



Anti Vivisection WA (Inc)

ABN 17 235 544 910

Past Patron: Sir Walter Murdoch

“Working to end experiments on animals!”

3 March 2004

Project Officer - Xenotransplantation
Health Ethics Section,
NHMRC (MDP 100)
GPO Box 9848
Canberra ACT 2601

Dear Sur/Madam

Re: Xenotransplantation Research How should Australia proceed?

I have been instructed by the Committee of Management and Members of **Anti Vivisection WA (Inc)** to provide a submission in reply to the Response Paper “Animal-to-human transplantation research: How should Australia proceed?”

What does Xenotransplantation mean?

Firstly, we noted that the XWP (Xenotransplantation Working Party) assumed that from indications expressed in the first round of submissions it received, respondents were mainly referring to “organ” transplants and not the other animal cell or tissue transplants.¹

We believe, however that the main “focus” of the Discussion Paper calling for public response was based on animal organ transplantation, and that the XWP had already identified that animal cell and tissues transplantation, albeit in a somewhat broader range,¹ that are currently in general use.

However, given the XWP’s assumption we therefore wish to point out that for the purpose of this submission, our use of the term “xenotransplantation” means to encompass **all** animal cells, tissues and organ transplantation.

Should Xenotransplantation be allowed to proceed?

Despite the proportionally high number of submissions that directly opposed xenotransplantation in “first round” submissions received by the NHMRC² and the amount of public opposition received to date, it did not appear to deter the XWP from making up its collective mind that xenotransplantation should proceed even at this preliminary stage.

This assumption whilst appearing quite regularly throughout the Response Paper has never been more clearly indicated than that in *“The way forward for Australia - Section*

¹ Response Paper, paragraph 1.16

² Response Paper, paragraph 2.10

12”³ and also in “A guide for the community - Section 12 The way forward”⁴

This then begs the question to be asked, “Will the XWP be prepared to accept that Xenotransplantation would not proceed if after the second round of public consultations the same (or better) ratio of 66 to 25 against xenotransplantation (or approximate two thirds against) is obtained?”

When I asked this question of Dr Sparrow after the Public Consultation Meeting in Perth (16/02/04), he answered simply by saying the XWP can only make recommendations to the NHMRC. However it is quite obvious that the NHMRC will respond in accordance with those recommendations and given the XWP’s proposal in the affirmative then it seems that xenotransplantation is a foregone conclusion despite widespread community opinion against xenotransplantation!

If we don’t do it someone else will!

Furthermore, we were also extremely disappointed to note that the XWP deems that “a total ban on xenotransplantation”⁵ would “force research offshore” or “prevent progress in other areas”. How would this be so?

Certainly the veiled “threat” of research moving overseas is definitely not a valid justification for allowing xenotransplantation to proceed in Australia. In fact we believe that xenotransplantation research would cause future funding to be turned away from more important and relevant human studies and preventing progress in “other areas”.

Inadequate Flowchart & Flawed Processes

Throughout the Response paper, the XWP have readily passed the onus of animal to animal transplantation approvals back onto individual HREC (Human Research Ethics Committees) or AECs (Animal Ethics Committees) of individual institutions, yet we note in Figure 11.1 (*Flowchart showing proposed regulatory progress*)⁶ that approval (or non-approval) by HREC/AECs is the **final** stage in the process.

AECs and HRECs should be situated in the **first** stage of any proposed research program, and then if such research program were approved then the next step would be for the researcher to approach the National Committee for further approval.

Also currently both HREC and AECs occupy equal levels in the proposed flowchart process. There is no provision for either ethics committees holding a separate review of the proposed experiment or in the event of a conflict of approval (ie one says yes and the other says no)? The NSW Agriculture AWU adequately highlighted this anomaly in their Submission X070⁷.

Further, if an experiment is not approved the researcher can apply to another institution for sponsorship. Procedures must ensure that in the situation where a researcher has approached another institution the researcher must reapply at the National level for a completely **new** certificate (of approval). Basically, this notifies the National Committee of the different institution and new circumstances. This is another important reason why the HREC/AECs should be at the beginning of the process and not at the end.

³ Response Paper, paragraph 12.6

⁴ A guide for the community, page 20

⁵ Response Paper, paragraph 2.28 to 2.31

⁶ Response Paper; page 136

⁷ Response Paper paragraph 11.54

The Role of AECs

One could also ask how many times would an AEC be permitted to reject animal research programs before an institution becomes aware that they are possibly losing lucrative research grants? We think undue pressure will be placed on AECs, especially on individual AEC members, to provide blanket approval for all xenotransplantation experiments.

Furthermore, as AECs are all self-regulatory thereby whilst purporting to follow codes of practice and guidelines, there is no legally binding provision for them to do so and there is no legal consequence for breaching any standards. Who is going to put up their hand to highlight a breach of any codes and to whom are they going to report this breach? One would expect their tenure at the institution would be short lived.

Valid Points and New Questions

Many of the respondents to the Discussion Paper have made some extremely valid points, which we believe compels further discussion. For this reason we have submitted a detailed analysis of the Response Paper by examining it closely, tackling each paragraph where we felt an extremely important point needs to be re-addressed.

We also wish to point out with some of our comments we have simply posed questions. This is due to the fact that we feel that a particular topic has not been adequately debated and requires far more serious deliberation.

We have included as part of our submission an excerpt from “Diaries of Despair” by Uncaged Campaigns of the UK, who have uncovered atrocities committed on animals in the name of Xenotransplantation. We believe that the XWP cannot make valued judgements without reading these compelling reports written by the researchers themselves.

We also urge the XWP to view the video footage available from Uncaged Campaigns at www.xenodiaries.org before committing Australia and Australians down the perilous path of xenotransplantation.

Xenotransplantation is fraught with danger and still remains morally and ethically wrong. We do not believe that permission should be granted for the misleading and cruel pseudo-science known as “xenotransplantation” to be permitted in Australia!

Yours faithfully

For and on behalf of the Members

Lindsey Linfoot (Mrs)
President
Anti Vivisection WA (Inc)

(Encl)

Xenotransplantation Research How should Australia proceed?

What is xenotransplantation?

1.7 *Researches are working out the science of animal to human transplantation.... [Xenotransplantation] would only be attempted if the animal-to-animal studies show successful outcomes.*

What constitutes “successful outcomes” and how can they be measured given the vast range of species, procedures, personal interpretations, conditions, etc?

About this Response Paper

1.15 *“However, not all interest groups were represented among the respondents...”*

Will we be having public consultation hearings until the XWP receives the answer they want to hear?

Introduction

Response to submissions

2.4 *“...recipients of transplants, diabetics or other people who might have a direct interest in the benefits of xenotransplantation.”*

This paragraph also refers to the lack of response from transplant recipients and the perceived “benefits” which still not been worked out. How many times do we have to submit a “NO” response?

2.11 *“The good of the community as a whole and the rights of animals must outweigh the good of the few who may possibly benefit from xenotransplantation.”⁸*

First round submissions against xenotransplantation totalled **66 to 25**.

Arguments against animal-to-human transplantation

2.12 *It is entirely unacceptable to ... bring an animal into existence for the express purpose of “harvesting” its body parts for organ transplantation into humans...⁹*

We do not have the moral or ethical right to breed animals solely for the supply of their body parts or tissues for xenotransplantation.

Arguments in support of animal-to-human transplantation

2.14 *“Necessary due to shortage of human tissue for transplantation.”¹⁰*

What’s wrong with promoting “Drivers Licence” donations? Furthermore, in a recent news article by the Sunday Times (22/02/04) the issue of promoting human organ donors was tackled at length with over 4 pages devoted to the David Hookes Foundation to promote human organ donations and the very important aspects of human-to-human organ donors.¹¹

The role of guidelines

The relationship between guidelines and research

2.25 *“Rather the purpose of guidelines is to provide a cautions framework within which unsafe or unsuitable research would be effectively blocked, while potentially safe and beneficial research may be allowed to proceed under strictly monitored conditions”*

What constitutes “potentially safe and beneficial” - The concept of ethics committees whilst

⁸ Lene Martine (Sub X007)

⁹ Naomi & Michael Mairou (Sub X013)

¹⁰ Professor Bernie Tuch, Diabetes Transplant Unit (Sub X016)

¹¹ Sunday Times 22/02/04 – Article attached.

giving the impression of some sort of oversight doesn't really work due to the "anonymity" of the members of the said committees.

What about having a complete ban?

2.30 *A total ban in countries such as Australia, may also force research offshore?*

The "threat" of research moving overseas is definitely not a valid justification for allowing xenotransplantation to proceed in Australia. Getting in first does not make xenotransplantation any more ethical or safe!

What does xenotransplantation research involve?

Why consider animal-to-human transplantation?

3.9 *"Unfortunately while transplants have become more frequent and successful, and the number and scope of the procedures have increased, the number of donors has not risen to the same extent. In Australia, as elsewhere in the world, there are not enough donors available."*

All the more reason to promote human organ donations! The recent case with the untimely death of legendary cricketer David Hookes shows the benefits and effect that high profile organ donors can have on the general public.¹²

3.10 *"The costs to society of these shortages can be measured in the deaths and illness of patients; in emotional, social and economic costs to their families; and in direct and indirect economic costs to the wider community."*

All the more reason to promote human organ donations, as funding for xenotransplantation research will cost millions and millions of dollars and still cannot be assured of ever reaching any practical success rates. This is a highly subjective statement to measure "costs" in this manner. Emotional costs to families would not be eased by the concept of xenotransplantation. It would merely add to the burden that families face in these circumstances. Greater amounts of immunosuppressive drugs would now be pumped into the patient making them susceptible to other infections, etc. **A classic case of "the operation was successful but the patient died"**

3.12 *"...scientists now feel that the major problems associated with animal transplants (such as rapid rejection of the transplant) may be overcome by genetic modification of the source animals."*

Genetic modification (GM) of plants (and animals) has not yet been perfected and there is vast contention it will ever be. GM has certainly not been accepted by the wider community and is viewed with alarm and mistrust and definitely not without reason. The use of GM in the xenotransplantation issue appears to be trying to solve one problem with another.

Preclinical studies

3.21 & 3.22 relate to preclinical studies using animals.

What would be the limit to the number of animals used before a procedure was to be considered "safe" or "unsafe"?

4 Ethical overview of animal-to-human transplantation

Crossing the species barrier

4.10 *"... religion was the main concern about crossing the species barrier by putting animal tissues into human beings. However this view was not substantiated by the submissions from representatives of a number of major religions"*

Whilst various church leaders have declared within the Response Paper that there is nothing in the

¹² Sunday Times 22/02/04 – Article attached.

religious teachings to say that xenotransplantation is wrong there is nothing in the bible to say it *IS* right! This delves into the realms of “religious theology” and would be an entirely different debate altogether. Xenotransplantation NEVER existed at the time when the Bible or Koran was written.

Animals treated as human property

4.23 “...mainstream view in society is that it is acceptable to use animals for the benefit of humans.” .

We do not subscribe to this view, as we believe that vivisection is cruel, unethical and morally wrong it is also extremely dangerous to humans. Information regarding animal experimentation is generally kept away from the public arena and furthermore it is also “sanitised” before being released to the media. The public do not really know what is being done in their name and with taxpayer money.

Genetic modification of animals

4.28 “Genetic modification of source animals involves inserting some key human genes to help make animal transplants behave more like human transplants.”

The points raised concern only not “humanising” the animal before using its body parts for human treatment but whether the animal can now be protected under human rights and discrimination laws? How much human gene insertion to an animals DNA constitutes these new rights?

4.29 “...genetically modifying animals for many years in agriculture”¹³

With regard to the above statement this is not necessarily true. Cross breeding sheep, chickens or any animal is not genetically modifying their DNA.

GMOs are developed by blasting DNA code with genes from another species. “Genetic modification (GM) involves exchanging or splicing genes of unrelated species that cannot naturally swap with each other” and “A specially-designed “gene gun” fires dozens of metal slivers like bullets at target cells. The tiny pellets, usually of tungsten or gold, are much smaller than the diameter of the target cell, and coated with genetic material.”¹⁴

There is a huge groundswell of opposition to this “hit and miss” technology being introduced into the (human) food chain. We still do not know the consequences of such technology.

Use of primates

4.35 “...non-human primates should not be allowed to be used... not only for the potential spread of retroviruses or other infections ...”

This is the problem faced by the introduction of xenotransplantation. It has so many flaws that are apparent right from the start.

4.36 “...that nonhuman primates may not be used as source animals for human xenotransplantation products on both safety and ethical grounds.”¹⁵

Further, if intelligence only was the barrier to being used then these animals have extreme cognitive abilities and other “intelligence” skills. They can display very human characteristics and some have a greater intelligence than mentally handicapped people. Definitely, nonhuman primates should not be used for xenotransplantation or for preclinical animal-to-animal trials.

Impact on human identity

4.58 “The Salvation Army also finds no biblical objection to xenotransplantation on the grounds of loss of identity.”

¹³ International Xenotransplantation Association (Sub x077)

¹⁴ <http://www.thecampaign.org/News/nov01j.htm>

¹⁵ RSPCA Australia and RSPCA UK (Subs X050 & X091) stated

Once again xenotransplantation was not around when the bible was written therefore the argument is “if the Bible didn’t refer to xenotransplantation then its OK?” We don’t think so!

4.62 *Islamic law if the following conditions are met: Point 2 “is not transplanted at the moment”*

This could never eventuate because of the preparation time for a patient to receive a transplant (including anti rejection drugs, etc.) Point 4 refers to “no physical, mental, psychological or moral degeneration would take place in future because of transplantation.” Patients (and doctors) cannot predict how they will feel after undergoing xenotransplantation (even if successful) and what happens when the transplant (cell or organ) fails. Counselling might prevent some misgivings but could never be guaranteed as once the transplant had taken place the patient has an animal organ in their body.

Ethical conduct of animal-to-animal studies

4.76 *“The RSPCA believes that current controls do not give adequate consideration to the welfare of animals involved in xenotransplantation studies, nor do they do justice to the seriousness of the ethical questions this research raises.”*

There are still huge doubts that the controls and guidelines governing xenotransplantation and other subsequent research are adequate.

The need for public debate

4.80 *“There is an obligation to ensure that the community understands the technology, the ethical considerations and the risks.”¹⁶*

What risks would the community be prepared to accept? What does this mean? Would doctors (or the patient) be prepared to accept a risk and the responsibility especially to the wider community? What actions would they be prepared to take if the risk unpredictably infected the community as a whole?

Conclusion:

4.84 *Two main questions: Is animal to human transplantation ethical? That is should medical therapies based on live animal products be considered at all? And How should xenotransplantation research be conducted.”* That is, if we agree that it is acceptable to develop therapies based on live animal products, how should the research associated with its developments be conducted?

4.85 *“The conclusion reached by the XWP is that, overall, society favours the use of animals for the needs of humanity.” “...it is merely a reflection of the prevailing view; which has been substantiated by moral arguments from many different cultural perspectives.”*

Viewpoints taken from the religious or cultural perspectives are based on theologies and doctrines. We do not believe that given the uncertain quantities of xenotransplantation that any decisions can be made in this light.

4.86 *“...minimise animal welfare concerns.”*

This statement does not take into consideration that people disagree with xenotransplantation for many reasons and whether animal welfare concerns were minimised or not does not make xenotransplantation any more palatable or ethical.

4.87 to 4.90 *“...prevailing view that using animals for the needs of humanity”*

Once again this refers to trying to justify the rightfulness of xenotransplantation.

4.91 *“...animal to human transplantation research proposals should consider the effects of the research on society as a whole, including those who oppose the use of animals in this*

¹⁶ (NSW Health (Sub X090))

way...

Those who justify xenotransplantation (especially those researchers that conduct experiments on animals) cannot fully understand the effects of on those who are opposed to it! This statement seems just condescending claptrap.

5 Animal Welfare

General considerations on the use of animals for medical purposes

5.2 & 5.5 *“...the majority view is that some use of animals in biomedical research is justified to safeguard and improve health, and to alleviate suffering of human beings and other animals.”* And *“When judging the acceptability of procedures involving animals in biomedical research, an ethical decision must be made about whether any pain and suffering caused to the animals can be justified by the potential benefit of the research involved to humans or other animals”.*

We do not understand the XWP's context of the term “other animals”! If ethics were truly the case then xenotransplantation would not be considered at all! The “alleviation of suffering” in relation to “other animals” would not be considered— this so-called alleviation of suffering is applicable (in these circumstances) for humans only.

Regulation of animal research

Aust code of practice etc

5.10 *“However, there is no provision for national oversight of animal research...”*

With reference to AECs, all members sign confidentiality agreements that preclude them from informing other groups whether national or local. Further if the NHMRC cannot offer protection to animals (and that's not its purpose) then what good is an AEC?

5.12 *The central goals of the Code of Practice...”*

There are no independent bodies (and we stress independent) that have immediate access into any of the research facilities. Once again “confidential nature of the experiments” would override any access to independent bodies and there is no provision for the protection of whistle blowers.

Functioning of AECs

5.26 *“A properly functioning AEC should work to ensure that all views are taken into account...”*

This works in the hypothetical world but not the real world. There are no measures taken with regard to a “wrong decision” and there are no repercussions with regard to law or responsibility if any law, decision or code is breached. There is entirely no protection for the animals. We do not know who are on ethics committees or what they have passed or not passed. Confidentiality clauses protect institutions.

5.28 *“..oversight provided by a national committee and NHMRC guidelines for the care and use of animals in xenotransplantation research should also help to alleviate these problems.”*

The general community are still none the wiser for knowing who these individuals are that are making these bold decisions on their behalf! This will not “alleviate the problem”.

Gene insertions

5.50 *“The presence of a transgene may also affect the animals ability to perform normal behaviour. Beltsville pigs for example (genetically modified to express additional growth hormones) experienced such extreme welfare problems that normal behaviour was impossible for them. They suffered from lethargy, lameness, lack of coordination, thickened skin, gastric ulcers, sever synovitis, degenerative joint disease, pericarditis and*

endocarditis, cardiomegaly, paraketosis, nephritis and pneumonia.”¹⁷

We refer to our comments in regard to Paragraph 4.29 and that GMO research has not been perfected.

5.51 *“...the XWP recognised that adverse effect may occur, for example, because the transgene damages the genetic material of the host egg when it is inserted...”*

Because animals cannot communicate we cannot begin to understand any “adverse” effects unless they are blatantly obvious, we can only observe abnormal behaviour. Abnormal behaviour can also be affected by environmental conditions, food and other natural occurrences.

5.53 *“Cell culture has been promoted by animal welfare groups as a better alternative to using whole live animals for medical research.”*

This is true but only when cell cultures TOTALLY replace animals in research and not used in conjunction with or as a supplement to animal research. Research involving animals is misleading and dangerous to the community.

Removal of organs and tissues

5.56 *Bullet Point 2: “removing the required organ or tissue while the animal is alive under a range of anaesthetic procedures (and possible recovery of the animal.)”*

“Possible recovery” gives the (false) impression that the animal may recover and lead a normal life. The animal will not receive any benefits for removal of any of its tissues or organs and certainly will not be “pensioned off”. Keeping animals once they have “served their intended purpose” would have a financial cost so therefore this would not be considered by any institution or research facility.

5.58 *“When animals are killed without anaesthesia, requirements for humane killing set out in the Code of Practice must be followed.” Further “where practical, tissues from animals being used should be shared among investigators...” “in animal to animal” thus avoiding the slaughter of additional animals”*

This does not avoid the slaughter of additional animals but merely provides the availability of additional organs for transplants; one would assume that the same number of animals would be used. Further we presume that results to date indicate that a “successful” outcome involves using transgenic animals raised in sterile conditions and the practice of gaining organs from slaughterhouses would not conform to the requirements for these animals to be raised in “sterile conditions”. Therefore we could also assume that the intended transplant would fail given that researchers have not followed their own requirement for specifically bred animals?

It also flies in the face of minimising risks and preventing cross contamination!

Animal welfare consequences of xenotransplantation research

5.65 *“...highest standards of welfare”.*

We do not believe that AECs could ensure the “highest standards of welfare” since they approve an animal experiment but do not physically monitor it. There is also circumstances of ill treatment by animal carers and there is no protection from the animals or any “whistle blowers” that may decide to speak up. What processes are in place to ensure FULL compliance by an animal researcher?

Numbers of nonhuman primates bred and used

5.72 *“As with any animal use, researchers are required to justify their choice of species...”*

This is once again a very subjective issue. We do not believe AECs can offer any protection for animals given that the justification comes from the researcher intending to conduct an experiment

¹⁷ Humane Charities Australia (Sub X033)

and that nonhuman primates will be specially bred in research breeding colonies.

5.74 *“Some respondents argue that nonhuman primate studies should not be permitted in Australia...”*

We also argue strongly that it is morally and ethically wrong to use nonhuman primates in experiments due to their extremely enhanced cognitive capabilities and higher intelligence.

Importation

5.75 *“...were concerned about the welfare issues involved in transportation.”*

We are aware that there is a large primate-breeding complex at the National Macaque Facility at Werribee and of the proposed breeding colony at Churchill.

Housing, confinement and husbandry

5.79 *“It is up to individual AECs to approve the specific standards of housing and care at individual institutions.” Further “...current breeding programs are generally regarded as sufficient to supply demand in the present research environment.”*

Is this including the numbers that would be required for xenotransplantation if it were to be allowed? Once again we dispute the ability of AECs to adequately supervise research once underway. AECs are all self-regulatory thereby whilst purporting to follow codes of practice and guidelines, there is no legally binding provision for them to do so.

Impact of procedures

5.80 *“The impact that procedures involved in xenotransplantation research would have on primates...”*

We stress the “cognitive” abilities of nonhuman primates. Also we refer to researchers own notes that are publicised on the website Diaries of Despair¹⁸ and as attached to this submission.

5.81 *“...problems that arise when primates have received additional organ transplants at other body sites.”*

We believe that this suffering is totally unjustifiable and should not be allowed or condoned. We provide the following examples of the pain and suffering that baboons at Huntingdon Life Sciences (UK) underwent between 1994 and 2000:

* Notes from Xenotransplantation “Diaries of Despair”:

Baboon X240f:

Day 1 “Quiet but alert.”

Day 4 “...active if approached.”

Day 11 “...active if stimulated.”

Day 25 “...slow movements.”

Day 28 “Small soft gingival swelling.”

Day 32 “Vomit in cage.”

Day 48 “...clinging to cage front.”

Day 58 “Large vomit in cage.”

Day 73 “Quiet on cage floor...”

Day 81 “Quiet, eyes partially closed...
Appears tired and weak.”

Day 95 “Body and head tremors.”

Day 98 “Reluctant to move.”

Day 99 “Sacrificed...”

Baboon X205m:

Day 1 “Quiet”

Day 2 “Transplanted heart possibly fibrillating.”

Day 5 “Vomit on cage floor.”

Day 11 “Transplanted heart seems very large
and
possibly discomforting animal.”

Day 14 “...swollen and red, seeping yellow
fluid.”

Day 20 “Keeps holding area where transplanted
heart is.”

Day 21 “...sacrificed.”

¹⁸ www.xenodiaries.org

5.82 *“...complaints were received and prepared a report which sets out their concerns in detail”*

This is a clear indication that animal welfare standards and codes of practice can be set but the various institutions do not have to follow them and can and do frequently breach these codes. This does not help the animals that have suffered or are still in the “care” of the particular establishments. There is no protection for animals at all!

5.83 *“...some studies will be required using nonhuman primates as the transplant recipients.”*

This just indicates one of examples where the decision to have xenotransplantation proceed has already been made by the XWP.

XWP response (use of nonhuman primates)

5.86 & 5.97 *“...develop a new supplementary policy for the use of animals in xenotransplantation research.”*

There is still no protection for the use of animals in research this is just providing another policy or code of practice.

Impact of procedures

5.92 *“...to achieve scientifically valid results.”*

Subjective, how can this be measured? What constitutes a scientifically valid result?

The nature and extent of the genetic modification

5.101 *“...but will be assessed by individual AECs based on in-depth knowledge of the species.”*

Firstly this is putting the onus back on an AEC. It would be extremely hard to have an AEC whereby all its members have an “in-depth” knowledge of several entire species, ie rats, pigs, baboons, etc. There is no possibility of all members of an AEC having an “in-depth knowledge” as required by this clause.

5.103 *-“This reduces the need for any of the procedures described in paragraph 5.102”*

How does “using eggs obtained from sows killed at abattoirs” etc, reduce the distress caused to animals used in genetic modification and cloning procedures? Firstly, the eggs (from slaughtered sows) would not be “pathogen free” and secondly, researchers would still be surgically inserted the eggs into laboratory bred pigs.

The unpredictability of outcomes

5.106 *“...An additional uncertainty that is created by genetic modification of pigs to make their tissues and organs more compatible with human transplant recipients is that the pigs may become susceptible to human infections.”*

This statement acknowledges the problems of cross-species infections and that infections can work both ways. Humans will have the ability to wipe out other species of animals by cross infecting them with human viruses. If there is any possibility that this may happen then we also can assume that it **will** happen.

Wastage of animals

5.107 *“... However, the use of materials from abattoirs (such as eggs obtained from pig ovaries) and cloning techniques involving cultured cells reduce the number of live animals used.”*

Mere speculation, there is no measurement in place that would lead to this conclusion. Assuming that xenotransplantation has not been authorised yet, how can figures gathered and how can XWP anticipate there would be a reduction in the loss of animal lives? Then what about the numbers of mice, dogs, rabbits, etc. that would be used during animal-to-animal studies?

National oversight of animal use in xenotransplantation research

5.113 *Third bullet point “...the final decision over the approval of any project involving the use of animals must remain in the hands of the relevant institutional AEC.”*

We need an urgent overhaul of the rules governing AECs. We do not believe AECs are independent or are able to monitor and control experimentation in the institution once an experiment has been approved. We have seen that they are self-regulatory and in the proposed flowchart in Figure 11.1 in paragraph 11.51 of the Response Paper, their authority in the scheme of things is extremely low.

Guideline on animal welfare

5.124 *“...whether xenotransplantation is “acceptable” has yet to be debated and determined.”¹⁹*

We categorically agree with the sentiments contained in that statement.

Conclusions

5.127 & 5.129 *“...has also decided to produce a policy statement on the use of animals in xenotransplantation research to assist AECs to assess and monitor such studies.”*

These rules whilst sounding as if they are designed to protect animals have no bearing on the treatment of the animal when it comes down to the nature of the actual experiment.

6 Alternatives to animal-to-human transplantation

Human organ and tissue donations

6.5 *“despite these efforts, for most tissues and organs, in Australia as elsewhere, there are not enough donor tissues and organs available for transplantation.”*

We disagree that there has been any serious “efforts” made to the alternatives as listed. We need to seriously address this issue NOW because human donors are far more compatible and ethical than using “source animals”. See news articles attached.²⁰

Improving donation rates

6.7 *Point two If the problem lies in a lack of organs for transplant, then wouldn't it be better to put serious efforts in investigating means of increasing organ donation?”²¹ .*

This seems the most logical and beneficial option for humankind and the most ethical and human for animals and we refer to our comments for Paragraph 3.29 pointing out the value of high profile individuals canvassing for human organ donations.

The best method to promote human organ donation rates was put by an individual at the Public Consultation Meeting held in Perth on 16/02/04, whereby he suggested, “if you aren't prepared to donate an organ you shouldn't expect to receive one” (or words to that effect).

6.11 & 6.12 *“...the prospects for long-term survival have been promising.”*

This indicates that human organ and tissue donation has the most promising outcome for human transplant recipients.

6.13 *“...However, unless there is a dramatic increase in the number and quality of donations, the development of animal transplantation therapies may ultimately prove to be a valuable alternative that will maximise the number of people who can be successfully treated.”*

¹⁹ Animals Australia (Submission X050)

²⁰ Sunday Times 22/02/04 – Article attached

²¹ (Respondent details confidential)

Would xenotransplantation be stopped once the human donations increased? We would hope so! What do the XWP consider as an acceptable level of human donations? We further comment that the “successfully” treated statement gives the false impression that xenotransplantation actually works.!

Presumed consent

6.2 *“I do not feel that “presumed consent” has been adequately explored...”²²*

We believe further and intensive campaigning on the merits of presumed consent need to be addressed.

6.23 *“Systems that could address the short-term need – presumed consent, changes to hospital procedures and payment for organs – are not in place because it is assumed the social, emotional and ultimately political objections they raise cannot be overcome ...”²³*

A statement like this highlights the need to campaign strongly for the use of human donations as opposed to animals used for providing us with spare parts. This is not an insurmountable problem it merely requires people to discuss the issue with loved ones. All of us have the ability to provide the answer to the current available organ shortages. It would be far more cost effective for society to embrace this concept than that of subjecting animals and eventually humans to the suffering anticipated with xenotransplantation and its additional baggage of lifelong monitoring of xenotransplantation recipients.

6.26 *“...the system of presumed consent would not work well in Australia because of cultural factors associated with the diverse multicultural population...”*

Why would this not work any better than any other country or using a diverse species of animals? Statistical data proves human to human transplant patients have a better and longer chance of survival. 93% success rate for human-to-human heart transplants with a life expectancy of approximately thirteen years was quoted at the Perth Public Consultation meeting recently (16 February 2004).

One of the members of the public also quoted that they felt that “if you don’t list yourself as willing to donate (an organ) then you shouldn’t expect to receive one” which we think is an extremely valid point and should be advertised more in the interests of increasing human organ donations!

Use of organs from living donors

6.32 *“The left lobe of liver can be removed from an adult and transplanted into a child with a relatively low risk of complications or death of the donor. However an adult recipient requires donation of the right lobe of the liver. This procedure has been associated with a significant complication rate and occasional deaths of donors, and is not in routine practice in Australia.”*

If complications such as quoted above exist just in the different use of the same donated human organ to different age groups in human recipients, how can bringing in a totally “wild card” with animal sourced organs expected to achieve a better success rate?

Human external therapies

6.36 *“Primary cultures of human liver cells can be set up from relatively small samples of human liver; such as transplant discards...” and “...Early trials using human cell external liver support therapy for people with liver failure have shown similar results to those obtained using pig cells...”*

Once again, there are significant indications of a better success rate with the use of human tissues. We believe the use of xenotransplantation would provide dangerously misleading results.

²² Kerrie Donaldson (Submission X092)

²³ Queensland Health (Sub X014)

Further, the Response Paper pointed out the huge anomalies, which exist with use of the same organ, ie liver, within the same species and for the same procedure, ie adults and infants and where portions of an organ have to be used instead of the whole organ, especially in case of dialysis.

Human cell therapies

6.37 *“Recent scientific work on the culture of human stem cells has raised hopes for future therapies to repair human organs and treat a range of diseases.”*

6.39 *“Comments in the submissions received were generally in favour of human stem cell research.”*

We believe this is a more acceptable method of research whereby it is based on human therapies for human results.

Artificial organs

6.41 & 6.44 & 6.46 *“However, at this stage there is no clear indication whether the human or animal therapies will have an advantage in any particular clinical circumstance.” “...artificial organs therapies” “Improving transplant outcomes...”*

All paragraphs are very true therefore reinforces that animal studies cannot be extrapolated to human conditions and illnesses.

Preventative programs and lifestyle education

6.48 *“...The cause of Parkinson’s disease is unknown but the illness is not related to poor lifestyle choices; other neurological diseases, such as Huntington’s disease are genetic.”*

Obviously genetics play an important part in the susceptibility of disease. While the concept of identifying “bad” genes and therefore preventing pregnancy in some individuals may seem somewhat repugnant, it would be far more tragic for parents to cling to the false hope that a xenotransplant might provide some miraculous outcome.

Further at the Public Consultation Meeting held in Perth on 16 February 2004, some members of the XWP panel conceded that lifestyle played quite a large part in the cause of illness.

Quite obviously, a change in the general population’s lifestyle would prevent a major portion of those requiring transplants from being on waiting lists and allowing those that became ill due to other causes to receive transplants from human donors.

Conclusion:

6.51 *“Organ and tissue donations are required to overcome a large range of diseases and conditions. Xenotransplantation is only one of a number of approaches that might be used...”*

We believe that any amount of funding directed into xenotransplantation research will be wasted. Funding should be directed instead towards human based research.

6.52 *“Although vigorous efforts are needed to increase the number of human donations... it is unlikely that such efforts will overcome the extreme shortfall”*

We argue that the use of money towards animal based therapies will certainly not change this situation. Human organ donations would increase we just need to concentrate on this method and not on xenotransplantation.

6.53 *“In terms of the various alternative therapies that are currently being researched, the XWP felt that Australia should be able to opt for the therapy that is considered the most efficacious and safest at the time.” “Before agreeing to proceed with a trial of animal to*

human transplantation, the proposed regulatory committee will need to consider all alternative therapeutic options available...”

We would assume this could only eventuate after many years of countless animal experiments. Already findings with human to human transplantation (allotransplantation) are showing promising results, whereby xenotransplantation studies carried out in other countries are only showing extremely horrendous results eg. Baby Fae, etc.

6.55 *“Until we can more accurately identify the best option for particular diseases and conditions, it may be the best to adopt an integrated approach involving a range of different options.”*

We think that the use of xenotransplantation will only exacerbate the problem of finding the best approach to tackling human disease!

7 Resource Issues

Overview: “Should there be a more extensive discussion of resource allocation for xenotransplantation research and clinical trials now, or can these issues be postponed until it becomes clearer that xenotransplantation is likely to become a reality”.

There definitely should be more attention paid to resource allocation. It’s a bit late to undo funding or get money back once the point of “no return” has been reached. Equally there needs to be checks and balances in place with regard to research grants and other financial issues to prevent a point of no return. The NHMRC and more relevantly the XWP need to be over one hundred percent sure that they have succeeded in finding the “Holy Grail” and how could this ever be measured?.

Resource allocation

7.1 *“How xenotransplantation research fits with the general scheme of medical research that should be funded must be explored and justified.”²⁴*

It seems apparent to many respondents that the XWP has already made some decisions when it comes to funding, etc, that it is “beyond the scope” of the XWP and its decision making process.

7.2 *“...address the shortage of organ donations than spend money on animal-to-human transplantation.”*

We thoroughly concur.

7.4 *“In preparing the Discussion Paper, the XWP thought that it was beyond the scope of the working party to consider the full economic impact of animal to human transplantation research (Discussion Paper, Section 3.4)”*

We believe that this is a paramount factor in this area. At what point does it become too expensive or inappropriate to continue with xenotransplantation? All aspects of funding needs to be addressed and fully considered now before any authorisation is given.

Public funding:

7.7 *“Research grants are awarded on the basis of scientific quality, as judged by peer review.”*

What consideration is given to ensure that the grants are not given where duplicate experiments are being conducted in other countries or institutions? What checks are in place to take the onus off AECs when supplying for authorisation for research grants and how is “value for money” measures weighted.

²⁴ Human Research Ethics Subcommittee of the Department of Human Services South Australia (Submission X055)

Access:

Access costs have been discussed with the view to availability of xenotransplantation to those who cannot afford the costs and whether the taxpayer should fund this area.

We believe that this line of research would be a total waste of taxpayer money, and would certainly not be in the best interests of the community or serve the “common good”. How could this be measured and who would be in the position to monitor “access”?

7.23 *“...it is impossible to predict what public funding may be made available to set up transplant units in public hospitals...” Further “...the pattern of funding is likely to be the same as that for similar procedures, such as allotransplantation.”*

This is very true and given that setting Australia down the path of xenotransplantation is fraught with potential and highly probable risks we believe that no amount of money can protect the community from the dangers. How much money has been directed to allotransplantation?

Costs

7.25 *“Some [respondents] anticipated that a cost-benefit analysis of animal transplants would be poor”*

We concur! The costs associated with human organ donation is only in terms of cross-matching donors with patients, maintaining the organ during transportation and having the patient prepared for the operation. Voluntary or self-funded, community based groups provide many of these (cross-matching) services. However, the hidden costs of providing genetic modified animals, housing, feeding, medication, sterile conditions, transportation, animal husbandry and veterinarian staff, etc far outweigh the alternatives of cost-effectiveness provided with allotransplantation!

It seems a fair observation that the NHMRC have “lots of money” and are just finding new ways to spend it.

7.31 *“...there is still considerable uncertainty about the practicalities” of xenotransplantation. There is a call for the “non biased” assessment of xenotransplantation before proceeding with any form of clinical study.*

Each day we read about new outbreaks of viruses that have “jumped the species barrier”.²⁵

7.33 *“...the current costs of treating people with diseases such as renal failure is also very high: one year of dialysis is estimated to cost \$50,000-\$70,000 per patient...”*

How much money is going to be spent on animal-to animal then animal to human transplant research? We believe a far lot more!

Liability:

It is far too late to apportion blame when something has “gone wrong”. There is no technology that can fully guarantee to be one hundred percent risk free. When something does go wrong all the people involved in this research will all duck for cover and fob any blame off with “we had all the checks in place”. We will not be convinced that there can be any safe procedures while manipulating genes and xenotransplantation.

There are still dangers and risks associated with blood transfusions requiring the need to be heavily screened for BSE (Bovine Spongiform Encephalopathy, AIDS (Acquired Immunodeficiency Syndrome), hepatitis and other contagions before being transplanted. In the case of BSE, blood donations are refused from donors who have visited the United Kingdom for more than a 2-month period since 1985.

8. Will animal to human transplantation work?

²⁵ Refer to attached News Articles.

“Any proposed clinical (animal to human) xenotransplantation trial must be based on preclinical (animal to animal) studies that demonstrate therapeutic benefit to the participants.”

Can we assume from this statement that the animals that are to undergo the preclinical studies will be suffering from a (natural) pre-existing condition that will be alleviated by the procedure and therefore directly and therapeutically benefit from the trial?

Animal external therapies

8.2 *“The use of a whole pig liver for such perfusion invokes an immune response similar to that described for animal organ transplants...”*

Once again there exists a anomaly occurs with the use of a partial organ and use of a whole organ.

8.3 *“Skin grown from the patient’s own cells is less likely to be rejected...”*

Taking cells and tissues from the patient and treating them with their own cells THUS preventing rejection and therefore the body would not require to be overloaded with immunosuppressive drugs causing infection or the body to be open to viral attacks.

Animal cell therapies

8.6 *“ACTs can provoke an immune rejection response...”*

Further indicating that the body’s immune system has to be completely incapacitated.

Immune rejection

8.12 *“Certainly, if the transplant survives the initial HAR and DXR responses, it will be subjected to the same adaptive rejection processes that occur for human-to-human organ transplants...” and “...we will not know how big a barrier to successful xenotransplantation this will prove to be until HAR and DXR are overcome”.*

There are so many different possibilities to xenotransplantation that it could not be considered a viable proposition in the distant future so how many animals will have to suffer in the meantime?

Anatomical and physiological barriers to AOT

8.13 *“...there appear to be no insurmountable physiological barriers to the use of pig hearts and kidneys”*

There is no guarantee that there will NOT be any unforeseen and irreversible effects of using another species.

8.22 *“The XWP has been advised that researchers in the field are aware of these issues...” Further “major obstacles are to be expected...”*

Referring to the problems associated with 8.17 to 8.21 in reference to pig kidney, heart, lungs, liver and final transplantation into human recipients. This is reminiscent of the “how long is a piece of string” and the emphasis being on two words “... researchers HOPE that pig hearts and kidneys MAY function...”

Use of genetically modified pigs

8.25 *“Researchers HOPE that any genetic abnormalities identified in founder pigs can therefore be screened out and that other possible problems MAY be overcome by cross-breeding”*

Hoping to screen out genetic abnormalities does not guarantee success.

Animal-to-animal studies

8.30 *“Overall, most researchers in this field agree that the preclinical testing of xenotherapies can best be carried out using primates...”*

I am sure that they would agree when they are the ones receiving the research grant.

8.34 *“The XWP felt that any xenotransplantation therapy should be tested in baboons before human trials can be undertaken.”*

There has been approximately thirty years of serious human-to-human transplantation already documented with clinical trials and anecdotal evidence. This is a retrograde step for research to begin trials all over again is a sheer waste of money and animal lives.

Effectiveness of animal therapies

Animal external therapies

Bioartificial livers

8.36 *“Since the 1960s, whole pig, calf and baboon livers have been used intermittently to externally perfuse blood from patient with liver failure, but such trial have been largely discontinued because of concerns about infection and problems of immune rejection.”*

Since these trials were discontinued due to risks of infection and problems of immune rejection why is the XWP proposing to allow Xenotransplantation to proceed when there will be exactly the same problems encountered with immune rejections and with similar risks of infection and why after 40 years does the XWP feel that these problems will be overcome with xenotransplantation?

8.37 *Table 8.1 (page 91) Number of patients 10; “A significant improvement in symptoms. All bridged to a liver transplant but 2 died after transplantation. No severely adverse events...”*

Death we would presume to be a MAJOR adverse event!

Animal-to-human trials

8.46 *“...thought that these results, combined with the animal to animal data, did not show enough improvement to warrant further clinical (animal to human) trials..”*

How many trials need to be conducted until a decision is made to discontinue studies in that particular area? Many respondents have indicated that these trials cannot be justified for further research.

8.48 *“Nevertheless, the clinical trials to date have provided some encouragement for researchers...”*

This statement is of course true, if they didn't show “encouraging” results the research grant would be rejected or cancelled.

Animal organ transplantation

8.51 *“This infectious risk meant that nonhuman primates were no longer considered to be suitable donors for AOT. Researchers therefore turned their attention to pigs...” Further “A single pig-to-human heart transplant carried out in the early 1990s survived for less than one day.”*

There is no guarantee that viruses especially PERVs will not become apparent until some time down the track. Therefore creating a huge risk to the community at large. SARS, Avian Flu (H5N1) and others are still cropping up when least expected.²⁶

Animal-to-animal studies

8.53 *“Clearly, these studies show only short survival times, even when the recipient animals were heavily immunosuppressed, their blood was treated to remove antibodies that might cause rejection and in some cases, their spleens were removed to further suppress their immune response.”*

²⁶ Refer to attached News Articles.

The prognosis for human patients does not look good if removing spleens is the remedy for “anti rejection” treatment and preventing rejection in animal experiments.

8.55 *“Table 8.3.....Although these pigs have answered important biological questions, they are not the definitive answer on genetic manipulation for animal-to-human transplantation.”*

We believe that this would be an important factor for NOT allowing xenotransplantation to proceed.

8.57 *“UKXIRA (2001) “It seems, therefore, that the likelihood of whole organ xenotransplantation being developed within a clinically worthwhile timeframe is increasingly remote.”*

What more could we possibly add?

Definition of therapeutic benefits

8.59 & 8.60 & 8.62 *“...The XWP asked if it was possible to define a reasonable criterion for success in animal to animal studies, on which progression to clinical trials (animal to human) can be based.”*

The terms “reasonable” and “based on effectiveness” are highly subjective and we ask how this could possibly be determined given the diverse requirements of individuals.

8.66 & 8.67 *“Therefore if there is a viable animal therapy available, it may be possible to select a subgroup of patients for whom the potential benefits would be worth the risk” and “...(such as the known serious side effects of immunosuppression) would also need to be taken into account in both the decision to allow a trial and individual patient selection.”*

In all circumstances, the actual transplant may be a success but the patient dies due to the immunosuppressive side effects. It would not be possible to keep a patient functioning without their own body defences system working at some stage during their life.

Conclusion

8.72 *“Finally, the NHMRC is concerned to make sure that if any animal to human transplantation trials proceed on this basis, they occur within a framework that ensures highest ethical standards possible for the animals and humans involved and that protects the safety of the community at large.”*

Where xenotransplantation has existed in other countries the animals have not been treated ethically, even with “guidelines” established (HLS) further the NHMRC cannot make any guarantees that that community will not be at risk.

9 Risks of infection (Safety)

Main community concerns

9.2 *“...the risk of a new infectious disease emerging in humans however small, is not acceptable...”*

We concur with this statement. One human death due to an unforeseen event such as a transmitted virus in another human (perhaps sitting on a train) is not acceptable.

9.4 *“[viruses] that do not cause disease in their non-human hosts, still impose a potential risk to humans under such conditions. ...may modify themselves, once transmitted to humans and become severely pathogenic, HIV-1 which originated from non-human primate species, is an example of such a virus...”²⁷*

The risk is far too great for dabbling with xenotransplants.

²⁷ International Xenotransplantation Association (Sub X077)

9.5 *“minimal risks”*

What is minimal risks? Any risk has the potential to have serious consequences. This is just a term and cannot be measured.

9.6 *“...(SARS), which were coordinated by the World Health Organisation and government agencies, were effective in controlling the outbreak.”*

Not for the people who died and the death of hundreds of thousands of animals. Controlling is not the same as preventing.

General infection risks from animal-to-human transplantation**Known disease agents**9.9 *“...a number of respondents were concerned that known pig diseases may be a greater problem than indicated...”*

Yes this is totally an unknown area. Viruses or diseases not yet detected cannot be measured.

Novel and evolving disease agents9.13 *“...more serious public health concerns about the risks of animal to human transplantation...”*

This concern cannot be underestimated.

Porcine endogenous retrovirus (PERV)**The evidence**9.23 *“Central to the debate about PERV is research that shows that, to date, of over 200 human patients who have received animal to human therapies, none has become infected by PERV.” Further “However many of these were found to have some pig cells circulating in their bloodstream, which was unexpected (Paradis et al 1999).”*

This is totally unacceptable and goes to show to expect the unexpected!

9.25 *“Other researchers have also reported PERV viral expression (activation) in pig to mouse transplant experiments (Van der Laan et al; 2000)”*

Already the bells are starting to ring!

9.27 *“Alternatively, some researchers are turning their attention to pig breeds (eg ‘minipigs’) that do not carry the type of PERV genome that has been shown to infect human cells in culture.”*

How can safety precautions and risk prevention be put in place when such variations can be seen within the same species. More bells and whistles!

Animal external therapies:9.29 *“If animal external therapies (AETs) are perfected...the risk of transferring PERV or other pathogens may be considered minimal.”*

This is not a fact because AETs have not been perfected and the transmission of pathogens is a serious risk. What is considered “minimal” in this instance?

Animal cell therapies:9.30 *“In animal cell therapies (ACTs), risks may vary according to the procedure used. ...encapsulation of the transplanted cells may help to block the transfer of any infectious agents from the transplant to the recipient...” And further “...Such results indicate that current microencapsulation techniques will not be sufficiently robust to contain infectious*

agents, which remain viable for as long as the transplant.”²⁸

Presence of infectious agents need to be monitored, not only for as long as the transplant but for the life of the patient due to the antibodies that would have built up in their blood stream.

Animal organ transplants:

9.31 *“Animal organ transplants present the highest risk of infection because more tissue is transplanted...” and “... including direct association with the blood supply of the recipient, which would continue over the long term...”*

Risk of infection and other biological hazards can remain dormant or undetected for years. What may look “promising” can turn out to be quite the opposite a few years on. We must not allow even the smallest risk to endanger the health of the community.

XWP Response:

9.35 & 9.42 *“The XWP envisages that the role of the national xenotransplantation committee, working according to NHMRC guidelines, will be to engage the necessary expertise to independently review...in the light of the most recent research evidence as it becomes available.”*

This is akin to shutting the stable door after the horse has bolted. Many studies will be conducted all costing hundreds of thousands of dollars and there would still be no time limit and each case would still be proposed to go ahead as it would be the “most recent” of the studies.

How safe is safe?

Risk versus benefit

9.40 *“Many respondents stressed that the risk of a new infectious disease emerging is too high a price to pay for the unproven benefits of animal therapies to date.”*

This does not just apply for current technology but applies to any future developments. There can be no guarantee of safety or prevention of new diseases or viruses.

9.41 *“An important aspect of risk assessment is the seriousness of the consequences, or the impact, if the risk event occurs.” Further “...and any investigator undertaking animal to human transplant trials would be required to submit documented procedures that address those issues.”*

There is an important word here and it is “IF”. Rest assured that if there is the slightest chance an infectious breakout can occur it WILL occur and it has in the past. Mistakes do happen and even natural events or travel cause contamination or spread of disease, radiation, or pollutants, ie Chernobyl, H5N1, Exxon Valdez, AIDS, etc.

Risk management

9.43 & 9.46 *“Factors that affect the risk of infection....include the conditions under which source animals are reared, genetic modification of source animals, how the xenotransplantation product is produced, what health care infection control procedures are used during and after the procedure, the type of procedure involved, and the level of immunosuppression of the patient.”*

There are other factors that have not been included such as: length of monitoring of the recipient’s condition (for their lifetime), recipient’s lifestyle and contact with the general public, disposal of the body and organs if the recipient dies (ie at the funeral director), or community protection from infection say for police or ambulance at a motor vehicle crash, or blood transfusion, etc.

International cooperation

9.53 *The International Xenotransplantation Association has drawn serious attention to “xenotourism” aspect of xenotransplantation, including how would recipients be monitored and*

²⁸ Dr Anthony Raizis (Sub X034)

that this situation has not been addressed by any of the authorities of any country where xenotransplantation has been allowed to be conducted.

It is all very well to say there is current monitoring and regulation in place eg for the recent outbreak of SARS, however SARS is transmitted unknowingly whereby xenotransplantation is a conscious decision made by the recipient and their close contacts.

Management of an infectious disease incident

9.54 *“...transplantation research protocols should include procedures for the management of a public health risk if an adverse event occurs...”*

Serious health risks of cross species infections and viruses are already being experienced and the WHO and other governments are battling to contain spread of viruses (we are referring in particular to SARS and H5N1).

The battle is enormous; we should not even be considering any further possibilities for cross contamination. We are currently witnessing the mass slaughter of poultry in Asian countries, could the world sustain another loss of a food source, ie pigs?

Further the cross infections work both ways and species could become infected with human viruses to cause massive loss to various herds and flocks.

Conclusions:

9.56 *“Like other animals, including humans, pigs carry many disease agents. Most of these are well known to microbiologists...” “...there should not be a significant risk of dangerous infections in animal transplant recipients.”*

Any risk would be significant!

9.57 *“However, some disease agents have only recently been identified and are less well known. These include the endogenous retroviruses, such as PERV...” “For many people, such a risk appears unacceptable, especially when the benefits that can be delivered through animal therapy procedures are uncertain.”*

We thoroughly concur and we should not even be considering this type of study. We need to get back to basics of human organ donation and human studies.

9.58 *“Tests have also been developed to monitor transplant recipients for infection.”*

This could mean lots of things however does not alter the fact that when an infection is discovered what happens then? Do we euthanise the recipient to prevent further infection? Do we also euthanise any person they may have come into contact with? We think not! However the problem remains real so how do we contain any outbreak of disease?

9.60 *“Trials with an unacceptable level of risk should not be allowed to proceed.”*

How would this be monitored? An “unacceptable level of risk” what is an acceptable level?

10 Managing animal-to-human transplantation trials

Overview

Guideline 4 (Consent)

The research protocol must include:

(a) procedures which when followed ensure that the consent of potential research participants is obtained after the necessary information is provided (Guideline 3) and which allow the participant to take a reasonable period to think things over and discuss the information provided with their close contacts; and

(b) consent forms that clearly set out what is being consented to, including the need for ongoing

and long-term surveillance for possible emerging personal and public health risks; and

(c) procedures for collection of signed information sheets (or equivalent) from close contacts of research participants.

The above is truly frightening! How can people consent to a procedure that cannot be guaranteed? What rights do close contacts have to withdraw their consent at a later date? Would a spouse or *de facto* relationship be considered to be a close contact? What happens in divorce or separation issues? How would the health of children be monitored? When can the rights of the community overtake the rights of the individual? Does this cover close friends and/ persons who come into short term contact eg taxi drivers?

“Screening and testing of close contacts were seen as essential to any management strategy.”

Does this also mean if a patient consents to undergo a xenotransplantation procedure, those close contacts who do not agree are removed from contact with the patient for the life of the transplant? Or does it mean the patient cannot go ahead with the transplant? What a terrible pressure to be placed on a “close contact”? “It’s the dog or your baby?” in a new form.

Who are the “research participants”?

10.6 *“...criteria need to be developed to define a “close contact” ...*

XWP Response

10.11 *“... contacts should be considered as research participants for the purposes of complying with compensation and insurance arrangements...”*

Information sharing and consent

10.19 *“Possible feelings of loss of identity that might be experienced by animal transplant recipients...”*

We refer to other transplant problems such as “1998 (Sep) France first hand transplant that was successful in short term but removed in February 2001 at the patient’s request.”²⁹ “However, one should remember that since these surgeries are still in the experimental stage, all of the patients are carefully selected and have the least risk of problems resulting from the surgery.”³⁰

Ethics of monitoring and follow-up of trial participants and contacts

Is lifelong monitoring and follow-up acceptable?

10.29 *“...Research participants and their close contacts may become unwilling or unable to continue to cooperate.”³¹*

How can people be prevented from say living in the country and not being available for clinical follow-ups and checks? What will happen to people who refuse to participate – gao! them?

10.31 *“There seems no alternative to life-long monitoring but it is hard to envisage how it can be managed and harder to judge how we would react in a worst-case scenario in which an Ebola-like disease emerged.”³²*

10.33 *“...more attention should be paid to the investigator’s evidence of safety.”*

We do not believe that there can be any minimum limit placed on safety. What happens to the investigator if their evidence proves false or unforeseen?

Ethical and social responsibility of the research participant

²⁹ www.rnw.nl/science/html/hand010717.html

³⁰ http://biomed.brown.edu/Courses/BI108/BI108_2003_Groups/Hand_Transplantation/costa.html

³¹ Maren Child (Submission X030)

³² Armadale Health Service Ethics & Research Committee (Sub X048)

10.35 “...only time will determine what the requirements of “participation” will be.”³³

10.37 “it will be essential to select research subjects who appear capable of fully understanding the potential impact of their behaviour...”³⁴

We refer to the fact that we believe that screening does not guarantee that research subjects will adhere to social responsibilities or life long monitoring.

Costs and compensation

There certainly has not been enough thought of costs and budgets in this section. The cost to the community has not been adequately covered, especially in the costs of compensation, insurance, legal liability for the medical profession and NHMRC to the community. We also refer to the fact that Section 7 dealing with Resources Issues in the Response Paper only covers approximately ten pages.

The XWP in its conclusions stated “*Participation in animal to human transplantation trials will be free to the patients involved, as the costs of such research will be borne by the research sponsors*” and then qualifies it by saying “*To date, research sponsors may not have adequately assessed all the costs involved in conducting animal to human transplantation...*” This is only refers to the animal to human clinical trials not the animal-to-animal preclinical trials required to “perfect” the technique. How much will this cost?

Overall XWP response (ethic of long-term monitoring and surveillance)

10.48 *Bullet points: “the participants understand that although they retain their right to withdraw their consent for further medical treatment (ie withdraw from the trial) at any time, they will not be able to withdraw from long-term monitoring and surveillance; and “ the close contacts also understand the requirements for long-term monitoring and surveillance:”*

Again, what will happen to them if they don’t want to comply? It’s OK to say that there is mechanisms in place already as for SARS, but SARS does not involve life long monitoring of the patient and close contacts which would be the case with xenotransplantation.

Conclusion

Definition of research participants and close contacts:

10.49 “...research participants in animal –to-human transplantation trials should be defined to include the transplant recipient only...”

This would certainly keep costs and compensation claims down but not protect the community.

10.50 “...close contacts should be closely involved in the information sharing process...”

If this is approved then all the previous concerns for cross contamination and spread of viruses will be for nothing. There will be no protection for the close contacts other than “we gave you a leaflet to read and you signed you have read it”.

10.51 “...will need to be worked out on a case by case basis.”

Who will be designated responsible for this and how will this be enforced?

Information sharing and consent arrangements

10.56 “*Consent to participation in the trial should be separate from consent for long-term monitoring and surveillance as participants will retain the right to withdraw from the former but not from the later.*”

Once again what would the penalties be – gaol or fines or both?

³³ Kerrie Donaldson (Sub X092)

³⁴ International Xenotransplantation Association (Sub X077)

Monitoring and follow-up of participants and contacts

10.60 “...[xenotransplantation] be allowed to proceed only if the trial protocols include validated processes for monitoring and surveillance of public health risks of research participants and close contacts.”

If close contacts are not required sign consent forms because they are “not research participants” as designated in 10.50 but the research participant (recipient) does, how can “validated processes for monitoring and surveillance” take place?

Further should it be a requirement that animal organ recipients, prior to undergoing a xenotransplantation, sever all ties with family and close contacts rather than subjecting them to the rigours of lifelong monitoring and surveillance?

Does this monitoring of close contacts finish after the recipient has died?

Has the XWP satisfied itself that lifelong monitoring and surveillance of recipients and close contacts complies with an individual’s basic civil rights and privacy laws?

11 Regulation of animal-to-human transplantation research

General considerations

11.3 “... even if such research [xenotransplantation] is allowed to proceed, it will be many years before any therapies involving animal-to-human transplantation become routine clinical practice.”

Human organ donation is currently happening now and is quite advanced. Recipients of human organ donations have an above 90% chance of survival with approximately a ten year life expectancy. By funding research into this area will surely increase this again? Increasing the donor rate will also provide a good resource for tissue and organ transplant products.

11.5 “It is also a requirement of the NHMRC that all NHMRC funded research be conducted in compliance with this code and any other related NHMRC policies on the use of animals. Compliance with this requirement is overseen by the NHMRC AWC.”

It is already pointed out in the Response Paper that this is only a code of practice and not enforceable on private institutions. There is no “teeth” in this requirement as AECs are not legally bound to monitor experiments they approve.

11.7 “... the NHMRC Research Committee formed a subcommittee known as the Gene and Related Therapies Research Advisory Panel (GTRAP)...”

GTRAP would never be a truly “independent body”.

11.10 “...HRECs should not approve research that involves gene and related therapies without the prior approval of both the institutional bio-safety committee and GTRAP.”

11.11 “...there is currently no guarantee that GTRAP’s decision will be final.”

Give with one hand take away with the other.

Regulation of research involving gene technology

11.23 *Bullet points: “Source animals modified by gene technology are classified as genetically modified organisms (GMOs)”*

Would this distinction then be passed on to the recipient of an organ received from a GM animal?

- “...the researchers will need to obtain a licence from the OGTR;”
- “xenotransplantation of genetically modified material does not involve an “intentional release” of a GMO; and...” If transplanting an organ from a genetically modified animal into a fully informed recipient is not “intentional” then what is?
- “live animal transplantation products for use in humans would be classified as GM products under the GT Act, which means that they would not be further regulated by the

OGTR...”

Then what is the purpose of “obtaining a licence from the OGTR” as in the previous bullet point under this paragraph number? It appears all mirrors and slight of hand to give the appearance that there are strict regulations in place.

Therapy-specific considerations

11.29 “...Accordingly it [XWP] suggests that the regulatory regime adopted should focus on safety, efficacy, animal welfare etc, on a case-by-case basis.”

This then enables side stepping of procedures or protocols set in place by this Response Paper and any subsequent “Guidelines”.

Therapeutic Goods Administration discussion paper

11.43 “It now appears likely that xenotransplantation and gene therapy will be included as high-risk therapies under a revised TGA Act. The new legislation will ensure that clinical trial applications will have to follow the CTX application route and that there will be no access to the Special Access Scheme.”

Completely refutes the arguments of many of the points in Section 11.

Comments from Gene and Related Therapies Research Advisory Panel

11.44 “Based on the information provided in the Discussion Paper, GTRAP supported model 1 as the referred model...”

GTRAP are biased as they will be expanded to become the focus of xenotransplantation approval.

XWP proposal for the regulation of xenotransplantation research

National assessment and approval for animal-to-human transplantation trial proposals

11.49 “...and the new developments with respect to revised TGA legislation for biological therapies and decided to propose model 1 as its preferred model for the regulation of xenotransplantation...”

This model needs considerable work in our opinion. The decisions made are still based that animal to human trial will commence in a reasonably short time frame. Whilst it is prudent to have a mechanism in place it appears rather opportunistic given that animal to human transplants have not been “perfected”.

11.51 “...If TGA approval is granted, institutional ethics committees (HRECs and AECs) will be able to consider the trial for inclusion in the research program of their institution. These proposed arrangements are shown in Figure 11.1”

This approval process seems somewhat akin to “putting the cart in front of the horse.” See also our comments for paragraph 5.113.

Firstly whilst we are opposed to xenotransplantation outright, serious consideration has not been given to the pressure placed on the individual AEC and its members. Given that all authorisations from other groups and organisations have been received the AEC then has to give approval to the proposed research program based on the ethical treatment of the animals required for the study.

Further the HREC/AEC are listed in the same process box instead of being totally separate entities. Therefore are they in the same room when the decision is made so to speak?

In Figure 11.1 (Flowchart showing proposed regulatory progress) that approval (or non-approval) by HREC/AECs are both at the same level of process. There is no provision in the flowchart for either ethics committees to each hold a separate review of the proposed animal experiment and approve or disapprove the experiment. There appears to be no thought taken in regard to this issue.

Which of the AEC or HREC holds the ultimate power, for example if the HREC approves an experiment and the AEC does not (or visa versa)? And how does the Working Party propose to

resolve this issue?

The flow chart provided in Figure 11.1 (page 136) should be in two stages.

Stage 1.

Sponsor applies to the individual HREC/AEC* for approval in principle to the study. This allows the two ethics committees chance to evaluate the proposed study without the pressure of financial gains. If the ECs do not approve such research study at this early stage then it would be pointless for the researcher to approach the national bodies for approval. Thus avoiding a waste of the National Committee's time and saving money.

Stage 2

If the sponsor gains approval either from the first HREC and AEC or from another institution's HREC and AEC then it should progress to the next stage of getting approval from the National Committee.

*An important consideration should also be whether approval is required from both the HREC and the AEC before the trial can commence or does one hold more authority over the other?

As an organisation working to end experiments on animals it is not the intentions of Anti Vivisection WA (Inc) to write up the processes for XWP's procedural flowchart, suffice to say however that the whole process is flawed and needs much more serious attention than it has been given.

National oversight of animal-to-animal studies

11.55 *“In particular, respondents noted that it is difficult for AECs to uphold the principles outlined in the Code of Practice because individual committees do not have access to the “bigger” picture of what research has been done elsewhere...”*

This is very true and there is no process in place for “whistle blowers” where they would be in breach of signed confidentiality agreements. Mechanisms need to be in place to protect those who speak out against a proposed research study or one in “progress”.

Committee membership

11.62 *“An AWC member could not be expected to be truly independent...”*

From the word “independent” we assume to mean “unbiased” and this would apply to all types of AWC memberships. The layperson with animal welfare background (Category C or D) could be seen as not being independent if they said “no” too many times. However this should also apply to say the AWC members who were themselves scientists and therefore would be more inclined to say “yes” to all research studies.

Terms of reference

11.68 *All points.*

One important step has been missed out of the terms of reference; **the power to veto any experiment or research proposal.**

11.71 *“...in overseeing the monitoring of xenotransplantation clinical trials...” and further “...should have such powers for both animal-to-human transplantation trial and animal-to-animal studies.”*

This should be regularly monitored and without prior notice having to be provided.

Registry for recipients of xenotransplants

11.80 *“An additional role for any national xenotransplantation committee may be to maintain a registry of recipients...”*

How would privacy considerations be implemented whilst ensuring that all future contact and monitoring checks would be carried out? Would close contacts also require an autopsy upon death?

Appeals

11.81 *“... appeals process both for researchers and for the public...”*

How would the public gain the information to lodge an appeal for a research procedure or study? Usually this information is extremely confidential in nature and would not be available for public scrutiny.

Conclusion

11.86 *“The XWP therefore now proposes that model 1 be adopted...”*

This decision should not be made at this point in time. There are still too many questions to be asked and considered. This is a bit of railroading on the XWP's behalf.

11.87 *“If the national committee approves the proposal, it will be able to be considered further by institutional HRECs and AECs and a CTX application for use of the xenotransplantation product in a clinical trial can be forwarded to the TGA”*

This statement does not appear to follow the procedures proposed in the flowchart!

11.89 *“Under the recommended arrangement, neither the institutional ethics committees nor the TGA would be able to approve trials that have not been approved by the national committee...” Further “an appeals process will need to be developed so that researchers can appeal decisions that do not allow their research to proceed.”*

This should be the other way around and that the AEC and HREC should be the first to give approval. We believe that public should be able to be apart of the appeals mechanism so that individual AEC/HREC members can also appeal a decision.

We refer to our comments in our covering letter.

12 The way forward for Australia

This whole section is devoted to the XWPs proposal for xenotransplantation research to proceed in Australia.

We refer to our comments in our covering letter where we believe that the XWPs proposal is far too advanced given that the proposed research is still in the early stages of public consultation..