs 9.1 - 9.4).
- 10.45 It is difficult to predict what the effects of xenotransplantation might be on individual recipients and, in particular, how people's views of their body and of their identity might be affected by xenotransplantation. This highlights the need for more research in this area. **The Working Party recommends that counselling of xenograft recipients should include discussion of the possible personal impact of xenotransplantation. The Working Party further recommends that research should be initiated to assess the personal impact of xenotransplantation on potential and early recipients** (paragraphs 9.5 - 9.15).
- 10.46 It is highly unlikely that xenotransplantation would eliminate the need for human organs. Xenotransplantation would probably become part of a range of treatments used alongside human organ and tissue transplantation, and the use of artificial substitutes. It is very important to indicate to potential and actual human donors that their gift will be no less precious if it becomes part of the range of available treatments. There is a great responsibility, therefore, on xenotransplant teams, on the media and on those responsible for influencing public opinion to ensure that the reporting of developments in xenotransplantation is as accurate, balanced and unsensational as possible. It should be made clear that, for the foreseeable future, xenotransplantation will not solve the shortage of organs and tissue for transplantation and that there will still be a pressing need for the donation of human organs (paragraphs 9.16 - 9.20).

Implementation of recommendations

10.47 This report has set out the many ethical issues raised by the development of xenotransplantation. In the view of the Working Party, responding to these issues will require the establishment of an Advisory Committee on Xenotransplantation (paragraph 10.31). **The Working Party recommends that the proposed Advisory Committee on Xenotransplantation should produce guidance on best practice and revise that guidance in the light of experience. The responsibilities of the Advisory Committee should include:**

- ▶ **assembling and assessing information about the possible risks of disease transmission, and on that basis making recommendations** (paragraph 10.26)
- ▶ **establishing a regulatory mechanism to ensure that the appropriate infectious organisms are eliminated from source animals** (paragraph 10.27)
- ▶ **developing guidance on the monitoring of future recipients of xenografts and maintaining a register of xenograft recipients** (paragraphs 10.28 - 10.29)
- ▶ **approving any xenotransplantation trials involving human recipients and the centres that may undertake such trials** (paragraph 10.32)
- ▶ **overseeing issues of consent and conscientious objection** (paragraphs 10.34 -10.41)
- ▶ **assessing the impact of xenotransplantation on individual recipients** (paragraph 10.45)
- ▶ **facilitating debate and assessing attitudes to xenotransplantation** (paragraph 10.46).

No xenotransplantation trials involving human recipients should proceed until the proposed Advisory Committee on Xenotransplantation is in place and the above issues have been addressed.

10.48 A particularly wide range of concerns is raised by xenotransplantation, about which people have differing and strongly held views. The Working Party has recommended that the development of xenotransplantation should continue subject to rigorous regulation to ensure protection for potential human recipients and care for animal welfare. Public debate about the ethical issues raised by xenotransplantation will continue. This report is intended to contribute to that debate.