From: Brett Lidbury
Date: Friday, 19 February 2016 1:22 pm

Subject: Response to question taken "On Notice"

Re: Senate Environment and Communications Legislation Committee - EPBC Amendment (Prohibition of Live Imports of Primates) Bill 2015

Dear Committee,

During the recent Senate Enquiry conducted on the 5th February 2016, I took a question “on notice” regarding the comparative costs of NHP research to an alternatives approach, not requiring animals. On responding to this question I requested the help of Ms Helen Marston, CEO Humane Research Australia (HRA), who also presented testimony to this enquiry.

Please find attached three documents that should assist with the assessment of this question, two of which are from a previous Senate Enquiry (via HRA). The “Facts” document was prepared by HRA, and as well as some figures pertaining to NHP research costs (scroll towards the bottom), there are a range of other opinions and analyses that may be useful to consider, including some examples of alternatives.

In terms of comparison to an alternative (non-animal) approach, this is very difficult to assess since there is usually institutional support provided to support animal house facilities, including staff. There is also institutional support that is difficult to calculate for researchers (like myself) who do not use animals (except of course, for the maintenance of animal colonies and facilities).

An individual comparison I can provide is on a current study where I am the Chief Investigator – this is a project on Chronic Fatigue Syndrome (CFS) - ME, which attracted funding from the Judith Mason Foundation.

As an alternative approach we recruit human volunteers, collect data and apply sophisticated machine learning methods to disease patterns, to explore in future via other in vitro techniques (this approach replaces a mouse model of CFS/ME).

For an approximately 2-year project that covers my part-time salary (0.3), clinic costs and tests, pathology testing, specialist immune system assays, partial genetic testing, and investigator travel, we have a budget of **$202,745.00**.

Again, there are a number of associated costs for both approaches that are difficult to capture so this comparison is not exact; however, I hope it provides some insights that will assist your deliberations on this important matter.

Thank you again for allowing me to be involved in this Senate Enquiry.

With best wishes.

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Brett A. Lidbury, Ph.D.
Associate Professor,
Pattern Recognition & Pathology
The John Curtin School of Medical Research,
Department of Genome Sciences
College of Medicine, Biology & Environment
The Australian National University
Canberra ACT 2601 Australia

W :http://jcsmr.anu.edu.au/research/genome-sciences/lidbury-group

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Senate Community Affairs Committee

ANSWERS TO ESTIMATES QUESTIONS ON NOTICE

HEALTH PORTFOLIO

Supplementary Budget Estimates 2013-14, 20 November 2013

Question: E13-198

OUTCOME: 1 – Population Health

Topic: Non-Human Primates in Experiments

Type of Question: Written Question on Notice

Senator: Rhiannon

Question:

a) How many primates are currently being held in each of the government-funded non-human primate breeding facilities?
b) For each facility, please provide current information for each species: numbers; ages; sexes; state of health.
c) What are the costs to the Commonwealth per facility?
d) Please provide the history of births and deaths in these primate facilities including, but not restricted to (please date all information):
    i. number of births per species and by sex;
    ii. number of deaths per species and by sex; For each death please provide: species, date, age, sex, attributed cause of death and please provide the documentation associated with the death
e) What is the range of causes of death of primates in the facility?
f) How many of the primates in the facility are used for research or any related purposes?
g) What is the number of research protocols each animal has been subjected to?
h) How many of the deaths are as a result (direct or indirectly) of research procedures? For each death please state:
    i. the history of procedures that the animal underwent?
    ii. What was the species; age; sex; date of death; attributed cause of death.
i) Are any primates being used under licence (or any other method) for research (or any other purpose) by bodies other than Commonwealth agencies, authorities, companies or departments?
j) What are the names of those bodies and their locations?
k) How many primates are held by each body and at which location?
l) Please provide the history of births and deaths while at these facilities including, but not restricted to (please date all information): number of births per species and by sex; number of deaths per species and by sex; for each death please provide: species, date, age, sex, attributed cause of death.
m) What is the range of causes of death of primates in the facility?

Answer:

a) and b)
The National Health and Medical Research Council (NHMRC) provides an annual contribution towards funding the infrastructure for these facilities to provide non-human primates for medical research within Australia.

Responsibility for regulatory oversight of the care and use of animals in these facilities rests with the relevant state government.

c) The NHMRC makes annual contributions to two facilities to ensure that high welfare standards are maintained and to support the supply of animals for NHMRC funded research. The annual contributions are $500,000 for the National Non-Human Primate Breeding and Research Facility and $195,000 for the The National Baboon Colony.

d) to m)
The NHMRC does not have access to this information. Responsibility for regulatory oversight of the care and use of animals in these facilities rests with the relevant state government.

Senate Community Affairs Committee

ANSWERS TO ESTIMATES QUESTIONS ON NOTICE

HEALTH PORTFOLIO

Supplementary Budget Estimates 2013-14, 20 November 2013

Question: E13-199

OUTCOME: 1 – Population Health

Topic: Non-human primates in experiments

Type of Question: Written Question on Notice

Senator: Rhiannon

Question:

a) How many grants have been made that involve using primates?
b) Who/what body was the grant given to?
c) What was the purpose of the grant?
d) What was the dollar value of the grant?
e) What is the purpose of the research or activity?
f) What were the species, sex and numbers of primates used for each project?
g) What projects that involve primates is the NHMRC currently considering funding? For each project please detail:
   i. Who or what body or organisations?
   ii. For what amount?
   iii. What is the stated purpose of the research or activity?
   iv. What are the numbers and species of primates proposed?
h) Please provide names and numbers of relevant people if I need to obtain any further information on the above series of questions.

Answer:

a) Over the previous 10 years, the National Medical Research Council (NHMRC) has offered grants for 60 applications that involved non-human primates.

b) and d)

Grant recipient	**Number of grants**	**Value of grants**
Australian National University	1	$0.6 million
Centre for Eye Research Australia Ltd	2	$1.7 million
Macfarlane Burnet Institute for Medical Research	1	$0.5 million
Monash University	20	$11.0 million
University of Adelaide	2	$1.1 million
University of Melbourne	18	$12.0 million
University of New South Wales	3	$1.6 million
University of Queensland	2	$0.7 million
University of Sydney	9	$3.6 million
University of Western Australia	1	$0.5 million
University of Western Sydney	1	$0.5 million

c) and e)
Medical research including studies into hepatitis C and liver disease; neuroscience, vision, neurology and brain diseases; xenotransplantation, kidney disease and organ transplantation; immunology, virology, HIV and cancer vaccine development; heart disease and pulmonary vascular disease; prenatal and mother's health; and cystic fibrosis.

f) The NHMRC obtained information relating to this question from the final reports provided by grant recipients at the completion of each project. Currently, final reports are available for projects awarded funding that commenced between 2005 and 2009. In these projects, 303 non-human primates were used including 209 marmosets, 51 macaques and 30 baboons, 13 of the reports did not specify the species. The NHMRC does not have data regarding the sex of the animals used.

g) No research projects are currently under consideration. The 2014 research application process has begun, and applications close 5 March 2014. These will then undergo peer review, and recommendations for funding will be made in the second half of 2014. Following recommendations for funding, any non-human primate research will need to adhere to the NHMRC Policy on the care and use of non-human primates for scientific purposes.

h) Requests for additional information, should be directed through the office of the Minister for Health.

FACTS ON PRIMATE EXPERIMENTATION IN AUSTRALIA

Recent Examples:

Primates are used in a variety of research experiments in institutions around Australia. A summary of some of the experiments carried out on primates in Australia include:

The University of Melbourne **fixated the heads of two male macaques** to make them focus on visual stimuli and allow for recording. This type of fixation when performing neurological experiments is called the "halo method"; a circular aluminium frame encloses the entire scalp and is fixed to the skull using 6-8 stainless steel pegs. To record brain activity 2.5 mm diameter holes were drilled in the skull and electrodes were inserted. The monkeys had to release a lever to indicate whether one grating stimulus was different from another. They were later killed by means of a lethal injection of sodium pentobarbitone and their brains were sectioned and examined under a microscope. [1]

In seeking an animal source of islet cells for Diabetes sufferers, **baboons underwent an immunosuppressive regime** before being infused with a culture of pancreatic cells obtained from genetically modified 1 to 5 day-old piglets. They were monitored for one month to investigate the antibodies which developed and the rejection of the transplanted material. This involved slice biopsies taken from their livers. At the end of the study the baboons were anaesthetized, their livers were removed for further study and they were then killed. [2]

The University of Sydney **used the retinas from the eyes of eight marmosets**, four males and four females. The animals were killed by means of an overdose on sodium pentobarbitone, and their eyes were removed and dissected. The relevant sections of the eyes were then prepared and mounted on slides to be viewed under a microscope to investigate a distinct group of amacrine cells. Prior to being used in this study the marmosets were also used in an experiment that took electrophysiological readings from their visual brain centres. To date that experiment has not been published, so the details of what the marmosets were subjected to are unknown. [3]

Forty-four pig-tailed **macaques were infected with Simmian Immunodefiency Virus (SIV)**, either intrarectally or intravenously. Thirteen macaques received SIV or HIV vaccines that were ineffective in controlling the SIV infection. Thirty-one macaques were infected with SIV and then received antiretroviral therapy. Of these 31 macaques, 10 macaques remained unvaccinated, and 20 macaques received one of two peptide-based SIV vaccines. The vaccinations were administered from 4-10 weeks after SIV infection. The macaques had blood withdrawn from their femoral vein while sedated with ketamine. The macaques were killed before developing simian AIDS. [4]

The **kidney tissue of 25 adult marmosets** was used by the Royal Adelaide Hospital and University of Adelaide in an attempt to study renal pathology. Nineteen of the monkeys were killed and six kept alive for associated weight loss observation. Of the 19 killed, 15 had previously been used in fertility studies and 4 in immune biology studies. Some of the reasons cited for their use by the researchers was because of their 'small size promoting ease of animal husbandry', that 'they are not endangered', and their 'rapid generational turnover'. The marmosets were killed by means of inhalational anaesthesia via cardiac puncture. [5]

Earlier research (2009 - 2012):

- Marmosets used in **auditory cortex studies** and then killed at Monash University [6]
- **Preclampsia experiments** were conducted on pregnant baboonsat the Heart Research Institute, Newton NSW. Invasive procedures on pregnant and non-pregnant baboons resulted in the death of a baby and mother baboon [7]
- Eight baboons used and killed to study the **healing process of shoulder tendon surgery**. The eight female baboons, all over 15 years of age, had been used in experiments and breeding programs all of their lives and, scheduled for death, and were taken from the Australian Baboon Breeding Colony to be used in this highly invasive experiment [8]
- **Visual cortex studies** on marmoset monkeys at the Australian Regenerative Medicine Institute at Monash University, where, marmosets aged from one day old, have had their brains exposed whilst recordings of the visual cortex were made [9]
- **Cerebral cortex studies** on primates at the Centre for Cognitive Neuroscience at the University of Queensland [10]

- Owl monkeys used in **malaria research** in Queensland [11]

Click here for a more extensive listing of Australian research involving primates

"As an expert on the welfare and well-being of non-human primates, I believe that using these individuals in research is inherently immoral. Social structure and the opportunity for normal interactions with not only conspecifics (members of their species) in general, but their family members in particular, are crucial for the physical and psychological well-being of non-human primates. The privation of captivity is compounded by the kinds of experiments imposed on these individuals, which often cause intense pain and suffering which cannot be alleviated until the individual is killed. Although they are similar to human beings in some ways, non-human primates are sufficiently different to make them poor surrogates. Only studies on people can provide us with unquestionably useful information about human structure, function and pathological conditions which will be invaluable in understanding and treating human disorders. We are an intelligent and capable species. If we use our intelligence compassionately, we can find ways to answer the questions we have without harming and killing non-human primates."

- Nedim C. Buyukmihci, V.M.D.

Emeritus Professor of Veterinary Medicine

School of Veterinary Medicine

University of California-Davis

Suitability as models for human disease:

Chimpanzees are the species most closely related to humans. The chimpanzee genome (complete genetic material) is 98.77percent identical to that of humans, therefore, researchers argue that chimpanzees will be the species most likely to replicate human outcomes in scientific (biomedical and toxicity) testing. However this small genetic variation between human and chimpanzees accounts for very significant differences in the way diseases affect the two species.[12] Chimpanzees are not currently used in Australian research, and those primates that are used have even wider genetic variation to humans, meaning that the differences in results would be greater again.

Universally accepted in scientific experiments involving human and non-human animal subjects, is the principle that the benefits must exceed the costs. Between 1995 and 2004, 749 papers on biomedical testing on chimpanzees were published worldwide. Ninety-five of these were randomly selected and not even half were cited in subsequent papers. Of those that were cited, only 14.7 percent were mentioned in the abstracts indicating relevance to tackling human diseases.

The degree to which a journal is circulated within the scientific community affects citation rates, therefore, citation rates are not an entirely objective measure of the importance of that research.[13] However, if chimpanzee studies are published in lower impact journals, then the logical reflection is that they are not important in the studies themselves. This calls into question the value of chimpanzee experiments, the majority of which make little noticeable contribution to biomedical advancement. Of the original sample, no chimpanzee study made an essential contribution to papers which had well developed methods for combating human diseases. Brown stated, “It is always problematic to what extent such models reflect the human situation."[14]

Despite chimpanzees being the most genetically similar animals to humans, experiments on them have not provided substantial

contributions to biomedical research. Therefore, it is logical for us to question, that if the most genetically similar animal to humans is an ineffective model, then how can the use of more genetically distant animals assist us? Such concerns – both scientific and ethical – are being recognised around the world where their use in research is being phased out.

"Monkeys are very poorly representative of human biology and diseases, including crucial research areas such as HIV/AIDS, malaria, neurodegenerative diseases, cancer, and many others. They continue to be used in experiments due to their superficial similarity to humans, but it is increasingly clear that countless and important genetic differences exist, which combine to generate vastly different biologies, disease susceptibilities and pathologies. Monkey experiments are therefore inherently misleading, and can never reliably inform human medicine. The sooner science leaves them behind, the better - not just for monkeys, but also for billions of people relying on science for cures and treatments for diseases that blight their lives."

- Jarrod Bailey, Ph.D.

Senior Research Scientist, BUAV

Statistics 2006-2013:

The following table shows the number of primates used in Australian research between 2006 and 2011 (the latest available). Not all states have provided annual returns showing the numbers of animals used in research, so the figures below could be considered to be conservative.

Year	2006	2007	2008	2009	2010	2011	2012	2013
VIC	128	65	90	186	282	313	235	176
NSW	122	147	323	484	184	27	18	22
TAS	-	-	-	-	-	-	-	-
SA	-	-	32	30	n/a yet	n/a yet	n/a yet	n/a
NT	n/a	n/a	n/a	-	n/a	n/a	n/a	n/a
WA	33	-	n/a	n/a	n/a	n/a	TBR	21
QLD	n/a	n/a	n/a	58	n/a	n/a	n/a	n/a
ACT*	-	5	-	10	n/a	n/a	n/a	n/a
TOTAL	283	217	445	768	466	340	253	219

NB: ACT figures are from ANU and CSIRO only. TBR = To Be Received. n/a = Statistics were not made available by the State or Territory Government.

Breeding Facilities:

There are three NHMRC-funded non-human primate breeding facilities in Australia.

Despite this however, between 2000-2014, Australia imported:

- 331 pig-tailed macaques (Macaca nemestrina) listed on the International Union for Conservation of Nature (ICUN) Red List of Threatened Species as vulnerable to extinction (from Indonesia)
- 250 crab-eating macaques (Macaca fascicularis) listed on the IUCN Red List from Indonesia
- 71 owl monkeys (Aotus lemurinus grisembra) listed on the IUCN Red List from the US.[15]
- 37 marmosets (Callithrix jacchus) from France
- 1 marmoset (Callithrix jacchus) from Switzerland
- 10 crab-eating tailed macaques (Macaca fascicularis) from France.

The NHMRC supports the use of national breeding colonies (NBCs) for macaques, marmosets and baboons. In addition to the provision of research grants, the NHMRC makes annual contributions of $500,000 to the National Non-Human Primate Breeding and Research Facility and $195,000 to the National Baboon Colony.[16]

Over the period 2013-2014, the NHMRC has awarded 14 grants to applicants who indicated they would involve non-human primates in their research:[17]

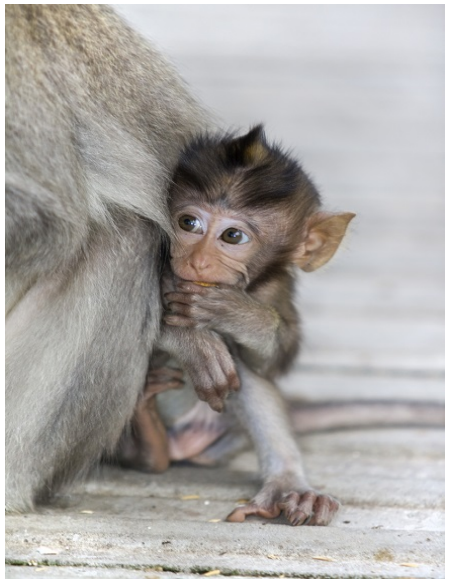
Grant Recipient	No. of grants	Value of grants
Australian National University	1	$0.51 million
Centre for Eye Research Australia Ltd	1	$0.85 million
Monash University	8	$5.27 million
University of Melbourne	2	$1.95 million
University of Queensland	1	$0.75 million

University of Sydney	1	$0.59 million

This research included studies into vision, hearing, brain physiology, stroke, diabetes and vaccine development.

Furthermore, the NHMRC also funds research on primates overseas, such as inflicting heart attacks on macaques at University of Washington.

Alternatives:



The development of several international centres and university departments for the furtherance of non-animal alternatives in scientific testing around the world shows that there is interest in this option. The Fund for the Replacement of Animals In Medical Experiments in the United Kingdom has examined non primate alternatives in five areas of medical research[18]:

Malaria: There have been several in vitro (literally meaning, in a test tube) studies on human cells that have been used to examine the malarial parasite. These have included developing imaging technologies for visualisation of malaria molecules in living human cells, such as human liver cells. Human volunteers have been used to study the effects of specific genes, the product of which could be induced into a vaccine. Further, the human volunteer studies can be used to show gene expression in the malarial parasite, including the influences on the survival of the parasite.

Cognition: Human imaging is the keystone to understanding the human brain. It replaces primate experiments with ethical, human volunteer subjects. Different brain scans can produce impressive amounts of accurate data, without the need for invasive techniques. Where brain lesions are needed, fully reversible lesions can be created safely on people. Human subjects are also able to respond to verbal instructions. This is invaluable to scientific understanding within cognition research.

Stroke: Due to the failures in animal and primate models in current stroke research, there is more potential in the development of

techniques to research strokes in humans. The techniques can include computer aided technology, brain imaging scans, in vitro studies, and the development of co-cultures using human cells and brain slices to study cell activity post mortem.

AIDS: Non-animal techniques can be used to provide insight into the HIV virus and AIDS, such as screening the genetic makeup of hundreds of HIV sufferers, to determine susceptibility to the virus. Mathematical analysis and statistical prediction can be used to map the acquisition of the infection, its viral state, and how the disease escapes immune control. In vivo (within a live organism) and in vitro studies, along with molecular research using tissues and cells, have also proved to be some of the most successful non-animal tests to date assisting with understanding the disease and subsequent drug production.

Hepatitis C (HCV): Mathematical modelling has been the most successful method for advancing the understanding of the HCV virus in human patients. In vitro systems have also proved effective.

Research on non-animal testing alternatives for these diseases has created a positive trajectory for the development of non-primate alternatives, should they be given the resources. Australia needs to step up to the mark and become a leader in this area - not continue with archaic and unethical research on primates.

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[12] The Jane Goodall Institute, 'Chimps in Captivity: The Great Ape Protection Act Fact Sheet', http://www.janegoodall.org/chimps-GAPA-fact-sheet, (accessed 9 July 2014).

[13] A. Knight, 'Chimpanzee experiment: Questionable contributions to the biomedical process', Alternatives to Animal Testing and Experimentation, vol. 14, special issue, 2008, pp. 119-124.

[14] P. Brown, 'Blood ineffecivity, processing and screening tests in transmissible spongiform encephalopathy', Vox Sanguinis, vol. 89, no. 2, 2005, pp. 63-70.

[15] Data obtained from CITES (Convention on International Trade in Endangered Species of Wild Fauna and Flora), to which Australia is a signatory.

[16] Senate Community Affairs Committee, 'Answers to estimates questions on notice', Health and Ageing Portfolio, Budget Estimates 2013-14, 20 November 2013, question E13-198. Available at: http://www.aph.gov.au/~/media/Estimates/Live/clac_ctte/estimates/sup_1314/DoH/Answers/198.ashx (accessed 9 July 2014).

[17] Senate Community Affairs Committee, Answers to Estimates Questions on Notice, Health Portfolio, Budget Estimates 2015-2016, 1-2 June 2015. Ref No:SQ15-000408.

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