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# THE COSTS AND BENEFITS OF ANIMAL EXPERIMENTS

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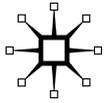
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# The Costs and Benefits of Animal Experiments

Andrew Knight

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# Abbreviations

ADME	absorption, distribution, metabolism, and excretion (see Glossary: <i>kinetics</i> )
AIDS	acquired immunodeficiency syndrome
AVA	Australian Veterinary Association
AVMA	American Veterinary Medical Association
AWA	US <i>Animal Welfare Act</i>
AWIC	Animal Welfare Information Center (US)
CA	chromosomal aberration
CAL	computer-aided learning
CCAC	Canadian Council on Animal Care
cDNA	complementary DNA (see Glossary)
$\chi^2$	chi square (statistical) value (see Glossary: <i>chi square test</i> )
CI	confidence interval (see Glossary)
<i>df</i>	degrees of freedom (see Glossary)
EBM	evidence-based medicine (see Glossary)
EC	Commission of the European Communities
ECVAM	European Centre for the Validation of Alternative Methods
EPA	Environmental Protection Agency (US)
ESC	embryonic stem cell (see Glossary: <i>stem cell lines</i> )
EST	embryonic stem cell test
FDA	Food and Drug Administration (US)
FE	finite element analysis (an engineering technique)
fMRI	functional magnetic resonance imaging
GC	genotoxic carcinogen
GLP	good laboratory practice
GM	genetically modified (see Glossary)
GMP	good manufacturing practice
HCV	hepatitis C virus
hESC	human embryonic stem cell
HIV	human immunodeficiency virus
HPPC	Hans Popper Primate Center (Austria)
HPV	High Production Volume Challenge Program (US)
IACUC	institutional animal care and use committee
IARC	International Agency for Research on Cancer (World Health Organization)

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IdMOC	Integrated Discrete Multiple Organ Co-culture system
ILSI	International Life Sciences Institute (US)
IRIS	Integrated Risk Information System (EPA)
LAL	limulus (horseshoe crab) amoebocyte lysate test
LGDW	laser-guided direct writing
LIF	leukaemia inhibitory factor
LLLT	low-level laser therapy
MEP	Member of the European Parliament
MHC	major histocompatibility complex
mRNA	messenger RNA
MTD	maximum tolerated dose (see Glossary)
NCI	National Cancer Institute (US)
NCRR	National Center for Research Resources (NIH, US)
NGC	non-genotoxic carcinogen
NHP	non-human primate
NIH	National Institutes of Health (US)
NOAEL	no observed adverse effect level (see Glossary)
NSAID	non-steroidal anti-inflammatory drug
NTP	National Toxicology Program (US)
NYBC	New York Blood Center
NZVA	New Zealand Veterinary Association
OECD	Organisation for Economic Co-operation and Development
OR	odds ratio (see Glossary)
PAB	polyclonal antibody
PBBK	physiology-based biokinetics (see Glossary: <i>-kinetics</i> )
PBPK	physiology-based pharmacokinetics (see Glossary: <i>-kinetics</i> )
PD	pharmacodynamics (see Glossary: <i>-dynamics</i> )
PET	positron emission tomography
PK	pharmacokinetics (see Glossary: <i>-kinetics</i> )
QA	quality assurance
QSAR	quantitative structure–activity relationship (see Glossary)
REACH	Registration, Evaluation and Authorisation of Chemicals testing programme (EC; see Glossary)
RP	relative predictivity
SAR	structure–activity relationship (see Glossary)
SC	stem cell (see Glossary: <i>stem cell lines</i> )
SHE	Syrian hamster embryo

SVM	School of Veterinary Medicine
TCR	T cell receptor
ToM	Theory of Mind (see Glossary)
USDA	United States Department of Agriculture
WHO	World Health Organization

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# Series Preface

This is a new book series for a new field of inquiry: Animal Ethics.

In recent years, there has been a growing interest in the ethics of our treatment of animals. Philosophers have led the way, and now a range of other scholars have followed, from historians to social scientists. From being a marginal issue, animals have become an emerging issue in ethics and in multidisciplinary inquiry.

In addition, a rethink of the status of animals has been fuelled by a range of scientific investigations which have revealed the complexity of animal sentience, cognition, and awareness. The ethical implications of this new knowledge have yet to be properly evaluated, but it is becoming clear that the old view that animals are mere things, tools, machines, or commodities cannot be sustained ethically.

But it is not only philosophy and science that are putting animals on the agenda. Increasingly, in Europe and the United States, animals are becoming a political issue as political parties vie for the 'green' and 'animal' vote. In turn, political scientists are beginning to look again at the history of political thought in relation to animals, and historians are beginning to revisit the political history of animal protection.

As animals have grown as an issue of importance, so have there been more collaborative academic ventures leading to conference volumes, special journal issues, indeed new academic animal journals as well. Moreover, we have witnessed the growth of academic courses, as well as university posts, in Animal Ethics, Animal Welfare, Animal Rights, Animal Law, Animals and Philosophy, Human–Animal Studies, Critical Animal Studies, Animals and Society, Animals in Literature, Animals and Religion – tangible signs that a new academic discipline is emerging.

'Animal Ethics' is the new term for the academic exploration of the moral status of the non-human – an exploration that explicitly involves a focus on what we owe animals morally, and which also helps us to understand the influences – social, legal, cultural, religious, and political – that legitimate animal abuse. This series explores the challenges that Animal Ethics poses, both conceptually and practically, to traditional understandings of human–animal relations.

The series is needed for three reasons: (i) to provide the texts that will service the new university courses on animals; (ii) to support the

increasing number of students studying and academics researching in animal-related fields; and (iii) because there is currently no book series that is a focus for multidisciplinary research in the field.

Specifically, the series will

- provide a range of key introductory and advanced texts that map out ethical positions on animals;
- publish pioneering work written by new, as well as accomplished, scholars; and
- produce texts from a variety of disciplines that are multidisciplinary in character or have multidisciplinary relevance.

The new Palgrave Macmillan Series on Animal Ethics is the result of a unique partnership between Palgrave Macmillan and the Ferrater Mora Oxford Centre for Animal Ethics. The series is an integral part of the mission of the Centre to put animals on the intellectual agenda by facilitating academic research and publication. The series is also a natural complement to one of the Centre's other major projects, the *Journal of Animal Ethics*. The Centre is an independent think-tank for the advancement of progressive thought about animals, and is the first centre of its kind in the world. It aims to demonstrate rigorous intellectual enquiry and the highest standards of scholarship. It strives to be a world-class centre of academic excellence in its field.

We invite academics to visit [www.oxfordanimaethics.com](http://www.oxfordanimaethics.com), the Centre's website, and to contact us with new book proposals for the series.

ANDREW LINZEY AND PRISCILLA N. COHN  
General Editors



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# 1

## Introduction

### Legal implications of chimpanzee ‘personhood’

On the basis of scientific argument that chimpanzees possess a *Theory of Mind*\* (ToM), and ought to be classified within the genus *Homo*, in 2007 advocates sought recognition under Austrian law of the *personhood* of a chimpanzee named Matthew Hiasl Pan (e.g. Balluch 2007). Success would mean that Matthew could no longer be considered property. He would become legally eligible for guardianship, on the basis that he was abducted as an infant, has been involuntarily confined in an alien environment for most of his lifetime, and has consequently been unable to fend for himself, or to safeguard his own interests. Through a guardian Matthew would be able to receive donations towards his living costs, and potentially even sue those responsible for his capture in West Africa in 1982 for acquired immunodeficiency syndrome (AIDS) and hepatitis research (Goodall 2006, Balluch 2007, Stafford 2007).

Matthew’s case is highly controversial, and its legal and philosophical ramifications would be enormous, should it be upheld. At the time of writing, Matthew’s advocates had not succeeded in the Austrian courts, and were appealing to the European Court of Human Rights. Whether or not they ultimately succeed, rapidly growing interest in such cases – including the publication of detailed legal foundations supporting the legislative personhood of chimpanzees (Wise 2000) – strongly suggests that Matthew’s lawsuit will not be the last of its kind.

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\* Explanations of many technical terms are provided in the Glossary at the end of the book. These terms are *italicised* where they first occur, or where additional explanation is provided.

## Moral implications of animal abilities

Matthew's case raises fascinating questions regarding the sensory, cognitive, and social characteristics necessary to confer a moral or legal right to protection from capture, social disruption, involuntary confinement, and *invasive* or life-threatening experimentation. It also raises questions about which species possess such characteristics, and to what degree.

Fundamental human rights, such as the rights to life, liberty, and freedom from torture, were first directly linked to the concept of *personhood* by the eighteenth-century German philosopher Immanuel Kant (Sturma 1999). Although such anthropocentrism has recently been challenged (e.g. White 2007, Benz-Schwarzburg & Knight 2011), classical concepts of personhood continue to rely on the possession of human-like psychological characteristics, such as consciousness and self-consciousness, the capacity to experience a wide range of emotional states, and the possession of key *cognitive* abilities, including those giving rise to culture, language, and *Theory of Mind*. The latter is a core consciousness-based capacity of human beings. Those possessing a ToM are considered able to ascribe mental or psychological states to themselves and others, including perceptual states such as seeing, as well as beliefs and desires (Premack & Woodruff 1978, Bischof-Köhler 2000).

In 2011 Benz-Schwarzburg and I reviewed in detail the scientific evidence for the existence of ToM in great apes, cetaceans, corvids, and other animal species (Benz-Schwarzburg & Knight 2011). In many respects chimpanzees such as Matthew possess the necessary mental characteristics; in other respects they might not. Combined evidence from multiple studies suggests they understand the intentions, goals, visual (and sometimes auditory) perception, and knowledge of other chimpanzees. The understanding that beliefs may be false (*false belief understanding*) demonstrates awareness of the difference between reality and mental representations, which is considered a core criterion for advanced ToMs (Onishi & Baillargeon 2005). Although evidence of such awareness in chimpanzees remains lacking to date, they seem able to understand others within a 'perception-goal psychology' (Call & Tomasello 2008, Kaminski *et al.* 2008, Krachun *et al.* 2009).

It is logically consistent to consider animals who possess such abilities as *non-human persons* who should be granted at least basic rights concordant with some of those granted to humans. One implication is that the moral boundary which ethical actors are obliged to respect is violated when such animals are used for a range of contemporary

human purposes, including involuntary confinement and participation in biomedical research.

Despite morally important similarities, such species nevertheless differ from human persons (as they do from each other). However, it remains reasonable to conclude that they should be included in the community of moral consideration. After all, so-called *marginal human persons*, such as the very young, old, injured, or ill, who lack the full range of psychological and social characteristics and abilities exhibited by healthy human adults, are nevertheless valued as persons. They are valued as partially conscious, partially self-conscious, or partially autonomous beings, with unique personalities, and are accordingly granted human rights.

The Kantian foundation for human rights stems from the ideal of the rational person and the principle that every person is equally rational, self-conscious, and autonomous. However, the case for the equal application of human rights transcends this core idea. No matter how equal all humans actually *are*, all are *considered* equal in dignity and rights.

### **Utilitarian basis for animal experimentation**

Current regulations governing animal experimentation fall far short of the moral consideration warranted by scientific advances in the understanding of key animal abilities and characteristics. Nevertheless, the interests of animals remain fundamentally important – at least in theory. The core principle underpinning animal experimentation regulation and policy is that the likely benefits of such research must outweigh its expected costs. Although considerable financial and human collateral costs do exist, the main costs are borne by the animals subjected to such research. And although such research may be directed at yielding benefits for animal species or the environment, the overwhelming majority is intended for human benefit, whether through the advancement of knowledge, through the development or toxicity testing of clinical interventions and consumer or industrial products, or through educational applications.

This *utilitarian* cost:benefit analysis underpins all fundamental regulation governing animal experimentation. *Directive 2010/63/EU on the protection of animals used for scientific purposes*, which directs such animal use in all EU member states, asserts that it is ‘essential, both on moral and scientific grounds, to ensure that each use of an animal is carefully evaluated as to the scientific or educational validity, usefulness and relevance of the expected result of that use. The likely harm

to the animal should be balanced against the expected benefits of the project' (EU 2010).

However, the contemporary widespread reliance on animal models in biomedical research and toxicity testing is heavily dependent on assumptions of human utility – and, in particular, of reasonable *predictivity* for human outcomes. Surprisingly, these assumptions have rarely been verified or, indeed, subjected to rigorous scrutiny of any kind.

Such untested or unfounded assumptions about the human utility of animal models have rendered utilitarian arguments for and against their use largely speculative to date.

### **Purpose of this book**

To judge the merits of animal experimentation overall, it is essential to have reliable information about the magnitude of laboratory animal use, the probable harms inflicted on animals, the human benefits realised, and the potential offered by alternative research, testing, and educational methodologies. Accordingly, these key topics are investigated in the corresponding parts of this book:

Part I (Chapters 2–4)	Animal Costs
Part II (Chapters 5–7)	Human Benefits
Part III (Chapters 8–9)	Alternative Strategies
Part IV (Chapters 10–11)	Educational Animal Use and Student Impacts

In addition, in each of the three fields of fundamental and clinically applied biomedical research, toxicity testing, and biomedical education, a key example is examined in greater detail.

### **Invasive chimpanzee research**

Chimpanzees are the species most closely related to humans, and consequently most likely to be generally predictive of human outcomes when used in research aimed at the development of human clinical interventions. However, their advanced cognitive, psychological, and social characteristics also raise exceptional animal welfare and ethical concerns when they are confined in research laboratories and subjected to invasive procedures. Both the likely benefits and the ethical costs are potentially maximised by such research. These costs and benefits are examined in detail in Chapters 4, 5, and 12.

### **Animal carcinogenicity testing**

In the field of toxicity testing, the accurate identification of previously unknown human *carcinogens* to which workers, consumers, or patients may be exposed offers greater potential public health benefits than the identification of all other toxins combined – by a considerable margin. Accordingly, the accurate identification of such carcinogens is crucial. However, due to a lack of human exposure data, carcinogen testing has traditionally relied heavily on animal studies. Chapter 6 examines the utility of such studies in accurately predicting human carcinogenicity, and in deriving hazard classifications for the regulation of human exposure.

### **Veterinary education**

Veterinarians must be able to perform a variety of clinical and surgical procedures on animal patients, including euthanasia, and must be familiar with the clinical signs of animal diseases. Accordingly, the justifications for invasive animal use are stronger in veterinary education than in virtually any other educational discipline. To critically assess the necessity of invasive animal use in education, it is therefore instructive to examine the case of veterinary education closely.

Participation in such animal use may also profoundly affect the development of attitudes towards animal welfare – which are fundamentally important in the case of veterinarians. However, such attitudinal impacts have been relatively under-studied to date. These topics are examined in detail in Chapters 10 and 11.

### **Conclusions and policy recommendations**

Animal experimentation is arguably the single most contentious issue in the wider debate concerning the rights of humans to use animals. However, detailed critical review indicates that, although uncertainties remain, sufficient evidence now exists to draw some key conclusions about the overall costs to animals, and benefits to humans, of invasive animal experimentation.

Examining and weighing these costs and benefits leads to important recommendations for the ethical oversight of scientific animal use, for the scientific *validation* and acceptance of both animal and non-animal experimental models, for the implementation of alternative research, testing, and educational strategies, and for the development of associated policy and regulation.

Appropriate recommendations are summarised, alongside an overview of existing regulation governing laboratory animal use in Europe and the US, in:

Part V (Chapters 12–13) Conclusions and Policy Recommendations

#### **Use of this book**

This book uses some technical language. To assist readers unfamiliar with them, many technical terms are explained in the Glossary at the end of the book. These terms are *italicised* where they first occur, or where further explanations are provided in the text.

Readers should be aware that approximations of summated totals and their numerical components in figures, tables, and the text are all correctly rounded from original figures, as are corresponding percentages. However, such rounded approximations do not always summate perfectly.

Concluding summaries are provided in all of the following chapters with the exception of those in Part V, which summarise the remainder of this book. Full colour versions of the figures may be viewed at [www.palgrave.com/animalexperiments](http://www.palgrave.com/animalexperiments).

#### **Intended readership**

This book is intended to serve all who are interested in the scientific and educational utility of laboratory animal use, and in alternative research, testing, and educational strategies. It may be of use to scientists and educators working with animals, or developing alternatives; to policy-makers, including regulatory agencies and legislators; to chemical and pharmaceutical companies and consumer product manufacturers, who are increasingly required to provide toxicity data on their products; to both undergraduates and postgraduates studying the ethical issues surrounding animal experimentation; to bioethicists and philosophers concerned with animal issues; and to members and supporters of organisations promoting scientific animal use, the protection of animals, and patient and consumer safety.

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## **Part I**

### **Animal Costs**

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