

# Contents

<i>List of Tables</i>	vii
<i>List of Figures</i>	viii
<i>List of Abbreviations</i>	ix
<i>Acknowledgements</i>	xii
<i>Series Preface</i>	xiv
1 Introduction	1
<b>Part I Animal Costs</b>	
2 Global Laboratory Animal Use	9
3 Types of Laboratory Animal Use	18
4 Impacts on Laboratory Animals	29
<b>Part II Human Benefits</b>	
5 Human Clinical Utility of Animal Models	39
6 Human Toxicological Utility of Animal Models	60
7 Factors Limiting the Human Utility of Animal Models	75
<b>Part III Alternative Strategies</b>	
8 Non-Animal Research and Testing Methodologies	97
9 Reduction and Refinement of Laboratory Animal Use	125
<b>Part IV Educational Animal Use and Student Impacts</b>	
10 Educational Animal Use	139
11 Effects of Harmful Animal Use on Students	167
<b>Part V Conclusions and Policy Recommendations</b>	
12 The Costs and Benefits of Animal Experimentation	179
13 Regulatory Developments and Policy Recommendations	194

vi *Contents*

<i>Glossary</i>	208
<i>References</i>	218
<i>Index</i>	249

## 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.

---

\* 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

#### 4 *The Costs and Benefits of Animal Experiments*

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.

## 6 *The Costs and Benefits of Animal Experiments*

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.



# Index

- 3Rs, 99
- academic freedom, 146
- adverse drug reactions, 40
- altruistic behaviour, 34
- American Veterinary Medical Association, 171–2
- Ames test, 109
- anaesthetic use, 26, 27, 33, 132
- analgesic use, 33, 132
- Animal Care Policy Manual*, 197
- animal ethics committee, *see* ethical review
- animal welfare, 196, 197, 204
  - positions of veterinarians, 171–2
- Animal Welfare Act*, 98, 196
- Animal Welfare Information Center, 197
- Animals (Scientific Procedures) Act*, 104, 198
- animals protected by regulations, 104–5, 194, 203
- antibody production, 130
- asthma research, 55–6
- Australian animal use, 12, 23
- Australian Veterinary Association, 171
- best practice in laboratory animal science, 205
- biological products, quality control, 112–13
- biomarkers of toxicity, 119
- block designs, 126
- body donation programme, *see* ethically sourced cadavers
- bone-seeking pharmaceuticals, 114
- Bovine Rectal Palpation Simulator, 161
- brain tissue cultures, 107–8
- British Veterinary Association, 171
- cadaver donation programme, *see* ethically sourced cadavers
- cadaver sourcing, 149
  - see also* ethically sourced cadavers
- Canadian animal use, 12, 23–6
- cancer costs, 61
- cancer predisposition of rodents, 81
- carcinogen identification, importance of, 60–2
- carcinogenicity assay, *in vitro*, 109
- carcinogenicity bioassay
  - ad libitum* (unrestricted) feeding, 87
  - animal welfare, 63
  - EPA and IARC assessments, 65–70
  - false positive results: calorie-induced, 88; dose-related, 87
  - history, 62
  - logistical challenges, 15, 63
  - maximum tolerated doses, 87
  - organs affected, 85–7
  - routes of administration, 82–3, 84
  - species used, 78, 79
  - utility, 64
  - validation, 72
- cardiac pathology research, 55, 56
- CD28-SuperMAB, *see* TGN1412
- cDNA microarrays, 117–18
- cell cultures, 105–6
- Center for Alternatives to Animal Testing, Baltimore, 97
- centres for alternatives, 205
- cephalopods, 104, 179
- chemical testing programmes, *see* Endocrine Disrupting Chemicals Research Program; High Production Volume Challenge Program; Registration, Evaluation and Authorisation of Chemicals
- Chimp Haven is Home Act*, 192
- Chimpanzee Health Improvement, Maintenance and Protection Act*, 199
- chimpanzees
  - breeding moratorium, 202
  - emotional capacities, 33
  - genome, 75

- chimpanzees – *continued*
- invasive research: advocacy of, 43; AIDS vaccine, 49, 202; animal welfare, 35, 77, 188, 204; biomedical knowledge advancements, 46–7; cancer, 49; costs, 202; HCV, 49–50; human healthcare advancements, 47–50; scientific fields, 43–5
  - legal protection, 1, 198–9, 201–2
  - numbers, 201–2
  - psychological abilities, 33–4, 192
  - retirement, 199
  - social characteristics, 34
  - Theory of Mind, 2
- chronological implications of educational studies, 159
- citation frequencies, 46–7
- client donation programme, *see* ethically sourced cadavers
- clinical training, 143, 158
- clinical trials
- safety, 118–20
  - timing, 52, 56
  - translation from animal studies, 51
- clinical utility of animal models
- case studies, 39–41
  - systematic reviews, 41–57
- colon cancer research, 57
- compliance with the 3Rs, 91, 98, 145, 202–3
- computerised modelling or simulation, 100–4, 121
- conflict between alternatives, 133–4
- conscientious objection by students, 144–5, 169
- consideration of alternatives requirement, 128
- Cosmetics Directive 76/768/EEC*, 16, 124, 187
- death, 140
- desensitisation-related phenomena, 173
- design of experiments, 126–7
- developmental stages of vertebrates, 104
- developmental toxicity assessment, 114–16
- Directive 86/609/EEC*, 195
- Directive 2010/63/EU*, 104, 194–5, 201
- discretionary toxicity testing, 130
- dissection, 139
- see also* preservatives, health hazards
- duplication of animal experiments, 205
- educational efficacy of humane teaching methods, *see* humane teaching methods
- embryonic stem cells, *see* stem cells
- Endocrine Disrupting Chemicals Research Program, 15–16
- environmental enrichment, 30, 31, 192
- EPA carcinogenicity assessments, 63–70
- epidemiological research, 121
- ethical review, 189, 195, 205
- ethically justifiable research, 192–3
- ethically sourced cadavers, 141–2, 145, 149
- ethics committee, *see* ethical review
- EU numbers of animals, 11
- EU regulations, 195–6
- European Centre for the Validation of Alternative Methods, 97, 190–1
- European Convention*, 195
- euthanasia, 140
- evidence-based research, 90–1
- expert systems, 103–4
- extrapolation
- between routes of administration, 82–3
  - between species, 81–2
- false belief understanding, 2
- false positive results, *see* carcinogenicity bioassay
- FDA petition for alternatives, 200
- FDA regulations, 200
- feeding regimes in toxicity tests, 87
- finite element analysis, 121
- fluid resuscitation, 55
- foetal bovine serum, 133
- Food and Drug Administration, 70
- formaldehyde, 167–8

- gene chips, *see* cDNA microarrays
- genetically modified animals, 12–15
- German universities, 50
- good laboratory practice, 131
- Great Ape Protection Act*, 201
- great apes, *see* chimpanzees
- Great Britain, *see* UK
- GreenScreen genotoxicity assay, 110–11
- grouping of similar chemicals, 101–2
- Guide for the Care and Use of Laboratory Animals*, 197
- haptic simulation, 161
- harm, 140, 148–9
- harmonisation of test guidelines, 131–2
- healthcare advancements, *see* clinical utility of animal models
- heart disease research, 55, 56
- hen welfare, 172
- hepatocyte assays, 111
- High Production Volume Challenge Program, 15, 98
- highly cited animal experiments, 50–1
- high-throughput toxicity assessment, 98
- housing of laboratory animals, 30–1, 75, 84
- human rights, 2, 3
- humane teaching methods, 140
  - animal welfare and regulatory aspects, 163–4
  - educational efficacy, 147–63, 168–70
  - faculty opposition: Australian, 144–5; causes, 146–7; international, 145–6
  - logistical benefits, 147, 159, 160
- hypersensitivity prediction, 114
- IARC Monographs*, 65, 71
- imaging techniques, 122
- Improved Standards for Laboratory Animals Act*, 196
- in vitro* assays, 108–12
- Institutional Animal Care and Use Committee, *see* ethical review
- Integrated Discrete Multiple Organ Co-culture system, 112
- Integrated Risk Information System chemicals database, 63, 78
- integrated toxicity testing, 122, 123
- interaction between alternatives, 133
- Interagency Coordinating Committee on the Validation of Alternative Methods, 191
- International Conference on Harmonisation, 131
- interspecies variation, 76–81, 85
- invasiveness of procedures, 22–6, 32–3
  - Australia, 23
  - Canada, 23
  - see also* anaesthetic use
- Japanese medical students, 168
- Kant, Immanuel, 2
- LD50 test, 130
- legal analogies, 179, 188
- legal protection
  - chimpanzees, 198–9, 201–2
  - educational animal use, 170
  - great apes, 198–9
  - primates, 200–1
- legislation, *see* legal protection; regulations
- libraries of humane teaching methods, 166
- limulus (horse-shoe crab) amoebocyte lysate test, 113
- liver constructs, 106
- longitudinal studies, 129
- low-level laser therapy, 55, 56
- Massey University, 169–70
- maximum tolerated doses in toxicity testing, 87
- medical advancements from animal experiments, 50
- meta-analysis, 126
- metabolite assessment, 111–12, 116–17
- methodological quality of animal studies, 53–4, 89–91

- microdose studies, 119
- minimally sentient organisms, 104–5
- moral consideration, 3, 180
- multifactorial designs, 126
- Murdoch University, 144
  
- nasogastric intubation, 158
- National Centre for the Replacement, Reduction and Refinement of Animals in Research, 97
- Netherlands, The, 132
- neurodegenerative disease models, 121
- New Zealand Veterinary Association, 171
- noise in laboratories, 30
- non-steroidal anti-inflammatory drugs, 40
- NTP carcinogenicity assessments, 71, 72
- numbers of animals
  - EU, 11
  - increases, 12–16
  - national regions, 12
  - UK, 12–14
  - US, 9
  - worldwide, 9–11
  
- Occupational Safety and Health Administration, 70–1
- organ cultures, 106
- organ–organ interaction, 111–12
- osteomyelitis research, 56
  
- P450-dependent monooxygenases, 75
- p-i concept, 113–14
- Pan, Matthew Hiasl, 1
- perfused tissue cultures, 107
- personhood, 2–3
- Pharmacopoeia Discussion Group, 131
- physicochemical evaluation, 100–4
- physiological distortion, 31
- physiology training, 158–9
- polyclonal antibody production, 130
- positive reinforcement techniques, 133
- precautionary principle, 179–80
- preservatives, health hazards, 167–8
  
- primate use, regulation of, 200–1
- psychological resistance to humane teaching methods, 146
- Public Health Service Act*, 199
- Public Health Service Policy*, 197
- Public Laws 89-544 & 99-198*, 196
- publication bias, 91
- pulsatile organ perfusion trainer, 162
- pyrogens, 113
  
- quality control of biological products, 112–13
- quantitative structure–activity relationships, 102
  
- rabbit pyrogen test, 113
- read-across, 101–2
- recommendations for policy, 203–6
- reduction alternatives, 125–31
  - extra-experimental reduction, 129–31
  - intra-experimental reduction, 125–7
  - supra-experimental reduction, 127–9
- reduction targets, 205
- refinement alternatives, 132–3
- Registration, Evaluation and Authorisation of Chemicals, 15, 61–2, 100, 103, 114, 130
- regulations
  - Animal Care Policy Manual*, 197
  - Animal Welfare Act*, 98, 196
  - animal welfare aspects, 196, 197, 204
  - Animals (Scientific Procedures) Act*, 104, 198
  - animals protected, 104–5, 194, 203
  - Chimp Haven is Home Act*, 192
  - Chimpanzee Health Improvement, Maintenance and Protection Act*, 199
  - chimpanzees, 198–9, 201–2
  - compliance failures, 91, 98, 145, 202–3
  - Directive 86/609/EEC*, 195
  - Directive 2010/63/EU*, 104, 194–5, 201

- regulations – *continued*  
 EU, 195–6  
*European Convention*, 195  
 FDA petition for alternatives, 200  
 FDA regulations, 200  
*Great Ape Protection Act*, 201  
 great apes, 198–9  
*Improved Standards for Laboratory Animals Act*, 196  
 primates, 200–1  
*Public Health Service Act*, 199  
*Public Health Service Policy*, 197  
*Public Laws 89-544 & 99-198*, 196  
 recommendations for policy, 203–6  
*Treaty of Lisbon*, 195  
 UK, 198  
 US, 196–7, 200  
*US Government Principles*, 197  
 use categories, 194, 203  
*Written Declaration 40/2007*, 200
- ReProTect project, 116  
 retrospective evaluation, 128–9, 205  
 re-use of animals, 129  
 reverse toxicology approach, 130  
*Roadmap for the Future*, 97  
 rounding of totals, 6  
 Rubaii, Safia, 170
- Saccharomyces cerevisiae*, 110  
 safety during dissections, 168  
 sample sizes, 125–6  
 scrutiny of scientific animal use, 204–5  
 searching for alternatives, 128, 197–8, 203  
 sentience, 104–5, 179  
 sharing and assessment of existing data, 100  
 shelter animal use, 140, 143–4  
 simulators, surgical, 161–2  
 sourcing of laboratory animals, 20–1, 29–30  
 species of laboratory animals, 18–20, 203–4  
 statistical analysis, 90, 125–6, 127  
 stem cells, 105–6, 114–16  
 stereotypical behaviour, 30–1  
 stress, 29–33, 83–4  
 stroke models, 52–4  
 structure–activity relationships, 102–3  
 surgical training, 142, 150, 151, 156–8, 161–2  
 surrogate tissues, 121  
 Syrian hamster embryo cell transformation assay, 109–10  
 systematic reviews of human utility, 41–2
- telemetric devices, 132–3  
 teratogenicity testing, 72–3  
 TGN1412 (CD28-SuperMAB), 39, 113, 118, 119  
 Theory of Mind, 2  
 three Rs, 99  
 tissue cultures, 105–8  
 toxicity testing  
   human predictivity, 73  
   *see also* carcinogenicity bioassay  
*Toxicity Testing in the 21st Century*, 98  
 toxicogenomics, 117–18  
 training of research personnel, 128, 132, 133  
 transcranial magnetic stimulation, 122  
 translation to clinical trials, 51  
*Treaty of Lisbon*, 195  
 Tufts University, 141–2, 145  
 types of animal use, 194, 203
- UK  
   anaesthetic use, 26, 27  
   genetically modified animals, 12–14  
   numbers of animals, 12–14  
   policy, 198  
   surgical training, 157  
 University College Dublin, 142  
 University of Colorado, 170  
 University of Illinois, 168–9  
 University of Sydney, 144  
 US  
   numbers of animals, 12  
   regulations, 9, 196–7, 200  
   *US Government Principles*, 197  
   use of animals, 20–2

- utilitarian
  - basis for animal experimentation, 3, 180
  - philosophy, 180
- vaccine testing, consistency
  - approach, 112–13
- validation of experimental models, 189–91
- variability of data, 126, 127
- veterinary attitudes towards animal welfare, 171–2
- veterinary education, 139–40, 172–3
- Vioxx, 40
- VirtualToxLab, 102–3
- World Veterinary Association, 171
- Written Declaration 40/2007*, 200

PROOF

PROOF