THE USE OF NON-HUMAN PRIMATES IN BIOMEDICAL RESEARCH: ADDRESSING THE REPLACEMENT IMPASSE THROUGH THE SOCIAL DYNAMICS OF SCIENCE

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Abstract

Non-human primate experimentation provokes passionate and opposing exchanges, particularly in the UK. This disagreement contributes to an impasse which in turn has prevented the exploration of the important question, if and how primate research could be ended This project aims to support the examination of this question of impasse presenting data on how it might be overcome by providing a novel and challenging perspective using a multi-method approach, and insights from science and technology studies, to better understand the animal research controversy.

The project primarily draws on data from face-to-face semi-structured interviews with primate users and with scientists who do not use primates across two areas of research, namely schistosomiasis and Parkinson's disease. This multiple-case study method was combined with a documentary analysis of primate reports produced by key stakeholders. The dataset was then analysed using a semi-inductive, thematic approach to identify how aspects of the social dynamics of science can help to explain the different viewpoints provided by participants. The analysis showed that issues of (i) competition and reputation, (ii) expectations, core sets and publications, (iii) entrenchment and policy, and (iv) ethics and speciesism are centrally relevant to a better understanding of the apparent stalemate in replacing primate experiments.

The key finding is therefore that the social dynamics of science play a critical role in explaining why the primate impasse persists, and can also help to understand how to overcome it. Constructive recommendations to achieve progress are made, focussing on improved collaboration and communication, increasing flexibility and explicit

examination of the ethical considerations. The thesis also draws conclusions on how best to ensure the necessary involvement of key stakeholders. Recommendations from this project also have wider implications for scientific practice particularly for those involved in alternatives to animal research, and for the field of science communication.

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Chapter 1: Introduction

Animal experiments can be traced back to the time of the ancient Greeks, when anatomical studies of dissected animals were done to overcome the taboos associated with vivisection and dissection of humans (see Franco 2013 for more detail). In more recent times, animal experiments have played a substantive role in important medical discoveries such as immunisation against diphtheria and tissue engineered organ transplantation (see AnimalResearch.Info 2014 for more examples). The seventeenth century saw the first real questioning of the scientific and moral reasoning behind animal use (Franco 2013). The modern animal research debate has its roots in the UK, which was the first country in the world to have specific legislation to control animal experiments (*The Cruelty to Animals Act 1876*) and where the first anti-vivisection organisation was founded in 1875. This organisation was called The Victoria Street Society for the Protection of Animals Liable to Vivisection and is now known as The National Anti-Vivisection Society (NAVS). The UK debate about whether or not animal experiments should be conducted is well known for its intense, emotive, and controversial nature (Matfield 2002); it receives significant media coverage (see for example Thew 2014 and Fox 2014), divides public opinion (Ipsos MORI 2014) and is increasingly political (Editorial; *Nature Neuroscience*, 2013).

This tension has resulted in vociferous arguments from organisations based on both sides of the debate, such as NAVS and the British Union for the Abolition of

Vivisection (BUAV)[1] campaigning against animal experiments, and Understanding Animal Research (UAR) and Pro-Test speaking in favour. The impact of the debate can clearly be seen when considering animal rights extremism, where individual activists and some organisations such as the Animal Rights Militia have gone beyond peaceful and legal protest, attacking researchers, biomedical facilities, companies and staff with any links to animal work. One high profile example was the Darley Oaks Farm guinea pig breeding business which was subjected to a campaign of intimidation and vandalism that culminated in the desecration of a management relative's grave and theft of her body (UAR 2014). Events such as this have resulted in the UK Government introducing legislation to tackle these extreme tactics, which has led to many of the most notorious activists being jailed (Matfield 2002; AREInformation 2013). These kinds of attack have declined in the UK in recent years, but they have been replicated in other countries in Europe and the USA (Paterlini 2013; Matfield 2002).

Within the general debate there is one particular area which provokes especially passionate and polarised arguments; that is the use of non-human primates (referred to as primates henceforth) in biomedical research and testing (Nuffield Council on Bioethics 2005). The evolutionary closeness and physical resemblance of the other primates to humans creates a psychological affinity that causes strong emotional and ethical reactions against using them in biomedical research, yet it is the similarities between us and them which form the scientific rationale for using them as experimental models. As will be discussed in subsequent chapters, primate users say that they only use primates when they absolutely have to, and opponents say that

[1] As of 1 June 2015 the BUAV became Cruelty Free International. Throughout this thesis it is referred to as the BUAV.

primate use must be stopped immediately. These opposing views seem irreconcilable, yet it could be said that, essentially, the two sides aspire to achieve the same aim of finding effective therapies and cures for disease without using primates. This is the primate use impasse; in which neither side seems able to move beyond the arguments to work towards this common goal. The controversial and emotive nature of the debate and impasse are outlined further below.

The existing examinations of the animal experimentation debate are largely framed in the context of discussing the morality of animal research or investigating a scientific controversy. The moral philosophy literature which considers animal experimentation is the more extensive of the two. While it is beyond the scope of this thesis to thoroughly review this body of knowledge, it is important to note that there has been specific moral discussion of primate experimentation. For example, Quigley (2007) argues that the main justifications for the use of primates in biomedical research, the 'least harm/greatest good' and the 'capacity' arguments are equally applicable to considering whether humans are appropriate subjects of biomedical research. She makes the case that the benchmark for deciding that primate experiments are morally justifiable seems to be whether we would carry out certain types of research on humans of a similar capacity. Therefore, if we decide that it is right to do such studies on humans then primate experiments are not necessary as the scientific evidence indicates human data is better. Conversely, if we decide it is not right to do the experiments on these humans then there is no good reason to do it in primates either (Quigley 2007). Moore (2008) also questions some of the ethical interpretations used for justifying primate research such as the teaching hospital fire thought experiment, where people would expect patients to be rescued before the laboratory animals, thus

humans think it is morally required to sacrifice animals to save human lives, so this can then be applied to medical research. But Moore (2008) argues that the two situations are not comparable because in the hospital scenario after the people had been rescued attempts would be made to save the animals, whereas in medical research the intention is that animals will be sacrificed.

It is clear that there is significant academic interest in the ethical analysis of primate research and there are examples of the scientific community discussing the topic. For example, Sughrue *et al*. (2009) aimed to provide a balanced examination of the ethics of primate stroke research using examples from the experimental studies they had undertaken. However, Rossi (2009) argued that Sughrue *et al* (2009) did not advance or defend any explicit ethical argument for the use of primates, but instead '*make a series of assertions regarding the scientific merits of the primate experimental model and a few respects in which the animals are (purportedly) not harmed*' (Rossi 2009, p.21). To some extent this example of a separation in the moral and scientific arguments illustrates why for the purpose of the current project a philosophical approach is not suitable, as the intention is to focus on the scientific viewpoints of those engaged in the research. Although, as discussed in later chapters, the findings of the present research indicate that ethics are an important dynamic in the primate debate the overall framing of the thesis is not in that context.

However, there are some key aspects of the philosophical literature that place this current piece of research into context. The 1970s saw the first rapid expansion of literature which academically addressed the ethical issues associated with animal experiments (Rollin 2007; Nuffield Council on Bioethics 2005), with authors such as

Ryder (1975), Singer (1975), Rollin (1981) and Regan (1983) arguing for higher moral status for animals. These publications are viewed by many opponents of vivisection as the cornerstone of their arguments and campaigns (Nuffield Council on Bioethics 2005). The moral status and capacities of animals are still the focus of theoretical discussions about the justification for and against animal use, as exemplified by the extensive coverage of the topic in the Nuffield Council on Bioethics (2005) report *The Ethics of Research Involving Animals*. There continues to be deliberation about how to assign moral status and what the consequences of reaching a conclusion might be. For example, Walker (2006) argues that the capacities-based view of moral status (i.e. when 'capacities' such as cognitive, social and emotional abilities are used to assign moral status, with beings with more complex capacities having higher moral status) is not sufficient to justify the contrast in the greater protection afforded to humans in regulations controlling research on humans versus that afforded to non-human animals in the regulations controlling animal experiments. There is also a broad literature discussing which normative theoretical framework should be applied to animal experimentation, with the key paradigms considered being consequentialism, deontology and virtue ethics[2] (See Nuffield Council on Bioethics 2005 and Dolan 1999 for further details).

[2] The Nuffield Council on Bioethics (2005) provides a nice summary of these three paradigms (p.49) describing them as follows. *Consequentialism* – according to this approach the moral value of individual human actions, or rules for such actions, is determined primarily by their outcome. Such approaches do not usually put strong emphasis on the inviolable rights of moral agents or subjects. Utilitarianism is an important type of consequentialism. *Deontology* – the name of this theory is derived from the Greek *deon*, which means duty or obligation. In this theory certain actions are right or wrong independent of their outcome. Instead, their rightness or wrongness is defined by a formal system, which defines certain actions as intrinsically right or wrong. Rights of moral agents or subjects can be violated if they are not treated according to the principles derived from the system. The concept of animal rights is a form of deontology. *Virtue Ethics* – according to this approach moral value depends less on duty to follow rules given by formal systems, or on duty to maximise beneficial consequences, than on the character of the moral agent. A virtuous moral agent is someone who deliberates and acts in a way which displays virtues such as justice, truthfulness and courage.

In contrast to the moral philosophy literature there has been relatively little scholarly empirical investigation of the animal experimentation debate and, as noted above, it is usually framed in the context of examining a scientific controversy. Nelkin (1995) uses animal research as an example of '*Controversy as a Moral Crusade*' (p. 451) in her analysis of the dynamics of science controversies as expressions of political tensions and moral reservations about the value of certain scientific practices. Michael and Birke (1994a) also note the moral character of the animal experimentation controversy when they illustrate, using Collins' (1988) concept of the 'core set', that scientists attempt to dictate the terms of the debate by trying to control who has a legitimate voice. The concept of the core set is discussed in much more detail in Chapters 3-6.

Much of the existing literature focuses on two main approaches. First, research looks at public attitudes toward animal experimentation and the experimenters (Lund *et al.* 2012), and the roles they play in shaping policy (Schuppli and Weary 2010; Von Roten 2009) and legitimising the practice (Hobson-West 2012). Second, authors aim to understand the debate over the use of animals, often by investigating how people on either side of the debate view themselves; the issues involved in animal experimentation; and those that oppose their stance. Paul (1995) did this through the use of questionnaires, while others have used ethnography (Holmberg and Ideland 2010) or interviews (Hobson-West 2012; Michael and Birke 1994a). Although this literature questions how animal research is justified and examines the persistence of the status quo, there is very little, if any, exploration of how to resolve the debate or move away from biomedicine's reliance on animal models.

Work investigating other areas of contentious science indicates that a productive way to gain a more comprehensive understanding of the animal experimentation debate and to explore possible resolutions could be to adopt science and technology approaches such as the 'theory of expectations' (Brown and Michael 2003) and 'core sets' (Collins 1988); see Chapter 2 for further explanation of these concepts. Wainwright *et al.* (2006) examined the highly contentious area of embryonic stem cell research using the analytical motif of expectations to offer insight into why difficulties exist in getting potential therapies to move from the laboratory bench to treating patients in the clinic. Mulkay (1999) used the rhetorics of hope and fear to explain differences in the arguments presented in the debate about the rights and wrongs of human embryo research and assisted reproduction. As noted above, Michael and Birke (1994a) had already used the core set concept in the context of animal research, and Hedgecoe (2006) combines core sets and expectations to understand the disagreement over the continued citation of a controversial scientific result in the field of Alzheimer's disease research.

Within the general topic of animal experimentation there are studies that focus on specific types of animal use, such as genetically modified animals (Schuppli and Weary 2010) and xenotransplantation (Brown and Michael 2001). However, it appears that none of the current literature is specifically aimed at understanding the controversy surrounding primate experiments, despite this being a dominant feature in many of the discussions about animal experimentation.

Therefore, to expand current knowledge in this area of scientific controversy and introduce a novel standpoint from which to explore it, this thesis specifically examines

the primate experimentation debate, and unusually investigates the impasse that exists and how it might be overcome using a multi-method approach.

This introductory chapter will explain the rationale for conducting this research, give an overview of the aim, research questions, design and process and, finally, outline the structure of the thesis as a whole.

1.1 Rationale for Research

The decision to undertake this research project was borne out of personal experience with the polarised nature of the primate experimentation debate and frustration at how to move constructively beyond it. As yet, it appears no one has actively investigated whether replacing primate use is feasible and, if it is, how to practically achieve it. A new approach is needed if the debate, and indeed the science, is ever to move forward. In order to do this it was decided that it was important to talk to the scientists in fields of research where primates are used, to get to the perspectives that cannot be reached simply from reading the literature. The multi-method approach used to do this is briefly outlined below and is described in detail in Chapter 2. It involved using qualitative methods and integrating science and technology studies with more traditional scientific enquiry. This is, as far as I am aware, a unique way of studying primate use. The remainder of this section provides the background to the polarisation of the primate debate and explains why it was important to undertake this study.

Primate Use in UK and Europe

Over the past decade, there has been a downward trend in primate experiments in the EU. In 2011 (latest available statistics), 6095 primates were used for experimental purposes in the EU (European Commission 2013a), with UK research accounting for the use of 1459 of these animals. The majority (3435) of the animals in the EU statistics were used in toxicological and other safety evaluations, followed by research, development and quality control of products and devices for human medicine and dentistry and for veterinary medicine (1375), and fundamental biological studies (631). The remainder were involved in education and training[3], and other types of experiments.

When considering the UK alone the picture is slightly different and, over the past two decades, the number of primates used has fluctuated around 3000. In 2011, there was a significant fall in the number of primates involved in experimentation with the fewest ever (1459) recorded. However, in 2013 for the second year in succession the number of primate experiments increased to 2202 (Home Office 2014a). In addition, there has been concern raised that the development of genetic techniques (making genetic alterations of primates more practical) could lead to a substantial rise in the number of primates used (Combes and Balls 2014). At present, the primates used in the UK include the Cynomolgus macaque (*Macaca fasciularis*), the Rhesus macaque (*Macaca mulatta*) and marmosets and tamarins, with the first of these making up the majority. In line with the EU, the majority (78%) are involved in safety (toxicity) testing, particularly in relation to pharmaceutical safety and efficacy evaluation.

[3] As of January 1 2013 this use is no longer permitted under Directive 2010/63/EU

Despite relatively low levels of usage in Europe, laboratory primates have received increasing regulatory protection in recent years. The European legislation which controls animal experimentation, *Directive 2010/63/EU*, does so through a system of authorisations. The breeders, suppliers and users of experimental animals have to be authorised and registered, as do their establishments. Before any animal experimentation can go ahead the researcher must apply for authorisation to conduct their proposed project. To be authorised the project must meet the following criteria; be justified from a scientific or educational point of view or required by law; the purposes of the project justify the use of animals and; the project is designed so as to enable procedures to be carried out in the most humane and environmentally sensitive manner possible. The procedures can only be carried out for certain purposes, such as translational or applied research for the assessment, detection, regulation or modification of physiological conditions in human beings, animals or plants. When the original European legislation controlling animal experimentation, *Council Directive 86/609/EEC,* was revised in 2010 and the new *Directive 2010/63/EU* adopted, there were a significant number of changes that focused on primate use. In the original Directive, only one Article (Article 18) specifically mentioned primates, requiring them to have individual identification marks and for that identity and their origin to be recorded. In the new Directive, there are more than ten Articles which specify conditions regarding the use of primates, including two that are dedicated to primates: *Article 8 Non-human primates* and *Article 28 Breeding strategy for non-human primates*.

As well as being more specific in regard to primates, the new rules also distinguish primates from other species, with unique conditions applied to them. For example,

primates can only be used for four out of nine permissible purposes for which animal experiments are allowed to be conducted, and there has to be scientific justification that the purpose of the procedure cannot be achieved using any other species. There is further restriction on the translational or applied aspects of primate experiments, in that they can only be undertaken with '*a view to the avoidance, prevention, diagnosis or treatment of debilitating or potentially life-threatening clinical conditions in human beings*' (Article 8, p.40). In addition, all facilities where primates are used must be inspected at least once a year (Article 34); researchers cannot simplify the administrative process when primates are involved (Article 42); and the origin and species of primate must be reported in the annual statistics (Article 54). The Directive also places special emphasis on reviewing if and how primate use can be reduced or replaced, as illustrated by all projects involving primates having to undergo retrospective review to evaluate whether the objectives of the project were achieved and what harms were inflicted on the animals (Article 39), and in the setting apart of primates in Article 58, which deals with reviewing the Directive:

> *The Commission shall review this Directive by 10 November 2017, taking into account advancements in the development of alternative methods not entailing the use of animals, in particular of non-human primates, and shall propose amendments, where appropriate.*
>
> *The Commission shall… conduct periodic thematic reviews of the replacement, reduction and refinement of the use of animals in procedures, paying specific attention to non-human primates, technological developments, and new scientific and animal-welfare knowledge.* (p.51, author's emphasis)

The reasoning behind this increased protection for primates is succinctly described in the preamble of the Directive:

> *Having regard to the present state of scientific knowledge, the use of non-human primates in scientific procedures is still necessary in biomedical research. Due to their genetic proximity to human beings and to their highly developed social skills, the use of non-human primates in scientific procedures raises specific ethical and practical problems in terms of meeting their behavioural, environmental and social needs in a laboratory environment. Furthermore, the use of non-human primates is of the greatest concern to the public. Therefore the use of non-human primates should be permitted only in those biomedical areas essential for the benefit of human beings, for which no other alternative replacement methods are yet available.* (Preamble 17, p.34-35)

This extract nicely illustrates why primate use stands out from the general animal experimentation debate. The following section describes in more detail the basis of the primate debate and its controversial and emotive nature.

The Primate Debate

In the context of overall animal experimentation, the use of primates appears minimal, accounting for less than 0.1% of all the animals used in the UK and throughout European research and testing facilities (Home Office 2014a, European Commission 2013a), yet there is a highly visible and polarised debate about primate experimentation. Provocative and often distressing images of primates in cages and undergoing experiments dominate many antivivisection campaigns (Kugler 2014). There have been several high profile campaigns and exposés aimed at stopping their use, improving welfare and preventing their transportation, with a recent example being the BUAV's *A Living Nightmare* campaign (BUAV 2014) detailing an undercover investigation into primate use in a German research facility. There have

also been several reports published by the scientific community specifically to address primate use; for example, the Weatherall Report (Weatherall 2006) and the Bateson Review (Bateson 2011). By contrast, such explicit discourse is not evident for the most commonly used experimental animals, rodents and fish.

The two opposing viewpoints on primate experimentation can be characterised as follows: that their use is scientifically necessary and that their genetic similarity to humans makes them essential models for understanding and developing treatments for human diseases (Bailey 2014). In contrast, opponents focus heavily on ethical and welfare-related issues, highlighting the significant physical and psychological costs to these animals when used experimentally. Discussions revolve around the evidence that primates are highly social animals that have complex behavioural and environmental needs with the ability to understand some of what has been, and will be, done to them; and to empathise with their cage-mates. This is said to be compounded by the nature of the procedures to which these animals are often subjected (Bailey 2014; Hudson-Shore 2013), which is highlighted in the Animals in Science Regulation Unit Annual Report 2012 (Home Office 2013). The report notes that in 2012, seven project licence applications involving primates in procedures of potentially substantial severity were referred to the Animal Procedures Committee, which under UK law provides independent advice to the Home Secretary about issues related to the regulation of animal experimentation. Substantially severe procedures were defined, at the time, as those '*that may result in a major departure from the animal's usual state of health or well-being. These include: acute toxicity procedures where significant morbidity or death is an endpoint, some efficacy tests of anti-microbial agents and vaccines, major surgery and some models of disease, in which*

welfare may be seriously compromised' (Anonymous [2000], section 5.42). It should be noted that a section of the opposition to primate use community does question the scientific validity of primate research in addition to making the ethical and welfare arguments (e.g. Bailey 2010; Bhogal *et al.* 2005), but there are very few detailed evidence-based examinations of the scientific value of primate experiments (Conlee and Rowan 2012).

There seems to be no obvious way to resolve the gap between these two positions, and there has been very little dialogue about how to do so. As noted above, there is a body of texts dedicated to discussing the ethics of animal research which span the period from the 1970s (such as Singer 1975) to the present day (such as Rollin 2007). These usually call for a greater moral status for animals including 'animal rights' (Regan 1987) or are written from the perspective of the ethics involved in legislative control of animal experiments (i.e. utilitarianism and the cost/benefit decision; Hudson and Balls 2012). However, there is very little, if any, academic appraisal or discussion specifically focused on why the primate aspect of the debate persists and how, or if, it can be resolved.

One exception to this is the proposal to move toward the 'zero option'; that is, to progressively eliminate the need for any experiments on primates, which was first put forward in 1995 (Balls 1995). It was principally proposed at this time to counter pressure in Europe to fund expensive primate breeding programmes whose purpose was to provide sufficient animals for experimentation. Balls' (1995) point was that the level of demand was unknown, as was the proportion of such demand that was truly

scientifically justified, and that, if the Three Rs principles[4] were rigorously applied by the time the additional primates were available, they would not be needed. The proposal received a mixed reaction and, in 2000, Balls reiterated the importance of the Zero Option, giving seven main reasons to adopt it; moral, behavioural, scientific, logistical, safety, economic and the Three Rs. He proposed eight ways to achieve it, including a decision to end the use of primates by a certain date; support for the development of alternatives to procedures currently deemed as an essential use of primates; active discouragement of the use of more than mild procedures; and active discouragement of the use of invasive surgical techniques (Balls 2000). The proposal did not include an immediate ban on primate use but, instead, emphasised the need to make the necessary efforts to replace primate experiments. However, there have been no further attempts to develop a full strategy incorporating practical actions, evidence, research and/or input from stakeholders and, as such, the Zero Option has not, so far, been adopted or widely discussed.

This brief overview of the primate debate illustrates its emotive and controversial nature but shows how important it is in the context of animal experimentation from a scientific, ethical and legislative point of view. It underpins why a new perspective is

[4] In 1954 UFAW commissioned Dr William Russell and Mr Rex Burch to conduct a systematic study of the ethical aspects of laboratory techniques. This resulted in the publication of their book *The Principles of Human Experimental Technique* (Russell and Burch 1959) in which they described the Three Rs concept of *Replacement, Reduction and Refinement* as a way in which the inhumanity directly or indirectly involved in performing potentially painful experiments on animals can be diminished or eliminated altogether (Russell and Birch 1959). That is, *Replacement* of experiments and studies on animals with other methods; *Reduction* of the number of animals used in each experiment or for a specific purpose; and *Refinement* of experiments on animals towards more humane practices. At the time their findings went largely unnoticed but as the antivivisection movement progressed in the 1970s and 80s the book became important and now their concept forms the core of the new European legislation. The Three Rs underpin the regulations and are explicitly cited as requirements meaning that scientists wishing to conduct animal experiments must ensure that where possible a non-animal procedure is used, that the number of animals is reduced to a minimum, and that procedures, breeding, accommodation and care are refined to minimise any possible pain distress or lasting harm to the animals.

needed. The following section outlines the approach taken in conducting the present research project.

1.2 Research Questions, Design and Process

This section outlines the overall aim of the project, the research questions examined in order to fulfil the aim and the methodological approach taken in order to address the polarisation of the primate experimentation debate.

Aim:

To understand the impasse in the animal research debate about whether primates should or should not be used, by examining how biomedical research scientists view the opportunities and challenges of primate use, to determine if and how the impasse can be overcome.

Research Questions:

1. What arguments/justifications are given for and against using primates in biomedical science?
2. Are there differences in the justifications/arguments between:
    a. Different fields of research?
    b. Different specialist users?

3. To what extent do the social dynamics of science help to explain the continued impasse in the debate?
4. What are the policy implications for primate use and scientific practice?

Methodology

As noted above, an unusual multi-method approach was used involving a mixture of qualitative methods. The main stages of research are summarised here, with further details and reasoning described in Chapter 2.

This thesis does not contain a traditional literature review; instead a documentary analysis of primate reports published since 1986 (see Chapter 3) was conducted. The aim of this was to identify how the opposing sides of the debate present the scientific arguments for and against primate use, and to provide answers to the first research question. The documentary analysis also enabled the identification of important areas of primate research from which to choose the case studies that followed (see below), and provided the first indications that the social dynamics of science do indeed have a role to play in explaining the primate experimentation impasse.

Given the limitations of a PhD study and the complexity of the subject matter, this project focuses on two case studies. The two contrasting cases, research into Parkinson's disease and schistosomiasis, are used collectively in an effort to broaden the applicability of the findings. The choice of cases is explained and justified in Chapter 2. Before conducting interviews, it was necessary to undertake a review of peer-reviewed publications for each case study. This was done for the purpose of

aiding general understanding of the scientific aspects of each research area, initially identifying prospective interviewees, and developing the interview schedule.

In order to determine how research scientists view the opportunities and challenges of primate experiments, to answer research question 1 in more detail, and to provide answers for question 2, semi-structured interviews were conducted. A schedule (see Appendices 2 and 3) was used for the interviews to provide structure, but with the flexibility to enable changes to be made and for participants to have some freedom in their answers. For each case study, ten interviews were conducted with experts who either used or had never used primates. All the interviews were recorded and fully transcribed and the transcripts analysed.

The transcript analysis revealed key themes related to the social dynamics of science, which provided answers towards research questions 3 and 4: namely, competition and reputation; expectations, core sets and publications; entrenchment and policy; and ethics, speciesism and 'others'. In interpreting the data an objectivist approach was adopted, viewing the participants' responses as direct access to their experiences and views, rather than using a constructivist approach which would see them as narrative accounts. It is acknowledged that the objectivist approach is taken less often than the latter, but the decision was taken after deliberating about the various assumptions attached to these different interpretative frameworks and, as outlined in Chapter 2, the benefits and limitations of the chosen approach were carefully considered.

The methodological approach was initially underpinned and guided by several theoretical Science and Technology Studies (STS) concepts, which are briefly

outlined here but are described in more detail in Chapter 2. Elements of the 'Strong Programme' (Bloor 1991) are used to sustain the neutrality of the thesis, in terms of explaining both sides of the debate and adopting a symmetrical style of explanation. The work of Gilbert (1976; 1977), Thorpe (1973) and Scott (1990) on referencing as persuasion and assessing documentary sources was taken into account when conducting the documentary analysis. The 'Theory of Expectations' (see for example Brown 2003; Hedgecoe 2006) provided some of the impetus for analysing the primate reports as a medium for translating and stabilising information and shaping people's ideas and expectations about the primate debate. As noted earlier the concept of 'core sets' as defined by Collins (1988) has previously been used in examining animal experimentation, and this partly influenced the decision to conduct interviews in order to access the views of the key scientists in each field. The social appraisal of technology literature (see for example Stirling 2008) also contributed to the decision to conduct the documentary analysis. This is because the primate reports can be seen as a means of engaging the public in the primate experimentation debate and thereby involving them in the decision-making surrounding it. The final section of this chapter explains the structure of the thesis and introduces the key findings.

1.3 Structure of the Thesis

Having introduced the basis of the study and outlined the aim of the project and the research questions addressing that aim, the structure of the remaining thesis chapters will now be explained and the contribution of each chapter towards supporting the aim of the thesis described.

Chapter 2 gives a detailed account of the multi-method approach taken to conduct this research. It outlines the key methodological decisions made throughout the course of the project and explains why the study design is the most appropriate way to answer the research questions and to address the aim of the thesis. The chapter describes the practical methods undertaken for each phase, such as the documentary analysis, case study choice and interview technique. In addition, Chapter 2 explains the theoretical approaches that influenced the practical decisions and those that were adopted in analysing the findings, in particular the objectivist view of interview data.

Chapter 3 reports the documentary analysis of primate reports and represents the first phase of the research project. This chapter is not a traditional literature review as the aim was to conduct a more in-depth analysis to identify how the opposing sides of the debate present the scientific arguments for and against primate use, and so to provide answers to the first research question. The chapter also describes the first indications that the social dynamics of science do indeed have a role to play in explaining the primate experimentation impasse. Therefore, in conjunction with Chapters 4 and 5, Chapter 3 informed the answer to the third question regarding the extent to which the social dynamics of science help to explain the continued impasse in the debate. The findings presented in this chapter guided the choice of case studies for the second phase of the project. Therefore, Chapter 3 is a combination of background information and data.

Chapter 4 covers the case study on schistosomiasis vaccine research. It reports the results of the empirical work undertaken on this case. It contributes to the thesis by providing evidence that supports the conclusion that the social dynamics of science

are essential for explaining the continued impasse in the primate debate and, in conjunction with Chapter 5, indicates that there are important differences in the justifications given for and against primate use between different fields of research and different specialists – but that there also many similarities. Together with Chapters 3 and 5, Chapter 4 supports the recommendations made in the final chapters of the thesis in relation to overcoming the impasse and the implications for primate use policy and scientific practice.

Chapter 5 examines the second case study, on Parkinson's disease research. As in the previous chapter, it reports an analytical summary of the data collected during the interviews. In addition to the contributions noted above, this chapter provides more detail on the comparisons between the two cases to avoid repetition. This chapter and Chapter 4 outline the key social dynamics which emerged from the data. Considering how these dynamics interacted and impacted on the primate debate was essential for understanding the impasse and making recommendations to overcome it.

Chapter 6 draws together the findings from Chapters 3, 4 and 5 and directly addresses the research questions posed. It illustrates that the social dynamics of science do help to explain the continued impasse in the primate debate and that they could account for some of the observed differences between the two case studies and the views of the specialists involved in them. It explores the intricate relationships between the various dynamics such as competition and reputation, the impact they have on the impasse and the consequences that the findings have for existing social thinking, including where they support or contradict it.

Chapter 7 discusses how the aim of the thesis has been achieved by describing the implications for policy and practice. Recommendations for overcoming the impasse, founded on the evidence and discussion detailed in the previous chapters, are presented. Central to the recommendations are: improving collaboration and communication; increasing flexibility in scientific practices; and addressing ethical considerations surrounding experimental models. Chapter 7 also acknowledges that the recommendations cannot be implemented in isolation, and the consequences for current policy and practice and the key stakeholders that will need to be involved are discussed. As with any research project, there are limitations and avenues for future research, and these are also described and reflected upon here, in particular how to widen the applicability of the findings and areas that could add value to existing STS literature.

Overall, this thesis shows that, despite the persistence of the animal experimentation debate and, in particular, the polarisation surrounding the use of primates, by using an unusual multi-method approach it is possible to gain a deeper understanding of the debate and to make recommendations for ways to overcome the impasse. This project has identified the arguments involved, the differences in the justifications given between different fields of research and different specialists within those fields and, importantly, that the social dynamics of science are essential to explaining the continued impasse in the primate debate and how to overcome it. In addition, it has shone a light on the complexity and multifaceted nature of the problem, showing that there are not only the two established positions of for and against, but tensions within and between scientists engaged in animal experimentation. The findings mean that it can be concluded that in Parkinson's disease and schistosomiasis research the impasse

preventing a move towards replacing primates can be overcome. The insight gained from the study has enabled the making of specific, constructive recommendations for how to begin to achieve this.

Chapter 2: Methodology

2.1 Introduction

Following the description of the study rationale in Chapter 1, this chapter will outline the key methodological decisions made throughout the course of the project in more detail and explain why the chosen research design is the most appropriate way of addressing the aim and objectives of the thesis. The chapter is chronological and describes the practical and theoretical approaches taken for each phase of the research, namely; documentary analysis, multiple-case study choice, peer-reviewed literature review and interviews, including aspects such as interview strategy and analysis. The theoretical approaches that influenced the practical decisions and those that were adopted in the analysis are summarised at the end. The rationale for including this theoretical literature here is the semi-inductive approach taken in designing the study. That is, the intention was not to test a hypothesis about the topic based on existing practical and theoretical knowledge as one would if following a deductive approach (Hammond and Wellington 2013). Instead, the aim was to see what emerged from the data in terms of the social dynamics of science and the associated theoretical frameworks. However, the indication that such dynamics could be important for interpreting the primate research impasse and the decisions about empirical approaches taken (documentary analysis and interviews) were informed by the existing literature. Hence, the process was not wholly inductive.

2.2 Research Techniques and Qualitative Methods

2.2.1 Primate Report Documentary Analysis

In place of a traditional literature review a documentary analysis of primate reports was conducted to gain greater insight into the debate and to identify how the opposing sides present the scientific arguments. This also influenced the case study choice detailed below and provided the first indications that the social dynamics of science have a role to play in explaining the primate experimentation impasse.

The advantages of analysing textual data are summarised well by Silverman (2006). Texts provide rich (revealing presentational subtleties and skills), naturally occurring (documenting what participants are actually doing in the world, without being dependent on being asked by researchers), accessible (usually readily available) data which have real effects in the world (influencing how we see the world and the people in it and how we act).

This documentary analysis is the first of multiple methods employed in this study and represents the first phase of the research. The second phase, (described later in section 2.2.2) was a multiple-case study comparing two cases, Parkinson's disease and schistosomiasis. This second phase involved a review of the scientific peer-reviewed literature associated with, and qualitative semi-structured interviews with scientists involved in, the two fields of research.

Using multiple methods in this way gives richer understanding than looking at the science or social aspects separately could, with the focus being on enriching and completing knowledge. The documentary analysis provides information on the arguments that characterise the primate debate, which are presented by opponents and proponents of primate experimentation but not scientific users of primates or alternative models. It informs and complements the semi-structured interviews. The interviews provide an opportunity to further examine why these arguments persist and gather detailed information on the views of those directly involved in the research, regarding the opportunities and challenges of primate research, which are not readily accessible via other sources. As such this approach was not designed as a strict attempt at triangulation as defined by Flick (2014) as '*the combination of different methods, study groups, local and temporal settings and different theoretical perspectives in dealing with a phenomenon*' (p.183). However, undertaking multiple methods was done in the spirit of Denzin and Lincoln's (2000) understanding of triangulation as a strategy to add rigor, breadth, complexity, richness and depth to the findings.

Rationale

Primate reports rather than traditional scientific peer-reviewed papers were analysed because they represent the special focus that is placed on primates within the general animal experimentation debate. In particular they illustrate the polarised nature of the issue and are unusual in containing scientific citations but not being peer-reviewed, so are somewhat less restricted than scientific papers in their content and structure.

As noted above the reports are not peer reviewed and have not been critically assessed collectively. It was important to analyse these reports because, as Brown (2003) argues about press releases, they translate and stabilise information that might otherwise go unnoticed in the wider world and they are characterised by language and discourse that would never appear in traditional peer-reviewed texts. They also serve as a space to construct expectations about biomedical research and carry them to a wider audience, so are useful for shaping peoples' expectations about the field in much the same way as review papers (Hedgecoe 2006). The reports can be seen as impacting on society's views of primate research and in some cases have been aimed at influencing policy and regulatory decisions. Since, in processes of social appraisal, substantive perspectives call for participation in decision making, including the involvement of lay people (Stirling 2008), then, an additional function of these reports could be to engage the public in the primate experimentation debate. This makes them an important tool in altering the course of such experiments and thus worthy of analytical investigation.

The majority of reports identified using the strategy outlined in the next section were analysed with the criteria for inclusion being as follows. The documentary analysis was conducted on reports which have a scientific focus, in that they contain information on the experimental use of primates in research and testing; as such any report that is purely welfare, transport, housing and husbandry or ethics based was excluded from the analysis. Of the 18 reports analysed (Appendix 1), ten specifically discuss the ethical aspects of primate research and testing, illustrating that it is an important factor in the debate. However, although it can be difficult to dissociate the ethical argument from the scientific one, as one is often used to support the other,

evaluating the ethical discourse is beyond the scope of this analysis, which aimed to identify how the opposing sides of the debate present the scientific arguments for and against primate use and what those arguments are.

In addition the reports had to be accessible to anyone when circulated and be published in Europe between 1986 and July 2007. The implementation of the *Animal (Scientific Procedures) Act 1986* (ASPA), represents a major milestone in the protection of laboratory animals and in the regulation of animal experimentation in Great Britain, so presented a logical starting point. The decision to focus on Europe was partly due to the time restrictions associated with a PhD study, accessibility to reports including language considerations, and the European origins of the animal experimentation debate. There were no exclusions based on author, publishing organisation or on the length of the reports. Therefore, reports were from organisations both for and against the use of primates in biomedical research.

Report Identification

Due to the nature of these publications (i.e. not in peer-reviewed journals) it was not possible to use traditional citation databases to identify possible reports for inclusion in the analysis. Instead, the following strategy was employed in an effort to minimise the chance of omitting any relevant reports. The majority of the reports were identified through personal association with FRAME (Fund for the Replacement of Animals in Medical Experiments), where I am currently the Scientific Programme Manager. As a recognised stakeholder in this area of research, FRAME often receives reports of this nature from the authors. Each of the reports held by FRAME was

checked for further citations. An internet search was then conducted with the *Google* online search engine using various search terms (table 1). For each set of search terms the first 100 results were checked for relevance (conducted October 2007). In order to check for other literature that might relate to relevant reports an *ISI Web of Science* search between 1986 and 2007 was conducted using the search terms detailed in table 1. The publications/available resources pages of stakeholders' websites were also checked for relevant links or references (table 2).

Table 1: Search terms used in Google online search engine (www.google.co.uk) and ISI Web of Science (WOS) to identify primate-based scientific reports (conducted October 2007)

Google	**WOS**
Animal experiments	Primate AND Report AND Review
Animal report	Medical AND Primate AND Review
Ban OR stop primate use	Primate AND Biomedical AND Review
Essential primate	Primate AND Research AND Review
Medical primate	Primate AND use AND Report
Monkey report	
Primate biomedical	
Primate experiments	
Primate report	
Primate research	
Primate use	
Primates report	

Table 2: Stakeholder websites checked for primate based publications (conducted October 2007)

Name	Home page
Altweb	http://altweb.jhsph.edu/
Animal Aid	http://www.animalaid.org.uk/h/n/AA/HOME/
Biosciences Federation	http://www.bsf.ac.uk/default.htm (no longer available)[5]
Biotechnology and Biological Sciences Research Council	http://www.bbsrc.ac.uk/
British Union for the Abolition of Vivisection	http://www.buav.org/index.php[6]
EU Primate Network	http://www.euprim-net.eu/
Fund for the Replacement of Animals in Medical Experiments	www.frame.org.uk
Medical Research Council	http://www.mrc.ac.uk/index.htm
National Antivivisection Society	http://www.navs.org/home
National Centre for the Replacement, Refinement and Reduction of Animals in Research	http://www.nc3rs.org.uk/
Primate Info Net	http://pin.primate.wisc.edu/
The Royal Society	http://royalsociety.org/
Wellcome Library	http://library.wellcome.ac.uk/
Wellcome Trust	http://www.wellcome.ac.uk/

Analysis

The content of each report was analysed taking into account: i) the areas of research covered, ii) the main arguments/conclusions about those areas, iii) whether these were referenced and iv) if any references were repeated in different reports. The findings are discussed chronologically to aid in the assessment of whether the arguments presented have changed over time and, if so, how. In analysing the reports their persuasive nature had to be taken into account because, as Scott (1990) noted in his discussion of sincerity in scientific discourse, authors may try to '*present matters in a*

[5] In 2009 the Biosciences Federation merged with the Institute of Biology to become Society of Biology (https://societyofbiology.org/).
[6] As of 1 June 2015 became https://www.crueltyfreeinternational.org/.

favourable or unfavourable light in order to enhance the standing or espouse the beliefs of a group to which he or she belongs or is committed' (p.23). This is a strategy, which given the emotive and controversial nature of this debate, is highly likely to be a characteristic of these public reports. It was also important to consider who the intended audience for each report was, as this can affect the intended meaning of the text and can alter the possible interpretations of it (Scott 1990).

When reading the reports, I attempted to avoid impressing my own perspective, that of a scientist and interested stakeholder, onto the analysis. However, as a member of the intended audience of these reports, how I interpret them is of general interest and may indicate how others might receive them. In order to induce as much neutrality as possible in the analysis, making judgements about the validity of the justifications given for the arguments presented was avoided. Instead, the focus was on what arguments and justifications are given and how and why they are given in the manner that they are.

The reports (Appendix 1) are cited by a number in square parentheses. The fields of biomedical research to which they refer have been categorized (see table 3) to allow for a more coherent analysis. The assigned categories are mainly based on those presented in the Royal Society for the Prevention of Cruelty to Animals (RSPCA)/FRAME report [2], with additional categories added when necessary. The fields of research initially covered by the documentary analysis are highlighted in bold in table 3. These are the fields that are covered in ten or more of the reports (i.e. over half), as it is reasonable to assume that these represent the most important fields in terms of scientific and lay opinion. Fields one to five were excluded from the analysis

as they are very general and, as such, too wide ranging to be adequately evaluated here; they would require a dedicated review of their contents. The emphasis of this analysis is biomedical research, so the field of toxicology (number 17, table 3) has been excluded, as this is based on satisfying safety regulations and not on the pursuit of advancing biomedical science. As the analysis progressed it became clear that the resulting report was too extensive for the current study. Therefore, the documentary analysis presented in this thesis (Chapter 3) largely focusses on the fields of Parkinson's disease (PD) and schistosomiasis research which were subsequently chosen as the case studies (see below), so is consistent with the presentation of the interview data later in the thesis (Chapters 4 and 5). However, when data related to Alzheimer's disease and other infectious disease including HIV/AIDS provides important contrast and support to the findings from PD and schistosomiasis they are included.

Table 3: Categories of research reviewed in primate reports including the number of reports containing information on that particular category.

	Scientific Field	No. of Reports
1	General Model	13
2	General Physiology	8
3	Neuroanatomy	11
4	Neurophysiology	15
5	Neuropathology	10
6	**Parkinson's Disease**	11
7	**Alzheimer's Disease**	11
8	Behaviour	6
9	Drug R&D	9
10	Dentistry	5
11	Reproduction	6
12	**Infectious Diseases including Schistosomiasis & HIV/AIDS**	10
13	Immunology	3
14	Vaccine Testing	7
15	Transplantation	4
16	Toxicology	12
17	Biotechnology	5
18	Experimental Husbandry & Behaviour	2
19	Experimental Surgery	1

2.2.2 Case Study Selection

According to Ragin (1992), 'casing' or deliberately making something into a case is '*an essential part of the process of producing theoretically structured descriptions of social life and of using empirical evidence to articulate theories*' (p.225). In attempting to academically appraise the primate debate and impasse, conducting case studies, therefore, was an appropriate choice, particularly as '*cases are invoked to make the linking of ideas and evidence possible*' (Ragin 1992, p.225). In addition, as the specific area of investigation was views on primate experiments which occur in different fields of research within science it seemed logical to adopt a cases study approach because as Bryman (2008) explains '*...the case is an object of interest in its own right, and the research aims to provide an in-depth elucidation of it* (p.54). The

semi-inductive approach taken in this project is also compatible with a case study design, which when the research strategy is qualitative tends to take an inductive approach to the relationship between theory and research (Bryman 2008).

A multiple-case study was undertaken using a comparative framework that is two contrasting cases were studied using the same methods, because social phenomena can be better understood when '*they are compared in relation to two or more meaningfully contrasting cases or situations*' (Bryman 2008, p.58). The decision to conduct two rather than several case studies was due to the resource and time limitations associated with a PhD study, which limited the ability to adequately address the complex and extensive nature of each individual area of scientific research identified in the documentary analysis. However, the selection of two cases strikes a balance between the recent arguments for a greater use of case study research that involves more than one case and the criticism that a multiple-case study approach can lead to researchers paying less attention to the specific context and more to the ways in which cases can be compared (Bryman (2008).

This research focuses on two case studies; schistosomiasis, a parasitic disease, and Parkinson's disease, a neurodegenerative disorder. These two cases contrast in various ways as outlined below. As Flick (2014) recommends, this choice has been accomplished by purposive sampling, with the cases being selected to represent different aspects of the primate research controversy. In terms of choosing the cases a maximal variation approach to sampling has been taken, whereby the cases are as different as possible to disclose the range of variation and differentiation in the field (Flick (2014). These are instrumental case studies (Silverman 2005), but they are used

collectively to achieve the overall aim. That is, they are examined individually to provide insight into the primate impasse in their respective fields, but the findings from both are used to examine how that impasse might be overcome. By choosing contrasting examples, it may be possible to make recommendations for primate research more widely, because, as Silverman (2006) notes, '*The generalizability of a piece of qualitative research can be increased by purposive sampling guided by time and resources and theoretical* sampling' (p.311). The documentary analysis described above was used to identify these two cases and the rationale for selection is described below.

Case Study 1 – Schistosomiasis vaccine research: This is a field where the number of primates used in the search for a vaccine is relatively low, involving relatively mild procedures conducted during the end stages of the research process. It is also an example of the study of a parasitic disease that, despite affecting over 200 million people, is a relatively low profile Developing world disease when compared to the second case study, which often receives media attention and large amounts of funding.

Case Study 2 – Parkinson's disease treatment: In contrast to Case Study 1, this is a field of research where much of the research is fundamental in nature. Parkinson's disease is a neurological disease primarily of the Western world, in which primates are used to facilitate the search for effective therapies or a cure. It involves more primate use than schistosomiasis and the procedures are relatively more severe. The polarisation in this case seems very strong and much more contentious both ethically and scientifically.

2.2.3 Peer-Reviewed Literature Review

After selecting the case studies, peer-reviewed literature for each one was examined. In his guide to writing a dissertation literature review Randolph (2009) identifies the purpose of a literature review as being three-fold; i) demonstrating knowledge, ii) producing a publishable document and iii) identifying the influential researchers and groups in a field. In this sense the case study literature reviews were not traditional. Although they were used to identify relevant experts for interview, the aim was not to demonstrate knowledge in a publication/report, but to gain insight into the two fields of research, to aid with general understanding of the scientific aspects of each case.

The rationale for conducting these reviews conforms to a selection of Hart's (1998) reasons for reviewing literature, namely: discovering important variables relevant to the topic; synthesizing and gaining new perspective; establishing the context of the topic; enhancing and acquiring the subject vocabulary; and identifying the main methodologies and research techniques that have been used. This helped a great deal with preparing for the interviews, establishing pertinent areas for further investigation in the interview stage and designing the interview schedules (Appendices 2 and 3). As such these aspects are detailed in this chapter but the review as a whole is not reported.

The reviews were narrative in nature in that they were done to describe and discuss the state of the science of the two specific cases from a contextual point of view (Rother 2007). However, as detailed below in order to improve transparency and be as inclusive as possible a more systematic approach to sourcing and selecting the

literature was adopted; with an explicit search strategy devised and criterion-based selection being uniformly applied (Rother 2007).

Schistosomiasis

The peer-reviewed literature was identified via electronic searches of the WOS and PubMed databases. The primary search terms were "Schisto* OR Bilharzia" in the title or key words, limited to the years 1986 – 28 August 2008 (when the search was conducted). As with the primate report analysis the implementation of ASPA in 1986 represented a logical starting point. The results were imported into Endnote. This first search returned over 13,000 papers, therefore a strategy to find the most relevant papers was undertaken. Endnote was searched and duplicate entries removed and then certain papers excluded; see table 4 for the exclusion criteria, rationale and search terms used. The abstracts of the remaining papers were checked to ensure any remaining extraneous papers were removed; the criteria for these exclusions are given in table 5.

The identified papers that were available via the University of Nottingham's electronic journal subscription portal were then read in more detail. The main conclusions from each were categorised based on the type of model used, for example, two of the categories were primate models and rodent models, which were then subcategorised into species (baboon/macaque/chimpanzee for the former and mouse/rat for the latter), and the main research aim such as, attenuated vaccine or self-cure. Findings from these were summarised and listed with the reference. This continued until no new information was extracted. Although effort was made to

ensure as many papers and as much information as possible was included in the review complete saturation was not as important as it is in traditional narrative or systematic reviews as the main aim was to develop a personal knowledge base to inform the next stage of the project rather than answer a specific research question. In addition, the intention was to explore and, in some cases, check the findings from the review with the interview participants.

This collated information was used to identify the scientific rationale for using primate or other animal/non-animal models for schistosomiasis vaccine research. In addition, the review informed the interview schedule as it revealed controversies, knowledge gaps, influential outcomes and important discoveries. As explained below (section 2.1.4), the literature was also used to identify experts for interview and improve the rapport and flexibility in the semi-structured interviews.

Table 4: Strategy used to identify relevant peer-reviewed articles about schistosomiasis vaccine research: Exclusion via bibliography search.

Exclusion criterion	Reason	Search term(s) used in Endnote
Review	Not reporting new findings	"Review" in Title OR Notes OR Reference type
Proceedings	Usually reports work that is in progress, has previously been published or is about to be published	"Proceedings" in Title OR Notes OR Reference type
Workshop or Meeting	Usually a report of the conclusions and/or recommendations of the workshop/meeting not original research	"Workshop OR Meeting" in Title OR Notes
Snails	Removing papers solely focused on the host of the parasite and not on vaccine research	"snail*" in Title OR Keywords
None of the authors based in Europe	Time constraints	The following terms were all used in Author Address sequentially, results were checked and any without collaborators in Europe were excluded "US OR USA OR United States of America" "Japan OR China" "Australia OR New Zealand" "Egypt OR Brazil OR Brasil" "Kenya OR Ghana OR Nigeria" "Canada OR Mexico" "India OR Saudi Arabia" Papers with no address or where it was missed by the terms above were excluded
Non-English abstract	Do not have the resources to translate papers	"English Abstract" in Notes (match words)

Table 5: Strategy used to identify relevant peer-reviewed articles about schistosomiasis vaccine research: Exclusion via abstract content.

Exclusion criterion
No abstract available
Infection risk/rate/transmission
Schistosomiasis associated with other diseases
Diagnosis and methods of diagnosis
Treatment not vaccination
Not main focus/cursory mention
Snail ecology/infection/control (missed in previous search)
Meeting report/review (missed in previous search)
Parasite biology not related to vaccine development
Schistosomiasis aetiology/progression/clinical condition
Schistosomiasis species that do not infect humans
Economic evaluations
Behavioural studies
Study methods
Not English (missed in previous search)
Duplicates (missed in previous searches)

Parkinson's Disease

The strategy used to identify the Parkinson's peer-reviewed literature differed slightly from that for schistosomiasis. An electronic search was conducted in the *WOS* and *PubMed* databases. From an initial examination, and based on the experience from the previous search, it appeared that the majority of the *PubMed* results were duplicates. Therefore, it was felt that it was sufficient to use only the *WOS* results.

The primary search term used was "Parkinson*" in the title OR topic, limited to the years 1986 – 22 February 2010 (when the search was conducted). This returned over 60,000 papers, so the results were refined within *WOS*, imported into *Endnote* and further distilled using the criteria in table 6. As with the previous case study, the abstracts of the remaining papers were checked to ensure any remaining extraneous papers were removed; the criteria for these exclusions are given in table 7.

Table 6: Strategy used to identify relevant peer-reviewed articles about Parkinson's disease research: exclusion via bibliography search and refinement terms.

Exclusion criterion	**Reason**	**Refinement term(s) used in WOS**	**Search term(s) used in Endnote**
Review/Proceedings/Workshop or Meeting	Not reporting new findings/reporting work that is in progress or previously published/reporting of the outcome of workshop/meeting not original research	Document Type=(ARTICLE)	
Non-English abstract	Lack of resources to translate papers	AND Language=(ENGLISH)	
None of authors based in Europe	Time constraints	AND Countries/Territories=(HUNGARY OR ENGLAND OR WALES OR GERMANY OR IRELAND OR LITHUANIA OR CZECH REPUBLIC OR ITALY OR SERBIA MONTENEG OR FRANCE OR SPAIN OR NORTH IRELAND OR ARMENIA OR NETHERLANDS OR CROATIA OR MALTA OR SWEDEN OR SLOVENIA OR ESTONIA OR BOSNIA & HERCEG OR SWITZERLAND OR BULGARIA OR AUSTRIA OR SLOVAKIA OR FINLAND OR UKRAINE OR BELGIUM OR YUGOSLAVIA OR DENMARK OR	

Exclusion criterion	Reason	Refinement term(s) used in WOS	Search term(s) used in Endnote
		SERBIA OR POLAND OR SCOTLAND OR CYPRUS OR TURKEY OR NORWAY OR LATVIA OR GREECE OR REP OF GOERGIA OR PORTUGAL OR RUSSIA OR LUXEMBOURG OR ALBANIA OR BYELARUS OR USSR OR CZECHOOLOVVAKIA OR FED REP GER)	
No Abstract	Time constraint for identifying relevant papers		"a" in Abstract
Papers on methods of diagnosis	Removing papers not solely focused on treatment research		"Diagnosis" in All Fields
Papers not primarily focused on Parkinson's disease	Removing papers where Parkinson's is only given a cursory mention		"Parkinson" in Abstract (checked and removed remainder) Then searched sequentially for the following in All Fields and removed after checking abstract "White AND Syndrome" "Schizophrenia" "Alzheimer's OR AD" "Huntington's"

The identified papers that were available via the University of Nottingham's electronic journal subscription portal were then read in more detail. The main conclusions from each were again categorised based on the type of model used and

the main research aim such as, surgical or pharmacological therapy. Findings from these were summarised and listed with the reference. As with the first case study, this continued until nothing new was being identified, and the collated information was analysed and utilised in the same way. For example, it was used to identify the scientific rationale for using primate or other animal/non-animal models and to inform the interview schedule.

Table 7: Strategy used to identify relevant peer-reviewed articles about Parkinson's disease research: Exclusion via abstract content.

Exclusion criterion
Diagnosis and methods of diagnosis (missed in previous searches)
Describing symptoms or clinical signs
No direct reference to PD (missed in previous searches)
Side effects of known treatments
Not main focus/cursory mention (missed in previous searches)
Causative agents/ susceptibility
Meeting report/review (missed in previous search)
Sociological studies of PD management
Compound structure
Mechanism of action of treatments/MPTP
Drug interactions
Brain anatomy/morphology/physiology (not directly related to PD)
Aging studies
Vision research
Pathogenesis
Case studies
Tissue storage
Drug sensitisation/ Drug delivery
Toxicity
Genetic screening
Movement studies (of patients)
Imaging substances
Economics of treatment

2.2.4 Interviewing Relevant Experts

Interviews were the most suitable method of data collection for this project because as Liamputtong and Ezzy (2006) highlight:

a. they provide a way of discovering the subjective meanings and interpretations that participants give to their experiences
b. they allow aspects of social life such as social processes to be studied, which could not be achieved any other way
c. participants' responses are less influenced by direct pressure from peers, so they may be more prepared to discuss sensitive matters
d. participants can find the experience rewarding

Points a and c were particularly important given that scientists' views on a controversial topic were being sought. Point d was also found to be true with several participants expressing thanks for making them think about the topic again and/or giving them the opportunity to revisit or talk about their work. Other methods such as focus groups or ethnography were unsuitable; in the former case because the aim was to generate in-depth information about the views of individuals and in the latter, because of time constraints and wanting to seek the scientists' views rather than an understanding of the environment in which they worked.

These interviews allowed exploration of the scientific issues/questions that arose from the literature review and a more in-depth look at the social dynamics apparent in the prior documentary analysis. They have allowed detailed access to expert perspectives and exploration of some of the nuances of the debate. As part of the case studies, the intention was to investigate: (a) whether there are differences between the work of the

specialists within in each field (i.e. the core set, see 2.2.3 for more detail), (b) how that work is represented and (c) what impact this has on the perception of primate experiments. Another purpose was to reveal if the status quo (continuing primate use) is due to the actions of key scientists; again to determine this it has been essential to speak to those scientists. The interviews are important, therefore, for constructing answers to each of the research questions; in particular whether there are differences in the justifications/arguments between the fields of research and the different specialists and to what extent the social dynamics of science help to explain the continued impasse in the debate.

Interview Strategy

For each case study, ten interviews were conducted with experts involved in each of the two fields – see below for details on how these were identified and accessed. Table 8 provides an overview of the participants for each case. Interviews lasted between an hour and two hours with one exception of just over 40 minutes. They were all conducted in the participants' offices within their academic institution, with one exception which was conducted in a café over lunch.

Table 8: Overview of the academic position, background and range of participants for the two case studies

Schistosomiasis Vaccine Research	Parkinson's Disease Treatment Research
Academic Position	Academic Position
5 Professors	3 Professors
3 Senior researchers/lecturers	7 Senior researchers/lecturers
2 Postgraduate researchers	(figures include 2 clinicians)
Models Used	Models Used
5 Have worked with primates	4 Have worked with primates
5 Have not worked primates	6 Have not worked primates
Location	Location
6 Different academic institutions in the UK and France	7 Different academic institutions in the UK and Ireland

The interviews were semi-structured to give the flexibility to make changes during the interviews, while still providing enough structure to ensure that the information most relevant to meeting the aim of the study was collected. This involved using an interview schedule (Appendices 2 and 3) consisting of several themes, each having several prompt questions depending on the response of the participant (see below for more details). Thus, as the interviewer I shaped the discussion, as the questions were influenced by the research aims. However, by using this semi-structured approach rather than an open-ended one, the aim was to allow participants to use their own ways of defining their environment, work and viewpoints, and to raise important issues not contained in the schedule, whilst, at the same time, avoiding creating an interpretive problem for the participants in worrying about what is relevant (Silverman 2006). Each interview was recorded and was stored in accordance with the University of Nottingham research guidelines. As Liamputtong and Ezzy (2006) note, recordings provide a level of detail and accuracy that are not obtainable from memory or by taking notes. Indeed, a further advantage of recording is that as the interviewer I was able to concentrate on maintaining flexibility in the interview such as, following up

interesting points, probing when necessary and highlighting inconsistencies in responses rather than making extensive notes on what was said (Bryman 2008).

The interview recordings were fully transcribed in an ongoing manner in order to make the process more manageable. While the majority of the analysis of the resulting transcripts was done when all the interviews in each case were complete it is important to note that the production and use of transcripts are essentially 'research activities' (Atkinson and Heritage cited in Silverman 2006), involving close, repeated listening to recordings that can often reveal previously unnoted recurring features of the organisation of talk. Therefore, taking this consecutive approach to transcription allowed for some initial analysis in terms of raising awareness of emerging themes (Bryman 2008) and identifying areas in the interview schedule that needed to be developed or changed as the interviews continued. The transcription process and analytical approach taken are described in more detail in the Transcription and Analysis section (p.53)

The schedule design was the same for both cases with examples specific to each field of research being substituted as necessary. The schedules (Appendices 2 and 3) were designed to cover certain themes that had arisen from the documentary analysis and literature review with the aim of gathering data relevant to the research aim and questions, in particular questions 2 to 4. They are divided into background, and five themes;

1. Expectations and justifications used in biomedical research
2. Scientific controversies and misunderstandings
3. Perceptions of biomedical research

4. Shaping biomedical research, barriers and facilitators
5. Views on implications for primate use policy and regulation

The background section included questions about factual aspects of the participants' career and research to enable a rapport to be developed before tackling the more in-depth or difficult questions. Each theme represented an aspect that was considered to be important for understanding the primate debate impasse. Within each theme there was a maximum of six questions. The initial question was a general introductory question to begin and guide the conversation, with the remaining questions acting as probes to clarify answers if necessary or as follow up questions to pursue the implications of a given answer. As far as possible the questions were designed to be impartial and encourage detailed responses rather than one-word answers. The schistosomiasis schedule was adapted when it became clear, after the first couple of interviews, that a question in theme 4 regarding a change of emphasis in their work (see Appendix 2) was causing confusion. Experience gained during the interviews, also informed some slight changes of emphasis in some of the questions in the schedule in some instances. For example, specifically asking some Parkinson's disease participants about the problem of research moving abroad, when they did not spontaneously mention it.

All interviews were face-to-face, with the exception of one of the Parkinson's disease interviews, which, due to time constraints for the participant (I14NP), was conducted over the telephone. Face-to-face interviews are preferable for this kind of study as they have been reported to: result in a better response to sensitive items; decrease the social distance between the interviewer and respondent; and allow participants to self-generate what is on their minds (Shuy 2002). Therefore, in undertaking the telephone

interview, it was important to be aware that the participant might be more likely to avoid the more sensitive/controversial aspects of my schedule. Aquilino (1994) describes how this is often due to problems with the participant being less persuaded by the confidentiality claims made by the interviewer. Therefore, to try and avoid these problems the anonymity of the data was emphasised and in general it was felt that a good rapport was established. In addition, the participant (I14NP) gave extensive answers that did not differ significantly in terms of detail from the other interviews.

During one of the schistosomiasis interviews, the recorder malfunctioned and approximately half of the conversation was not recorded. However, the participant (I8P) later agreed to go over some of the main points again so that they would be recorded. A transcript for the missing parts was written using the notes taken during the interview and a copy of this was sent to the participant to ensure they were happy that the conversation had not been misrepresented.

Expert Identification

When deciding who to interview a purposive sampling approach was taken in order to ensure that those that were interviewed were the most relevant to the research questions being asked (Bryman 2008). Indeed Bryman (2008) notes that '*many writers on sampling in qualitative research based on interviews recommend that purposive sampling is conducted*' (p.458). In contrast probability sampling was not appropriate for this study as the research questions were aimed at a particular category of people (biomedical scientists) within specific fields of research (PD and

schistosomiasis) rather than a wider population and although some generalisation might be possible the intention to conduct case studies means that the focus is on those specific occurrences rather than broader applicability (Bryman 2008).

Identification of experts to be interviewed was done via a variety of means. The papers collected for the literature review were used as the basis for the purposive sample, as it was assumed that those who were the most prolific publishers were likely to be very active within their fields so be more likely to give a rounded and current overview of the research. The papers were organised by first author using the bibliography software Endnote. Authors who had published four or more papers were highlighted and their current research status investigated, initially using the addresses given in the papers and then, if necessary, using the internet search engine *Google*. Having identified those that were still active with available email addresses, the most senior researchers in each associated group were targeted for initial communication, as it was thought that these would have the greatest amount of experience and could give an overview of the group's work in the field. In addition, certain experts were identified from presentations/posters at conferences and via previous association with FRAME and other Three Rs organisations.

Additionally, a snowballing approach was adopted where participants were asked if they could recommend anyone to approach and, on one occasion, this led to an extra unsolicited interview with another member of the research team on the same day. Snowballing was appropriate in these circumstances as the sampling frame (i.e. the list of all the units within a population from which a sample is selected; Bryman 2008) was limited by identifying researchers via the literature as this was dependent on them

having published research so it was not possible to have a complete list of all researchers in each scientific field from which to draw a sample. It must be noted that seniority was not a definitive criterion; hence the interviews with two post graduate researchers, who were conducting extremely relevant research and who, it was thought, might have a different outlook on the field. The recommendations of other relevant researchers by participants also provided reassurance that a good breadth of respondents was being targeted, as many of those identified by participants were among those approached. There was also reasonable coverage in terms of the fields of research, with representatives from most of the main research aims identified by participants and the peer-reviewed literature review being involved.

Location and Access

The interviews were conducted in academic institutions, with the exception of the one conducted in a nearby café (in the telephone interview, the participant called from their academic institute). Location was not used as a criterion for deciding which interviews to conduct as this was decided purely by where the research is carried out.

The controversial nature of animal experiments, particularly primate use, and the sometimes violent response by animal rights extremists towards researchers involved in it (see Chapter 1) meant that access to the identified experts required a particularly sensitive approach. It was extremely ethically important to give consideration to the scientists' safety and to attempt to mitigate any negative consequences that might arise from participating (Bryman 2008). To this purpose all responses were treated as confidential and transcripts coded and anonymised. Information regarding

participants' names and contact details were stored securely and separately from the interview recordings and transcripts. The project received ethical approval from the University of Nottingham and adhered to its research code of practice. The process for gaining access is detailed below.

In order to gain access to the identified experts, an initial approach letter on University-headed paper was sent via email requesting assistance with the PhD project. It outlined the sponsor, the research aims, the intention to conduct interviews and the themes that would be explored in them. The letter also detailed the steps to be taken regarding confidentiality and anonymity, and the ethical approval. Agreement to be interviewed was taken as consent to participate, but in addition at the beginning of each interview participants were asked to confirm their willingness to proceed and be recorded. The anonymity aspect was also reiterated at the beginning of each interview, and on concluding the interview all participants were given my contact details should they have any concerns or queries at a later stage.

For schistosomiasis the approach letter led to immediate acceptance by some participants. Having conducted the first round of interviews the snowballing approach also aided with access as well as identification of potential participants, in that some of those interviewed offered to act as a referee/gatekeeper. Those who had not responded were contacted again and it was emphasised that other participants had recommended that they be spoken to. This was very successful, there were no refusals and only one expert did not reply, with another not being able to fix a suitable date for interview. Indeed, as detailed above, this strategy led to an extra unsolicited interview at one institution. In the case of Parkinson's disease it was envisaged that the snowball

approach might need to be utilised more extensively as the primate models used in this field are more contentious and so the researchers might be more reticent to participate. However, it was pleasantly surprising that the majority of the targeted experts were willing to participate. Of those contacted, three did not reply, one accepted but was unable to arrange a suitable date for the interview and three declined due to other commitments or because they were no longer working in the field.

Transcription and Analysis

Each interview was transcribed verbatim by me and given a code number to ensure anonymity. Flick (2014) notes that as yet no standard has been established in terms of how exact or comprehensive a transcription has to be, arguing that:

> Where linguistic and conversation analytical studies focus on the organization of language, this kind of exactness [formulaic rules for transcription] may be justified. For more psychological or sociological research questions, however, where linguistic exchange is a medium for studying certain contents, exaggerated standards for exactness in transcriptions are justified only in exceptional cases… (Flick 2008, p.389).

Given that the intention was to conduct a thematic analysis of the transcripts it was important to transcribe the interviews in full to ensure that nothing important was missed and to facilitate comparison within and between the cases. This included making note of pauses, stresses and emphasis but not the fine grained details required for conversation or discourse analysis such as, prolongation of sounds, turn taking, in takes of breath and measuring periods of silence to the tenth of a second (Bryman 2008). Neither conversation analysis or discourse analysis were suitable for the purposes of this project, the former because it focusses on how the patterns in

naturally occurring talk elucidate hidden aspects of interaction (Scott and Marshall 2005) and the latter as it is constructionist approach concerned with the strategies people employ in trying to create different effects (Bryman 2008).

It can be argued that thematic analysis is one of the most common approaches applied to qualitative data (Bryman 2008). Yet, as Bryman (2008) discusses, unlike other strategies such as grounded theory, it does not have an identifiable heritage or defined set of criteria or techniques. However, this method offers practical means to pin down activities in qualitative data analysis, particularly when the research aims beyond developing a theory from the material (Flick 2014). Indeed, Braun and Clarke (2006) argue that thematic analysis '*offers an accessible and theoretically flexible approach to analysing qualitative data*' (p.77). In their paper on using thematic analysis in psychology Braun and Clarke (2006) provide a useful outline of what thematic analysis is and give guidelines on how to conduct it in a more deliberate and rigorous way.

Given the semi-inductive approach taken in designing the present study, thematic analysis as defined by Braun and Clarke (2006) as '*a method for identifying, analysing and reporting patterns (themes) within the data*' (p.79), is an appropriate methodological framework to adopt. Therefore, in the process of transcribing and analysing the interview data (described below) Braun and Clarke's (2006) six steps for searching across a data set to find repeated patterns of meaning were considered. These are:

1. Familiarising yourself with your data
2. Generating initial codes
3. Searching for themes
4. Reviewing themes

5. Defining and naming themes
6. Producing the report (Braun and Clarke 2006, p.87)

The following describes the stepwise process of transcription and analysis of the interview data. As noted above transcription (or familiarisation with the data) was completed in an ongoing manner but the analysis in terms of coding and identifying themes was conducted once all of the interviews in both cases had been completed and transcribed. This allowed comparison across all participants' response within and between the cases.

Each interview was transcribed verbatim into an electronic Word document. Any names of places or people were omitted to reduce the chances of participants being identified. Participants were given a code number and each transcript file was given an anonymous code name.

Each transcript was then manually analysed, using insight from Science and Technology Studies (STS; see Section 2.2), to highlight information that is relevant to understanding which experimental models and techniques are used to investigate schistosomiasis vaccines and treatments for Parkinson's disease from a scientific perspective, and what the benefits and problems are with each of them. In addition, responses that had social science consequences were identified, such as utterances related to conflict in a field or building expectations.

These sections of the transcripts were then grouped (or coded) and examined to decipher what the main emerging themes were. The categories/codes used were; expectations, drivers, barriers, justification, knowledge creation and model choice.

The extracts were not limited to one category if it was felt that they were illustrative of more than one. This continued until all extracts had been assigned to a category. The categories were collated and the relevant extracts gathered together to identify the key themes described in Chapters 4 and 5. It was important to consider if there were any contradictory data and what impact they might have on the findings, and to be aware of any omissions in the data, as what the participants have not said may have consequences for how the debate on primate use is framed.

Once the themes were identified they were examined to see how they linked together and how responses within them differed or concurred between different types of participant and between the two cases. In much the same way as Bryman (2008) describes, the comparison allowed the distinguishing characteristics of the two cases to act as springboard for the theoretical reflections about the contrasting findings. When reporting the findings of the analysis, quotations that were illustrative of the majority of the responses or that represented a significant contradictory or unique viewpoint were chosen. Thick description was adopted, that is quotations were more than a sentence or a few words, in order to provide context, validity and richness to the analysis.

In terms of interpretation of the data, an objectivist approach was adopted, in that the participants' responses were taken as giving direct access to their experiences and views rather than seeing them as narrative accounts, that is, from a constructionist viewpoint. This decision was taken after deliberating about the various assumptions attached to these different interpretative frameworks and, as outlined below, carefully considering the benefits and limitations of the chosen approach.

There is a great deal of literature which discusses the use of interviews as elicitation of accounts. This stance is foundered in constructionism, that is, interviewer and interviewees are actively engaged in constructing meaning. This means that interview responses are not taken as simply true or false, but are displays of perspectives or moral forms which draw upon available cultural resources (Silverman 2006). A useful discussion of the basis for treating interviews in this way is given by Dingwall (1997). In summary, he proposes that when interpreting interview data the analyst must consider that the interview situation is never an occasion where the respondent can tell whatever story they like. There is always a deliberate topic that the interviewer is interested in. Therefore, the interview is a joint accomplishment involving interaction which should be analysed in terms of impression management. That is, the respondent will be concerned about demonstrating competence as a member of the community under study and will do so in response to intentional or unintentional cues given by the interviewer about what is or is not acceptable about their answers. For the constructionist this places emphasis on the interaction or how the respondents create meaning as a topic in its own right, so 'accounts' are not representations of the world but are part of the world they are describing.

Critics of constructionism argue that it suffers from narrowness by focussing on the properties of social interaction and seemingly denying the value of treating interview data as saying anything about any other reality than the interview itself. That is, it focusses on the 'how' questions rather than the 'what' questions. Silverman (2006) notes that this means that many interview researchers complain that following a constructionist position results in a '*…focus on the conversational skills of the*

participants rather than on the content of what they are saying and its relation to the world outside the interview' (p.131).

In contrast to the constructionist approach, in viewing data as real, in and of themselves, objectivists assume; that research participants can and will relate the significant facts about their situation; that the researcher remains separate and distant from research participants and their realities; that the researcher represents the participants and their realities as an external authority and; that the research report offers participants a useful analysis of their situations (Charmaz 2002). Abraham (2002) proposes that objectivist realism provides a theoretical framework for producing knowledge and for gaining knowledge of the historical, economical, psychological, political and sociological explanations and implications of technological risk and benefit. He argues that this does not imply that knowledge is never socially constructed but rather that it is not wholly constructed, for example;

> In the case of scientific research involving the natural world this is because of objective natural mechanisms which exist and have properties independently of scientists (e.g. cell proliferation), even though the social activity and organisation of science is needed to produce knowledge about them. (Abraham 2002, p.307)

He goes on to say that realists can be sceptical about scientific knowledge claims and that in fact they tend to challenge such claims much more deeply and comprehensively than relativists/constructionists because they can include a degree of examination of the validity of the claims. van Zwanenberg and Millstone (2000) also feel that realism can acknowledge that social factors affect scientific activity but that it does not feel the need to explain scientific developments purely in terms of those

factors. They also argue that realists have more appreciation than scientistic and relativist analysts do of the reliability and robustness of certain parts of science.

Having chosen the objectivist approach it is acknowledged that there is a literature surrounding what some argue are 'problems' which can distort participants' responses. Denzin (1970) provides a useful list of these, which are now used to describe how it is believed that many of the issues about interpreting the data as actual experiences were either overcome or, at least, taken in to consideration in the present study.

Respondents possessing different interactional roles from the interviewer – This relates to respondents possibly assigning a different role to the interviewer, so the situation is not respondent/interviewer, but instead it might be teacher/pupil, male/female etc. In essence this may not be as problematic as it seems if the interviewer adopts the role indicated by the respondent; in actuality it might improve the relationship and make talking easier for the interviewee. In this study this was not particularly a problem, with the exception that sometimes it was felt that a small selection of the participants took on a teaching role in some instances. This was dealt with by accepting the 'lesson' passively and then moving on to the next question. This aspect of Denzin's discussion of problems that might distort participants' responses may also not be as relevant today, because as a society we are much more aware of the interview and are exposed to them daily in the media (e.g. newspapers, magazines internet blogs and television). Scientists are also increasingly expected to engage with the public by grant-giving bodies and their institutions, so are much more familiar with the role of interviews and how they are conducted.

Problem of 'self-presentation' (of the interviewer) especially in the early stages of interview – To address this, an attempt was made to remain neutral and approachable and to build a rapport with the participants. Fontana and Prokos (2007) explain that to establish a rapport '*the researcher must be able to take the role of the respondent and see the situation from their viewpoint rather than superimpose his or her pre-conceptions upon them*' (p.116). Therefore, having a scientific background and reviewing the peer reviewed literature was advantageous in developing and maintaining the rapport as it enabled an understanding of the vocabulary and culture of the participants (Fontana and Frey 2000). Denzin (1970) argues that rapport varies by dimensions such as class, perceived social status and consensual meaning conveyed by the interview, and that the closer the fit is in these dimensions between the interviewer and the interviewee the greater the rapport will be. Despite the benefits of rapport the interviewer must avoid 'going native' and becoming a member of the study group so foregoing their academic role (Fontana and Frey 2000). Taking these various recommendations into consideration an attempt to establish a rapport with each participant was made in the following way. The interviews began with questions asking for factual information such as academic position and time spent working in the area to ease the participant in to the interview. They were asked about their work prior to the more controversial questions so that they could discuss something familiar and agreeable to them before tackling the more difficult questions. A passive voice was used when asking questions, that is, aggressive questioning was not used – the questions were not phrased to indicate a right or wrong stance. Finally, general terms were deferred to such as 'others have said' or 'the literature indicates' rather using 'I' or indicating that they were personal thoughts.

Problem of 'volatile', 'fleeting' relationships to which respondents have little commitment and so can fabricate tales of self that belie the actual facts – This relies on participants feeling that the interviewer will not have objective evidence to counter fabricated 'tales' and the risk of it is thought to be amplified if the probability of future encounters is low. Given that the interviews were conducted as part of a PhD project and all of the participants are familiar with the process and methods that accompany such a project they would have been aware that background research on their field will have been conducted, and that their peers/associates would be spoken to as well. In addition, because of the association with FRAME it is reasonable to think that many, if not all, of the participants would perceive that I had some knowledge of the situation under investigation. Therefore, taking these factors into account, they would be less inclined to give false responses that I might be able to question the authenticity of. In terms of a volatile/fleeting relationship there was no experience of any of the indications that this was the case such as the participants breaking off or refusing to answer questions. Neither was there experience of any 'flooding out' or apparent embarrassment that meant that the participant could not carry on, or that it was necessary to intervene to change the topic or move the interview on.

Difficulty of penetrating private worlds of experience – There were several instances that indicate that this was not an issue in these interviews. Where participants were particularly aware of my background and association with FRAME there was no hesitation to talk about the negative aspects of their work, which might have been expected if they were telling me what they thought I would want to hear rather than their experiences. Some of the participants that did not use primates still said they

would be needed to some extent. So they were not 'preaching' alternatives or reluctant to say primates might be needed, as you might expect them to be if they were uncomfortable with the situation or giving an account based on what they thought might be deemed acceptable. Many also wished me luck with the project and were interested in the findings of the thesis and any publications that arise from it. Denzin (1970) also proposes that the interview should be viewed as a special relationship which has often been freely entered into, and one in which information is exchanged. As such any information which is given freely may be assumed to be more valid. In the interviews none of the participants were coerced in any way to take part, and to strengthen the free-giving of information all were assured of the anonymity of the data so that they had fewer worries of negative consequences from their responses.

In addition, Holstein and Gubrium (1995) cite tell-tale phrases such as 'if I were in his shoes' or 'wearing my professional hat', which participants use to signal shifts in roles, indicating that they are active narrators weaving skilful, appropriately located, stories (accounts). There is a very low incidence of this kind of phrase within the interview transcripts.

The relative status of interviewer and interviewee – This can cause problems if there is inequality between the two. For example, if the interviewee is superior to the interviewer they may talk past them, perhaps in a lecturing or dismissive tone. Equally, if the interviewer perceives the interviewee to be of lower status they may force their morality on to them or talk down to them, all of which may influence the participant's response. The interview can be seen as a transaction or understanding wherein the interviewer gets access to and can direct the participants' communications

and in return the participant is assured there will be no reprisal. So, in order to maximise self-expression of the participant and create a free atmosphere, a degree of equality in the interview is desirable. This might be a fit in backgrounds or status for example.

In my experience the inequality of all of the participants being of higher status in an academic context (i.e. postdoctoral or above) than me was balanced by the respect that is given to the PhD process and outcomes. I never felt that I was being talked down to, and all the participants engaged with me an open manner.

The 'context' of the interview (e.g. home, work, hospital) – Denzin (1970) contends that few studies succeed in locating interviews within the same situational class (e.g. homes, offices or laboratories), which may lead to between-class variance making it difficult to justify comparability across interviews. The fact that all of the interviews were conducted in the participants' offices within their academic institutions helps to mitigate this problem. Even with the exceptional interview that was conducted in a café, the participant had chosen that location and it was still within the academic sphere as it was frequented by the University staff and students. Thus participants were comfortable and secure, and were able to discuss research within a research setting in each interview.

It is acknowledged that this objectivist approach to the analysis of the interview data could be seen by some as contradictory to the stance taken in the documentary analysis. Taking into consideration the persuasive nature of the primate reports could be seen as quite a constructionist reading of them, with the concern perhaps being

about how the reports are assembled and evaluated rather than their content *per se*. Silverman (2006) notes that from a constructionist position researchers are interested in texts as 'topics' but not as 'resources'. However, in the documentary analysis in this study the reports were treated more as a resource to establish which fields of scientific research were seen as important in the context of concerns about primate experiments and to identify what the main arguments in the primate debate were. Although the analysis involved interpreting why those arguments might have been presented as they were, this was not just about how they were presented, but rather what theoretical paradigms might underpin them. Therefore, it was once again used as a resource to inform the next stage of the project both in terms of highlighting that the social dynamics of science could, as hinted in the existing literature, play an important role in understanding the primate impasse, and in choosing the case studies and developing the interview strategy.

2.3 Theoretical Rationale

Elements of the 'Strong Programme' of science and technology studies (STS) (Bloor 1991) are used to sustain the neutrality of the thesis. The Strong Programme is defined by four tenets in which Bloor (1991) says of a proper sociology of knowledge that;

1. It would be causal, i.e. concerned with the conditions that bring about belief or states of knowledge. Naturally there will be other types of causes apart from social ones which will cooperate in bringing about belief.

2. It would be impartial with respect to truth and falsity, rationality or irrationality, success or failure. Both sides of these dichotomies will require explanation.
3. It would be symmetrical in its style of explanation. The same types of causes would explain, say, true and false beliefs.
4. It would be reflexive. In principle its patterns of explanation would be applicable to sociology itself. Like the requirement of symmetry, this is a response to the need for general explanations. It is an obvious requirement of principle, otherwise sociology would be a standing refutation of its own theories.

The second and third of these are mostly utilised within this thesis, in that both sides of the primate use debate will be described without making an *a priori* distinction as to which is right or wrong. The principle of symmetry will be adopted with the same resources used to explain each side's beliefs. The Strong Programme may at first seem incompatible with the adopted objectivist/realist approach, as it is frequently classed under the label of 'social constructivism' (Bloor 1999) and allied with a more relativist reading (Kochan 2009). However, Lewens (2005) argues that the Strong Programme is compatible with realist thinking and provides an accordant interpretation of each of the four tenets. For example, Lewens feels that the reading of the symmetry principle given in the following quotation from Barnes and Bloor (1982) gives nothing for the realist to disagree with:

> Our equivalence postulate [an alternative name for the symmetry principle] is that all beliefs are on a par with one another with respect to the causes of their credibility. It is not that all beliefs are equally true or equally false, but that regardless of truth and falsity the fact of their credibility is to be seen as

> equally problematic. The position we shall defend is that the incidence of all beliefs without exception calls for empirical investigation and must be accounted for by finding the specific, local causes of credibility. [Sociologists of knowledge] simply investigate the contingent determinants of belief and reasoning without regard to whether the beliefs are true or the inferences rational. They exhibit the same degree of curiosity in both cases (Barnes and Bloor 1982 in Lewens 2005).

He feels that this is a problem:

> …of explaining why certain beliefs, or practices of inference, are found credible by those who hold them. Even realists agree that true beliefs can be explained causally, and beliefs about what reasons are good reasons need causal explanation too (Lewens 2005).

This indicates that this approach is appropriate for this thesis, as it is the views of scientists that are being sought and, so long as an awareness of possible reasons for those views is maintained, then the Strong programme is applicable in helping to preserve an element of neutrality in the analysis and presentation of results.

In addition, when looking at scientific controversies, such as cold fusion or in this case whether primates are the best model for a disease, it is important to take a symmetrical approach to avoid seeing losing participants as being unreasonable (Sismondo 2003). Given that participants in disputes or debates always have, what at least seem, to them, good reasons for taking the positions that they do, then there should be an attempt to decipher the forces behind those reasons for both protagonist and antagonist viewpoints on primate experimentation.

The following summarises the key theories that initially influenced this study. It is included in this chapter because of the way in which these approaches have influenced the methodological design. It is acknowledged that this summary of theoretical

frameworks is not an extensive review but instead provides an overview of the point from which the research began. The intention from the outset was to see what emerged from the data in terms of social dynamics of science and the associated theoretical frameworks. The findings from the documentary analysis (Chapter 3) and case studies (Chapters 4 and 5) revealed the key social dynamics at play in interpreting and understanding the primate debate impasse, which formed the structure of the discussion in Chapter 6 (i.e. competition and reputation, expectations, core sets and publications, entrenchment and policy, and ethics, speciesism and 'others'). Therefore, throughout the thesis as each dynamic is presented the associated literature is described and critiqued. In Chapter 6 the direct consequences for existing social scientific thinking are specifically detailed. Indeed, Jensen and Holliman (2009) note that this type of inductive approach, which does not necessarily fulfil all aspects of Glaser and Strauss 'Grounded Theory' has been adopted by many qualitative researchers. In their research of certain forms of science communication Jensen and Holliman adopt this inductive orientation, while acknowledging that it is not possible to start completely from scratch their approach '*has also been informed by theoretical perspectives and methodological approaches that we have found to be persuasive*' (Jensen and Holliman 2009 p.57). In a similar vein the following theoretical frameworks are those which initially informed and guided my methodological approach.

2.3.1 Referencing as Persuasion and Assessing Documentary Sources

Gilbert (1976) examined the creation of scientific knowledge through the writing of research papers. He noted that citations within research papers are used to establish

the authority of the author's argument, but that the reader of the paper may come to a different conclusion than that of the author. He also suggested that, given the way that knowledge claims are constructed, it is extremely difficult for a scientist to achieve recognition when proposing an alternative to an established model. In a later paper, Gilbert (1977) described the use of references as persuasive tools, with the most effective way to justify an argument being to cite papers that the intended audience believe present well-founded, valid results. However, not all relevant articles are equally valuable for achieving this, leading to selective citation. Prior to Gilbert's discussion, Thorpe (1973) made the interesting observation that there are 'taken-for-granted references' within scientific discourses that become acknowledged as valid evidence in support of arguments or new/counter hypotheses, without ever being critically re-evaluated. These concepts are extremely relevant to understanding how the various parties construct the primate debate and for examining why certain arguments are used to establish authority. In analysing relevant reports and scientific papers, their persuasive nature has to be taken into account because, as noted earlier due to the controversial nature of the debate could mean that authors present matters in a favourable or unfavourable light to improve the standing or beliefs of the group they belong to Scott (1990).

2.3.2 Theory of Expectations

The theoretical framework, the 'Theory of Expectations', provided some of the original impetus for analysing the primate reports, because, as Brown (2003) argues about press releases, they translate and stabilise information that might otherwise go unnoticed in the wider world, and they are characterised by language and discourse

that would never appear in traditional peer-reviewed texts. They also serve as a space in which to construct expectations about biomedical research and carry them to a wider audience, and are useful for shaping peoples' expectations about the field in much the same way as review papers (Hedgecoe 2006). This choice was shown to be appropriate as the documentary analysis indicated that, in several ways, this framework can be applied to the primate experimentation controversy and possibly to biomedical science more generally. This includes the use of sickness narratives to create space for and justify morally challenging research (Brown 2003 and Mulkay 1993) and using examples of established techniques to serve as a basis for visions of future benefits in an attempt to shift the emphasis of the research (Brown 2003 and Hedgecoe 2006). Hypothetical future benefits are also offered by the scientists to legitimise the costs to the primates retrospectively being seen to be morally unjustifiable (Brown 2003). There is an apparent hype/disappointment cycle (Brown 2003 and Konrad 2006), where expectations have been raised but beneficial outcomes remain elusive, resulting in a rapid downturn in expectations and a shift in the type of research conducted. When discussing the use of expectations or 'visions' in emerging biotechnologies, Hedgecoe and Martin (2003) argue that:

> …the creation of a bioethical discourse around a controversial technology is important as it provides a negotiation space to explore the socially acceptable limits of the technology and acts as a means of enrolling support from key actors (p.329).

The theory of expectations has previously been used to consider why hype and overly optimistic forecasts of the benefits of scientific research might have been made, and how that might affect the reputations of the scientists and their organisations (Pollock and Williams 2010). Pollock and Williams (2010) argue that expectations can be

performative or 'self-fulfilling prophecies', in that because people are convinced by the claims, they continue to fund and conduct research into them. This may well be the case for primate-based research or indeed may be a way forward to increase investment in alternative techniques, and so is considered in the analysis in Chapters 3 to 5.

It has also been established that expectations are the outcome of competition, with the most vociferous actor/group being the most likely to have their expectations disseminated widely enough for them to be seen as a normative anticipation of the future (Brown 2003). How this relates to the use of primates and the consequences for explaining the path of biomedical science is explored later in Chapters 3 to 5.

2.3.3 Core Sets

The 'core set', defined by Collins (1988) as '*the group of technically informed specialists who participate in the resolution of scientific controversy through their esoteric technical activity*' (p. 728), has previously been examined in the context of the animal experimentation controversy. Michael and Birke (1994a) investigated how scientists involved in animal experimentation restricted access to their core set and placed criteria on whom they regarded as having legitimate membership and thus a voice in the debate. The decision to conduct interviews was partially guided by this theoretical framework as, in order to interpret how primate experimentation is viewed and justified, the core set of primate researchers and alternatives users had to be accessed. In addition, as Collins (1999) discusses, relying entirely on published literature may give a false sense of what are the salient and important aspects of

research within a field, because as an 'outsider' I might interpret published papers as being significant to the field, whilst those within the field may actually see them as marginal or may even ignore them altogether. In order to better understand the predominant interpretation of the published literature it was necessary to have access to members of the core set and even perhaps the 'core group' (the members of the core set who hold the dominant view-point). Exploring this relationship between what is published and how that is controlled and interpreted by the different layers of the community helped in the interpretation of what is driving certain areas of research and why there may be barriers to others. This literature contributed to understanding the observed interactions and helped in explaining why certain actors have more or less influence on biomedical science and its perceived value.

More recently, Hedgecoe (2006) combined the ideas of the 'core set' and the theory of expectations to explain why a disputed link between carrying a certain gene and reduced response to the Alzheimer's disease (AD) drug Tacrine continues to be cited. Whether a combination of the concepts of the core set and the theory of expectations can explain the continuation of the primate experimentation controversy is explored in Chapter 6.

2.3.4 Social Appraisal of Technology

This literature provided further reasons to analyse the primate reports. Since, in processes of social appraisal, substantive perspectives call for participation in decision making, including the involvement of lay people (Stirling 2008), the reports could be seen as engaging the public in the primate experimentation debate. Indeed, in some

cases the reports have been aimed at influencing policy and regulatory decisions. As many of the reports have a specified outcome, to end or promote primate research, one would expect '*strong justification*' for that outcome. It is argued that deliberate conditioning of the framing of the appraisal of technology, or in this case the failures/successes of primate experiments, will provide a promising means to secure the desired outcomes (Stirling 2008). In Chapters 4 and 5 this framework helped in explaining how and why scientists provide different levels of justification for their work and whether some of the findings are examples of 'sound science' being used to legitimise certain decisions within biomedical science policy/practice, even when the evidence is equivocal (Millstone and van Zwanenberg 2002).

2.4 Conclusion

The primary focus of this research is to examine and understand the controversial primate experimentation debate in an effort to determine if the stalemate which exists in moving towards replacing such studies can be overcome, and if so how. This chapter explains how the different phases of the project were designed to effectively and rigorously conduct the research, including the methodological decisions and the analytical approaches that were taken in the process.

The description of the multi-method design adopted in this project highlights how combining different approaches has enabled a new perspective on this complex, polarised topic and provides a powerful means to qualitatively investigate scientific controversy and practice. This chapter sought to show that although strategies such as documentary analysis, and thematic analysis of semi-structured interviews are not

well defined in current methodological literature they can be effectively implemented in conjunction with a multiple-case study to elucidate the nuanced complexities of how and why an area of scientific debate exist and persists. Comparing contrasting cases enables important identification of the dimensions and interactions within the social dynamics of science that are different or similar between cases, which in turn allows possible solutions to overcome the identified impasse to be distinguished.

On reflection the decision to adopt a semi-inductive approach to the design and analysis of this project resulted in a sound basis from which to build the research in a coherent way. The methodological decisions to conduct a documentary analysis and interviews were guided by the existing theoretical literature, but by not restricting the analysis to those theories, important details about the influence of other social dynamics such as entrenchment and competition could be identified. The nature of the interviews as one-on-one, face-to-face allowed access to viewpoints that are often regarded as difficult to reach. Providing assurance of anonymity, and my own scientific background were also important for building the trust and rapport that helped the participants to feel comfortable and confident in providing those views.

Combining methods in the way that is described in this chapter enabled appropriate cases to be identified and provided a rich data set from which to make the comparisons to answer the research questions and make recommendations to meet the overall aim.

The next chapter presents the documentary analysis which represents the first phase of the methodological approach described here. The second phase of the study, the case study interviews are detailed in Chapters 4 and 5.

Chapter 3: Documentary Analysis of Primate Reports

3.1 Introduction

In terms of the broader thesis, this chapter represents the first phase of the project to identify what arguments are given and to compare and contrast how they are presented by the opposing sides in the debate. It describes the in-depth documentary analysis of reports describing primate experimentation, so combines background information and data. The rationale and methods are detailed in Chapter 2 (2.2.1). In summary, 18 reports published 1986-2007 were analysed and classified as anti-primate use or pro-primate use. This classification was based on whether the organisations or individuals responsible for the reports were known to support or oppose primate use. When the stance was unclear then the decision was based on the amount of pro-primate versus anti-primate use content the report contained. If the reports are discussed they are referred to as anti-report or pro-report, and cited by an allocated number in square parenthesis (Appendix 1).

The reports range in length from six to 147 pages and many are professionally produced including photographs. Table 9 describes the appearance and overall style of the reports. The content of each report was analysed with the aim of establishing how the authors of each one attempt to make their claims. The findings incorporate descriptions of the scientific claims made and are divided by the theoretical themes; persuasive referencing, expectations, and cores sets, which enable understanding and

explanation of why those claims are made and how they impact on the primate debate. As described in Chapter 2 the final report which resulted from this analysis was too extensive for the current study. Therefore, to provide consistency with the case studies presented later the primary focus in this chapter is the findings resulting from the reporting of research into; Parkinson's disease (PD) – a chronic neurodegenerative disorder leading to severe motor impairments and cognitive dysfunction; and schistosomiasis – a macroparasitic infection, which can lead to a variety of chronic symptoms, such as abdominal pain and seizures. However, where data from the other diseases analysed is particularly important to provide contrast and/or additional support relevant in the overall context of the thesis these are reported.

Table 9: A summary description of the appearance and style of the primate reports analysed in the documentary analysis. Appendix 1 contains further bibliographical detail.

Citation Number	Report	Stance	Description
1	Anonymous (1987) *The Use of Non-Human Primates as Laboratory Animals in Great Britain.* UK: FRAME and Committee for the Reform of Animal Experimentation (CRAE).	Anti-primate use.	A5 pamphlet style with a primate logo on the front cover. Text only inside with red titles and blue main body text. Contains 17 references. 16 pages.
2	Hampson, J. *et al*. (1990) *An RSPCA/ FRAME Survey of the Use of Non-Human Primates as Laboratory Animals in Great Britain 1984-1988*. UK: FRAME.	Anti-primate use.	A5 booklet style with a black and white photo of primates eating in an open cage, and the organisations' logos on the front cover. Black text only, including tables. Contains 314 references. 68 pages.

Citation Number	Report	Stance	Description
3	Crawford, D. (1994) *Paradise Lost: A review of UK Primate Research*. UK: BUAV.	Anti-primate use.	A4 booklet style with no images or logos. Black text only. Contains 44 references. 141 pages.
4	Ruhdel, I.W. and Sauer, U.H. (1997c.) *Primate Experimentation a Report on the Use, Supply and Housing Conditions of Primates used for Scientific Purposes Within the European Union*. Unknown: European Coalition to End Animal Experiments.	Anti-primate use.	A4 booklet style with a black and white image of a primate behind bars and the organisations logo on the front cover. Black and white photographs of primates in the wild, in cages, undergoing procedures and photographs of their capture and transportation are interspersed throughout the document. Text is black, including tables. Contains 99 references. 88 pages.
5	Bottrill, K. (2000) *A Report on the Use of Non-Human Primates in the European Union*. EU: Unknown.	Anti-primate use.	A4 booklet style with no images or logos. Black text only. Contains 163 references. 104 pages.
6	Langley, G. (2002) *Phasing Out Primate Use in Belgian Laboratories*. Belgium: Global Action in the Interest of Animals.	Anti-primate use.	A4 booklet style with no images or logos. Black text only. Contains 213 references. 85 pages.
7	Smith, J.A. and Boyd, K.M. (Eds) (2002) *The Use of Non-Human Primates in Research and Testing*, UK: The British Psychological Society.	Pro-primate use.	A4 booklet style with a stylised front cover, including the logo of the publisher. Black text only, including tables. Contains 87 references. 59 pages.
8	Scientific Committee on Animal Health and Animal Welfare (2002) *The Welfare of Non-Human Primates Used in Research*. EU: European Commission.	Pro-primate use.	A4 booklet style with the European Commission logo on the front cover. Black text only. Contains 477 references. 135 pages.
9	Animal Procedures Committee (2002) *The Use of Primates Under the Animals (Scientific Procedures) Act (1986) Analysis of Current Trends with Particular*	Pro-primate use.	A4 booklet style with a coloured front cover, including photographs of primates. Black text only, including tables and graphs. Contains 32 references. 39 pages.

Citation Number	Report	Stance	Description
	Reference to Regulatory Toxicology. UK: Animal Procedures Committee.		
10	Creamer, J. and Phillips, T. (Eds) (2005) *My Mate's a Primate Evaluating our Relationship and Behaviour Towards our Fellow Primates*. UK: Animal Defenders International.	Anti-primate use.	A4 booklet style with a coloured front cover mainly consisting of a colour photograph of the faces of a person and a chimpanzee, it includes the organisation's logo. The report also includes information on primate use in entertainment, for bush meat and as pets. Colour photographs of primates in the wild, in cages, undergoing procedures and with people are interspersed throughout the report. The main text is black, with titles and highlighted quotations from the main body of text in green. Contains 50 references. 52 pages.
11	Chapman, K.(2006) *Opportunities for Reducing the use of Non-Human Primates in the Development of Monoclonal Antibodies a Workshop Report*. UK: NC3Rs.	Anti-primate use.	A4 booklet style with a colour photo of a primate and the two organisations' logos on the front cover. Black text only, including graphs and tables. Contains 69 references. 30 pages.
12	Langley, G. (2006) *Next of Kin a Report on the Use of Primates in Experiments*. UK: BUAV.	Anti-report use.	A4 booklet style with a coloured front cover, including a photograph of a primate in a cage and the logos of the organisation. Colour photographs of primates in the wild, in cages and undergoing procedures and photographs of traps and laboratory equipment are interspersed throughout the report. The main text is black with titles and quotations within the text in purple and graphs in colour. Contains 290 references. 98 pages.
13	Taylor, K. (2006) *Still Dying of Ignorance? 25 Years of Failed Primate AIDS Research*. UK: BUAV.	Anti-report use	A4 booklet style with a full page black and white photograph of a primate in a cage on the front cover. The title on the front cover is in red and the back cover is red. The front cover also has the organisation's logo. The front cover photograph is repeated on the header of each page

Citation Number	Report	Stance	Description
			in the report and black and white photographs of laboratory equipment appear on two pages. Black text only with larger text for the introductions to each section. Contains 106 references. 15 pages.
14	Anonymous (2006) *The Case for an EU Ban on Primate Experiments.*UK: Animal Aid.	Anti-report use.	A4 booklet style with a black and white photograph of a primate with a head implant in a cage and the organisation's logo on the front cover. The photograph from the cover is repeated in the header of each page in the report and the title of each section is written horizontally in the side margin of each page as well as in the main text. Black text only. Contains 16 references. 6 pages.
15	Creamer, J. and Phillips, T. (Eds) (2006) *The Primate Nations the Case Against Laboratory Research on Primates*. UK: Animal Defenders International.	Anti-primate use.	A4 booklet style with a coloured front cover consisting mainly of a colour photograph of a primate in a cage it includes the organisation's logo. There is a colour photograph of a primate on the inside front cover but no further photographs. Black text only. Contains 113 references. 20 pages.
16	Anonymous (2006) *Primates in Medical Research*. UK: Medical Research Council and Wellcome Trust.	Pro-primate use.	Square pamphlet style with a blue cover consisting of the title and then a collage of disease names in various sizes of text. Colour photographs of primates in cages, undergoing minor procedures and being trained are interspersed throughout the report and colour photographs of people, medical images (e.g. brain scans) and equipment. Main text is black with blue titles and case studies are presented in separate blue boxes. Contains no references. 21 pages.
17	Weatherall D. (2006) *The Use of Non-Human Primates in Research A Working Group Report Chaired by Sir David Weatherall FRS FmedSci*	Pro-primate use.	A4 booklet style with a green cover including a black and white photograph of two primates. Main text is black with a green header on each page and green boxes to highlight case studies and recommendations. Includes tables

Citation Number	Report	Stance	Description
	[The Weatherall Report]. UK: The Academy of Medical Sciences, Medical Research Council, The Royal Society, Wellcome Trust.		and graphs in black and green. Contains 350 references. 147 pages.
18	Anonymous (2007) *Response to the Statement of the EU Scientific Steering Committee on the Use of Non-Human Primates (NHP) in Biomedical Research*. UK: Animal Defenders International.	Anti-primate use.	A4 booklet style with a blue front cover, including a large black and white photograph of a primate and smaller blue-toned photographs of people using alternative techniques, such as microscopy. It includes the logos of the organisations. Further blue-toned photographs of people involved in alternative methods are found on the back cover. Black text only including tables. Contains 100 references. 19 pages.

3.2 Persuasive Referencing

Introduction

As noted in Chapter 2 (2.3.1), Gilbert (1976) examined the creation of scientific knowledge through writing of research papers and explored '*references as persuasion*' (Gilbert 1977 p.115), including selective citation. Scott (1990) also commented on authors of scientific discourse presenting matters in an unfavourable or favourable light to support their stance. This section describes how the reports provide clear examples of persuasive referencing but that the form it takes and the successful application of it varies depending on the overall stance of the authors. It also describes interesting findings which indicate that 'balanced referencing' could be being adopted

in two of the reports as a means to improve the credibility of the authors overall stance. The findings are presented under the sub-headings Parkinson's disease and Schistosomiasis, but where examples from other fields of research are pertinent they are also included within these sub-divisions.

Parkinson's Disease

The authors of reports dealing with PD appear to use persuasive referencing with varying degrees of success and in both obvious and less explicit ways. Several anti-reports ([3, 4, 10, 15 and 18]) appear to use persuasive referencing when refuting scientific justifications for using 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) primates – the controversial MPTP primate model of PD was developed after the discovery in 1982 that MPTP induced Parkinsonism in young adults (Langston *et al.* 1983). For example, the British Union for the Abolition of Vivisection (BUAV) discusses scientific drawbacks of the model, including differences in aetiology of the two syndromes leading to a host of variations between human PD and MPTP primates, such as an absence of Lewy bodies (intra-neuronal inclusions). Central to the argument is this quote, '*There are differences* [with human PD] *in that tremor is not a marked feature of the MPTP syndrome in marmosets'* (Rose *et al.* 1989, p.308), which in isolation is apparently convincing as it is from a group well known for its primate research in this field. However, while Rose *et al.* (1989) identified several limitations of the marmoset (*Callithrax jaccus*) MPTP model, they still conclude it will be useful in studying early stage disease. Their report [3] comes to a different conclusion than that of the original research, a fact which is concealed by selective quotation. This may not be deliberate as Gilbert (1976) observed; '*...scientists who*

cite a paper may find and evaluate 'conclusions' other than those intended by the author' (p. 295), depending on the scientific perspective with which the reader approaches the work. Here, Crawford's [3] perspective is one against using primates so he has taken the above as a conclusion in support of his ideas rather than those of the authors of the paper. It could be, as Gilbert (1976) proposed, that Crawford is ignoring claims within Rose *et al.* (1989) which do not seem consistent with his perspective, so is perhaps inadvertently using persuasive referencing to reinforce what he sees as failure of the MPTP model.

There is some evidence that anti-authors are sporadic or inefficient in their use of persuasive referencing, particularly when discussing alternatives. For example, Crawford [3] fails to use citations when asserting that alternatives to MPTP primates are already in use and will be much more likely to produce useful and relevant results. Because these claims are not substantiated by references, it is difficult to establish, from this report [3] how realistic these ideas were considered at the time. This illustrates the importance of '*references as persuasion*' (Gilbert 1977, p.115) to verify a new knowledge claim. In constructing knowledge claims, scientists are required to demonstrate that the procedures/models used are standardised and widely recognised already (Gilbert 1976). Here, the established model is primate experiments and Crawford [3] is proposing new alternative models, which is recognised as being extremely difficult to achieve recognition for (Gilbert 1976). Therefore, to persuade the scientific community and other interested parties of the veracity of these new alternative models, the author needed to provide persuasive references. The reader is likely to be less convinced as to whether the proposed alternative techniques can replace established primate experiments because Crawford [3] fails to relate

alternative models to current knowledge, how they then advance that knowledge and illustrate the new models incorporate appropriate techniques and theories.

Another BUAV report [13], which presents arguments against primate use in acquired immunodeficiency syndrome (AIDS)/human immunodeficiency virus (HIV) research, is of particular interest here. As in other reports, the key differences between simian immunodeficiency virus (SIV; the primate equivalent to HIV) and HIV are given, but the author's [13] choice of supporting citations is surprising in some instances and in others is superficial, when more detail would have strengthened the presented argument. For example, she notes SIV is not as virulent as HIV and does not produce severe illness, but fails to describe the genetic reason for this as provided by the cited reference (Hardman 2006), which gives the scientific context for the difference. In the same way as Crawford [3], Taylor [13] uses citations to draw conclusions that the authors probably did not intend. For example, Gardner and Luciw (1989) are cited as evidence for differences in presentation of symptoms between macaques and humans. They discuss advantages and limitations of various models, but overall they advocate using macaque models. This approach is somewhat unusual given that this report [13] has a specified outcome – to end primate AIDS research – and as such one would expect 'strong justification' for that outcome. It is argued that deliberate conditioning or framing of the appraisal of technology, or in this case failures of primate experiments, will provide a promising means to secure the desired outcomes (Stirling 2008). Therefore, it seems unusual that this author has not given stronger justification, which may explain why primate experiments continue to dominate AIDS/HIV research as well as indicating that anti-authors may be unaware of the impact persuasive referencing can have, so are using it sporadically.

It is apparent that some anti-authors are developing their persuasive technique. For example, the European Coalition to End Animal Experiments (ECEAE) [4] refutes what they identify as claims made that major findings concerning PD originate from primate experiments by presenting a literature search that shows approximately 90% of publications on PD from 1984-1996 were based on human studies. They argue this indicates that scientists consider patient studies to be more relevant than primate ones. This is a compelling argument for opponents of primate research. However, the report fails to give a full account of how the search was conducted; doing so would have strengthened the claims made by giving the reader reassurance they had sought to omit their biases as anti-primate advocates. Unlike the Crawford report [3], this one provides references in relation to alternatives to primate models, which illustrate how methods such as Positron Emission Tomography (PET) and *in vitro* cell systems can be used to study PD. But it does not indicate how or when these techniques could replace the primate model or why they have not already. Ruhdel and Sauer [4] appear to be developing a more 'scientific' approach to presenting their claims. By this I mean they are using references to demonstrate the veracity of their proposed alternative approaches in an attempt to show they have '*followed the correct procedure for uncovering the truth'* (Gilbert 1976, p. 285).

When reporting on a second neurological disorder, Alzheimer's disease, Ruhdel and Sauer [4] use 'scientific' citation again but provide an interesting example of a different kind of reference. They justify the inappropriateness of using elderly primates in AD research by quoting primate users Podlisny *et al.* (1991) and Bons *et al.* (1992) expressing doubt over the contribution of primate models to AD knowledge. However, it is unclear if they read these papers independently or have

simply taken the citation from Crawford [3] or another source. The misspelling of Podlisny (Podlinsky in [4]) and a slight error in the Bons *et al.* quotation indicate the latter is most likely true. If so, this may be an example of 'taken-for-granted references' which Thorpe (1973) defines as:

> …an original empirical study. The findings of which become accepted and thereafter acknowledged as valid evidence in support of argument or for the generation of new hypotheses or counter hypotheses without presentation of critical re-evaluation. (Thorpe 1973, p.361)

Ruhdel and Sauer could have accepted these quotations without consulting or assessing the original papers, particularly if this is a case of the original study fading away from consciousness and only the quoted findings becoming relevant-in-use (Thorpe 1973).

The pro-primate reports contain very little discourse regarding the MPTP model. The Boyd Group, a forum for dialogue on contentious issues in laboratory animal use, merely include a case study advocating the suitability of MPTP marmosets for studying acute pharmacological interventions, but not for surgical treatments for PD, in order to '*...illustrate the kinds of fundamental and more applied benefits that might be sought from such work*' ([7], p.16).

The pro-*Weatherall Report* [17], includes the MPTP model, but requires contextualisation. It was commissioned by organisations with a long history of funding primate research (The Academy of Medical Sciences, Medical Research Council [MRC], The Royal Society and the Wellcome Trust) although it is emphasised they played no part in determining the contents of the report, which were

written by members of a working party. For reasons that become clear throughout this chapter, this report is deemed pro-primate use.

The report [17] gives an unreferenced list of deficiencies of primate models that were submitted to the authors by various stakeholders. From personal experience, I am aware that many of those stakeholders provided references to support information they submitted to the report. During the consultation period for the report [17] I co-authored the FRAME submission to the Weatherall group which contained many references. Following the publication of the report [17] FRAME solicited views about its contents and recommendations from the organisations that had contributed to it. As part of this FRAME asked the responding organisations to provide a copy of their original submission to the Weatherall group (if it had not already been published). From these submissions it was clear that scientific literature had been cited to support claims that were being made by many of the stakeholder groups. This appears to be a clear case of selective citation by the report's [17] authors, as they seem to have ignored all references that could validate a claim which opposes their stance that primate use is necessary. It is impossible to say if this was a deliberate attempt to cast doubt on opposing assertions, but given that the sponsors state it is an '*independent report into the scientific basis for the past, current and future role of non-human primates in research*' (sponsors' statement), it seems unusual that the report provides some references for pro aspects of the discussion but none for the counterpoints. It could be that the authors did not accept the validity of claims made in the submitted citations so did not want to imply any acceptance by including them (Gilbert 1976), but for a balanced evaluation of the arguments, submitted evidence should be presented to the reader and reasons for not accepting the counter arguments explained.

Further evidence of this selective citation by omission can be seen in the pro-*Weatherall Report* report's [17] treatment of AIDS/HIV research. It claims primates are vital for investigating pathogenesis of HIV and for developing treatments. The authors note limitations of primate models that have been extensively discussed in previous reports. However, they provide no references for these limitations, yet when a counterargument is made, citations are given. Similar to some anti-reports not providing any pro-primate evidence, the pro-reports give very little if any consideration to alternatives to primates in the case of AIDS/HIV. This in itself is selective citation. For example, the *Weatherall report* [17] does not discuss any alternative methods of researching AIDS besides an explanation of a transgenic mouse model that might be useful in investigating 'prime-boost' vaccines. Instead it directs the reader to two reviews on different approaches to developing HIV vaccines. Given the stated aim of this report, this seems very superficial compared to the coverage that primate models receive, and given that even a cursory search of the literature reveals a great deal of AIDS/HIV research is conducted without using primates.

Schistosomiasis

One anti- [2] and one pro-report [17] cover schistosomiasis studies. Both use persuasive referencing, although the anti-report does this in an unusual way.

The anti-report [2] presents an unexpectedly positive account of the schistosomiasis research. Hampson *et al.* [2] describes five studies spanning 1984-1988 by the same lead author (Sturrock), which used olive baboons (*Papio anubis*) to investigate induction of resistance to reinfection and curative drug therapy for schistosomiasis.

These studies conclude that this primate model produced different results to earlier findings in mice, and that consequently, rodent results should be extrapolated to humans with caution. They found a positive therapeutic action from a test compound and chemotherapy that could be the basis of evaluating the effects of treatments for human infection. While the report [2] is mostly descriptive the tone is relatively pro-primate use in this case, detailing the positive conclusions of the citations that support using baboons in this field and providing a pro-primate quotation from one of the papers:

> …Primates, in many ways better than rodents, though too expensive for general use, remain invaluable for testing the relevance of rodent findings to man (Sturrock 1986 in [2], p.46)

There is no criticism of the work or counterpoints made, which given the anti-primate use stance of the RSPCA and FRAME, tends to lead the reader to believe this work was justified and provided some benefit toward treatments for the disease. However, at least one of the citations provides some cause for questioning the asserted usefulness of the baboon model when it concludes:

> So far, though, the weight of our evidence and that from previous studies indicates that baboons develop neither hepatic fibrosis nor collateral circulation comparable to that seen in man or mice. If this is so, it limits the usefulness of baboons for investigating schistosomal liver fibrosis. (Sturrock *et al.* 1988, p.46)

Unusually, the report [2] did not describe this finding even though it is obviously more in keeping with their viewpoint. This appears to be a case of persuasive referencing through selective citation but in the opposite direction than would be expected. It is difficult to know why the authors omitted this, but it may be they think

that the evidence is strong and do not feel a counter argument would be credible so have not made one. Alternatively, perhaps they are purposefully not trying to persuade the reader as would be expected, given that the majority of the other reports do.

One explanation for purposively not being persuasive, and in some instances actually being more persuasive in the opposite pro-direction, may be that the FRAME/RSPCA report [2] was trying to remain neutral and present both sides of the debate in the hope of adding credibility to their overall stance of being against primate use. This analysis suggests that this could be because they wanted to avoid accusations of bias so were overly 'neutral'. This is strengthened when the general discussion is taken into account. This section clearly lays out the concerns the authors have about primate work and justification for it, which was not present in the individual disease sections, for example:

> The most striking impression gained from our survey…was the uneven quality of the research itself and of the way it was recorded in the published literature ([2], p.61]
>
> Most of the papers contained no justification of choice of species, and in many cases the impression is given that animals were used merely because they happened to be around…([2], p.63)

Therefore, it may be that, as I term it, the 'balanced referencing' used earlier in the report was done to give a more impartial impression, so when the authors make their final summaries about the survey, the reader would be more convinced that they had made a reasoned decision about their claims, so giving them more credibility.

This application of 'balanced referencing' to persuade the reader of an overall anti-stance and give greater strength to the suggested alternatives was also evident in

Bottrill's anti-report [5], especially in her discussion about AIDS/HIV research. This particular example also illustrates a unique example within all these reports of an explicit conflict among primate users as to whether a primate (chimpanzee) model should be used. The AIDS/HIV section of Bottrill's report [5] exhibits a lack of selective citation when it provides a referenced account of the different models available for studying AIDS/HIV, such as the severe combined immunodeficiency (SCID) mouse and the feline immunodeficiency virus (FIV) cat, including the benefits and limitations. The author [5] presents justifications for using chimpanzees, and the refutations of the claims associated with them, more or less equally. Noting for example, the Biomedical Research Centre (BPRC)'s opinion that chimpanzees are useful in vaccination studies to investigate protection against HIV infection, as they do not develop AIDS, so they may have something in common with long-term HIV survivors; as well as the Paul Ehrlich-Institute (PEI) opposition that this may result from evolutionary adaptation to the virus in chimpanzees, but not humans, so can be studied in other species of primate. This could simply be reflective of the conflict within the field at the time as Bottrill notes, '*This* [chimpanzee research] *is an issue on which there currently appears to be a lack of consensus within the scientific community*' ([5], p.74). However, to be associated as a member of that community she has possibly reported it in this way in order to give credibility to other aspects of the report that would be seen as more anti, such as suggestions for reducing primate use, or using alternatives, so improving the likelihood of them being accepted. Therefore, this may be a means of becoming accepted into the 'core set', that is, the experts in the field who participate in resolving this particular scientific controversy (Collins 1988), which is discussed in more detail in section 3.3.

The AIDS/HIV discourse also included only the second example of explicit conflict within all of these reports, this time regarding which overall research aim was most appropriate. Two anti-reports [4 and 5] questioned if trying to develop a vaccine was the right approach to take. This was the only disease in these publications where the foundation upon which expectations about primate models – and to some extent alternatives – were being constructed, was questioned. This contention about which overall aim a field of research as a whole should work toward was more evident in the interview stage of this project (Chapters 4 and 5), so why there were not more examples in the primate reports is perplexing. The nature of these reports may provide some explanation. They are publicly available and generally aimed at influencing policy and/or garnering support for the stance they advocate. Therefore, authors may want to present a 'united front' so as not to detract from the overall message they are trying to impart on the reader, by avoiding indicating that there may be disagreement about it.

The pro-report [17] provides evidence of more traditional persuasive referencing. The discussion about primate use in schistosomiasis studies is based on a single submission from one research group and hence the entire primate related citations, except for one, have members of the group as authors. The report uncritically summarises the findings of the group's four cited papers as:

> Research over the last ten years has shown that non-human primates are the only animals for which it is possible to produce infections that closely mimic those in humans in every aspect of the complex life cycles of the parasites. ([17], p.54, my emphasis)

The citations provide evidence for a physiological argument for using rhesus macaques (*Macaca mulatta*) and olive baboons as infection models for schistosomiasis, based on features of these species that facilitate a study of concomitant immunity allowing a more realistic schistosome worm burden to be achieved, which is not easily replicated in rodent models (Wilson and Coulson 1998; Wilson and Coulson 1999). Primate models also permit the direct measurement of worm burden to more accurately evaluate the efficacy of a candidate vaccine, rather than requiring indirect measurements, used in human trials, which overestimate protection from infection (Kariuki *et al.* 2004). However, the report [17] does not describe any of the beneficial research conducted in other species that is evident in some of the same citations. For example, much of the discovery and development of potential therapeutic candidates has been a result of studies in mice (Wilson and Coulson 1998; Wilson and Coulson 1999), humans, and by using *in vitro* techniques (Capron *et al.* 2005; Wilson and Coulson 1998). This appears to be a clear example of selective citation to persuade the reader of the report's stance that the primate should be used in this area. This is strengthened further when examining the report's [17] assertion:

> …it seems <u>inevitable</u> that non-human primates will be required for their [potential vaccines] evaluation. ([17], p.54, my emphasis)

Supporting this is an example of a current vaccine trial that '*…requires non-human primates for its development*' ([17] p.54). The citation (Capron *et al.* 2005) given for this features work in primates, but this is talked about in conjunction with parallel studies on cattle and humans, which appear to have given the same results as the primates, begging the question: is it inevitable to use primates or could cattle studies

perhaps be used instead? Additionally, the majority of the discussion in Capron *et al.* (2005) revolves around studies on rats, mice and humans, none of which is described by the report [17].

This report [17] has made bold statements about the need for primates based on one group's submitted information, with no indication of any checking of the assertions made by that group or any description of alternative models that have and could be used. Therefore, as well as being a case of selective citation, this could be related to the reputations of the submitting group. The authors of the report [17] may have viewed this research group as being the 'core set', which is discussed in more detail in section 3.4.

Summary

This analysis shows that the primate report authors use persuasive referencing in describing Parkinson's disease and schistosomiasis research, and indeed for other scientific fields, such as Alzheimer's disease and AIDS/HIV. What is more interesting in the context of this thesis is the different ways that anti and pro-reports do this. Opponents and proponents attempt to create scientific knowledge for and against using primate models by using references as persuasive tools (Gilbert 1977). Importantly, they do it slightly differently. Pro-authors selectively cite by omission that is, they do not include any (or very few) references for alternatives or for papers questioning the necessity of primate models. Whereas, anti-authors show some omission regarding limitations of proposed alternatives, but in general tend to selectively cite by selective quotation from papers advocating primate use that is,

quoting out of context. These approaches might be expected as Gilbert (1976) noted '*...a citation used to justify an argument suggests that the author recognizes the cited claim as contribution to knowledge*' (p.287), so pro-authors may not want to be seen as endorsing alternatives or anti-arguments, thus do not provide references. The anti-reports appear to conform to Gilbert's (1976) finding that a published article may contain a number of possible knowledge claims, from which the reader will select those most relevant to their interpretative stance whilst ignoring others, and which might be completely different to the author's own conclusion. Additionally, anti-authors may feel criticisms which apparently come from the primate user community will be more credible and be less likely to be dismissed by that community. There is also evidence that anti-authors are perhaps not as adept at utilising selective citations as pro-authors but that this might be improving in some instance.

In addition, this analysis has revealed an interesting departure from the existing literature regarding referencing as persuasion. Anti-reports [2] and [5] show a distinct lack of traditional persuasive referencing. Instead, Bottrill [5] in particular presents citations and discussion for both aspects of the debate, including expectations and supportive quotations for primate and alternative models alike. This opposes what would be expected by Gilbert (1976 and 1977) and others. It may illustrate that Bottrill felt that presenting as balanced a discussion of the situation as possible would give credibility to her overall stance by avoiding accusations of bias. So I have termed it 'balanced referencing as persuasion'. It could be a further illustration of an attempt to be more 'scientific' or 'rational' so as to be accepted by scientists conducting the work (i.e. the core set) as a valid voice in the debate.

Persuasive referencing was not used in isolation, as the next section illustrates it was often combined with another strategy for gaining support for the claims made, that of building expectations.

3.3 Expectations

Introduction

As noted in Chapter 2 (2.3.2), expectations are used to understand mobilisation of resources for, and acceptance of, emerging technologies via construction and dissemination of expectations about benefits that might accrue from those technologies. This analysis shows that this theoretical framework is applicable to scientific techniques and models as well as to emerging technologies. There are interesting contrasts between how pro-authors and anti-authors appear to utilise expectations, including the use of sickness narratives. Again the focus is on PD and schistosomiasis research, but examples from other fields of research are included.

Parkinson's Disease

Some authors appear to present information to support their assertions about which experimental models will be most beneficial for understanding PD and other diseases that can be understood by considering the theory of expectations, including utilising 'sickness narratives' to convince readers of the importance of said benefits. However,

the emphasis on expectations is slightly different dependent on the stance of the report.

As described in the previous section anti-reports focused on the MPTP primate model in their discussions. They did not consider primate experiments conducted for the purpose of investigating Deep Brain Stimulation (DBS) – a surgical intervention that involves implanting electrodes into patients' brains to control the symptoms of PD. In contrast the pro-reports seem to use DBS as their flagship for showing the necessity and success of primate studies. In particular the *Weatherall Report* [17] focuses on the '*instrumental*' (p.74) role of MPTP primates in developing '*particularly effective treatment* [DBS] *in certain patients*' (p.74). It gives an historical overview of how DBS was developed from primate work in the early nineties. This account is based on information submitted to the authors by researchers in the field and does not include supporting citations. It could be that expectations developed about the role of primates in DBS have become '*collective expectations*' (Konrad 2006, p.431; i.e. have become unattributable to specific groups or individuals), with scientists taking them into account and assuming others will too. Collective expectations can take on the status of '*taken-for-granted self-evident assumptions that no longer have to be justified*' (Konrad 2006, p.433), so the authors may have felt it unnecessary to validate the assertion that primates were essential in this particular area.

The report [17] argues primates could be needed in future research on stem cell therapies, citing studies with early results in this area. Similarly to the anti-report [12] below, the authors have put their expectations into current context in an attempt to show that their visions of future primate use are realistic and achievable (Brown

2003). They included a section emphasising the debilitating nature and financial implications of PD, so are utilising 'sickness narratives' to put greater importance on the expectations they are building, as Brown (2003) argues; '*...the telling of sickness narratives in the context of technological promotion is a powerful means of creating research space, attractive investment and justifying morally challenging research*' (p.8). This is discussed in more detail in the schistosomiasis section below.

As the previous section illustrates, anti-primate reports use persuasive referencing to discredit pro-primate evidence but not to bolster their own claims about alternatives. Instead, they appear to construct expectations about alternatives. The anti-primate BUAV/ECEAE report [12] provides the most comprehensive discussion of possible alternatives to MPTP primates. However, unlike in previous reports this includes fully referenced examples of what has already been discovered via the alternative methods involved. This account provides optimism that at least some aspects of primate PD research can and will be replaced. Importantly, this might be an example of Brown's (2003) using precedence to build expectations about alternatives in order to gain acceptance for them. By illustrating how technologies/techniques have already been implemented and have led to recognised and accepted findings, the authors are providing validation for the expectation that these methods can replace primate studies in this field, in order to convince readers their vision of the future is achievable. This is also evident in the BUAV report on AIDS research [13], where there is a referenced section on '*Future 'alternative' methods of understanding and treating HIV*' (p.11), which describes various non-animal methods and how they '*provide a huge hope for the future*' (p.11).

This building of expectations by anti-primate report authors has not always been as evident, as illustrated by the lack of examples in the schistosomiasis section below. Instead, it appears to have developed over time with the examples above being some of the most recent. In the interim between the report featuring schistosomiasis [2] published in 1990 and the later reports above [12; 13] both published in 2006, other reports illustrate a gradual shift towards presenting information that can be understood as expectation building. For example, in Crawford's 1994 report [3] there is no evidence of expectation building, other than the important exception that it features a sickness narrative, beginning '*AIDS is a new and terrifying disease, that has already afflicted millions of people around the world*' (p.120). As noted above and described later, sickness narratives are something which this analysis has found to usually be associated with pro-reports. Given the relatively low number of scientific citations in his report Crawford may be using this to add justification to his anti-stance. By highlighting disease severity to illustrate damage that is being done by what he claims is a delay in development of a vaccine due to wrongful reliance on primate models.

A few years later (1997c.), Ruhdel and Sauer's report [4] again contains very little evidence of expectation building, with the exception of another unusual use of a sickness narrative. They document a primate study conducted to understand the cause, origin and progression of Bovine Spongiform Encephalopathy (BSE) with the aim of finding a treatment. BSE is one of a group of diseases of the brain known as transmittable spongiform encephalopathies (TSEs), which affect humans and animals. The documented study revealed similar histological results in the primate brain as those in a human variant Creutzfeldt-Jakob disease (vCJD) brain, suggesting BSE was a causative agent of vCJD (Lasmézas *et al.* 1996). Ruhdel and Sauer [4] deny this

work could make any contribution to combating the BSE crisis. They defend this by detailing the severity of procedures involved and describing how the animals will suffer, for example:

> This means that the animals will suffer all the terrible stages of the disease…The destruction of the brain is manifested in behavioural changes, motor disturbances and violent convulsions, to name but a few. ([4], p.14)

This appears to be a sickness narrative, which parallels those given by pro-primate reports, but instead of focusing on the suffering of the human patients; these authors are using it to highlight the suffering of the animals involved. In doing so they are perhaps attempting to garner sympathy for the animals in order to gain support and acceptance for their view that the cost to primates in terms of suffering is not outweighed by the proposed benefits of the work, in much the same way primate users might use sickness narratives to add importance to the benefits they are proposing.

Schistosomiasis

As noted previously, one anti- [2] and one pro-report [17] cover schistosomiasis studies. There is a distinct difference between the two in regards to expectations. In this field of research the reports present limited data relating to expectations so this section contains several examples from other fields covered by additional reports to compare and contrast in more detail how the two sides of the debate differ.

In the anti-report's [2] discussion of schistosomiasis there are no examples of descriptions of the present or future benefits of alternatives that could be understood as expectations building, or any comments on failures of promises made about primate

experiments, which are evident in other anti-reports (see below). It is difficult to explain why this might be the case from this limited information, However, there is a lack expectation building throughout the report [2] not just in the case of schistosomiasis research. Therefore, it could be indicative that the authors were unaware that highlighting the usefulness and future beneficial consequences of the alternatives research could act to increase acceptance and resources for it. This is supported by the fact this report was published earlier (1990) than all of the others (with the exception of [1]) and as noted in the previous section it appears that the anti-authors have only recently begun to exhibit these techniques.

Fifteen years later the pro-report [17] presents the stance that primates have and should still be justifiably used in evaluating schistosomiasis vaccines. In doing this the authors provide references to previous successes with primate models and then justify their assertion that '*...it seems inevitable that non-human primates will be required*' ([17], p.54) for evaluating the new approaches to schistosomiasis vaccine development, by giving an example of preliminary work that shows positive results to this effect. Therefore, they are showing precedence for the promised benefits while at the same time placing them in current context to illustrate that they are realistic and achievable expectations.

In addition, the report [17] begins with a sickness narrative describing how and why it is important to develop an effective schistosomiasis vaccine, thus building up the importance of the expected benefits they then describe. This particular report [17] uses sickness narratives extensively for the majority of diseases it discusses. For example, the report describes how AD affects patients including its '*insidious onset*' ([17],

p.78) and how the cost implications related to the care of those patients is set to rise as incidence increases. This strong emphasis on the debilitating effects of AD is not seen in any of the other reports, but it does add credence to the observations of Crawford [3] and others over ten years earlier, that scientists engaged in primate research were using the severity of the illness to justify their research rather than whether it will ever provide any actual benefits for AD sufferers.

Crawford [3] argues that proponents of primate AD models make unsupported claims about their usefulness. He feels the seriousness of the condition is used to justify primate experimentation or to imply such research is the only hope for sufferers, when in fact it has diverted resources away from non-animal alternative methods that have so far led to the most progress. This observation is credible as it is established that telling sickness narratives in this way is a powerful means of creating research space for and justifying morally challenging research (Brown 2003 and Mulkay 1993). Ruhdel and Sauer [4] and Langley [6] also express concern that fear of the disease is being exploited by primate researchers to justify invasive and unrelated studies in AD. Therefore, it may be that the context into which Shakespeare (2006) put this is most appropriate. He talks about a 'cure rhetoric', where the scientific and medical community and sometimes people with a disease and their families, represent patients as being desperate for a cure in order to draw public attention and garner charitable or government funding. The controversial nature of primate procedures involved in AD research, and the often fundamental nature of the work, could be the reason why this pro-report [17] and other primate proponents indicated by the anti-reports have used sickness narratives and cure rhetoric in an attempt to add further justification to their claims and to make the expected benefits appear more important.

An interesting contrast in relation to expectations is that anti-authors focus on failed expectations whereas pro-authors do not. For example, the AIDS/HIV discourse illustrates the role which expectations can have in developing a scientific field. Anti-authors such as, [4], [6] and [13] argue that promises about AIDS/HIV primate models remain unfulfilled, with no human vaccine being available despite decades of primate research. They contend that these failed expectations make primate research unjustified. As future benefits are used to legitimise costs in the present (Brown 2003) this viewpoint does not seem unreasonable. However, the pro-report [17] defends the expectations, arguing that it is unrealistic to expect rapid answers and that the longevity of the work merely reflects the complexity of the problem. This may also be a valid comment, as Konrad (2006) notes crucial expectations are typically the last to be ascertained, and there is often uncertainty as to what constitutes success or failure.

Anti-reports [4, 6 and 13] also argue that there has been a clear shift away from using chimpanzee HIV models. Again this seems to be framed as a consequence of failed expectations resulting from physiological and genetic differences as well as logistical and financial restrictions. This is best illustrated by the BUAV [13] introducing chimpanzee research with '*A history of broken promises: how primate research has failed us*' ([13], p.5). Brown (2003) and Borup *et al.* (2006) suggest that exaggerated promises (hype) about technologies are necessary to attract sufficient interest and funding but this leads to inevitable disappointment as unforeseen problems arise and organisational and cultural factors come into play, which can '*...foster a kind of historical amnesia*' with past disappointments tending '*...to be rationalized such that they present a reduced threat to new successive expectations*' (Borup *et al.* 2006, p.290). The primate reports indicate that this cyclic operation of expectations is

applicable to scientific models as well as technologies. Historically HIV-chimpanzee research appears to have undergone a hype/disappointment cycle (Brown 2003 and Konrad 2006), as expectations were raised in the early 1980s that chimpanzees would provide a vaccine for HIV, attracting increased funding and leading to a boom in studies. However, failure to produce any beneficial outcomes meant this rhetoric of hype could not be maintained, and by the late 1990s there was a rapid downturn in expectations and scientists (and funding) shifted from chimpanzees to other primates. As illustrated by a citation from Ruhdel and Sauer [4], which details the US National Institute of Health (NIH) redirecting money for chimpanzee research to other primate models as it sees chimpanzees as an '*…inferior animal model for AIDS pathogenesis…*'(Cohen 1996, p.590). The pro-report [17] confirms that this shift has occurred by concluding that the chimpanzee has now been replaced.

Pro-reports [16 and 17] provide very little discussion of alternatives, so do not construct expectations about them, which is not unusual given that they want to create acceptance for primate models, not alternatives. However, they do not take the opportunity to question promises made about alternative models in the same way anti-authors do about primate ones. This seems unusual at first, but it may be they are concerned about being construed as unethical, given the value now being placed on the Three Rs in legislation and by funding bodies and publishers (Chapter 1).

Interestingly, none of the reports discuss the ethical implications of implementing alternative techniques and technologies, despite recognition that they can be ethically problematic (Smith and Boyd 1991). This implies that alternatives are seen as morally acceptable when compared with the strong ethical objections to animal use or perhaps

ethical considerations have not been taken into account; commenting on this is difficult and would require further investigation beyond the scope of this thesis. However, as Hedgecoe and Martin (2003) observed for pharmacogenetics, alternative advocates have possibly attempted to construct expectations that distance the alternative methods from the seemingly more serious ethical problems surrounding animal experiments, in an effort to shape alternatives as more ethically sound.

Summary

This analysis shows that expectations were a feature when the reports covered PD, but not so much when they discussed schistosomiasis, particularly the anti-report [2]. However, this could be related more to the age and format of the report [2] than to the field of research *per se*, as the later interviews indicate that expectations are important for understanding some of the schistosomiasis researchers responses (Chapters 4 and 6).

These findings indicate that different aspects of the theory of expectations concept help to explain the opposing sides of the debate. Pro-authors construct expectations by making promissory statements about benefits that will accrue from primate studies and extensively use sickness narratives to strengthen those promises. There is also evidence of collective expectations indicating that justifications for primate work may be taken-for-granted. Pro-reports do not attempt to question or discredit expectations related to alternative methods. In contrast, anti-reports repeatedly use 'failed' expectations in primate research to argue it is unjustified. The descriptions of failed expectations also provide evidence that the concept of hype/disappointment cycles

(Brown 2003; Borup *et al.* 2006) could be applicable to scientific techniques and models as well as to emerging technologies.

Whereas pro-authors appear to use persuasive referencing and create expectations to support their claims about primates, anti-authors almost exclusively rely on the latter to justify their assertions about alternatives, particularly in later reports. The reason for this may be two-fold. Firstly, because alternatives are novel and challenge the established primate models, it is more difficult to gain acceptance, associated funding and expert interest for them (Gilbert 1976). Therefore, emphasising benefits that will accrue from alternative studies may be the most effective way of mobilising the necessary resources to cause a shift in research emphasis towards replacing primates with these methods. Indeed, the reports themselves provide a platform for building expectations and disseminating them to a wider audience than is possible with peer reviewed literature. Due to the controversial nature of this debate this may be the most efficient route for establishing visions of the future of biomedical science as mainstream viewpoints. Secondly, it can be seen that expectations are the outcome of competition (Brown 2003), so it may be that anti-authors have noted how pro-authors have used expectations to so far win this 'competition' and are now adopting the same approach in attempting to overcome them. The use of a sickness narrative focussing on animals [4] may illustrate this.

PD and AD are both neurological disorders generally associated with aging, which have limited symptomatic treatments available, yet the reports present the associated primate work differently. While authors build expectations about methods they are advocating in both areas, there was a greater use of sickness narrative or cure rhetoric

in AD. In particular, anti-authors showed awareness of researchers using the seriousness of the condition to justify primate models and were concerned that fear of the disorder was being exploited to justify invasive and unrelated studies. Sickness narratives are used to create space for and justify morally challenging research (Brown 2003 and Mulkay 1993), indicating that in AD scientific justification for using primates may not be as strong as in other fields. It could also explain why this was not evident in PD, where primate studies are more directly applicable to the human disorder, and in some cases have been translated into treatments. It could also indicate an underlying pressure on scientists to provide an applied justification for their research in order to secure funding for it, which is not explicit in these reports but which became apparent when speaking to scientists during the case studies (Chapters 4 and 5).

The final section of this chapter describes how the reports indicate that 'core sets' could be important in explaining some aspects of the primate debate and indeed why certain authors have presented their arguments in the manner that they have, as detailed in this section on expectations and the previous one on persuasive referencing.

3.4 Core Sets

Introduction

As noted in Chapter 2 (2.3.3), the concept of the 'core set' was conceived and defined by Collins (1988) as '*the group of technically informed specialists who participate in the resolution of scientific controversy through their esoteric technical activity*' (p. 728). In 2006, Hedgecoe described it as providing an explanation for '*how scientific communities respond to experiments, controversy and outside influences*' (p.723). The findings from this analysis support this description. Interestingly, the importance of the concept of a core set is only suggested in the discussions relating to infectious diseases such as, schistosomiasis and BSE, but not in the coverage of neurological diseases, PD and AD.

Parkinson's Disease

There is nothing in the reports that is indicative that core sets might be applicable to understanding the arguments which are presented regarding primate experiments in PD or in the other main neurological disease discussed, AD. As noted below this might be related to the nature of the field and number of specialists working in it. It is also consistent with the findings from the Case Study 2 interviews, which indicated that core sets were less influential in PD research than in schistosomiasis (Chapter 5).

Schistosomiasis

In contrast to PD there is some evidence that the core set concept could be important in explaining the framing of some of the justifications given in schistosomiasis and other infectious disease including the balanced referencing described earlier.

As described earlier (section 3.1), pro-report [17] made statements about the need for primates in schistosomiasis research based on the submissions of one research group. This appears to be a case of selective citation as there is no indication of any checking of the assertions made by that group or any description of alternative models that have and could be used. This uncritical acceptance of the submitted information could also be related to the reputations of the submitting group. The authors of the report [17] may have viewed this research group as being the core set that is, the experts in the field who participate in resolving this particular scientific controversy, and as outsiders they did not question the assertions they made or look for counter evidence. Hedgecoe (2006) describes this effect as '*enchantment*' (p.742) with the outsiders being further from the scientific fact so seeing it as more certain and straightforward.

In their earlier report, Ruhdel and Sauer [4] make an interesting observation about the value which scientists attribute to science itself and as a consequence to animal experiments. They note that despite a great deal of epidemiological evidence suggesting a causative link between BSE and vCJD, scientists still feel obliged to distrust their personal conviction until they have experimental evidence to support it. Thus, the primate experiments merely confirm what they already know. This also appears to be 'enchantment*'* as the scientists are members of the core set (i.e. actively engaged in the experimentation at the heart of the primate controversy) and as such

always show an element of doubt about their findings, whereas those outside the core set and further from the actual science are more certain about that science (Hedgecoe 2006). Hence, the scientists feel the need to provide evidence to justify their opinions, even when it most likely would not be required by those said to consume their findings in a wider context. Why the core set appears influential in these infectious disease examples, but not in the neurological examples, may be related to the small and specialised nature of the fields. That is, the influence of those in the core set is more pronounced and any competition or controversy between them has a magnified impact on the direction of the field and techniques and models adopted.

As noted previously (section 3.1), two anti-reports [2 and 5] appear to be attempting 'balanced referencing' when discussing work being conducted in several areas of research including schistosomiasis [2]. As Michael and Birke (1994a) noted, scientists in the animal experimentation controversy place criteria on who can be a member of the core set. Therefore, attempting to present a more balanced account could be a means to be accepted into the core set and be seen by scientists as a credible voice in the debate. This could have the consequence of being able to then influence those scientists and the direction of research away from primate use, with a greater chance of novel ideas (i.e. alternatives) being seen as valid and realistic.

Summary

This analysis has revealed an interesting difference between the fields of research: a possible influence of a core set of scientists in the reporting of primate infection models. In the pro-report [17] it seemed that the authors may have seen the group who

submitted evidence as the specialists that are solving the controversy about the validity of the schistosomiasis primate models (i.e. the core set), so did not question their evidence. An anti-report [4] observed the relationship core set scientists had with their own findings, noting that BSE scientists were distrusting their personal conviction and epidemiological evidence until they had experimental primate data to support it. Both of these examples could be seen as enchantment (Hedgecoe 2006). It is unclear from this analysis why core sets may be influential in the field of infectious disease but not of neurological disorders, but the case study findings later in the thesis (Chapters 4 and 5) indicate it may be related to the size and specialisation of these often relatively small fields of research, with disagreements about appropriate research strategies being more pronounced among fewer lead scientists.

3.5 Conclusion

The central aim of this analysis was to distinguish what kinds of scientific arguments are given in support of and against the use of primates in various areas of research, and to decipher how they are presented and framed by the two sides of the debate, that is, pro-primate use and anti-primate use. This analysis has shown that the debate about using primates in biomedical science is still controversial, not just between proponents and opponents but also within scientific disciplines. It has revealed that authors utilise persuasive referencing and expectations to convince the reader of their particular stance, and core sets may be influencing some areas of research. There are differences in disease framing and in how these theoretical themes explain the two sides of the debate. The anti-primate reports use persuasive referencing to discredit pro-primate

evidence but not to bolster their own claims about alternatives. Instead, they appear to construct expectations about alternatives, while extensively highlighting failed expectations of primate studies to argue that they are unjustified. In contrast, pro-authors apparently use persuasive referencing and expectations, especially sickness narratives, to show the reader their primate research is justified and beneficial, but do not attempt to discredit alternative models. Perhaps most interesting was evidence of balanced referencing as persuasion, which was not predicted by existing literature.

There was also the intriguing observation that the anti-authors appear to alter the emphasis of their argument presentation over time. Together, a slight improvement in persuasive referencing, extensive use of expectations and possible balanced referencing indicate that anti-authors may be shifting to a more 'scientific' way of presenting their arguments. This could be due to anti-authors having to address the scientific grounding for alternatives, due to more pressure being placed on research scientists to do so, as awareness of alternatives increases, which was more apparent in the interviews (Chapters 4 and 5). In addition, anti-authors may be attempting to engage with scientists at the same level. The modern anti-movement has an ethical foundation of questioning the morality of experimenting on animals rather than the scientific justifications as such (see Franco 2013 for an overview of this). This means that many anti-authors may have had less experience in a more scientific arena so are only just developing similar approaches to pro-authors who mostly argue the scientific aspects in reports like these. In addition to simply attempting to discredit primate studies, anti-authors now appear to be drawing on scientific work in the expanding alternatives field and presenting it as the scientifically justified means of investigating diseases. In utilising references and expectations, they show that they follow the

correct scientific procedures; that is, presenting experimental work on alternatives, which has been done using the same scientific practices as the primate work. Theoretically, this makes it more difficult for primate scientists to dismiss claims as unscientific or misinterpreted without appearing to have double standards; whether this occurs in practice still remains to be seen. Significantly, research scientists seem unaware of this shift in approach, as during interviews (Chapters 4 and 5) neither primate nor alternative users made any specific comments about it. Therefore, it may be a phenomenon associated with this kind of publication or more likely may only be in its infancy, but it presents an interesting area for future research.

In the context of the overall thesis these findings provide the basis from which to enter the second phase of the project, looking at two of the featured cases, PD and schistosomiasis research in more depth. The contrasts between the reporting of the primate experimentation in PD and schistosomiasis research, such as differences in the use of sickness narratives and the potential influence of the core set, informed my purposive choice of these two fields as my case studies, Chapter 2 details the full rationale for this choice. This analysis suggests that these two cases provide an interesting comparison from which to investigate the primate debate. Given that the theoretical themes are applicable across both fields it provides further impetus to examine in more depth, through interviews with the scientists conducting the research, how important the social dynamics of science are in understanding the impasse in the debate. The results of this second stage are reported in Chapters 4 and 5. The consequences of the findings from this documentary analysis and the two case studies for understanding and overcoming the primate debate impasse are described in Chapters 6 and 7.

Chapter 4: Case Study 1 – Schistosomiasis Research

4.1 Introduction

The next two chapters present an analytical summary of the themes that emerged from the case study interviews. The interview process is described in detail in Chapter 2, along with the rationale for choosing schistosomiasis as a case study. The analysis builds upon information gleaned from the documentary analysis (Chapter 3). The findings indicate that scientists identify several challenges to and/or opportunities for replacing primates in this particular field, and that the social dynamics of science have an important role to play in explaining the participants' responses. These were important for understanding the primate impasse (Chapter 6) and developing the recommendations for overcoming it (Chapter 7).

Schistosomiasis is a macroparasitic disease caused by trematode worms affecting approximately 200 million people at any one time, with the majority of sufferers living in Africa (WHO 2010). Its complex lifecycle involves eight morphological stages and two hosts (mollusc and mammal). Five species of Schistosoma can infect humans causing chronic disease: *Schistosoma mansoni, S. japonicum, S. haematobium, S. intercalatum* and *S. mekongi*. The first two of these result in an acute schistosomiasis state and are the focus of most vaccine research. The disease is predominantly treated with oral doses of the drug Praziquantel (or Oxamniquine outside the US) but effectiveness varies, with rapid reinfection following treatment

making this an expensive option requiring substantial infrastructure (Butterworth *et al.* 1987). Additionally, evidence of resistance is emerging (Capron 1998, Butterworth *et al*. 1987); thus there is strong impetus to develop a preventative vaccine.

Early efforts were focused on a vaccine that would protect humans against natural infection. Although attenuated larvae induce a good level of immunity in various experimental models, consensus was that a non-living, defined vaccine would be easier to produce on a large scale, via recombinant DNA technology (Boulanger *et al*. 1991). So far, vaccine-induced immunity has been incomplete, with only partial protection being achieved (Capron 1998). For further historical insight on schistosomiasis vaccine research see Wilson and Coulson (2006).

In this and the subsequent chapter, participants are identified by a number and 'P' for primate user or 'NP' for not a primate user. I am identified as MH. For one participant, some identifiers include [NR] (not recorded). This refers to quotes taken in note form rather than transcribed, due to recorder malfunction (see Chapter 2 for details). Gender-specific pronouns are not used to avoid compromising anonymity.

Throughout the respondents' answers they justified science, being a professional scientist, conducting certain types of research and studying certain fields of research. This was done both explicitly and implicitly. Data fell broadly into four themes that I have described as: the Scientific Institution; Practical Science; Animals and Ethics; and Health and Ethics. Each theme is broken done into sub-themes to illustrate its nuances. Comparisons between primate and non-primate users are given where

applicable. This case study was compared to the second PD case study and any important observations are presented in the next chapter.

4.2 The Scientific Institution

Participants identified underlying factors that influence how science is done as a way of justifying their position and research. Using the language of Merton (1957) I categorised these factors as the 'scientific institution'; that is, processes ingrained in the fabric of science illustrating why scientists conduct science as they do. Data are presented under the following sub-themes: competition, reputation, knowledge acceptance and publication.

Competition

Participants identified the competitive nature of science as a whole as key to facilitating or restricting their work. This was sometimes explicitly stated, but also subtly inferred, for example I8P considers that they might eventually have been beaten to their discovery by another scientist working in the same area:

> …if I didn't discover it somebody over the pond would've discovered at the same sort of time… (I8P)

Some participants viewed competition as negatively influencing dissemination of research findings, by limiting information sharing and collaboration. Fear of having their ideas stolen or being '*anticipated*' (Hagstrom 1974, p.2) was crucial to

participants feeling that they or others in the field would not openly discuss their work. For example:

> Yes I think a meeting would be good bringing together the good and the wise….There might also be problems with getting people to reveal their new ideas. ([NR]I8P)

A relatively low level of collaboration could account for the apparent strength of the negative impact that competition seems to have in this field. While a small number of participants reported collaborating with others when choosing models, the majority of responses about collaboration called for more, in order to move the field forward. This included primate and non-primate users with the following statement summing up responses:

> …I think that's one thing that actually needs to be dealt with on a more serious level, larger groupings of collaborations across the field. (I7NP)

This indicates that collaboration might overcome some of the perceived competitive challenges to moving the schistosomiasis field forward.

Mixed opinions were expressed in reference to competition, in the context of which vaccine strategy or experimental model is likely to contribute most to the field. Some regarded competition as positively driving research effort to improve the chance of finding solutions – for example, I10P smiled when they spoke of their competition with another researcher and how it pushed them to pursue their chosen model and strive to make a contribution:

> …was a good friend of mine…we were extremely competitive together…and we had the entirely opposite view…But sometimes it happens that the relations are a little bit you know disturbed by {laughs} some conflicting results or findings but that's life and that's science. (I10P)

Meanwhile, others expressed concern that competition can lead to unnecessary and, in this case, morally unacceptable repetition of effort and/or experiments:

> …the one side of things that I find morally unacceptable should I say is when…the competitive nature of science means that sometimes there can be people reinventing the wheel on both sides of the Atlantic for example. Because you don't know what your competitors are doing. And that has happened on occasions. (I5P)

While this dual impact of competition has been documented (Hagstrom 1974), it is unclear how the scientist's role in the competition might affect their view of it or whether they use it as justification for how science is done. For example, it is reasonable that those who see themselves as 'winners' see competition more positively as opposed to those who class themselves as 'losers' who might be more negative about it. I6P did this by describing their research group as *the champions of the irradiated vaccine* and, despite using terms such as *warfare* and *battle* when discussing competing to get their strategy accepted, seemed to relish how it had pushed them to continue and develop new ideas:

> …when I first stood at Cambridge and said sorry folks it's all a result of the vascular changes…I was not popular…so then ensued a battle…That's when we came to work with people in the States who were like-minded and we kind of sorted that out to our satisfaction and eventually I think other people have accepted it…it's not an argument anymore. (I6P)

I3NP had recently won an award for their research and, while initially being negative about competition, went on to express that it could be useful for driving knowledge claims about alternatives:

> …I think also the fact that research labs tend to be competitive is not particularly helpful. Although it is helpful in some ways I think if you can prove from a scientific point of view that animal usage is not desirable then I think that can almost force people you know because it makes the data not publishable. (I3NP)

In contrast INP described several instances where they had been 'beaten' in the competition, and their negativity about this extends to withholding information so others cannot do the research. In essence the competitive environment may in this case slow down research, and INP seems well aware of this:

> What I tend to be more reluctant to do is to discuss ideas that I think will rock the boat…But you know if it's an idea that I want to work on and think I can work on I'm not going to go to a discussion group and let someone else because they have the resources to do it to you know give them the knowledge so that they can do it first…I'm gonna be dog-in-the-mangerish and say sod it. (INP)

Another participant (I2NP) describes *losing out* in publication, and expresses frustration that competition is delaying dissemination of their work and that this particular area of research is not seen as highly ranking in competition terms; it is not *sexy*.

Positive impressions of competition all came from primate users (except I3NP above). Therefore, the influence of competition on expectation building and how that might have influenced participants' responses needs consideration. Brown (2003) acknowledges that in a competitive environment the most vociferous voices are most

likely to have their expectations disseminated widely enough to become more generally accepted as 'what will happen', and will consequently attract more resources for their research. From this data it seems that primate users are currently winning this 'competition', but indications are that non-primate users are now more aware of this and are using it as a means to attract resources and acceptance for their work. For example, this participant recognises they have to 'sell' their research to get acknowledgment:

> …And it's something which I don't like but I think it's necessary in order to be able to sell your work you have to have something that makes it a saleable thing. (I7NP)

Additionally, participants identified, as Merton (1968) did, that scientists deemed to have a strong reputation in the field are at an advantage in the competition. In some cases this is disproportionate and possibly damaging for vaccine development. I5P's response to the question of whether those with big reputations influence the field summarises this:

> Yes. Too much sometimes…like in in other walks of life you get personalities who are able to sort of corner the market, they get the funding because of who they are not necessarily because of what they've produced…so it goes on it's self-perpetuating and not necessarily always for the benefit of everyone else. (I5P)

The full significance of scientific reputation is detailed in the next section.

In summary, the concept of competition in science was first indicated by Merton (1957) who discusses how emphasis on the value of originality in science leads to pressures to make contributions to knowledge and to be first to do so. While scientific

competition was addressed more extensively in the late 1960s and 70s (see Merton 1968; Hagstrom 1974; Barber *et* al. 1979), and despite its apparent role in the mechanism of the 'Scientific Institution', Bonitz and Scharnhorst (2001) noted it has fallen out of favour more recently:

> Less widely addressed in this literature is one aspect of science that is actually one of the necessary conditions for the functioning of science, namely "competition in science". Competition is one of the key mechanisms of the science system. Scientists compete for being first and for scientific reward institutions compete for the allocation of resources… (Bonitz and Scharnhorst 2001, p.37)

These findings indicate it is still an important influencing factor on how scientists conduct their research. It seems to impact on the direction and progression of the field; as such it deserves renewed attention. Particularly interesting is how perceived size and importance of the field may affect incidence of competition. Hagstrom (1974) posits:

> Competition and concern about it will be greatest in specialties perceived to be most important for further developments in science because the number of competent researchers relative to the number of known research problems will be greatest there. (Hagstrom 1974 p.12)

This does not appear to be applicable in this case as concern is high but schistosomiasis researchers perceive the work is deemed unimportant by those outside the field. Instead, it may be that because there are few aspects within the field to focus research on, then competition for resources and acceptance within the small community is more acute. This data indicates that, according to researchers, competition is influencing this field of research, but that its impact differs with the reputation and success of the scientist involved. This is intertwined with needing to

'sell' the research to gain resources and acceptance for it by being the most vociferous in building expectations about it.

Reputation

The influence of a person's reputation was a key factor in explanations of why certain areas of research within the field dominated, or were more readily accepted by the schistosomiasis community and funding agencies. There were positive examples of how those with a reputation have their ideas accepted, leading to trends in funding and further research. But many participants were quick to point out that while reputation can be positive for individuals or groups, it is not necessarily best for the field as a whole from a scientific perspective:

> I think after a while if you get to be a very well-known person that you end up having a sufficient weight or clout which allows you to continue peddling your point of view…there are certain of my colleagues in my field who I feel have continued to do it well past the sell by date of their particular point of view. (I7NP)

Another negative aspect was the influence certain people can have on the peer review process. Some participants felt there are individuals who, when acting as referees, blocked their research or at least slowed publication:

> …because of course all the work is peer-reviewed. And unfortunately it isn't always rejected on the grounds of whether or not it has merit it's rejected on personalities…I don't know how you get round that problem but it's there... (I5P)

This concern is found in other fields of science, for example stem cell experts recently published an open letter expressing concern that '*...a small group of scientists is effectively vetoing high quality science from publication in journals*' (Ghosh 2011).

Many participants commented on their perception of their own and close colleagues' reputations and the consequences of that for the field. Primate users tended to be more positive about their reputations and felt they had a greater impact on improving knowledge in the field, for example:

> …they were pioneers in the use of primates for understanding the evolution of schistosomiasis, and you can also usefully rely on their publications because they have been very seminal observations…and can be used forever. (I10P)

Conversely, non-primate users tended to see themselves as less influential, for example:

> …for me I'm not, if you are a very famous person you say something all people believe you, but if you are just very junior and young may be the more you say it the more people do believe {laughs}. (I4NP)

One primate user appeared to be an exception; when asked early in the interview what they felt was their most important work they identified some results that altered thinking at the time. But later in the discussion they indicated that as a researcher they were not important enough to contribute to moving the field forward:

> I'm not really important enough to attend things like that. There are others who would be able to contribute before me. ([NR]I8P)

Therefore, even those who do not expressly recognise themselves as having a particularly strong reputation, still indicate that they place importance on reputation as a means of influencing the field. I5P felt that association with a scientist with a good reputation was sufficient to increase the chance of justification and acceptance for research.

In summary, it seems that reputation may have a significant effect on how scientists perceive their ability to justify their research and knowledge claims to others and, as previously indicated, it has an influence on the impact of competition. This could be an example of Merton's *Matthew Effect* (1968) where eminent scientists gain disproportionately greater credit for their contributions to science, compared to relatively unknown scientists who get less credit for similar contributions.

Knowledge Acceptance

Participants placed emphasis on how knowledge claims are accepted, related to who needs to or should accept them and whether the claims are novel or established. Several participants view the field as belonging to a select few, identifying different groups of people they feel are knowledgeable about their work and/or could or should have an influence on the field, and the acceptability of that work. Some participants indicated that it was more important for their knowledge claims to be accepted by those within the group, and that views of those outside the group were less or not important. I5P thinks the public perception of schistosomiasis is low because of the nature of the disease, which may account for the participants not being particularly

interested in gaining acceptance from the public. But they still emphasise needing to influence those inside their group (i.e. other scientists):

> …So I don't think I'm influencing the general public in any way. I think it's more the scientific community that I would be looking to influence. (I5P)

This apparent lack of consideration for the views/acceptance of those outside the participants' main group(s) might be a result of how the outsiders are perceived or characterised by the insiders. For example, when discussing participating in workshops I6P was quite forceful in characterising those outside the specialist groups as being irrational and inaccurate, in comparison to their rational willingness to debate and provide justification for their *essential* research:

> …only insane individuals would suggest that [testing on prisoners], would not see the contradiction in what they're saying. You know for animal welfare but not people welfare…I'm always happy to debate. And to justify use of animal experimentation where it's essential, where there is no other way. (I6P)

Some participants expressed a less extreme view of those outside as having no or little understanding of the research/disease. In contrast to this were comments related to insiders possessing specialist knowledge which only they can understand or pass judgement on, indicating that specialist knowledge of the field could be a criterion for membership of the group. For example, I3NP argues that those outside do not present the correct information and indicates it is more difficult to explain knowledge claims to those who are not members of the specialist group:

> …they're [scientists] an important people to be involved in the debate cos some of the factual information involved in debates is sometimes not accurate I find. But…sometimes it's quite a difficult thing to convey non-specialists kind of thing but I think it should be done. (I3NP)

Participants indicated that only the specialist group could move the field forward, and that for those outside – whether they are other scientists or members of the public – to have any influence, would need to meet certain criteria or their input would not be valid. As noted in Chapter 2 these specialist groupings have been identified by Collins (1981; 1988) as the 'core set'. This may be another example of Michael and Birke's (1994a) observations that scientists involved in animal experimentation place criteria on whom they regard as having a legitimate membership in the core set and consequently a voice in the debate. Further support of this argument is found in responses indicating that within the core set there have been conflicts resulting in a 'core group' being created which holds the dominant view (Collins 1999). For example, I6P talks about how the work they were doing conflicted with the established model so they constructed a separate group within the area, which eventually became the dominant view:

> …it turned out to be the lungs, not the skin as all the previous workers had said…That's when we came to work with people in the States who were like-minded. And we kind of sorted that out to our satisfaction and eventually I think other people have accepted it…it's not an argument anymore. (I6P)

Another aspect of acceptability is the intrinsic nature of the knowledge. That is, participants often distinguished between what they saw as novel knowledge and what was seen as established knowledge. Gilbert (1976) noted that getting novel scientific ideas accepted is difficult, and this was illustrated by a couple of participants. For example, I3NP indicates that novelty is important for acceptance but qualifies this by adding that it should be put into the context of established knowledge:

> …we're slightly driven by publication as well so it has to be novel and it has to be referenced to what people have done before so you have to be aware…I

> very much felt with the paper…like I had to directly compare it to what had been done before to be taken seriously. (I3NP)

Discussion about novel knowledge was limited to publication, which is discussed in the next section. Here, emphasis appears to be on the impact of established knowledge. Some participants explicitly stated the importance of building on current knowledge, or described that this was what they were doing.

Some indicated that established knowledge was a factor in driving the direction of research. For example, I7NP suggests that as knowledge becomes established, it perpetuates more research in that area:

> …But yes I think we're all the time reading other peoples research ideas and there are things that often when two or three people are beginning to nudge towards something you then start looking at that area in more detail and it can then chime with something that you've always believed which is very nice. Or it challenges something that you think that is really difficult to accept but given the fact it's turned up two or three times it's worth more than just thinking this is an aberrant result… (I7NP)

Therefore, it appears that most participants place importance on the historical or established nature of knowledge when deciding whether to accept it or not.

Except for I7NP, all responses related to the impact of established knowledge were given by primate users. This may indicate that they place more emphasis on the established nature of their work. This may function as a means of showing that their research has a history, so can be more strongly justified.

In summary, this data indicate that Collins' (1988; 1999) 'core set' concept is important in understanding why certain viewpoints dominate in the primate impasse

and why it can be difficult for alternative models to be accepted or even acknowledged by sectors of researchers within a field. Certain schistosomiasis researchers appear to be placing restrictions on who can make knowledge claims, which is a factor in the slow progress of the field and in the difficulties of getting non-primate findings accepted. The reluctance to communicate with those 'outside' the specialist group could be accentuating the lack of cooperation related to competition identified above.

Publication

Participants see publication as an enormously important means of substantiating their knowledge claims, in many cases using it as a measure of their success. Although they do not always apply this in a self-reflexive context, they do see publication as a means by which others judge them. Only two participants did not mention publication.

Publication's importance was emphasised by apparent distrust directed toward research where findings were not published:

> …I mean the other disgraceful thing is that the results of that trial have never been published the actual results …I think it's questionable why these results were not published. (INP)

There is indication that <u>where</u> research is published is important for judging the validity of knowledge claims. When asked about difficulties with acceptance or dissemination of work, INP replied *no because I publish in crap journals*. This was said during a conversation where the participant was quite negative about the impact

of their work, and it was obvious they were disappointed not to be publishing in 'better' journals.

Not unexpectedly, here a participant emphasises that they must consider where they publish, aiming for higher-ranking journals to ensure their work has maximum impact:

> …we're in a very competitive field and we always try to publish in highest-ranking journals. Yes we're not all publishing in the top ranking journal all the time. So I think in that sense we are always trying to do better and we'll try and publish in the journal which is going to have the highest impact… (I7NP)

However, for some participants a journal's ranking did not guarantee the quality or importance of the work, especially according to I6P during an exchange about publication quality versus where it is published (the journal name has been removed as I6P requested not to be quoted):

> …Getting a paper that really changes the way people think that's hard. There's a journal called {name} which is one of the top journals…You could also describe it as the {derogatory name for journal omitted}, because to get in there you have to have something that's so you know kind of way out off the wall, trendy. There's fifty per cent chance it's rubbish. (I6P)

The following participant's response to what makes a piece of work seminal illustrates that even publication in one of the highest ranking scientific journals, Nature, does not ensure long term impact:

> …I mean you know very well that you can have beautiful papers in Nature and which are destroyed six months later and they're therefore at long term have no impact. (I10P)

Despite the theoretical difficulties of getting new knowledge accepted, illustrated by the emphasis on established knowledge in the previous section, novelty was cited by some participants as being an important factor in initially getting a publication noticed and possibly accepted. For example:

> …I mean we're slightly driven by publication as well so it has to be novel and it has to be referenced to what people have done before so you have to be aware. (I3NP)

Thus, there seems to be a dichotomy where novelty is both an opportunity and a challenge to gaining acceptance for knowledge claims. Myers (1985) argues that this is a result of a negotiation between the writer and the potential audience, because:

> …the researcher tries to show that he or she deserves credit for something new, while…the editors and reviewers try to relate the claim to the body of knowledge produced by the community. (Myers 1985 p.595)

I5P made an important point about the nature of publication, which was noted by others. They expressed regret that a great deal of data is never published as it is seen as negative findings. It seems this is 'lost' knowledge rather than useless knowledge because it still provides valuable indications of where research should go and what has already been explored. Indeed, I5P felt quite strongly that this information should be made available; to help speed up progression in the field by preventing repetition of 'unsuccessful' studies, but also to prevent unnecessary animal use:

> Plus the fact there are no journals of negative results…But nobody wants to hear negative data like that, so it never gets published. There is no repository for that kind of stuff and so I think there's a lot that's lost to the scientific community. Not just about animals but in general. But what can you do about it? But in the case of animals it does mean that sometimes things are wasted because somebody else tries out the same procedure. (I5P)

As well as scientific publication, respondents talked about publication in the context of media coverage. The majority of responses were negative about the hype the media such as, newspaper journalists, radio programmes and television reporters, puts on scientific findings. Participants expressed concern that hype can be wrong or unscientific and that it might be damaging to the reputation of the field, by causing disappointment when promises are perceived as not being achieved:

> …everybody just wants you know the cure for AIDS and this that and the other straight away…I guess they don't see the final consequences and might just think you know nobody's actually achieving anything… (I2NP)

I10P was particularly vocal about the media aspect, feeling there had been a shift toward greater use of media hype by the newer generation of scientists and this was all about self-promotion rather than science for which it is detrimental:

> I've been privileged to make the main part of my research activities at a period where science was still a very noble activity…people have changed and I say that science is a little bit polluted…there's a striking difference between the behaviour of an old man and an old generation, which are generally discreet at work and are not going to the TV or out to general newspapers every day and the rest younger people who are building up their reputation it's very striking. (I10P)

This observation was supported by responses from other participants, indicating it was necessary to 'sex up' your research in order for it to be noticed:

> …therefore you have to make your science sexy…And it's something which I don't like but I think it's necessary in order to be able to sell your work you have to have something that makes it a saleable thing. (I7NP)

Although there is negativity toward media hype there is also acknowledgement that it can generate interest and support for the research, for example:

> …it's again a balance attitude I would say between the necessity to provide proper information to the public who needs it. And if we need its support we need also to give them the proper information but on the other hand we have absolutely to resist to the temptation of delivery immature results or at an inappropriate time that's my point of view. (I10P)

In summary, the data indicate that participants identify scientific publication as an important means of gaining acceptance and justification for research. As noted in the previous section this can be influenced by the core set of scientists through the peer review process. The findings regarding uncertainty about hype illustrate the tension in the management of expectations identified by Brown (2003), where:

> …hype and the noisy clamour of future projection are indispensably central to the shaping of technology. And yet…we want to avoid the costly price of disillusionment, overshoot, hype and overselling. (Brown 2003 p.5)

Understanding how the schistosomiasis participants view hype, and how they do or do not create expectations through publications, has important consequences for overcoming the impasse. These are discussed in Chapter 7.

Scientific Institution Conclusion

These data indicate that the responses which can be analysed as being associated with the 'scientific institution' are an important means by which participants justify their research. Competition appears to be a particularly strong factor in this field, with reputation and the Matthew Effect seemingly affecting the influence it has and how it is viewed by the various participants. Participants placed greater emphasis on gaining acceptance from their peers, with publication being presented as an important way to achieve this. They see schistosomiasis as being an unknown disease to the public, and

view the public as well as some scientists as being outside the specialist group. The data suggest that the 'core set' concept is applicable here. As indicated in the documentary analysis (Chapter 3), it may be particularly influential in this field because of the relatively small pool of researchers and the limited availability of funding due to the low profile of the disease, making any competition or conflict much more pronounced. There was evidence of negativity toward expectation-building in the form of media hype that could be further restricting communication in this field. The chapter now turns to the second theme, scientists' views of the practicalities of conducting scientific research.

4.3 Practical Science

I have termed the second theme that emerged from responses, 'practical science' that is, the doing of science and the everyday encounters related to it. Participants used a variety of factors related to the practicalities of engaging in scientific experimentation to justify the research and/or models they use/used, including physiological reasons for model choice, research question and overall aims, policy and logistics, and alternatives.

Physiological Reasons for Model Choice

All participants described scientific reasons for their choice of whether to use a particular model or not. Typically these included descriptions related to physiology, parasitology, immunology and experimental methods and tools. A summary of

responses is given in table 10. In the documentary analysis (Chapter 3) the limitations of models were usually given by opponents of primate use; for example anti-reports presented extensive problems with primate models. Here, participants were willing to talk about the scientific limitations of their own and other models and, while this was not always spontaneous, it was freely discussed when prompted. Some participants gave information more readily about their own work: for example, I9P gave the limitations of each of the models they had used. Others gave problems with models they didn't use more easily than those they did: for example, I6P only gave cost and ethics as limitations of the baboon model they had used, whereas when discussing other models they gave several scientific problems. Additionally, some participants emphasised that due to the limitations of each individual model it was important to utilise more than one, in order to get a fuller picture of what was happening:

> …I'm not choosing between them [animal models] as you see I'm saying that each one has its own validity and I would say as each is inadequate to totally represent the picture you've got to actually probably do comparative things. (I9P)

Table 10: A summary of the 'scientific' reasons participants gave for and against using different experimental models for schistosomiasis vaccine research.

Model	Reasons for Use	Problems
Mouse	• Permissive to *S. mansoni* • Maintains parasite's whole lifecycle • Identifying diagnostic antigens • GM strains used to identify immune response class • Observing parasite migration • Many immune reagents available	• Heavy infection with few worms • Difficult to model chronic infection • No concomitant immunity • Subtle differences in immune response compared with humans • Too small for infection intensity studies • Circa 30% worm maturation
Hamster	• 60-70% worm maturation • Modelling skin penetration • Takes more parasites than mice	• Only permissive to *S. mansoni* and *S. haematobium*

Model	Reasons for Use	Problems
Rat	• Possibly self-cures – rejects worms as they mature	• Non- or semi-permissive to *S. mansoni* • IgE (allergic) response to worms
Rhesus Macaque	• Permissive to *S. mansoni* and *S. haematobium* • Realistic worm burden • Studying infection intensity • Possibly self-cures – eliminates adult worms • Long lasting immunity • Studying chronic infection • 80-90% worm maturation	• Needs multiple vaccinations/ infections for a relevant antigenic load • Sacrificed to get worm burden
Baboon	• Large size – realistic worm burden • Large worm burden without suffering adverse effects • Permissive to *S. mansoni* and *S. haematobium* • Studying infection intensity • Optimising vaccination • Studying chronic infection • 80-90% worm maturation	• Needs multiple vaccinations/ infections for a relevant antigenic load • Sacrificed to get worm burden • Lack of immune reagents • Pathology less intense than humans • Induced immunity decreases with time
Sheep	• Natural model of Schistosomiasis • Host to *S. mattheei* and *S. margrebowiei* which are related to *S. haematobium*	• Permissive to *Schistosoma spp.* which do not infect humans • Species specific animal vaccine
Cattle	• Natural model of Schistosomiasis • Studying natural infection effects on protection • Permissive to *S. bovis* which is related to *S. haematobium* • Permissive to *S. japonicum* • Non-invasive sample collection	• Not chronic infection • Cannot do long term safety studies • Species specific animal vaccine
Pigs	• Natural model of Schistosomiasis • Permissive to *S. japonicum* • Vaccine would treat humans and animals • High levels of protection with irradiated *S. japonicum* vaccine • Immunologically similar to humans • Similar mass to humans	• Not chronic infection • Self-cures over time so not directly analogous to human • Logistical problems of housing in laboratory
Human	• Studying age-related resistance • Uses fresh parasite isolates	• Immune response does not kill worms

Model	Reasons for Use	Problems
	reflecting true variability • Evaluating blood/sera based diagnostic tests • Studying pathology and clinical outcomes • Investigating acquired immunity • Studying chronic infection	• Cannot measure true worm burden • Sample sizes too small • Difficulty translating genome information into an intervention • No evidence of complete immunity • Complex factors surrounding age-related resistance
In Vitro/ Omics	• Identifying candidate molecules and site of expression • Studying parasite gene expression • Studying parasite strain variance • No selective pressure on parasites, as not passaged in animals • Developing diagnostic tools • Maintaining parasite lifecycle *in vitro*	• Available information needs fully cataloguing and annotating • Do not get full range of immune responses/interactions *in vitro* • Cannot grow adult worms *in vitro* • Does not provide information on how to present candidate molecules to stimulate the wanted immune responses

In summary, these responses indicate that, according to participants, there are many scientific reasons for and against using the various models available for schistosomiasis vaccine research, which are not immediately apparent from the literature. It is possible that this leads to the described need to use several models during investigations. Importantly, participants were willing in interviews to discuss the limitations of their models, which rarely occurs in publications like those analysed in Chapter 3 or in peer-review literature, where authors are ultimately focussing on the benefits of their claims to improve their acceptability.

Research Question and Overall Aim

The type of research question being asked was highlighted as a reason for model choice, with half of the participants mentioning it in this context. Raising the influence

the scientific question has on model choice may indicate a tendency to want to conform to the scientific 'norm', that is, to show they are conducting science in an appropriately logical way. Interestingly, several primate users emphasised that the question must be particularly important and vital to progressing the field when it came to decisions to use primates, for example:

> …the same is true of primate experiments again we move up several orders of magnitude in terms of expense, difficulty and ethical considerations we would only even envisage using a primate when there was completely vital question which is crucial or blocks our further studies on humans... (I9P)

A couple of participants also commented that the complexity of the disease means that, in order to answer all relevant questions several models need to be used.

It seems that there is interplay between the research question and the physiological reasons, that provides the scientists with a means by which to make the decision about the appropriate model(s) to use. It appears that some participants use this interplay to morally justify their choice when they note that only important questions should be answered using primates. This ethical aspect is explored further in the next section.

Another factor determining which questions are asked is the overall research aim the participant is following. From the peer-reviewed literature (see Chapter 2) three main areas of research for investigating schistosomiasis vaccines were identified: attenuated vaccines, self-cure and naturally occurring infection. These aims were checked with participants and they detailed two further examples; IgE (allergic) response and engineered/recombinant vaccines. Participants were relatively balanced in their descriptions of the pros and cons of the various aims they were most familiar with, but

there was obvious contention about which one should be pursued to reach a beneficial outcome.

In the documentary analysis (Chapter 3), overt reporting of conflicts within fields was rare. In contrast, in these interviews, participants were explicit about the disagreements surrounding which research aim should be used, including suggesting that more effort should be put into certain ones. Perhaps the most controversial aim and most illustrative example is that of self-cure. One participant in particular advocated this as a way forward:

> …now of course we can be inspired by spontaneous or self-cure mechanisms that are used by the rat for instance and this has been one of the reasons of the choice of this model for us particularly…(I10P)

Yet several other participants expressed that self-cure could never be beneficial and in some of their opinions should not be pursued further for example:

> I would not go down that route [self-cure]…The intrinsic mechanism is not likely to lead to a vaccine candidate. The irradiated vaccine is the best model and effort should be concentrated using the best models to find the antigens that can mimic that effect. **(**[NR]I8P)

Despite this conflict each of the given aims persists, so maybe this is a form of Hedgecoe's (2006) enchantment; with scientists in the core-set (these participants) being afraid to dismiss a model, just in case it does provide an answer. There may also be an influence of publication bias, as scientists have to focus on publishing the positive aspects of their research in order to keep interest and funding high, rather than expressing the negatives of other aims.

In summary, it seems the schistosomiasis participants tend to use the research questions as a means to justify their choice of model, especially when using primates. There was a great deal more discussion about the conflicts that are apparent in the field than there is in the primate reports and peer-reviewed literature, but seemingly counterintuitively, despite there being explicit views that some overall aims are better than others, they all continue to be explored. This may be inadvertently slowing progress in this field and was taken in to consideration when making the recommendations in Chapter 7.

Policy and Logistics

Participants identified policy and logistical issues that were affecting their choice of model and/or research aim, including comments on economic factors, availability of appropriate facilities and lobbyists' influence on policy.

National policy and political influence were viewed as having positive and negative effects on the schistosomiasis field. For example, the quote below illustrates that if there is a political need to follow a certain research aim, in this case vaccination, then it might outweigh the evidence of whether it is scientifically plausible or not. So even if results are negative, research might continue because policy dictates it should be done that way:

> I think if we hadn't demonstrated immunity in humans but we'd demonstrated such high levels of immunity in primates there would still be a push to develop a vaccine for schistosomiasis if the political will was there. (I8P)

Significantly, when asked how they might move the schistosomiasis field forward I3NP indicated it could be outside public health policies that are influencing the direction of the field, rather than a scientific agenda dictated by the schistosomiasis community:

> …there has been…an open research group to determine the score for determining the sort of research priorities from the public health agenda rather than from any other sort of agenda…So I think that's sort of that agenda has been pushed by the success of the control programmes, …it actually sort of came from not quite the research community sort of it came from the public health community. (I3NP)

I10P went as far as to say that scientists needed to engage with policy makers to help move the field forwards:

> …I think absolutely we need regular joint meetings not only between scientists but between science and policy makers and eventually industry people this is absolutely essential… (I10P)

As well as health policy influencing the scientific agenda, a couple of other participants indicated that the public and lobbyists may be directing research policy, for example:

> …the European Union you might say they're a stakeholder that they've already taken their point of view because they're being pressurised by the general public the voting public not to support working on primates…I think that they're taking more of just a reaction rather than to actually thinking it through…And I think as soon as you get into the stakeholders there's obviously the politics therefore lots of lobbyists who suggest you know saying this should be the case or that should be a case and…the stakeholders aren't completely independent in that sense because they've got people they're having to listen to. (I7NP)

Participants talked about economic limitations that specifically affected their ability to choose or use certain models. In particular, primates are perceived as expensive, and this can outweigh their scientific utility:

> … But working with baboons is much harder. They're more expensive, it's harder to get the funding. And so whilst I consider the baboon a much better model it's harder to get the data. (I6P)

This view was also expressed to a lesser extent regarding animal models in general. But expense is not just limited to animals; the vaccine strategy that can be pursued is constrained by financial costs associated with it:

> …But you still have the problem of keeping the damn things alive for long enough you know to distribute them to 200 miles from… It's gonna be expensive, that route. (INP)

There is some suggestion that whether a scientist uses a particular model or not may be decided by what facilities or animals are available to them. This may be especially true of primates as this participant recounts:

> …I think whether people use primates or not depends on availability the colleagues of mine who I know have worked on primates it's because those primates are actually available… And those people who haven't worked on primates it's largely because they're working in environments where they couldn't get access to primates… (I7NP)

I2NP further illustrates that logistical constraints might overcome the scientific utility of a model, in this case whether there are have adequate facilities for larger animals:

> …because it works absolutely fantastically in a pig and you know if you got the facilities to give a pig a nice house…that might be fine but you know if

> you're in a hospital you're not gonna have a herd of 40 pigs downstairs but you may be allowed 40 mice. (I2NP)

In summary, these responses indicate some perceived influence of policy, which can be positive for moving the field forward. However, others viewed policy more negatively because it can mean that an avenue of research persists even if it is not scientifically plausible. One respondent felt the public/lobbyists may be having too much influence by making knee-jerk political decisions rather than decisions based on facts. The data suggest that logistics and economic factors may be having more impact on the research agenda for these participants, as these factors were mentioned more than the political effects.

Alternatives

When making recommendations for overcoming the primate impasse it is crucial to establish whether there are alternatives to primate models currently available, or whether they could be developed. Therefore, participants were specifically asked about their thoughts on this.

The majority of participants (7/10), including both types of user, did not feel it was possible to replace primates completely in schistosomiasis research. However, many commented that their use could be confined to the later stages of testing prior to clinical trials, and alternatives could be used during the developmental phases. For example:

> …it's possible I think to a good extent…I don't think they would be necessary to use during the early developmental stages…I think there are a series of models…rats and mouse, in vitro or whatever and screening past human

> populations if you need that sort of information…Before you got to primates. I personally don't think that you could go in to humans before you went, without primates. (I9P)

Some participants were particularly adamant that it was impossible to replace primates but this was not confined to primate users as might be expected. In particular, INP, I7NP, I6P and I10P were unable to envisage not being able to use primates even when they were asked to theorise a situation where no primates were available, for example:

> There is no…I can't conceive of that situation arising ever, because I can't conceive of any new drug being used without having gone through the fullest… (INP)

Two of the three participants who did not give an outright 'no' were non-primate users (I2NP and I3NP), and they were uncertain as to whether it could be achieved or not. For example, I3NP gave several examples where they felt primates could be replaced or alternatives used, but towards the end of the interview seemed less certain, giving the following response when asked if a ban on primate use would impact on the field:

> I don't think so…although I guess I would hold the proviso that it would be if at some point in the future if somebody did come up with a really good vaccine that for scientific reasons which I don't quite know what they are would require primate use it would be a shame not to be able to do it I suppose. (I3NP)

The final participant (I8P) had used primates in the past but seemed sure progress could be made without them. I8P made several references to using pigs as alternatives to primates for example:

> …So that is one of the species which one could argue from the point of view of vaccine development, drug development might be the best way of avoiding using primates…that you could test those things in pigs. (I8P)

However, I8P was also conscious of their limitations, such as the possibility they may self-cure or that ethically it may not be any better to use the pig than the primate. I8P was not alone in considering the pig as possible alternative in at least some circumstances, as I4NP and I10P also mentioned it.

Additionally, I8P posed the potential for precedence in similar fields for taking vaccines straight into human trials and bypassing pre-clinical primate studies, for example:

> …in elephantiasis there is no relevant primate model so they have to test in cattle or straight in humans. You should check current practice in other areas with regard to what is done when there isn't a suitable animal model or intermediate animal model. (I8P)

Hookworm was given as another illustration of this, although I8P did note some problems with the models used, and I9P mentioned there were problems with the resultant clinical trials. Despite the described problems this does illustrate that the perception held by the majority of participants in this study, of primates *having* to be used pre-clinically, may be misplaced.

In summary, the majority of participants argued that it would not be possible to completely replace primates in schistosomiasis research. They placed particular emphasis on necessity at the end stages of the vaccine process prior to entering into clinical trials. This challenge may be due to safety fears and/or perceptions about regulation which are discussed in section 4.4. However, the inability by some even to

imagine not being able to use primates may indicate that their use is entrenched in this community, making it difficult to change to a different model. Collingridge (1980) discussed 'entrenchment' as the process by which a technology becomes firmly embedded in its use context, particularly through the establishment of supporting institutions or infrastructure, systemic interdependence, economic advantage, shared evaluations, and their mutual reinforcement. In doing so he highlights and accounts for the difficulty of removing, changing or controlling the technology. The lessons learnt from Collingridge's case study of entrenchment of technologies, namely that change is expensive, change is hotly debated and that in debate the status quo has an unfair advantage, may be able to explain why primate experiments have become the status quo and remain so.

It could also be that the alternatives have not been, or cannot be, developed for this final stage of the process. However, the responses of the two uncertain participants and of I8P above indicate that this is less likely to be the case.

Practical Science Conclusion

These findings indicate that, for schistosomiasis, the practicalities of doing scientific studies can impact on how that research is conducted and what decisions scientists make about which models to use. Participants openly discussed the scientific reasons why they do or do not use the various models available for developing a schistosomiasis vaccine. While it is not surprising that they would want to be seen to be conforming to the scientific norm or institution, what is most useful, is that not all the reasons given in the interviews are apparent from the peer-review literature,

indicating that scientists are more aware of the limitations of the science than they portray in publications.

Participants used the research question as a way to justify their model choice. There was explicit conflict about which overall research aim to follow but each one appears to persist. While there was evidence of a direct influence of policy, participants seemed to be more concerned about the impact that financial and logistical factors might be having on the direction of the field and which research was being facilitated. However, consideration must also be given to the subtle interplay between policy, economics and logistics, which was not explicit in these responses. In terms of alternatives to primate testing most participants felt that progress could be made without using primates during the developmental stages of vaccine research but that they would still be necessary during the end pre-clinical stage. However, there was some indication of precedence in other similar fields where primates had not been used in this manner, so the reluctance to accept that replacement might be possible could be related more to entrenchment and perceived need than an actual deficiency in alternatives.

4.4 Animals and Ethics

The third theme identified is animals and ethics. This involves talk about implications related to personal choices about animal use, the choice of species and the choices made by other parties. As the title suggests, ethical considerations are brought into play in each of these factors.

Personal Choices

When participants talked about model choice or dealing with the moral challenges of biomedical research there were several instances where they explicitly mentioned justifying the research to themselves, for example:

> …I think any scientist and any person obviously weighs up the costs and benefits in an ethical sense. And have to justify it to themselves…animals and humans for me have to weigh up personally against my personal morals and ethics… (I9P)

Participants indicated how they achieved personal justification. One particularly interesting and different response was given by I6P who seemed to be using humour about the nature of the animals to justify using them:

> …inevitably if you think about it the more distance the model is from us the less you're going to have qualms about it, it won't look like us, it will bite you. It'll smell horrible you know it won't be attractive. But it is you know a cute little baboon, Toto, then you know you clearly you must have feelings or qualms about what you're doing. And that doesn't hold for adult male baboons {laughs}, which are probably one of the most unpleasant creatures you would ever want to meet {laughs}. (I6P)

Some emphasised that the model they had adopted was ethically acceptable:

> Again it absolutely depends on what you're doing. I mean I would say what we're doing is not morally challenging but it's morally the opposite of challenging… (I2NP)

Others emphasised an awareness of, and action to meet, the health and welfare needs of their experimental animals:

> …at the moment policy is changing for animals we treat animals very carefully…Yeah as well as possible because at the moment very aware of the health of the animals particularly of cattle. (I4NP)

I7NP went further than their own treatment of animals feeling it was necessary for them to teach students to be more aware about the effort needed to look after laboratory animals:

> And it's something that I'm very keen on when we're dealing with students who do research projects in our laboratory that we insist that they go on the animal training course. Largely so that they get a much better realisation of what they're doing…they can actually realise that this [mouse] is not just something you can pick off the shelf and actually use. It is something that you have to put effort and energy in to looking after and it's a precious resource. (I7NP)

Another aspect is where participants place personal boundaries on what they are and are not willing to do. For example, the following participant's squeamishness means they would alter their work so they didn't have to use certain species. Intriguingly they see this as irrational, perhaps because it does not have a 'scientific' basis:

> I have pet cats and would feel uncomfortable using cats in research but I suppose that is irrational or hypocritical to just pick cats and dogs. I would choose not to go into that field of research and I would choose not to go for grants involving primates…I would be happier working with cattle and sheep…but it is not really rational. **(**[NR]I8P)

Importantly, there are some examples in which perceived ethical concern appears to have overcome the scientific utility of some animal models. I8P describes the abandonment of the cat as model for a different disease but it illustrates that this type of reaction can occur within this realm of research:

> We did have a group here working on cats when I first came here working on elephantiasis…the animals were recovered they sometimes of course they had to be dissected and worms taken out…Because of that people are reluctant generally to work on cats. That model is not since that time has not been worked on by anybody even though it's a very good model. (I8P)
>
> MH: Do you think that is because of the pet aspect of it?
>
> I'm sure it is, yeah. And I think that has delayed advances in that field. (I8P)

Secondly, I5P and I6P gave an example from schistosomiasis where ethical concerns related to experimental use of chimpanzees have, led them to the decision that, despite having used them in the past, they now feel they cannot. They make this choice even though, as the quote illustrates, they class chimpanzees as the best model for the job:

> Well I think the great apes…and I can say that having used them, great apes so yes it's something that it goes round in your head as to just how intelligent they are. How alike we are they are the best model without a doubt you know their physiology, the reagents work…So I wouldn't want now to go beyond that. (I6P)

In summary, these responses indicate it is important to participants to justify their work to themselves. They provided some examples of how they do this and suggest that they have personal limits as to which models and what type of research they will do. In some cases these limits appear to outweigh the scientific utility of a model. Birke *et al*. (2007) also found that research scientists and other lab workers often made reference to drawing a species or scientific technique line somewhere. They argue that, in order to cope with the moral dilemmas associated with animal experimentation, scientists have to learn to distance themselves from the animals they use by objectifying them as tools or data. However their findings, and those presented here, indicate that this does not always work and scientists are increasingly

acknowledging a relationship between the experimental animals and humans. Birke *et al*. (2007) summarise this ambivalence well:

> …however well they learn the psychological mechanism of distancing and treating the lab animal as just another tool of the trade, there is for many lab workers a naturalistic animal – a furry friend – there too. (Birke *et al.* 2007, p.107)

Choice of Species

Beyond the personal limitations on species choice noted above, throughout the study there are examples of participants differentiating the ease with which they can decide to use one species or another, or whether to use a species at all, with primates generally being given much greater consideration in one form or another.

When asked about knowledge gained from animal models I8P expresses more consideration toward whether or not to use primates – describing this as a dilemma rather than a simpler decision, as it seems to be with mice:

> …I mean there are people who will be testing things identified from that model natural immunity in humans, from that circumstance in mice… And I guess had that worked in mice really well then they would've then been faced with the dilemma of where do we go to next with this. (I8P)

As well as talking theoretically about species difference, it can also be seen in participants' descriptions of their actions. For example, here there is a difference in ethical consideration even between primate species, as chimpanzees were not sacrificed at the end of the study as a baboon or other animal would be:

> That wasn't possible in the chimpanzees for ethical reasons. So what happened at the end of the experiment is that the chimpanzees were treated in the same way that people would be treated that had schistosomiasis and then they were returned to the colony. (I5P)

In addition to putting species choice into an ethical context several participants specifically indicated that they were more comfortable working with rodents or livestock, for example:

> …I think you can actually more legitimately use those sorts of large experimental animals to be able to do your tests and in fact in the literature you do see a number of experimental vaccines being performed in cattle and pigs on those sorts of things. But I don't think it's as easy probably for ethical reasons to say let's just do all of these experiments in primates. (I7NP)

I2NP clarified why they were more comfortable with certain species by highlighting that it was easier to meet the needs of some species over others:

> I mean I'm not specious [sic] I think yes primates you know it's long lived and stuff like that but you know when the regulations are like against dogs and cats and horses because they're peoples pets I think you know a rat is somebody's pet and they're just as important…the advantages may be you can have the facilities to give them a good size house and accommodation…one has to be careful not to be specious thinking you know primates then you know dogs, cats are not necessarily higher than each it's what facility they can do and what benefits they would give. (I2NP)

Further indication that primates perhaps receive greater consideration was that the emphasis on the degree of necessity and scientific justification required to decide to use primates was higher than for any other species. For example, INP would need extensive evidence from other species before using primates:

> …what we would do is check it against mouse infections…then our route would be to do larger animal work…so in sheep or cattle…and then having

> done those one…could use those as justification for doing some primate experiments… (I1NP)

One participant even felt that special collaborative programmes should be in place before using primates:

> …So I think that you would be at an agreed end stage and I think you know to use primates in this context it would have to be one very very strong candidate…you'd wanna do it with some large scale collaborative programme… (I9P)

In summary, it appears that for various reasons many participants gave more consideration to the decision to use primate models over other models, whether they personally use them or not. They seem to be more comfortable working with other species such as rodents and livestock, as they do not flag up as many – if any – concerns about the ethical dilemmas or strong scientific justification that they indicate considering when thinking about primates. As I2NP hints at above, this may be a form of speciesism in action. Singer (1995) proposes, '*speciesists allow the interests of their own species to override the greater interests of members of other species*' (p.9). Here participants identify that they appear to exhibit speciesism towards animals such as rodents and cattle by giving them less consideration than primates. Although the participants have described it as such, this is not strictly speciesism as Singer (1995) defined it because if it were the participants would not give consideration to any of the animals. Instead, this more closely illustrates a sliding scale model (DeGrazia 2002) where animals are given consideration proportionate to their cognitive, emotional and social complexity, and perhaps in this case their relationship to society. This may make it easier to propose alternatives to primate models, including using other species.

Influence of Other Parties

Participants talk about the influence of other parties such as other scientists or regulators on the decisions regarding which experimental model to use. They do not see themselves as working in a vacuum, and comment on the ethical decisions about research made by other parties to justify their choices.

For example, I5P felt that a colleague found it much easier to suggest primate studies because they were detached from the actual work:

> …I think the primate work particularly got to me in a way that it didn't necessarily get to {name omitted} because of the fact that he wasn't the person at the coal face. (I5P)

When asked about the moral aspect of biomedical research, I7NP indicated they would be happy for other people to conduct the primate work but they would not want to do it themselves:

> I would feel uncomfortable dealing with primates for example. I feel less of a problem dealing with small rodents because I think they're telling me something which will feed on in to greater studies that other people will be more equipped to deal with rather than me. (I7NP)

As well as other scientists doing the work that might be ethically troublesome, participants also used the acceptance of peers and/or communities as a means of making the ethical decision for them or validating their choice. For example, I7NP and I9P both indicated that there should be scientific community agreement to use primates, so again displacing the ethical choice to one they are not personally responsible for:

> …I wouldn't want to just raise the money and go off and start sticking things in to monkeys myself I'd want it to be part of what the community considered to be a good thing and to be a worthwhile investment both financially and ethically. (I9P)

Participants did not explicitly state that it was society's place to decide whether animal experiments were morally right, but there was indirect suggestion that some participants were displacing the ethical choice to society. For example, by giving public acceptance as validation for the work they do:

> …it's very easy to justify to myself in terms of whether it's a worthwhile activity but it's also I think relatively easy to justify to in a more general sense to the public…and people are always interested…yeah people like what we do and I liked that fact…(I9P)

There was a suggestion that the choices of the communities affected by the disease should be taken in to account, so the moral decision is theirs:

> **…**The views of those suffering from the disease should also be taken into account. When their children are ill they would be happy for a treatment to be tested on a few mice. ([NR] I8P)

Another common strategy was to defer the decisions to regulators by using rules controlling animal experimentation as means to justify the research, with the indication being they are very tight; so if the work was deemed to meet the requirements demanded, then it must be justified. For example, when asked about emphasising reasons for model choice INP explained it has to be justified for regulatory acceptance, and when pressed further, the arguments presented have to be very good to meet the requirements:

> Unfortunately for that, perhaps rightly for the Home Office one has to produce strong arguments. (INP)

A second participant also highlights the complexity involved with regulatory acceptance by referring to the cost/benefit process that has to be performed; thus attempting to strengthen the validity this brings to the animal experiment:

> … I think any animal model where you can't see clearly the benefits that are likely to ensue would be unacceptable, but I mean given that [the] majority of the work that is done in the UK is done through the Home Office and you have to go through the cost benefit analysis I don't think there's anything that I could say shouldn't be done… (I5P)

I10P went as far as to say that the regulations mean the experimental animals may be treated better than some patients, so inferring the restraints imposed by the regulations tip the ethical balance in favour of the experiments.

I2NP expressed the view that, regulation might in fact be a means to encourage or even force scientists into greater ethical consideration particularly regarding primate use:

> …I imagine they're gonna have to use primates. But I think making it very difficult and regulating…I think these rules are very good and it will make people think twice about you know are there alternatives… (I2NP)

Some participants explicitly indicated getting funding validated their research choice:

> Our funding came from the European Commission and you know obviously at that time they thought it was appropriate for this work to be carried out it was all peer reviewed. (I5P)

As well as deferring the ethical choice to funding agencies indirectly, two primate researchers and a non-primate user indicated that funders have directly influenced an apparent shift away from experiments on primates. They noted that primate studies used to attract funding, but now funding agencies do not want them to be included in grant applications:

> …To encourage the field and you know get funding in and provide proof of principle, I think indeed those studies in primates did serve to bolster the field and encourage investment at the time. (I8P)

> …in the European Union there is such an antagonism to doing experiments with primates that I'm actually being steered away from that by people in the European Union say don't put this in to your grant application because we in the European Union don't like it. So in a sense the feeling is sufficiently strong to therefore them to tell me that in advance of submitting a grant. So I have taken it out of the grant and I'm not doing it as a result. (I7NP)

In summary, it appears that in order to justify their research choices, participants adopt a strategy of deferring the ethical decisions regarding experiments on to other parties such as other scientists, regulators, funders and to some extent society. Michael and Birke (1994b) identified that:

> …scientists distinguish themselves from a multiplicity of "others" and use the contrast to present their own practices of animal experimentation in a positive moral light (p.191).

They found that scientists were critical of these 'others', such as foreigners, the cosmetics industry, abattoirs, and clinicians, and portrayed them as negative in order to highlight that they are more humane, caring and morally superior. As the extracts presented above show, these negative 'others' were not apparent in the scientists' responses in this study. Instead they focused on the role these 'others' played in

determining the justification for and direction of scientific decisions. This indicates it is important to address the influence that 'others' as well as the scientists engaged in the experimentation might have when considering impacts on decisions about research direction, policy or recommendations.

Animals and Ethics Conclusion

This analysis indicates that participants attempt to ethically justify their research choices to themselves, and have personal boundaries that they do not necessarily class as rational. In some case these limits have outweighed the scientific utility of a model and they have ceased to use or avoided using it. This is indicative of the ambivalence that Birke *et al* (2007) noted when scientists attempt to objectify the animals they use to make it easier to justify their work. Participants expressed inconsistencies in how much consideration they gave to different species, with the decision to use primates seemingly needing greater justification and more thought than for other species. This 'speciesism' needs to be considered when proposing non-primate alternatives and in understanding why primates are seen as the very last resort in testing. There was evidence of participants distinguishing 'others' as being responsible for the justification for making certain decisions about experimentation, but this was not indicative of the critique of disreputable 'others' observed by Michael and Birke (1994b). Ethics, speciesism and 'others' are all important for understanding the impasse (Chapter 6) and in making and implementing the recommendations for overcoming it (Chapter 7). The ethical discussions were not restricted to animals; participants also talked about ethics in the context of patient health, as outlined in the next section.

4.5 Health and Ethics

The final theme of this analysis is Health and Ethics. Participants tended to talk about factors related to the impact of the disease, and the controls surrounding treatments for disease in the context of validating their research and justifying some of their choices. As in the previous theme these factors were discussed in practical and moral terms, this time under the sub-headings, disease severity, safety and regulation.

Disease Severity

Descriptions of the problems associated with schistosomiasis were used extensively by participants as a justification for their research. Seven participants discussed this, especially primate users, with five of the seven instances being from them. The following is a typical response:

> There are 200 million people infected with schistosomes you know this is the starting point of an argument why I should be doing this work. There are 200 million people infected there are 600 million people at risk the estimates of the number of people dying ranges from you know the thousands to the tens of thousands to the hundreds of thousands of people dying... (INP)

These responses exemplify the use of 'Sickness Narratives' in biomedical research. The term 'sickness narratives' was used by Brown (2003) to describe the telling of stories about the precarious futures of individuals who are desperate for treatment as a means of promoting technological advances, gaining research space and resources, and justifying morally challenging research. In venting irritation that certain 'Western'

diseases get the lion's share of funding, INP is illustrating how sickness narratives are utilised in an attempt to acquire resources for research:

> As we are doing about cancer research and heart disease and Alzheimer's and arthritis and multiple sclerosis and so on, other very debilitating diseases, there's plenty of money being spent on them there's plenty of animal research being done on them just because these people are poor…should not the same attention be paid to the disease that they are suffering from… (INP)

I9P emphasises the importance, to them, of ensuring a 'happy' outcome to the sickness narrative they use. They are keen to emphasise that those indicated as suffering in the narrative need to be engaged with the research, in order for it to be successful and accepted:

> …I mean if you're working in a village you have to make sure all the people in the village benefit from it you know…I mean you have to come away from a place saying not only have you found out things which were important to do and justified your time and money and everybody else but you've also actually they end up coming out the people are healthier and the people happier. (I9P)

Brown (2003) notes that combining expectations with the pathology of disease as sickness narratives '*takes place at enormous cost to those who, for however long, are persuaded to share in the hope*' (p.8). Therefore, I9P's emphasis might be a means of protecting those who stand to suffer the highest costs if hype and expectations surrounding the narrative fail to be realised.

Interestingly, one of the participants who did not use sickness narratives in their account expressed concern over their use:

> …yeah definitely that's although I think you can overstate that [impact of research]. Because I mean you can say that for any work on schisto whether or not it's likely to actually do anything useful… (I3NP)

In summary, this extensive use of sickness narratives may be related to the size of the field and the low awareness of the disease outside the schistosomiasis community, which as outlined in previous sections seems to result in limits on available funding, high competition for resources and difficulty getting acknowledgement for the benefits of the research. So participants may be attempting to improve awareness of the extent and severity of the disease in order to generate interest in their field, to garner resources and better understanding (Brown 2003). In the documentary analysis (Chapter 3) there were indications that some anti-primate authors, particularly in schistosomiasis, were not as effective as pro-authors at building expectations and winning the 'competition' for acceptance of their claims. In a similar vein, perhaps I3NP's response to sickness narratives and the limited use of them by non-primate users indicate that alternatives scientists have not yet perfected the approach of primate users to acquire resources.

Safety

When questioned about the possibility of completely replacing primates in schistosomiasis many participants (both types of user) expressed concern that this would lead to safety issues when giving candidate vaccines to volunteers and eventually patients. There were issues raised about the safety of certain therapeutic strategies, the impact of public perception of risk, and differences in international views on science, all of which could influence how they and others justified their research.

Several participants were concerned about the increased risk of adverse effects in human volunteers in clinical trials, and in the target patient population. This fear was expressed by non-primate users who in general did not think the primate was of great necessity for the majority of research in this field. For example, I7NP did not feel methods could be developed or improved to facilitate replacing primates, and one reason for this was safety:

> …we would have to therefore be very much more take leaps in the dark with respect to if we're going to progress through having an intervention strategy in humans. So therefore it would put the human guinea pigs or volunteers usually in those sort of phase 2 phase 3 trials very much more at risk (I7NP)

However, one exception was I6P. When asked specifically about finding another way to test the safety of vaccines they changed the focus of the discussion to the scientific aspects of why the primate was needed, indicating that, for them, safety was not an important reason for using primates.

Another related aspect expressed by several participants was concern that the type of therapeutic strategy might cause harm to patients and volunteers, for example:

> So if you immunise with this are you going to produce immune responses that would be deleterious?...For the human GST?...And in particular for instance a possible cross reaction with one class or such class of GST in humans that are essential for reproduction? So we have to be extremely careful about that and to perform a number of studies… (I10P)

Despite the concerns over this riskier strategy it was still being actively researched and at the time of the interview had moved into Phase III clinical trials.

I7NP made an interesting point that perhaps changes in public perception of risk have altered the level of testing and justification required before therapies can go into humans:

> …their understanding of risk and I think it's something that general public have a very very poor understanding of…one of the things is say if you took a vaccine and one in a hundred people will die as a result of the vaccine is that too big a risk? And most people will say it's too big a risk but on the other hand then you think if we went back 200 years to Edward Jenner they weren't really aware of one in a hundred they would think if 99 people were protected against smallpox that was a very good risk…But in today's society we think of that as being a very bad risk… I think that also goes through to using animals in scientific research understanding what the risk is or the benefits are… (I7NP)

In summary, these data indicate that participants may be reluctant to say that primates could eventually be replaced due to perceived safety risks. Despite these safety issues there is precedence for other anti-parasite vaccines going into human trials without primate pre-clinical data (section 4.2). This, in conjunction with examples wherein the risk issues raised about certain therapies *did not* lead to the research in those therapies being abandoned, suggests that safety might not be as big an issue as first indicated. This riskier approach could be related to the relatively high level of competition in this field (see 4.1) and the perception of losing out to other fields in terms of funding (see pervious section), because Barber *et al*. (1979) found in the case of research on human subjects that '*...researchers who did not do well in the scientific or in the local-institutional competition for rewards were more likely than others to be involved in studies with less favourable risks-benefits ratios for subjects*' (preface).

Regulations

While safety and risk underpin many regulations participants did not discuss legislation in this context. Instead participants focused on the role of regulation as a justification for primate research being conducted and for why it could not be replaced. These discussions centred on regulatory requirements to use primates, the level of regulatory control and a concern over research moving to countries with less stringent rules.

Some participants argued that primate models would eventually have to be used at the end of pre-clinical testing in order to satisfy regulatory requirements for conducting clinical trials, for example:

> …but I just don't see the regulatory authorities allowing any drug to go anywhere near a human if it hasn't gone through the fullest and to me that includes primates. (INP)

Some participants commented on the strictness of the regulatory controls regarding primate experiments, suggesting that they saw this as a way to validate the primate work was necessary:

> …When you start doing human experiments…you need to have a big file where you have to show that this vaccine has shown such and such properties in such and such animal species…in fact it's very difficult nowadays to get the permission of moving to humans because you have to go through an ethical committee you have to go to an executive committee and so on to get the permission of doing that without a number of arguments. (I10P)

In relation to this I2NP and I7NP expressed concern that researchers will move to conducting their experiments in other countries with less stringent controls:

> …it's such a shame because the regulations on animal use in Britain is so tight…it's great that people are aware and you know absolutely great that there are limits on what can be done but if it gets pushed too much the last thing you'd want is to push the science to other countries where you don't have these regulations… (I2NP, participant's emphasis)

I7NP thought that primate research could be stopped in Europe but cautioned that this would lead to it being conducted in other countries or by collaborations with researchers in those countries:

> I think you could remove primates from schistosomiasis research now…because it would be done in other continents…The Americans would continue to do it or Chinese or other nations…you would stop the use of primates in the European Union but you see the people who have an interest…seeing their work continued would just develop collaborations with other nations…Which maybe is a good thing. The downside is that with a lot of these other places for doing primate research don't have very strong control mechanisms…you are then leading into a weakening of the control of the experimental system on those animals… (I7NP)

In summary, these responses indicate that regulations are not seen as a challenge to conducting primate research, instead they are used as validation that the work must be necessary. There was concern over research being moved abroad where standards are lower and rules are less stringent, and this was used as a reason why primate experiments should not be completely banned. Similar responses were found by Birke *et al*. (2007) when they found that scientists were often explicit about being the 'good guys' by highlighting poor practices and less restrictive regimes in other countries. This is interesting from an ethical and scientific point of view because if primate studies are deemed as not being necessary/justified in Europe or if the standards abroad are unsatisfactory, would the scientific community be willing to accept the findings from such studies? This will be explored further in the second case study (Chapter 5).

Health and Ethics Conclusion

These findings indicate that factors relating to health, safety and regulations are used by primate and alternative users to justify their research, but there were some differences in how the various participants viewed these. Both types of user provided statements that can be classified as sickness narratives (Brown 2003), but primate users did this extensively, possibly because of the impact of competition and limited funding in this field. Safety initially appeared to be a significant challenge to replacing primates for both types of user. However, participants' examples of other vaccines being developed without primate data and risky therapeutic strategies not being abandoned suggests that in practice safety is not a major limitation. The data indicate that regulations are not seen as a challenge to primate experimentation but are in fact given as validation for the necessity of the work. The threat of work having to move abroad to less stringent countries was also given by some participants as a reason why primate use should not be banned. The differences in approach between primate and non-primate users and the impact of regulations are all considered in the recommendations to overcome the primate impasse (Chapter 7).

4.6 Conclusion

In conducting this analysis the aim was to access the views of primate and alternatives scientists regarding the opportunities and challenges of using primates in this field. This data has allowed me to look in more depth at the theoretical themes indicated in the documentary analysis, and to investigate whether there are differences between the work of the specialists within this field, how that work is represented, and what

impact this has on the perception of primate experiments and the possibility for replacing them.

This chapter discusses the analytical themes of: the Scientific Institution, Practical Science, Animals and Ethics, and Health and Ethics, in the context of the social dynamics of science, which explain the responses of the scientists involved in this study. The analysis indicates that scientists draw upon several factors related to those dynamics to justify their research choices and models – with some appearing to be more important than others. The data show many similarities between the responses of primate users and alternatives users, but this chapter describes that there are also some differences and highlights the possible reasons for this.. When compared to the PD case study, differences in the justifications given by scientists and how they presented them were apparent and are described in Chapter 5.

Within the theme of the Scientific Institution, participants indicated that competition was important and seen as more of a challenge than an opportunity to getting their knowledge claims accepted and for moving the field forward. This appeared to be related to the perceived low profile of the disease and paucity of collaboration due to fear of being anticipated (or scooped) by another researcher (Hagstrom 1974). Primate users were more positive about competition with non-primate users, seeing it as more of a problem for progression of their research. The participants' responses indicate an interplay between reputation and competition, with Merton's (1968) 'Matthew Effect' possibly explaining why those viewed as having the greatest reputation (in this case primate users) fare disproportionately well in the competition for resources and acceptance. Another important challenge revealed by the analysis was the lack of

established data for alternatives, as primate users strongly emphasised the existing knowledge related to their models. A further problem identified by both types of user was the lack of opportunity to publish negative results. Indeed, ter Riet *et al*. (2012) found that not publishing negative results appears to be prevalent in laboratory animal research and argue it is conceivable that:

> …non-reporting of "negative" research findings may hamper progress in laboratory animal research through unnecessary duplications of experiments and may lead to premature first-in-man studies. (p.1)

They suggest some possible solutions to this publication bias problem that will be explored in Chapter 7.

As well as challenges, participants identified some opportunities that were influencing the acceptance and direction of their research. These responses indicated an association between Collins' (1988) 'core sets', expectations in the form of hype (Brown 2003) and publication. They noted the importance of gaining acceptance from peers and of using publication to overcome problems with getting novel ideas accepted. However, a core group (Collins 1999) of primate researchers is dominating which knowledge claims are accepted and is limiting publication via peer-review. Several saw hype from media publication as problematic, but it was acknowledged that 'sexing up' or selling their research was a means to getting it published and accepted.

In terms of Practical Science, as would be expected, 'scientific' considerations were often given as justification for model choice. While the benefits of models were given more readily, participants seem to be very aware of the limitations of their models,

and are willing to discuss them even though they rarely appear in the peer-reviewed literature. The analysis indicates that research questions are used by participants to justify their model choice, and emphasis is placed on only the most important questions requiring primate studies. There is conflict over the best research aim to follow, with enchantment (Hedgecoe 2006) and publication bias perhaps preventing schistosomiasis scientists from identifying the best way to progress the field. In addition, this theme highlighted that the concept of entrenchment (Collingridge 1980) might explain why the idea that primates will be necessary for the final stages of the vaccine process persists, despite examples from other fields of research indicating that this is not always the case. External, rather than science, policy was perceived as driving the scientific agenda in this field, which was being influenced by the public and lobbyists, sometimes to the detriment of progress in finding a vaccine. Logistical issues were also identified as being problematic when using primates and other animals. In the PD case study it can be seen that there are subtle links between entrenchment and policy that are not so evident here (Chapter 5).

The Animals and Ethics theme revealed that, like those in the study by Birke *et al*. (2007), participants here have personal boundaries as to which species they will use, and these can act as challenges to conducting certain studies. This is linked to more consideration being given to primates and a kind of 'speciesism'. An important aspect to note here that was not included in the main analysis was that several participants spontaneously discussed the Three Rs concepts either explicitly or in descriptions of their actions. This implies that this concept may be an important means by which scientists justify their methods implicitly to themselves. Another important finding is that participants talk about the influence of 'other' parties such as other scientists or

regulators on the decisions regarding which experimental model to use. However, they did not talk about 'disreputable others', as scientists in Michael and Birke's (1994b) study did – with the possible exception of the public who misunderstand. Instead they focus on the role the 'others' play in providing justification for certain areas and types of research. A particularly interesting aspect of this was that European funders appeared to have shifted their emphasis away from primate studies, leading to them no longer being conducted. These 'others' are considered in Chapter 7 as they represent who or what else could be influential in affecting change in scientific attitudes or the course of the research and, as a consequence, in implementing the recommendations for overcoming the primate impasse.

The final theme of Health and Ethics raised two seemingly important challenges to completely replacing primates in schistosomiasis. Both types of user gave safety concerns as a reason why primates would be needed, particularly at the end stages of vaccine development. However, this seems less important when giving further consideration to the actions of the scientists continuing to work on strategies that raise safety concerns, and the precedence in other fields for pre-clinical primate studies to be by-passed. It may also be related to the regulatory requirement to use primates. Several participants including both types of user said they thought that regulations stipulated that primate data were needed before going into clinical trials. Therefore, regulation was framed as a challenge to replacing primate studies, including raising concern that the research would then move abroad to less stringent countries. The analysis again indicated that expectations in the form of sickness narratives (Brown 2003) are important for understanding why primate studies persist as the status quo. Primate scientists use sickness narratives more extensively than non-primate users.

There could be several reasons for this, which are considered in Chapter 6. For example, the primate work may be perceived as more controversial so needing stronger justification through emphasising how important the benefits are, or that the alternative users perhaps need to use this approach more to gain resources for their area of research.

This analysis reveals what scientists in schistosomiasis vaccine research identify as the main opportunities and challenges to their research, in particular their model choice. It indicates the factors which are important for the final phase of the project. These include the need to consider engagement with funders, policy makers and possibly lobbyists, and tackling entrenchment/regulatory perceptions about end stage use. The data from this and the next chapter also identified that some of the challenges and opportunities may be field dependent, and that different approaches will be needed for some aspects of the recommendations to overcome the primate impasse.

The next chapter presents the analysis of the interviews from the second case study looking at PD research, where the same themes were identified, but important comparisons and contrasts between the two cases are described.

Chapter 5: Case Study 2 – Parkinson's Disease Research

5.1 Introduction

This and the preceding chapter provide an analytical summary of the data that were collected in the semi-structured interviews described in Chapter 2. It reports findings from the second case study on Parkinson's disease (PD) and builds upon the documentary analysis (Chapter 3). Once again the participants' responses are presented in four themes: the Scientific Institution, Scientific Practice, Animals and Ethics and Health and Ethics. However, there are some differences in emphasis between this and the schistosomiasis case, which are highlighted within this chapter.

PD is a chronic neurodegenerative disorder leading to severe motor impairments and cognitive dysfunction. In industrialised countries PD is estimated to affect 0.3% of the entire population (de Lau and Breteler 2006). Parkinson's UK (2012; formerly Parkinson's Disease Society) estimates this to be 120,000 people in the UK. Since the 1960s, L-DOPA, a dopaminergic agonist drug, has been successfully used to treat PD. However, L-DOPA merely alleviates the symptoms of PD, can cause side effects and becomes less effective over time. This has led to other symptomatic treatments, such as other drugs, surgery, and dietary and rehabilitative management.

5.2 The Scientific Institution

As in the previous case (4.1), PD participants justified their research using underlying factors that influence how science is done under the Mertonian inspired theme 'Scientific Institution'. Again, data is presented under the sub-themes of: competition, reputation, knowledge acceptance and publication. Many PD responses echoed what was said in the schistosomiasis case, but some important differences were apparent in each sub-theme. Additionally, there was less distinction between the answers given by primate and non-primate PD scientists than there was between the different types of schistosomiasis users.

Competition

Chapter 4 identified that competition in science is an established concept (Bonitz and Scharnhorst 2001), and according to the interviews it is affecting the field of schistosomiasis research. PD researchers view competition as an influencing factor, but its impact seems to be less prominent.

As in Case Study 1, competition was seen as hindering progress in PD. Several participants discussed the problem of people not wishing to reveal their unpublished or new ideas due to the competitive nature of science, expressing this as a fear of being '*anticipated*' (Hagstrom 1974 p.2), for example:

> I think they're [working groups] useful to some degree <u>but</u> scientists are very secretive by nature Nobody is going to tell an audience of their very latest ideas the data cos you can't trust your colleagues to be quite frank. You learn

> the hard way that it's a very competitive world and that people will steal your ideas. So usually there's almost absolute ban on talking about something big in a laboratory until it's finished and you've got it in some way accepted for publication. (I11P, participant's emphasis)

In comparison to schistosomiasis, there were fewer comments on competition as a positive influence on the field, and less discussion about winning or losing the competition, with only one example from I16NP who described their research group as winning the competition for acceptance of their idea.

Fewer references to competition could indicate that it is not as influential in the PD field as it may be in schistosomiasis. Responses suggest that this may be due to collaborations between different researchers, both within and outside the PD field, overcoming the competition. Several participants commented on collaborations that they were either involved in or knew of and how, this had sometimes allowed significant progress to be made. For example, I16NP describes how the field of cell transplantation has been reinvigorated by collaboration, which has in turn attracted funding:

> That developed in to a working group on transplantation for Parkinson's disease that involved the leading people in Europe and that's now got new FP7 funding and that's now leading to a clinical trial… (I16NP)

This contrasts to schistosomiasis, where much of the discussion was about the need for more collaboration rather than it actually occurring. A factor in making this collaboration possible could be the involvement of 'core set' scientists (Collins 1981). The PD participants argued that when scientists with specific expertise were included the discussions were more open and honest, and the fear of losing a competitive edge was diminished, for example:

> …at the Parkinson's Disease Society where they've brought ten people together round the table for an afternoon where it was all signed nobody would repeat anything that moved out of the room. I probably learnt more in that afternoon than I did in the last two years about what people do where they're trying to get to and how that fits in with everybody else. (I13NP)

There was evidence of some reluctance even within the core set to disclose some information, which I19NP said was sometimes due to certain scientists' reputation:

> …it's very dependent on the make-up of the group, because obviously if people have big ambitions then it's very hard to get them to believe that they need anyone else to fulfil those ambitions … (I19NP)

However, this does not appear to be as problematic as it was in Case Study 1, which might be expected given the greater incidence of collaboration; because as Hagstrom (1974) identified, cooperating scientists are less secretive and communicate more.

The nature of PD research could also account for competition being less prominent. As the following participant illustrates, when there are many possible solutions to the questions in a field, the competition can be less intense (Hagstrom 1974):

> …and it's [competition] worse I think if you're looking for absolute answers. So that's always been a problem in the world of genetics. If you're looking for a gene that causes x and you find it that's great if you don't find it you're the second to find it no one's interested So you know it depends what your outcome is as well. (I19NP)

One participant indicated that it could be related to how close the scientist is to the PD patients as to whether they particularly engaged in the competition, with those that are closest or active clinicians being less likely to be competitive, and to be more open about their research:

> Or it's very easy when you're working in a lab to forget about the patients so you know unfortunately you have this dichotomy I would say that there are some people who are in it and working for personal progression and then there are people like {name omitted} and {name omitted} who keep the patients at the forefront of their mind. And they're very open about their research findings and they want to just move the field forward and not to you know keep their findings close to their own chest. (I14NP)

This seems plausible as schistosomiasis researchers seemed to have less regular direct contact with patients even though several had witnessed the infection's affects.

In summary, competition is not as prominent as an influencing factor for PD scientists as it appeared to be in schistosomiasis. Responses indicate that this could be due to a greater incidence of collaboration in PD. This might be related to translational closeness to patients, which appears to be a unique observation in terms of competition theory. There were no noticeable differences between the primate and non-primate user responses as there were in some instances in Case Study 1, perhaps because PD scientists make fewer references to competition in general.

Reputation

The reputation a person has is a key influential factor in participants' explanations, in both of these cases, of why certain areas of research are more dominant, or more readily accepted than others. The participants' responses in both cases were very similar with only slight differences.

When asked if individuals with strong reputations had driven the direction of research within the field, several PD participants answered yes. Some participants indicted that the reputation of the group or institution was important in how influential they could

be in altering the direction of research, or getting their ideas accepted, which was not apparent in schistosomiasis. For example, I17P talks about how training received in certain laboratories has influenced the theme of people's research, and stated that they are more willing to accept evidence presented by a laboratory with a good reputation.

Indeed, I14NP indicates that a reputable laboratory has to validate a novel finding for it to be generally accepted:

> I mean you can have serendipitous findings that can occur in any lab in any part of the world but usually I would say it would take a sort of a more established lab to validate or verify those serendipitous findings before everybody else is going to latch on if you know what I mean? (I14NP)

There were several examples given where reputation was having a positive impact, such as in getting funding and/or publications on an individual basis, or in driving research forwards and getting outcomes for the field:

> …it was also led by a very well respected neurologist and neuroscientist and he was very active in driving it forward and keeping everyone on track… (I16NP)

This might be expected from the perspective of the 'Matthew Effect', which Merton (1968) notes may result in '*...the distinct possibility that contributions made by scientists of considerable standing are the most likely to enter promptly and widely into the communication networks of science, and so to accelerate its development*' (p.60). This is probably contributing to the observations made about those with the greatest reputations receiving larger levels of funding.

Participant I20NP made an interesting unique observation that whilst having a good reputation was a positive thing and gave the person concerned some influence; they had to actively engage with the scientific community to take full advantage of it:

> …you get somebody who's solely interested in and pursuing the scientific findings and has no interest in sitting on committees and you know talking to the funding bodies and things like that. I guess that's generally a rare individual. But yes without doubt the people who are perceived as the leaders in the field will often be there or have that perception because they are well known to the field well known to the funders well known to the journals well known to the conference organisers. So it's certainly again another sort of snowball once you start getting recognition you can often build on that and increase your influence. (I20NP)

This was an unusual response in this study but it is not unexpected, as Merton (1968) noted '*…for science to be advanced…The innovations must be effectively communicated to others.*' (p.4). In line with Case Study 1, several PD participants highlighted that while reputation can be positive for the individual or group concerned, it is not necessarily best from a scientific point of view. Avenues of research can continue despite being very disappointing, or promising areas can be ignored on the say so of certain individuals or groups, with the following being a typical response:

> Yes there's no doubt that opinion leaders lead the field there's no doubt about that. Strong driving personalities in the Parkinson' disease arena have moulded where it's gone for a long time now… that can be good and bad sometimes it will drive a field on the right direction other times it could be completely wrong to drive the field on in that direction. (I11P)

Similar to the schistosomiasis scientists, PD participants identified that scientists with a big reputation can be negatively influential via the peer-review process, by blocking the publication of research they disagree with, for example:

> I think they can have a large influence over it yes cos they often end up reviewing everything else and therefore if it doesn't necessarily agree with their viewpoint they can be quite influential. (I19NP)

Perhaps the biggest difference between the case studies is when participants discuss their views on their own or close colleagues' reputations. The primate users were very positive about their reputation, as they were in the previous study. However, in contrast there are no examples of non-primate users identifying themselves as less influential in driving the field, or building new knowledge. Indeed, this non-primate user suggests that their reputation is good and has helped with driving the acceptance of the stem cell area of research:

> You can normally judge it by the number of invitations you get to talk about it and where you get asked to talk about it and the index is also how easy it is to publish and how much grant money you get. So cell therapies for Parkinson's disease because of the big push on stem cells has become a much more popular field. And therefore you know having been in it a long time before that began its easier to sort of have credibility in that field really. (I19NP)

In summary, the responses indicate that PD scientists see reputation as influential, and that its impact appears to be relatively similar in both cases. The findings suggest a broader applicability of Merton's (1968) 'Matthew Effect'. The main distinctions between the two cases were a difference in non-primate user PD participants' personal perceptions of their own reputation, and more emphasis in PD on group or institutional reputation. This may be due to broader avenues of research in PD resulting in a larger population of scientists engaging in research in this field, as opposed to schistosomiasis. Consequently, it could be easier to establish a reputation as an individual or group as less people are competing in the same area.

Knowledge Acceptance

Another factor evident in both case studies is how knowledge claims become accepted; including who needs to accept them and what form they take. This appears to be related to the kind of research conducted and the models used. Two distinct differences between this and Case Study 1 were related to public perception and novel research.

The majority of participants indicated that the acceptance/approval of their peers was important to them in validating what they had found, with some participants explicitly stating that the opinion of their peers was more important to them than the opinion or approval of the public:

> …but the public perception is not that important to me…You can't really give the level of detail to members of the public…more important to me is the way my work is received by other researchers in the field and also by the clinical people in the field, so the clinicians…the doctors who are actually going out there and talking to the patients. (I14NP)

A reason for this finding may be that participants are setting the public apart from those most closely involved in the research, and are seeing them as outside because they do not understand the evidence or the scientific process as whole:

> …and people then are like oh well how quick is it I mean how can we get this compound or hope when is it? And then you're like oh actually you know it was a very small trial and it was a very small effect and yeah it's interesting but…when is it gonna be that this could possibly have any benefit to you is who knows… (I18NP)

It seems that those placed outside are seen as less able, or even unable, to contribute to the scientific knowledge claims:

> If the aim of the meeting is to talk about a very important and tricky scientific point there's no point in having Mrs Smith the carer of Mr Smith who has Parkinson's disease there because she's not going to get anything out of it nor is able to contribute. (I12P)

The perception that those outside the scientific expertise cannot make valuable contributions seems particularly strong when it comes to people who take an anti-vivisection stance. There is resistance amongst some of the participants to engage with this group of people.

This reluctance to give anti-vivisectionist's contributions any consideration may be related to how those who classify themselves as inside the scientific expertise set, characterise those they see as outside. For example, participant I17P separates anti-vivisectionists from other outsiders in the context that they are irrational, compared to people who may not agree, but accept that there is justification for the work:

> Oh apart from the animal liberation type of people a lot have their negative feedback people would say that they would feel uncomfortable with the type of work but they see why it's necessary. (I17P)

This separation has parallels with Case Study 1 and with Michael and Birke (1994a), where scientists involved in animal experimentation, particularly those in the core set, place criteria on whom they regard as having a legitimate membership, and consequently a voice in the debate.

Despite describing having little consideration for public acceptance of their work, when asked how important public perception of their work was to them, several PD participants indicated that it was very important, and others suggested that it should at

least be taken in to consideration. This was not evident in the schistosomiasis responses.

The data suggest three main reasons for this. Firstly, in contrast to schistosomiasis, PD participants indicate that the public are acutely aware of PD and its affects, and want information about the research that is being conducted, which is nicely summarised in this quote:

> …and people are very interested. I mean certain things attract more interest than others. People are very interested in stem cells. People are interested in you know diseases of the brain because as we live older more of us will get it, so there's a vested interest in understanding it. So you know it's normally a pretty receptive audience when you go round and talk about these things. (I19NP)

This is unsurprising given that schistosomiasis is a disease associated with Developing countries, and so the European 'public' will very rarely come in to contact with it. This awareness may mean that it is easier to gain public acceptance of PD knowledge claims.

Secondly, there appears to be greater emphasis on the need for public support for PD research. This is twofold, in that participants talked in terms of accountability, with several noting they needed public acceptance because they were funded with public/charitable money, so they had to account for how that money had been used:

> Certainly we get some very good and very generous support…and of course they are supported and are accountable to Parkinson's patients and their families and caregivers and so on. So these are the people that we're really you know supposed to be making a difference for and because they actively have an interest in funding us I think we're beholden to some level to at least keep them informed about what we're doing… (I20NP)

Others indicated that they need public support as it manifest into a willingness to help with the research either as clinical volunteers or by donating tissues etc. for research purposes.

There is also an ethical aspect, in that if the scientist cannot justify it to the public then perhaps the work should not be conducted, which is explored further in section 5.3, but is illustrated here:

> I think scientists have a duty to go out and confront the public and talk about what they do and see how it goes down…If they can't explain why they're doing what they do then maybe they shouldn't be doing it may be they should be doing something else. (I11P)

The final reason is a more general drive by funders and the scientists themselves to increase public engagement. For example, I18NP talks about Research Councils specifically pushing for scientists to do more public engagement:

> …in general I think it's probably a good thing though cos you want people to be engaged in what kind of research is going on and you know people wanna know…I think a lot of the research councils are pushing towards this you know to disseminate our information to the public you know. (I18NP)

Therefore, it seems that public acceptance is relatively more important to PD researchers than it is to those working on schistosomiasis, possibly because of the perception that the public is not really aware of schistosomiasis. However, while PD scientists may feel that PD has a reasonable public profile some of the areas of research may not be so well known, as illustrated by I18NP who feels that public

engagement is important to increase the understanding and awareness of their model system:

> …the use of these very simple model systems like yeast and flies is you know somewhat new and people are still in general the public are quite surprised that you can do important disease research in simple systems. (I18NP)

As established in the previous case study (4.1), a second aspect of acceptability appears to be the nature of the knowledge, that is, whether it is novel or established. Unlike in Case Study 1, PD participants discussed novel knowledge quite extensively. Chapter 2 highlighted that theoretically it is difficult for scientists to achieve recognition when proposing alternatives to established knowledge (Gilbert 1976). Several participants indicated that it would be, or has been, a problem for them, for example:

> …sometimes I think we have struggled a lot with the graft work that has been quite a battle because it's been about technology and language between Europe and America in a way. And the transplantation work has been viewed very differently in Europe and the States and trying to get some of that work published has been and probably will continue to be quite tricky. (I16NP)

The participants that commented on this generally indicated that their ideas were eventually accepted, at least in part, but that it took time, persistence and further validation of the claims to achieve this.

Some of the PD participants indicated that novelty was in fact important in making knowledge claims more likely to be accepted, for example:

> But I think you know they kind of go hand in hand to some degree I think if you find something that's novel and interesting and you look at it in detail you probably gonna get a pretty good publication out of it. (I18NP)

No primate users described any particular difficulty with getting knowledge claims accepted, or mentioned novelty in the context of accepting the work of others. This could be because their work is already 'established', or that they place more emphasis on findings that come from an established background of work, for example:

> No it's building on work that was there because the evidence dictated that was the target so I went to do my research in one of the groups that was central in establishing it. (I17P)

Similarly to Case Study 1, the primate users were not alone in stating the importance of established knowledge, or in viewing their research as established in some cases. Therefore, there is an apparent dichotomy that, while theoretically and seemingly in practice, novel knowledge claims are more difficult to gain acceptance for, non-primate users appear to place special emphasis on novelty as a means of gaining acceptance. This could be because of non-primate users utilising newer, less established techniques/models, so they are overtly emphasising that novelty is good. However, as was true for some of the Case Study 1 participants, they appear to appreciate the difficulty of getting the novel claims accepted, and that to improve this they should in general put them into the context of historical or established knowledge.

In summary, knowledge acceptance was raised by participants in both cases, with established knowledge and approval of scientific peers apparently being important to them. However, in PD the responses indicate a dichotomy between novelty being regarded as a means to get scientific knowledge accepted, and it being difficult in practice to get such knowledge incorporated into the mainstream knowledge base. This was not seen in schistosomiasis, and appears to be limited to non-primate using

PD participants. This could be related to the perceived greater public perception regarding PD, and the comparatively newer or more unusual techniques being used by non-primate users making it necessary for them to focus on this aspect more.

Publication

Participants in both cases see scientific publication as important for substantiating knowledge claims, and as a means by which their success is measured by others and themselves. In the case of PD all of the participants talked about scientific publication in this context, although some placed more emphasis on it than others.

Bonitz and Scharnhorst (2001) note that, '*References to the published papers seem to be the "currency" in which the scientific community "pays" for useful work'* (p.38). Therefore, it is not unusual that participants signified that publishing was one of the factors they used as a measure of the success of their work, and as an indicator that it was accepted. This was done in several ways including emphasising the number of publications or citations.

Perhaps less obvious was the unusual suggestion by some participants that, while publication is the basis on which others or the 'institution' judged them, in some cases this was different to their own criteria for success. For example:

> …the motivation for my work is fundamental biological interest I have to justify my work to different people to regulatory authorities to government to university to grant agencies each of them have different sets of criteria. Usually they relate to things like publications…The papers I'm most proud of are quite different to the ones that the university flags up as high impact papers. (I15P)

Four PD participants identified that where a paper was published is important, and in a similar way to the schistosomiasis example, one pointed out that this did not necessarily guarantee the quality or importance of the work:

> …you've got to see them publish in good journals...You know just cos something's published in Nature or Science believe me doesn't mean it's right But there's not much publicity in the things that turn out to be wrong but there are things which are published in very good journals that are never reproduced by anybody else again. (I11P)

Once again the dichotomy of novelty being both an opportunity and a challenge to gaining acceptance is raised in this context, with two participants indicating that it is important for initially getting published, for example:

> But I think you know they kind of go hand in hand to some degree I think if you find something that's novel and interesting and you look at it in detail you probably gonna get a pretty good publication out of it. (I18NP)

Finally, as in schistosomiasis, some of the PD participants talked about the importance of publishing all data, especially negative data, in order to avoid unnecessary animal use. They expressed regret that this is often difficult to do, and is not seen as having as a high an impact, despite it being valid knowledge.

In addition to scientific publication, some schistosomiasis participants, and most PD participants, mentioned media reporting of research. Many of the responses expressed concern or negativity towards how media outlets portrayed scientific findings. There were general comments that this type of reporting is overly optimistic and dishonest:

> But I think it's more to do with the whole way the media presents science. I'm always disappointed about what comes out in terms of being simplistic it's the

> certainly in the media well my contacts with it honest an honest story is not a story it has to be wow bang or disaster. (I15P)

Several participants indicated that this over-optimism or hype can consequently create false hope, which in turn can be detrimental to the research field, and harmful to those suffering from the disease, with this being a typical response:

> …I mean there is obviously it's that way with everything though in the media right? I mean they hype everything right? Everything is very dramatic and they gotta...sell papers right so they need headlines. You know I think sometimes it's a bit unfortunate because I think you know I think it maybe gives false hopes to patients and patients families…I mean they're usually based on a scientific study that's interesting but it becomes overstated. (I18NP)

Despite the negativity expressed by some participants about the media, there were more positive responses than in the schistosomiasis case. For example, I17P indicated that engagement with media outlets was increasing:

> Yes more and more scientists are happy to be interviewed about their work and you can see that in the press as various successes are heralded. (I17P)

I20NP noted that, while concerned about the frustration caused by hype, they appreciated that it can generate interest in, and funding for, the research, which would appear to be a clear example of using expectations and hope about research to generate space and resources for it (Brown 2003):

> …I can certainly recognise that people get frustrated when you know big stories a lot of publicity and there's not always a tangible advance comes from that. One thing that it does often lead to that's not necessarily tangible for patients and those people directly affected it leads to greater visibility for a particular disease or syndrome or whatever it is at that time and that itself brings in well if people conduct it properly and capitalise on it should bring in a lot of charitable funding a lot of support not necessarily charity but from government as well. (I20NP)

In summary, it would appear, as expected, that publication is used by scientists in both cases as a means of measuring success and, perhaps more subtly, as a means of quality assurance, although, as noted by several participants in both cases, this is not definitive. Perhaps more interesting in the context of this project are the responses related to media coverage of the research. Although still citing negative aspects of media hype, PD participants tended to be more positive about the role of the media such as, newspaper, radio and television reports in gaining resources and acceptance for their research than the schistosomiasis scientists were. These findings indicate that despite disappointments, hype continues in both these case studies, suggesting that hype/disappointment cycles function in the process of scientific change as well as in the context of technological change that Borup *et al*. (2006) proposed; '*...expectations of technology are also seen to foster a kind of historical amnesis – hype is about the future and the new – rarely about the past – so the disjunctive aspects of technological change are often emphasized and continuities with the past are erased from promissory memory*' (p.290).

Scientific Institution Conclusion

Many of the findings related to 'scientific institution' are, as expected, generic to both cases, and possibly to biomedical research more broadly. Both cases show that the sub-themes described are not mutually exclusive, with competition, reputation, knowledge acceptance and publication being interrelated in various ways. Of greatest interest are areas where there is a contrast between the two cases, or between primate and non-primate users, which had to be taken into account when proposing the recommendations in Chapter 7. In particular, that competition appears to be less

important to PD participants, possibly due to greater levels of collaboration linked to the core set and nature of the field, as well as a potentially important relationship regarding the closeness of the researchers to the patient population. Descriptions of the influence of institutional reputation were also unique to PD participants. Despite there appearing to be less discrepancy in how primate and non-primate users viewed their own reputations in PD, there was still evidence of the 'Matthew Effect' (Merton 1968), with those with the greatest reputations being observed as gaining the most funding. The responses regarding scientific publication were similar to the first case including, the frustrations regarding publication of negative data. However, PD participants talked more extensively about publication via media outlets. They placed more emphasis on the impact of the public perception of their work, which might account for PD responders more positive attitude toward media hype and expectation building. Although not central to this project, given the apparent increasing interaction with media outlets in PD, these findings might be of interest to those studying the process of 'medialization' of science, that is, the changing relationship between science and the mass media, such as scientists being forced to engage with media outlets as a means to legitimate their research, or outcompete others for recognition (Rödder 2008).

5.3 Practical Science

As previously defined in Chapter 4, the second theme by which participants provided justification for their research and knowledge claims was that of 'Practical Science'. This is divided into: physiological reasons for model choice, research question and

overall aims, policy and logistics, and alternatives. There were some differences between the two cases, and when comparing primate and non-primate user responses.

Physiological Reasons for Model Choice

PD participants responded similarly to schistosomiasis researchers by describing many scientific reasons for their choice of experimental model, which are summarised in table 11. This included describing the limitations of theirs and others' models and emphasising that, due to deficiencies of each model, they had to use several different ones during the course of their research. Indeed, some were very explicit in saying none of the PD models were completely adequate, and this was not limited to either type of researcher, for example:

> I think the problem is we don't have a relevant model. And I think the only way round that is to use all the models because each model has its own benefit each mostly each model takes one small aspect of how the cells die and you can test a drug against that for example (I12P)

Table 11: A summary of the scientific reasons participants gave for and against using different experimental models for Parkinson's disease research.

Model	Reasons for Use	Problems
1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) Primate	• Develop dyskinesia • Investigating symptomatic treatments • Predictability due to back translation from humans • Develop akinesia • Postural instability • Bradykinesia • Acute doperminergic pathology • Studying onset of symptoms	• Not predictive for evaluating anti-neuronal cell death drugs • No tremor • Pharmacokinetic handling not predictive due to size differences (marmoset) • Not a progressive model (marmoset) • No non-doperminergic pathology • No lewy bodies (but same in human mptp cases)

Model	Reasons for Use	Problems
	• Studying onset of side effects of symptomatic treatments • Remains stable for many years Anatomically similar for implantation studies (macaques) • surgical targets are the same (macaques) • Scaling up/validating methods • No spontaneous recovery	• No alpha synuclein aggregation • Artificial lesion
Rodent (model type not specified)	• Drug metabolism and biochemical changes in the brain • Repeated dosing • Pharmacokinetic studies • Developing cell transplantation methods • Behavioural and cognitive testing possible • Neurochemical changes • Genetics	• Do not mimic symptoms • No akinesia • No postural instability • No tremor • Bradykinesia is very subtle • Limited ability to study L-dopa side effects • No cell spreading (in transplantation) due to small size • Cannot translate complex function • Different brain structure – surgical targets differ • Cannot do large scale genetic screening • Not experienced long term metabolic activity and exposure to damage that humans have
6-hydroxy-dopamine (6HD) Rat	• Investigating symptomatic treatments • Studying symptoms • Early and late stages of disease Non-dopaminergic symptoms • Dopamine neuron loss • Studying neuro-protective therapies • Can do several manipulations e.g. serotonin or cholinergic systems	• Not predictive for evaluating anti-neuronal cell death drugs • No dyskinesia • Have to use unilateral model as bilateral kills animals • Does not exhibit all symptoms of PD • No alpha synuclein aggregation • Not progressive • Stable lesion unlike PD • Purely doperminergic
Alpha synuclein Rat	• Mild Parkinson's like syndrome	• Limited dopamine neuron loss

Model	Reasons for Use	Problems
	• Studying gene mutations • Study aggregation • Gene therapy • Early stages of disease	
Rotenone Rat	• Parkinson like symptoms • Mechanistic perspective • Lesion less variable	• Severe (kills half of the animals) • Might lead to a biased sample population
MPTP Mouse	• Late stage PD model	• Not predictive for evaluating anti-neuronal cell death drugs • Neural protection does not translate to humans • No dyskinesia • No alpha synuclein aggregation
Genetically Modified (GM) Mouse (genetic alteration not specified)	• Pathways in cellular pathogenesis • Biochemical and molecular mechanisms	• No nigral cell degeneration • No lewy bodies • Very little if any symptomology • Late stages of disease • Not useful for cell replacement or protection • Small percentage of PD caused by gene mutation • Genetic redundancy • No progressive degeneration
Ubiquitin GM Mouse	• Rapid neuropathology (in 2-3 weeks) • Low variability • Ubiquitin system proteins conserved in humans • Study sporadic form of disease • Mitochondrial effects • Shows inclusions • Excessive neuro-degeneration	• Young animals so cannot study behaviour
Fruit Fly	• Genetic manipulation • Identifying therapy targets • Robust as many manipulation tools available • Can be made to express alpha synuclein to study aggregation Compound screening	• No natural alpha-synuclein expression • No microglia • Neuroanatomy different • Gene expression can differ • Lack of redundancy can result in compensatory mechanisms being missed • May be gene function

Model	Reasons for Use	Problems
	• Have a nervous system including glial cells • Behavioural observations possible • Identifying environmental toxins/causes • Rapid mutant generation • General biology conserved with human • Low genetic redundancy	divergence • Cannot test stem cell effectiveness
Worms	• Investigate mitochondrial function effects • Investigate protein handling • General biology conserved with human • Can observe some behaviours	
Yeast	• Genetic screening • Compound screening • Has human gene autologues • Can transfer human genes to study altering phenotype and rescuing it • Gene expression • Interactions • Identifying therapy targets • Cellular toxicity • Protein aggregation	• Cannot study neuron or synaptic processes
In Vitro	• Mechanisms of neuronal cell death • Protection against cell death • Allow large-scale screening • Drug mechanisms • Biochemical data • Primary cell culture – investigating areas affected by motor symptoms • Fluorescent imaging for cell interactions • Brain slices allow study of brain architecture • Gene identification • Cellular metabolic	• Lack of functional readout • Not completely predictive of what happens in brain • No information on vulnerability of aged brain • Cannot measure behaviours • Don't get full range of interactions • Artificial system • Use toxins so not replicating natural process • Different time course to disease • Disease isn't cellular

Model	Reasons for Use	Problems
	pathway mutations • Controlled system – low variation • Protein aggregation	
Post-Mortem Tissue	• Identification of disease processes in brain • Investigating anatomy and pathology of cells affected by disease • Identifying dopamine neuron death • Identifying disease pathology Changes in brain chemistry	• Cannot identify primary processes vs. consequences
Human Volunteers/Clinical Research	• Epidemiological studies (i.e. large sample) • Imaging studies • Disease processes • Understanding the disease	• Difficult to mimic clinical work in a lab • Cannot do brain manipulations

In summary, the consensus in these scientific reason responses between the two cases suggests scientific justification is not unique to this topic. This emphasis on scientific aspects is not surprising because if there was no concordance with human diseases there would be little point in conducting the research, and scientists would not receive authorisation to do it. As noted in the previous case, while it is important to know the scientific basis for the scientists' choices, what is more interesting and useful for the final stage of this project is the apparent willingness of participants to discuss the limitations of their own and other models, which is not apparent in the peer-reviewed literature and could aid negotiation of replacement strategies suggested in the recommendations in Chapter 7.

Research Question and Overall Aims

As in schistosomiasis, as well as giving scientific reasons, many of the PD participants explicitly said that the scientific question they wanted to address had a large influence on their model choice, as did the overall aims where some conflict was again evident.

Of particular note was that two of the participants (I15P and I19NP) indicated that the scientific question had to be specific and especially important, in order to justify using primates. I15P made this point on several occasions but this quote is representative:

> …you know in this field…I don't see any key questions that can only be addressed or require the use of primates. It's partly the nature of the questions too…it has to be conceptually better addressed in primates… (I15P)

Another aspect related to the scientific question is the overall research aim(s) that the scientist is working towards within the PD field. This can have a direct effect on which model a scientist decides to use. For example, I15P is discussing the possibility of a new strategy developing and that it may require primate models:

> …it could well be that the development of new trophic factor delivery strategies for neuro-protection…Because it's so fundamentally different to say transplantation I think that probably is an area that requires primate validation before trying systematically in humans. (I15P)

The literature review described in section 2.2.3 identified several areas of research that were being investigated in parallel within the PD field: surgical (DBS), surgical (cell transplantation), pharmacological (symptomatic), and pharmacological (neuro-protection). During the interviews these research aims were checked with participants. Similarly to schistosomiasis, responses indicated that there was conflict about which of these aims was the best to pursue in terms of finding an effective PD treatment. The

comments also suggested there were additional research aims that had not been identified, namely: surgical (viral vectors) and gene therapy Some of those working toward a specific aim were slightly more positive about that particular area of research, but in general the comments were relatively balanced, with some participants also highlighting the negative aspects of the aim they were pursuing.

Conflict about the research aims was subtly and explicitly stated in some cases. For example, I20NP has actively and openly avoided becoming involved in a particular aim pursued by some PD researchers:

> …indirectly I've been opposing a certain faction of the of the field that is obsessed with alpha-synuclein I say indirectly because I've actively avoided working on it cos I don't think it's worth it in with the type of approach that we take. I think some of the findings that have been done on that are not scientifically sound. I may well have said so in certain commentaries and reviews. (I20NP)

In contrast to schistosomiasis, where participants were more definite about which particular aims were best to work towards, several of the PD participants commented that rather than the research aims conflicting, or one being more likely to lead to an effective treatment, instead it was best to adopt a combination of strategies in the field as a whole, for example:

> I think we don't know enough now to say oh let's focus on our efforts put all our eggs in one basket and focus on this cos we just don't know what's gonna be the right way. I think maybe in ten years we will have a better idea what's gonna be the idea the best way but I think they're all equally important right now. (I18NP)

In summary, perhaps unsurprisingly in both cases, participants placed emphasis on the importance of the research question in their choice of model, and that the question

had to be especially significant when deciding to use primates. These findings provide important insight into the main research aims in these two fields, and reveal conflict among researchers as to which is the most appropriate for the field in general, which is not evident from the literature. There appears to be more enthusiasm among PD scientists for different research aims to be targeted in parallel, whereas, in schistosomiasis, participants were more often saying that a particular aim should take precedence.

Policy and Logistics

The role of politics and logistical factors in influencing research was evident to different degrees in both cases. In PD it seems that logistical aspects, such as cost and available facilities may be having a greater effect than policy on which areas of research are pursued.

In contrast to schistosomiasis, there was no evidence that participants viewed national policy as being influential in PD. There was very little discussion about policy, so the influence individuals or groups have on policy was not evident either. However, some responses indicate that anti-vivisectionists have been perceived as exerting pressure on the field that may have prevented some researchers from conducting primate work, but they have not particularly influenced any policies with regard to research strategy. Indeed this quote indicates this pressure has eased and can be dealt with:

> I think we've lived with the anti-viv movement for a very long time I think the biggest moves are any changes to legislation and changes to the financing streams. (I16NP)

Schistosomiasis participants discussed how economic limitations affected their choice of model, with primates, and to some extent other animal models, being perceived as being too expensive to use. This problem of the cost outweighing the scientific utility of a model was also evident in the PD case, with both primate and non-primate users commenting on it, for example:

> I mean it's very expensive doing mouse work you know… (I18NP)

One concern relating to economics that was consistently mentioned by both PD primate and non-primate users, but was not evident in schistosomiasis responses in this context, was the problem of increasing costs leading to the research and/or scientists moving away from Europe.

In contrast to other responses, participant I16NP noted that movement abroad may be beneficial, as there would be more funding available to conduct the research with more staff, which would result in improvements in the methodology:

> I think it's in some ways it's less of a concern because you can potentially afford more members of staff over there that they can give the drugs without necessarily knowing what they are and what they're meant to do. I would worry more about the care of the animals. (I16NP)

The issue of research moving abroad was also referred to in the context of regulation and is discussed further in section 5.4.

Several participants stated that logistics was a factor affecting which model was utilised. For example, this primate user was not alone in indicating that the availability of primates can be problematic:

> Well there have been problems it's largely a supply problem not anything else. We use marmosets and marmosets they're bred for research so we don't use I don't think we would use any feral animals wild captured animals at all. I think people who work with bigger monkeys than us have more of a problem with that. (I11P)

I11P then went on to suggest that working with cells was a much easier option in terms of them being readily available.

Similarly to Case Study 1, this non-primate user indicated that they could not use primates even if they wanted to because of their unavailability, and the lack of suitable facilities and infrastructure at their institution:

> Well I mean for financial and logistical reasons…I would never use primates because I just don't have the money or the resources or the infrastructure or the whatever to do primate research so that would be one reason for that. (I14NP)

In summary, in a similar way to schistosomiasis participants, PD responses highlight economic and logistical factors, including available facilities as having a significant impact on model choice, which can in some circumstances outweigh the scientific utility of a given model. However, the PD participants appear to see national policy as less influential in terms of research aims and model choice than schistosomiasis participants. Another contrast between the cases was the PD participants' comments on research moving out of Europe which did not appear in this context in schistosomiasis. There was very little distinction between the responses given by primate and non-primate users in either case, perhaps indicating that these factors are universal to all scientists independently of which model they use, or research aim they pursue, despite general indications in the media that primate research is distinctly affected by some of the issues raised here (e.g. Wadman 2012).

Alternatives

Key to understanding the primate impasse and whether it can be overcome is determining if there are any alternatives to primate models available, or any that could be developed. Therefore, participants were asked for their views on this. In PD, the data indicate that there is some uncertainty, but more participants than in schistosomiasis indicated that replacement was, or could be, possible. The statements sometimes had caveats, for example, I16NP feels that primates could be replaced in the development stage, but perhaps not during final testing:

> …I think the development of is possible, I think very few treatments are actually developed to a significant extent with primates. I think they are tested at the final stage in primates… (I16NP)

While the majority of positive responses were given by non-primate users, some primate users suggested that replacement models were needed, or were available in certain circumstances. For example, I11P went into great detail to describe the beginnings of the development of two new models that, on the face of it, would replace the less reliable MPTP primate model. However, they added that this might then go on to be developed in primates, but the potential is evident:

> So we have two events changes in protein handling and inflammatory change both of which we know occur are real and occur in all the areas of the brain which are effected by the disease. My suspicion is that we need to set up models around those two. We do have one…model looks to be quite a useful model it's still being evaluated. There are other models…which also look as though they could be useful and needed. At the moment most of it is in rodent… (I11P)

I12P was unsure about the need for primates as a second species, indicating that a lack of historical data might be the restricting the use of alternatives in a particular situation (neuroprotection), and this non-primate user made a similar suggestion:

> …I mean every time you go to a new system then you have to develop new tools…so I mean if you've got you know certain primate systems that have been very well characterised and that are understood very well from kind of a pharmacokinetic pharmacodynamic sort of standpoint…and how you then translate that data in to humans. If all that's in place from thirty years of research that's a powerful tool and to kind of reinvent the wheel yeah it's not a trivial task you know. (I18NP)

Other alternative models that were suggested included: pigs, rats, sheep, human post-mortem tissue, non-invasive human imaging and mice, all of which are noted in the recommendations to overcome the impasse (Chapter 7). In addition, there was some indication that there was precedence within the field to avoid preclinical primate testing, and to move directly in to clinical trials, for example:

> …I think in general success rate's been rather low from just going from mice to humans. I mean people they do it that's the norm. It's pretty normal to do compound trials in mice and then do you know tox testing in normal volunteers and then start clinical trials…I mean that's not unusual. But obviously it's also done where you go into primate models. (I18NP)

In terms of negative responses, those adamant that it was not possible to replace primate models were mostly primate users. All of the primate users made comments in this context with the following being typical:

> Difficult cos we have nothing to replace it with that's the trouble. If there were alternatives to be quite frank we'd be using them already. You know I can't think of any sort of any way you could after the rodent that would make it very easy to take a drug into humans. (I11P)

Whereas, non-primate users expressed uncertainty about primate replacement, with the following being a typical response:

> …obvious examples are if you wanna do gene therapy…in order to do that you have to look in aged monkeys…you really can't do that type of experiment in a rodent cos they don't have the same age and you don't have the same ability to deliver it over a bigger area which was really what it was all about…But for most treatments I don't think you need any primate studies. (I19NP)

Both primate and non-primate users gave reasons as to why it is difficult to replace primates in this field. These included: alternative models were not as good or could only be used in conjunction with the primate model; a lack of historical data for other models; low confidence in information from rodents translating to the human situation; a loss of scientific information when using simpler models and hesitancy in terms of safety when moving from other pre-clinical models directly in to humans. Participant I19NP made an interesting point in relation to this, that *in vitro* models had improved, and were capable of achieving much more than they used to, but that this information has apparently not disseminated widely throughout the field yet:

> …I think people understand the fact that you do have to use animals for certain aspects of the work I think what has become a unclear is that there are more things you can do in the dish. So in vitro studies are becoming are easier to do than they used to be. (I19NP)

In summary, in contrast to schistosomiasis, and despite the adamant statements from primate users to the contrary, PD participants gave more examples of possible alternatives to primates, and seemed more amenable to the possibility of replacing primates. There were hints of entrenchment in the comments related to change being difficult because developing a set of data similar to the historical information that is available for primates would be a huge task. However, unlike the previous case study,

it may be that in PD the entrenchment of the primate research is being compensated for by increasing flexibility in approach and techniques. Knot *et al*. (2001) argue that this can be achieved in terms of technologies by developing: i) robust technologies that are appropriate in several relevant futures, ii) flexible options (technologies) that are adaptable to changing circumstances, such as changing concerns, or iii) flexibility by variety, that is, maintaining different technologies that can serve the same function. The latter of these seems to be applicable in this circumstance.

Practical Science Conclusion

These findings indicate that participants in both cases refer to aspects of practical science when justifying their research decisions. As might be expected, giving extensive scientific reasons for model choice was apparent in both fields. Perhaps more important are the data showing that scientists in both fields are aware of, and are willing to discuss, the limitations of current models, and the contrast of PD participants' apparently greater enthusiasm for parallel research aims to be targeted, which both have a bearing on understanding the impasse and overcoming it (Chapters 6 and 7). Both sets of participants noted logistical barriers to choosing and using certain models, especially primates. However, schistosomiasis scientists placed more emphasis on the impact of national policy than PD scientists did, indicating that a dialogue with policy makers may be particularly important in that case. When discussing alternatives, PD participants appeared more amenable to the possibility of replacing primates, which indicated that 'flexibility' to the 'entrenchment' (Knot *et al*. 2001) seen in schistosomiasis may be at play. Flexibility may be easier in PD due to the higher public perception, relatively higher funding availability, and the

diverseness of the areas which can be studied, making it less costly to change from entrenched practices, and maintain a variety of approaches. In both cases the only major difference within this theme, between primate and non-primate using participants, was that primate users were more adamant that primates could not be replaced, whereas non-primate users were uncertain. Again this could be related to entrenchment and flexibility, with the financial, logistical, ethical and controversial nature of primate work highlighted throughout this project, meaning that primate users have invested heavily in the work. In contrast, non-primate using participants may not have to contend with the same degree of pressure in this context, making it easier for them to foresee adaptations to current practice (Knot *et al*. 2001).

5.4 Animals and Ethics

This analytical theme helps to explain factors identified by participants as influencing their decisions about animal experimentation, which involve moral considerations and fall under the sub-themes: personal choice, choice of species, and influence of other parties. Responses in both cases were similar, with a couple of exceptions that have consequences for the final recommendations (Chapter 7).

Personal Choices

As noted previously (4.3), participants made explicit reference to justifying the work to themselves when talking about model choice, and the moral challenges associated with biomedical science. In this case all of the primate users, and several non-primate

users, made references in this context. Something that was apparent in schistosomiasis, and evident in PD, was participants emphasising how important ethics were to them by highlighting that they feel it necessary to teach it to others, for example:

> … I teach a module on behavioural pharmacology here at taught masters level it's all about animal handling, welfare, ethics, maintenance all that kind of thing and I really enjoy it and it's all about teaching the students to have respect for the animals… (I14NP)

Participants indicated some of the ways that this personal justification was achieved. Firstly, by pointing out the faults of the animal; something which one schistosomiasis participant did in a jovial way, but here the response was serious:

> …I would also find it difficult to work with bigger monkeys. Marmosets look cute but to be quite frank they'll have your hand off as soon as you turn your back. So they're not shy about biting each other's fingers off if the two males get close to each other they're not cute… (I11P)

Similarly to schistosomiasis, several primate and non-primate using participants specifically emphasised the ethical acceptability of their models, including emphasising the priority they place on animal welfare. For example, I11P highlights their avoidance of unnecessary suffering even if it might disrupt the scientific findings:

> I really have some difficulty with anything that causes well it's difficult to define unnecessary suffering I we have round here really quite high standards about how far we'll go and if we think an animal is suffering then we put them down irrespective of how important that animal is. So we won't go too far. (I11P)

This emphasis on ethical self-justification is not surprising given as Wainwright *et al*. (2006) describe '*"...ethics", is becoming an integral part of maintaining the image of science*' (p.735) and Rollin (2007) notes; '*...society sees invasive animal research as a significant moral issue*' (p.525). Therefore, the scientists may feel more pressure to emphasise the moral consideration they have given to their career choices.

Another factor related to personal ethics is where each scientist places the limit on what research they will personally do, and which models they will use. All participants, with the exception of I13NP, gave some indication as to techniques or models they would not use. This was related to various factors, including severity and emotional attachment. It was often explicitly stated as their choice with the caveat that they did not have a problem with others doing it, for example:

> … I've always veered away from pain but I realise it has to be done. I personally have always been veered away from pain research for that reason. I've colleagues who do that and they have excellent endpoints in their project licence to make it acceptable. (I12P)

As in schistosomiasis there were examples where the participant indicated that their limit was perhaps not easy to rationally explain, for example:

> …at a flippant level I don't and won't work on eyes I'm squeamish and I don't and won't work on rabbits because I have pet rabbits and I have a great affection for them and you know completely emotional it's not rational, but emotions are to be respected not ignored. (I15P)

Again in PD there was some evidence that the perceived ethical concern appears to have overcome the scientific utility of some models, for example:

> The one that's shown the most promise is the rotenone model where the pesticide is given systemically…It hasn't been widely accepted and the other problem with that model is that it actually kills about half of the animals that are injected with the pesticide die…I mean people don't it's not ethically sound to use a model like that where you kill half your animals. (I14NP)

However, uniquely in this case, one participant described how the importance of the science had overcome his previous personal limit on working with mice:

> …it was actually kind of ironic that before I worked with mice I kind of said oh I'm never gonna work with mice cos I didn't think I could…was a bit disturbing to me to actually have to sacrifice an animal to do an experiment and these sorts of things. But I just happened to get very interested in that area of research and it you know that was kind of where it was going and it was important for us to look in that system… (I18NP)

In summary, these data show that participants in both fields place emphasis on ethically justifying the work to themselves. The ways the participants describe doing this are similar in most cases. Again, there was evidence of participants explicitly drawing personal ethical lines about which experiments they would conduct, which were seen by some as irrational and emotive, but could still outweigh the scientific utility of a model. However, one response did indicate that this was not always the case, as their personal limit had been altered by their perception that the science was too important not to use the model. As noted in the previous chapter, these types of response were observed by Birke *et al*. (2007), and this later example indicates that this mode of coping with the moral dilemmas associated with animal experimentation was successful for participant I18NP.

Choice of Species

There are several examples of participants differentiating the ease at which they can decide to use one species or another, or if an animal should be used at all. Again primates are generally given more consideration, but this is not universally the case.

There were several instances, similar to schistosomiasis, where participants indicated that primates were given more consideration in terms of the choice to work with them being a harder decision than it is for other species. This included setting them apart from other animals in requiring large and specific amounts of information before using them.

Two participants indicated that they give the highest level of consideration to humans for similar reasons to those given for limiting primate use. For example, I14NP indicated they set humans apart from other scientific 'models':

> I wouldn't consider the human say post mortem tissue or PET scanning or that kind of stuff to be model that would be proper clinical based or human sample work. (I14NP)

However, although primates appeared to receive the most consideration, in this case study two of the non-primate users indicated that the decision to use mouse models was not easy, for example:

> I really strongly feel you kind of need to have really covered all your bases before you decide to do a mouse experiment you know that obviously people are more emotionally attached to primates which I can obviously understand we all are but even the mice I think you kind of want to be. (I18NP)

A difference in the ethical consideration afforded to different species was also evident in some of the descriptions of the actions of participants. For example, I12P indicates their willingness to continue to care for primates rather than to cull them, whereas I19NP is somewhat blasé about sacrificing the smaller animals:

> …we've actually just extended the period that we can keep them to six years because they were so healthy that we felt it was ethically wrong to cull them at the end of four years so we've increased it to six years… (I12P)

> …you get more information from it but fundamentally with small animals you can always sacrifice them and do histology. (I19NP)

Apart from many participants generally appearing to be comfortable with using rodents, as they talked about them without expressing any concerns, there were no other indications that participants were particularly happier to use certain species, which contrasts to schistosomiasis. One slight exception to this was given by I18NP who indicated that perhaps people would be more comfortable working with livestock as opposed to primates, but they questioned if this is the right attitude to have:

> You know sheep obviously rats you know and these are probably important you know maybe they'd be good alternatives to primate models. But you know is the sheep you know any less worthy…I'm not sure I feel you know that much better about you know people working on pigs versus working on primates… (I18NP)

In summary, these findings indicate that in both cases, some participants give greater consideration to primates. Unlike in schistosomiasis, there was no explicit reference to speciesism. However, taking both case studies in to consideration it seems that this differential consideration may be more indicative of the established capacity-based model of moral status evaluation, where '*...beings with greater or more complex ("higher") morally relevant capacities have higher moral status than those with few*

or less complex ("lower") capacities' (Walker 2006, p.315). This is linked to the idea of humans serving as the standard being with full moral status, due to possession of multiple capacities, relative to which all other beings are valued. This is also known as the sliding-scale model (DeGrazia 2002).

Influence of Other Parties

The descriptions of the influence of other parties, such as regulators and other scientists, on decisions about model choice, given by participants in Chapter 4 are evident in PD.

The majority of comments made in this context indicated that the participant saw the decision of other scientists as a means to justify particular research. This was expressed by emphasis on being distant from the procedures, or that collaborators or colleagues do the work rather than them. Two participants also indicated that it was the scientific community as a whole that should be deciding what the correct action to take was, either directly as the first quote illustrates, or indirectly via peer-review as the second quote suggests:

> Well that happens in international meetings and local workshops well that is reflected in the ethical committees at the university and national levels and also there's like the Nuffield Centre for Bioethics where multiple people of various disciplines talk about problems and a way forward either in science or in society. (I17P)

> Inherent I mean if you were say putting in a grant application…anybody who knows anything will know that that's not gonna work…so I suppose you expect your reviewers will have some understanding of the models. (I14NP)

A second relatively common response was to explicitly talk about the ethical decision of society, which was not so overt in schistosomiasis. I15P was particularly vocal on this, making several comments. For example, noting that personal and societal ethics should be addressed:

> …I personally I feel very strongly and what I try and develop is to engage in any of this research you have to fulfil a double standard you have to have considered and abide by your own personal ethics…and you have to satisfy to a high standard the standards of the society as a whole in which we live. (I15P)

I20NP indicated that the model they use is accepted by society, and that society's decision not to raise concerns about it means that it is not regulated:

> I think it's illustrated by the fact that it's not legislated the use of these animals is not specifically legislated and no one ever appears to be too bothered about lobbying for fly rights things like that. No one else is particularly morally up in arms about it either. (I20NP)

As it was in schistosomiasis, the link to regulators validating the ethical decisions for the scientists was made on several occasions. This included comments on the high level of legislation that covers animal experiments, and that it should prevent any incorrect research.

Indeed, as in the first case, one PD participant indicated that primate research was more heavily regulated than human clinical work.

The strength of, and need for, regulation were discussed in the context of concerns over research moving abroad, but this is covered in section 5.4. Finally another two parties, the first of which was not mentioned in schistosomiasis, which were referred

to in terms of influencing decisions about models were the Ethical Review Process (ERP)[7] and the funders:

> …of course one has to continuously justify the use of primates both to the Research Councils which support my research and also to the ethics committee at the highest national level the Home Office. (I17P)

> …I believe that I should and it's required in the every grant application these days. You have sections which require justification independent ethical appraisal licensing rules and the rest of. (I15P)

It is implicit that funding is fundamentally important in facilitating biomedical research, as work would be impossible without it. The converse of this is that a lack of funding can slow or even prevent scientific progress. Participants provided several examples of both of these situations. Perhaps more interesting is that, rather than facilitate research that scientists want to do, funding and those providing it apparently dictate what research can be done. For example, I14NP indicates that funders, in fact, place emphasis on animal research, which may be a factor in why newer alternatives are more difficult to gain funding for:

[7] The Ethical Review Process (ERP) has been a feature of UK regulation of animal experimentation since 1999. In practice they functioned in much the same way as the Animal Welfare and Ethical Review Body (AWERB), which replaced them when the UK laws were updated in January 2013 to conform with the new EU Directive 2010/63/EU. Every establishment licensed to conduct animal procedures must have an AWERB. The AWERB's minimum required tasks are; a) advise staff dealing with animals in the licensed establishment on matters related to the welfare of the animals, in relation to their acquisition, accommodation, care and use; b) advise on the application of the 3Rs, and keep informed of relevant technical and scientific developments; c) establish and review management and operational processes for monitoring, reporting and follow-up in relation to the welfare of animals housed or used in the licensed establishment; d) follow the development and outcome (retrospective review) of projects carried out in the establishment, taking into account the effect on the animals used; and to identify and advise on elements that could further contribute to the 3Rs; and e) advise on rehoming schemes, including the appropriate socialisation of the animals to be re-homed. As a minimum membership the AWERB must have at least one of the establishments Named Animal Care and Welfare Officers (NACWOs) and Named Veterinary Surgeon (NVSs) plus a scientific member – if the establishment is a user establishment (Jennings and Smith 2015).

> But the drive is towards applied which means translational and the translational step you know between the bench and the bedside is the animals. So if you have an animal component in your research it's your much more likely to get funded. (I14NP)

In addition to the traditional biomedical funding agencies, several PD participants identified that Parkinson's UK was particularly influential in directing research for PD treatments. Parkinson's UK is a charity, which coordinates patient and carer groups, and funds biomedical research. There was no such advocacy group in the case of schistosomiasis, so in the context of this project this aspect is unique to PD. However, as the quote below illustrates it is not unique to neurodegenerative research more broadly:

> ….In the Huntington's Disease Society because it's a genetic disease and runs in families there's a completely different focus its discovery fundamental treatment for the future because it's their children who have this…they want to see you know it's too late for us but come up with something that will stop our children developing it… (I15P)

Unlike in the schistosomiasis case, there were no examples of PD participants seeing an apparent shift away from funding primate use. This could indicate that it may be easier in schistosomiasis than in PD to move away from primate use, as the funding options may not be available.

In summary, these findings, in conjunction with those from schistosomiasis, indicate that these scientists do not see themselves as working in a vacuum. Other parties have an influence on the research direction and choice of model system. Similar to the findings in Schistosomiasis, these 'others' were not portrayed as disreputable, which differs from the findings of Michael and Birke (1994b), who found that scientists were critical of the 'others' they deferred to. Instead, participants in schistosomiasis and PD

focused on the role of the 'others' in the model choice process. Because of this, these 'others' are considered in the making and implementation of the recommendations for overcoming the impasse (Chapter 7). For example, where the two cases particularly differed was in PD having an influential advocacy group. Therefore, it may be that the group needs to be consulted in some way for this particular case.

Animal and Ethics Conclusion

It is important to know what drives scientists' decisions to utilise certain models or to explore certain aims, in order to effectively understand the impasse, and make recommendations as to how to overcome it. This analysis indicates that, in both cases, participants try to justify their experimental choices ethically and the ways in which they do this has consequences for how the recommendations are designed, and in particular where they might need to differ from each other. Participants draw personal 'emotional' limits on what they are willing to do, which supports previous research by Birke *et al*. (2007), but there was some evidence in PD that this could be overcome, if the scientific case was strong enough. Particularly important for this project is the finding that participants in both cases appeared to give more consideration to primates, and exhibited a sliding scale attitude to how morally problematic models are. Participants from both fields identified that they did not see themselves as alone in making choices about animal models, highlighting other scientists, regulators, funders and society as having an influence. The latter of these could be understood as an example of Brown and Michael's (2001) 'switching', where scientists can be seen to swap between science and culture as they go from personal scientific reasoning for their choices to being part of societal decisions. As the influence of society is only

inferred in schistosomiasis rather than being explicit as it is in PD, PD participants might be regarded by Brown and Michael (2001) as more 'sociologically sophisticated'. Alternatively, these findings could be interpreted as ethical displacement, with participants potentially deferring the responsibility to regulatory frameworks, funders, society and other scientists to validate their own choices. Therefore, more constructivist scholars could argue this data could represent evidence of ethical boundary-work (e.g. Hobson-West 2012; Wainwright *et al*. 2006), as an example of the concept being useful in understanding how scientists ethically legitimise their research, particularly that involving animals. Participants did not limit their discussions on ethics to animals it was also considered in terms of the health of the patients that may come to benefit from their research, as shown in the next section.

5.5 Health and Ethics

In similar ways to the previous case (4.4), PD participants talked about factors related to the impact of the disease, and the controls surrounding treatments and patient safety. These moral and practical discussions are presented in the sub-themes: disease severity, safety and regulation. However, there were some differences in the impact that participants indicated these factors had, particularly disease severity and regulation, and between different types of user.

Disease Severity

In schistosomiasis participants used descriptions of the problems associated with the disease, or as Brown (2003) terms it 'sickness narratives', as a justification for their research. This was not such a dominant feature in PD. Indeed, only three participants made this kind of comment. Two were primate users, and all three had direct contact with patients either at present, or in the past. Instead, PD participants appeared to place more emphasis on the health benefits of their research, and on the complexity of the disease, in contrast to schistosomiasis where there was very little mention of these things. However, as in schistosomiasis, there was limited discussion centred on ensuring that those who were affected by the disease, or 'the sufferers in the sickness narrative', should be engaged with the research, in order for it to be successful, for example:

> The only way I can deal with it is I'm looking the patients in the eye and talking to the patients and the carers and understanding the need that they have… (I11P)

Brown (2003) notes that '*…the welding together of painful pathological biography and the fate of a biotechnological promise takes place at enormous cost to those who…are persuaded to share in the hope*' (p.8), so this might be a way of alleviating the damage that might result from sickness narratives, such as patients suffering intense disappointment when a promised therapy does not materialise.

In terms of health benefits six of the ten participants talked about the therapeutic advances made from their research, or emphasised how it has, or will, translate

positively into human medicine. All four primate users made comments of this nature. Of the non-primate users, I18NP made the most references to it, for example:

> …they may not understand why you'd wanna work with flies or yeast but I think it's important for them to understand how this can translate in to therapeutics for people. (I18NP)

It was also common to explain the variety of health effects within the condition, with many responses including comments on the complexity of the disease as a means of explaining why a variety of animal models were required, and/or why progress maybe slower than expected. All participants referred to this, with the exception of I13NP. For example:

> …it's a difficult question because depends on what aspect of the human condition, but if you were to say that there four key features of human Parkinsonism…Those would be what I would call the four pillars of Parkinson's diseases modelling and so far to be quite honest none of the models that are used in drug discovery research have those four pillars. (I14NP)

In summary, it seems that PD researchers, in contrast to schistosomiasis researchers, rarely use sickness narratives when justifying their research. This may be related to greater public awareness of PD, as illustrated by the quote below. This might mean that they do not find it necessary to describe the severity of the disease and its associated problems, as to them they are obvious or well known:

> …you know a combination of its disease research people are generally just interested in it more, or people the general public understands the concept behind it more. (I18NP)

Greater awareness could have resulted in more funding being available and, in conjunction with the relatively low level of competition identified in 5.1, might mean that PD researchers have not found it as necessary to use sickness narratives to raise the profile of the disease and/or generate resources. Instead, it seems PD researchers placed greater emphasis on promoting the health benefits of their research. Other studies have found this emphasis on promissory health benefits in the context of animal experimentation (Hobson-West 2012 and Birke *et al*. 2007), and it has been used in other areas of scientific controversy, such as stem cell biology (Wainwright *et al*. 2006). Primate users in particular talked about the health benefits. This may be because primate models are perceived as more controversial thereby needing 'strong justification', hence placing more emphasis on benefits. This might be expected given that European (*Directive 2010/63/EU*) and UK (*ASPA*) regulations governing animal experimentation require a harm/benefit analysis to be conducted, so only studies where the potential benefits outweigh the harms to the animals should be conducted.

Safety

When asked about the possibility of replacing pre-clinical primate models, all participants expressed some concern about the impact this would have on human safety. As with schistosomiasis, there appeared to be less confidence that results in other models would translate to humans, with the following being typical:

> And as a clinician who would have to then administer it to patients you would feel much more reluctant having to do it if you hadn't got that primate data. So if I…wanted to give you a gene therapy in to your brain, I could do it and you know I could base it on the rat stuff but I'd really really like to have seen some primate data… (I19NP)

Similarly, PD participants expressed concern about the safety of some therapeutic aims, in particular the need to proceed with caution with viral vector therapies. As the following quote illustrates, this may be related to the past problems with cell implantation that seems to have halted that area of research for several years, and which other participant also commented on:

> …I think there are a few potentials in the pipeline but they're risky strategies. The use of viral vectors has potentially got a lot of risks and that's what we're moving towards now…The problem is the transplantation I think highlights the potential problems that we have if we move too quickly we end up with side effects and then we devastate the field. And transplantation as a field as an area of research…took a big knock and well it was set back ten years by the development of side effects and the adverse publicity that gained. (I16NP)

Unlike in Case Study 1, there is no mention in PD of the public perception of risk, or of societal influences on safety. Perhaps this is related to PD participants seeing the benefits of the work as greatly outweighing the risk, especially given the emphasis on the health benefits of the work in the previous section.

In summary, there is a suggestion that despite the expressed safety concerns, there is precedence for clinical trials to go ahead without primate data, as shown in section 5.2, and as illustrated in the next section on regulation. There are indications in both cases that risk does not prevent therapeutic developments from moving forward, as evidenced by the re-emergence of cell transplantation studies, and the continuing development of viral vector therapies. Barber *et al*. (1979) found that, in the case of research on human subjects, '*...researchers who did not do well in the scientific or in the local-institutional competition for rewards were more likely than others to be involved in studies with less favourable risks-benefits ratios for subjects*' (preface). The findings in schistosomiasis would seem to conform to this, as relatively greater

competition was described by participants in that case, so the riskier approach might be explained in this context. However, this is less apparent for PD, although it could again be the case that the participants see the benefits as being much greater than the risks.

Regulations

As noted in Chapter 4, safety and risk are intrinsically linked to regulation, but again in PD, participants mostly talked about regulation as a barrier to primate research, or as a validation that the work conducted in their country was justified, that is, in a 'it is heavily regulated, so if it is legal it must be good' context. In contrast to schistosomiasis, there was very little evidence of PD participants asserting that using primates was a regulatory requirement. This low incidence of comments about regulatory requirements may indicate that this is a less important factor for these scientists. Indeed, when asked to clarify why primates could not be completely replaced, participant I13NP stated factors other than regulation:

> I don't think it's a definite step I think it's valuable it's another living system which everything is talking to each other in which is certainly more developed than a mouse system talking mouse or rat. I'm not sure what other system people use now. I know pigs have come back in but yeah I mean I think I would be more confident taking it as a person. (I13NP)

It may also be related to there being precedence for moving into human trials without primate data, as indicated by the following extract where regulatory bodies appear to be willing to accept rodent data alone in some cases:

> …you know these days a lot of compounds you know I mean just go straight to humans from mice I mean it's enough for most regulatory bodies to do if the data's strong enough and it makes sense that they will go from mice directly to humans. (I18NP)

What appeared to be a greater concern in the context of legislation for some primate and non-primate using participants was that regulations may be limiting primate research by making it more difficult to conduct the studies, and through increasing the cost, for example:

> They're fiendishly [expensive.] They're heavily regulated they're probably much more heavily regulated than clinical work. So I think they're expensive they're hard to find the places that do it they're heavily regulated and so I think people sort of shy away slightly from it… (I19NP)

In addition, as noted in earlier sections, participants were concerned about research moving out of Europe. Schistosomiasis participants spontaneously talked about this which prompted me to ask PD participants specifically about it. This accounts for there being more PD responses in relation to this, but not for all of them, as some participants mentioned it before they were asked. In either case, participants gave quite extensive comments about concerns that a European ban on primate experimentation would force scientists to conduct the research in countries where it is less heavily regulated, and that there may be consequences for animal welfare and scientific quality. For example:

> It would mean it would stop in England and maybe even Europe and it would carry on in China and it would be unlegislated. It would go to China and India and places where well it's already doing that because it's cheaper to do all these studies in China and India and everywhere else they have massive colonies, but it's completely unlegislated they can do what they like to the animals out there. So it would actually be a big mistake to stop it in Europe and in the UK it's not even as well legislated we don't believe in the States. They can do a lot more to the animals than we can do. (I12P)

I17P took this point further suggesting that as well as losing out on medical developments a movement abroad would have negative economic and intellectual impacts:

> But with it is all the loss of income because all the research is not just done by the researcher their jobs in the university there are many people involved all that will go with it and also if we are not involved in the discovery of it our science will…Economical intellectual everything. (I17P)

In summary, participants describe legislation as both a challenge to primate research (limiting the amount conducted), and as a justification for it. They also express concern that research will move abroad where it is not as well regulated. This raises important ethical questions about whether knowledge claims that come out of these 'less stringent' countries should be accepted by the scientific community. A complete investigation as to whether or not this argument should be used as a challenge to replacing primates in the UK and Europe is beyond the scope of this thesis, but it is considered briefly when discussing the impacts on the impasse (Chapter 6), and in making the final recommendations (Chapter 7).

Health and Ethics Conclusion

These findings indicate that factors related to health and ethics are identified as influential by participants in both cases, but the impact and emphasis placed on them differ in some important ways. Most obvious was the relative low use of sickness narratives by PD participants, who, unlike schistosomiasis researchers, talked much more about the health benefits of their work. In keeping with Brown (2003), it could be that PD participants do not see their work as being as ethically problematic as

schistosomiasis researchers do, or that they simply have greater resources at their disposal, so do not need to engage in this way. There were comparable responses regarding human safety with participants in both fields talking about risk to human health as a challenge to completely replacing primates, and identifying certain research aims as less safe than others. Baber *et al.*'s (1979) notes on scientists' risky behaviour, and the examples of continuing work, such as using viral vectors in PD, indicate that this may not be the challenge to research that it is initially described as. Again, in both fields participants identified regulation as a means of justifying their research, but it was given less as a direct barrier to conducting primate research in PD than it was in schistosomiasis. Instead, as in schistosomiasis, there was greater emphasis on it being a challenge because if primate use was banned in Europe the work would go to 'less stringent' countries where welfare and science might be 'questionable'. It would be interesting to conduct further research into this factor to see if it is a case of scientists painting other countries as 'disreputable others' (Michael and Birke 1994b), or of them performing ethical boundary-work to legitimise their actions (Hobson-West 2012), or both.

5.6 Conclusion

In analysing the interview data and comparing the two data sets, the aim was to access the views of scientists regarding the opportunities and challenges of using primates, in order to understand the primate impasse, and identify if it could be overcome in the two fields. These findings indicate that there are various factors to consider in this

endeavour, and suggest that several sociology and STS theories and concepts might be applicable in this context.

Each of the analytical themes revealed important social dynamics of science that are essential for understanding the primate impasse and, for explaining the similarities and differences identified between the two fields, and the different types of user. Considering the Scientific Institution highlighted the impact of competition in conjunction with reputation, as well as an association between core sets, expectations and publication. The role of entrenchment and policy was indicated in Practical Science. Animals and Ethics revealed the interplay between ethics, speciesism and 'others'. Finally Health and Ethics reinforced that expectations in the form of sickness narratives are essential for interpreting the primate impasse.

Throughout this and the previous chapter, theoretical concepts and literature that have aided the interpretation of the data, and provided some explanation for the findings have been identified. Most notably, the concept of 'competition in science' by scholars, such as Bonitz and Scharnhorst (2001) and Hagstrom (1974), helps to explain why competition is a dominant feature in schistosomiasis, and why collaboration is more likely in PD. Merton's (1968) 'Matthew Effect' appears to be in operation in both cases, with reputation being seen as influential by scientists in both fields. Gilbert's (1976) work supports participants' assertions about the difficulty of getting alternatives to established knowledge accepted, but does not explain the apparent dichotomy that novelty is also necessary, in order to make knowledge more likely to be accepted. The expectations literature (e.g. Brown 2003; Borup *et al.* 2006) helped with interpreting why there are differences in schistosomiasis and PD

participants' comments on the media, hype, and disease severity versus health benefits. The responses from participants regarding alternatives and replacing primates indicate that entrenchment (Collingridge 1980) and flexibility to compensate for it (Knot *et al*. 2001) could be applicable to scientific, as well as technological change. Finally, the discussions about animals and ethics, and health and ethics may be of interest to researchers of ethical boundary-work (e.g. Wainwright *et al*. 2006; Hobson-West 2012) and will contribute more broadly to the morality of animal experimentation literature (e.g. Walker 2006; Rollin 2007).

The conclusions discussed under each theme are important to consider in developing the recommendations for overcoming the impasse. This analysis has shown the intricate interplay within and between these themes and sub-themes, such as the links that participants express between, reputation, publication, knowledge acceptance and funding. Therefore, although they are presented in this and the previous chapter as distinct for the purposes of coherent reporting, these findings are not always mutually exclusive and will be considered together when applying them to understanding the primate impasse, and suggesting how to overcome it (Chapters 6 and 7). An additional finding not reported in the main analysis which could be influential in the implementation and dissemination of the recommendations was the participants' awareness of the Three Rs. This was shown by spontaneous implicit and explicit references by all types of participant. Participants were not directly asked about the Three Rs or animal welfare, yet many of them expressed views on how it made animal work acceptable. This may illustrate this is in the consciousness of scientists, perhaps due to societal pressure or increasing emphasis on the Three Rs in animal experimentation legislation.

The key differences in the scientific aspects of these two fields of research suggest that a general single set of recommendations is not possible, with some areas of the research being easier to propose replacements for than others. However, the findings reveal that some aspects will be universal, such as any proposals relating to publication or ethics related species choice. That being said, this analysis indicates that it is necessary to incorporate field-specific approaches to some areas of the two sets of recommendations. For example, focusing on improving collaboration in schistosomiasis and encouraging researchers in the field to conduct more public engagement. Whereas, in PD a target might be to incorporate dialogue with the advocacy charity and maintain, and expand their collaborations. The responses also reveal that where differences between primate and non-primate users were apparent, it might be important to target specific things at certain types of user. For example, primate users may need to be encouraged to develop more flexible approaches to compensate for 'entrenchment' in primate studies, or as shown in the documentary analysis (Chapter 3), non-primate users might need to construct more expectations about their research to attract more resources.

This and the previous interview analysis (Chapter 4) in conjunction with the documentary analysis (Chapter 3) inform the structuring, dissemination and hopefully implementation of the recommendations to overcome the primate impasse in schistosomiasis and PD detailed in Chapter 7.

The next chapter will consolidate the findings presented here and in Chapters 3 and 4 to discuss how the overall aim of understanding the primate impasse has been

achieved by identifying and appreciating how the social dynamics of science shape the arguments and justifications given about primate use.

Chapter 6: Discussion – Understanding the Impasse

This chapter draws together the findings of the analyses presented in Chapters 3, 4 and 5 and directly addresses the research questions outlined in Chapter 1, highlighting how the overall research aim has been achieved. The discussion is presented in two main sections: Introduction and Background, and Social Dynamics Involved in the Impasse. The latter describes how various social dynamics interact and impact on the primate impasse, as well as highlighting the consequences for existing social scientific thinking. This provides the basis for the recommendations and policy and practice implications presented in Chapter 7, as well as the possibilities for future research.

6.1 Introduction and Background

The role of animal experimentation in biomedical research has been debated throughout history with differences in opinions about its appropriateness being evident as far back as ancient Greece (Franco 2013). As noted in Chapter 1 this is particularly emotive when the experiments involve primates, due to their evolutionary closeness to people and their complex cognitive, social and habitat requirements. Over the past four decades there has been a continuing, consistently polarised discourse about whether or not primates should be used. This project was a consequence of personal experience with this polarisation and frustration with the impasse it creates. Ultimately, the two sides in the debate aspire to the same thing; for research to be done without using primates. Scientists insist they would not use primates if there was

another option, and those opposing primate use demand an immediate ban – yet neither side offers any constructive solutions to end primate experimentation. Instead the same arguments are repeatedly presented, as illustrated in the documentary analysis (Chapter 3) and somewhat in the case studies (Chapters 4 and 5).

As detailed in Chapter 1, the existing literature regarding the animal experimentation debate rarely, if at all, explores how to resolve the debate, move away from biomedicine's reliance on animal models, or specifically addresses understanding the controversy surrounding primate experiments. The lack of academic appraisal of the primate debate and ways to overcome the impasse, including what the impacts might be and how it could be achieved, was somewhat surprising. This led to the decision to undertake a new approach of applying social science methodologies, such as theory of expectations and core sets, to the primate experimentation debate. As noted in Chapter 1, previous work on animal experimentation (Hedgecoe 2006), stem cell research (Wainwright *et al*. 2006) and human embryo research (Mulkay 1993) indicated that this was a productive strategy to adopt. There is an underlying assumption within social science that gaining access to and working with animal research scientists is extremely difficult (Hobson-West 2010), because of distrust, particularly when dealing with controversial aspects of science (Jensen and Holliman 2009). This probably explains the paucity of studies which do so. However, my research aim was:

> To understand the impasse in the animal research debate about whether primates should or should not be used, by examining how biomedical research scientists view the opportunities and challenges of primate use, to determine if and how the impasse can be overcome.

As outlined in Chapter 2, in order to meet this aim a fresh perspective was sought using a multi-method approach to address the following research questions:

1. What arguments/justifications are given for and against using primates in biomedical science?
2. Are there differences in the justifications/arguments between:
    a. Different fields of research?
    b. Different specialist users?
3. To what extent do the social dynamics of science help to explain the continued impasse in the debate?
4. What are the policy implications for primate use and scientific practice?

This chapter will demonstrate that a greater understanding of the impasse is enabled through awareness of the arguments and justifications given about primate use, identifying the social dynamics involved, and appreciating how these dynamics shape the debate. As a consequence, Chapter 7 concludes that the impasse can indeed be overcome and presents recommendations for how this might be achieved.

6.2 Social Dynamics Involved in the Impasse

Through the documentary analysis (Chapter 3) and interviews (Chapters 4 and 5) it became evident that various social dynamics are at work in the primate debate, which help to explain both why the impasse persists and how it might be surmounted.

Speaking to scientists, rather than the public and other stakeholders, to get views on the opportunities and challenges posed by primate research has given the perspective of those intimately involved in the research itself. This, in conjunction with the multi-method approach, gives a richer understanding of the issue than would be possible by discussing the science or social aspects separately.

This section aims to illustrate that the social dynamics of science do help to explain the continued impasse in the debate, and that they may account for some of the differences observed between the two fields of research and between the different specialists. The sociological theories explored in the analyses in Chapters 3 to 5 highlight that there are several common factors which will contribute to overcoming the impasse in both fields of research, which are discussed here. Additionally, any consequences that these findings have for the existing literature are highlighted. However, the analyses indicates that there are field- and research aim-specific factors which need to be incorporated into overcoming the impasse and, these are explained as they arise.

In order to explain the influence of social dynamics on the impasse, this section explores the intricate relationship between the various dynamics such as competition and reputation, in conjunction with additional information gleaned from this project on the differences between specialisms and specialists within them. The discussion for each social dynamic includes a summary of the general findings relating to it, followed by two sub-sections: impact on the impasse and consequences for existing social scientific thinking.

6.2.1 Competition and Reputation

The interviews revealed that competition within the 'scientific institution' does have an impact on the primate debate. Despite there being a lack of contemporary literature and, as Bonitz and Scharnhorst (2001) noted, there being very little recent academic discussion about it, competition is key to understanding the mechanisms of science.

The dual impact of competition on science has been identified previously, with Merton (1957) noting that it functions to motivate scientists to make discoveries, but can also lead to deviant behaviour. Later, Hagstrom (1974) acknowledged that competition leads to allocation of scientific effort, but can have several negative consequences such as duplication, fraud and reduced communication. The findings from the present project support this and illustrate that scientists are acutely aware of the effects of competition on science, with participants discussing the competitive nature of their work both explicitly and implicitly. It also appears to be more widely accepted by scientists beyond the fields studied here, as shown by online blogs and essays such as *Competition in science: Driving science forward or a waste of resources* by cancer researcher Alexis Barr (2009), or the Explorable.com article *Competition in Science* by Florence Colantuono (2009).

Similarly, in describing the process of the 'Matthew Effect', Merton (1968) identified that reputation can be both functional and dysfunctional for different individuals within the scientific institution and at different times in their careers. He noted that scientists with established reputations are often given disproportionately more credit for their findings than those who have made similar discoveries but are less well known. In some cases this can mean that less experienced collaborating scientists are

overshadowed. But when looked at in the context of science communication, having a reputable scientist as co-author or collaborator can in fact boost the visibility of new discoveries and can lead to lesser known scientists gaining acceptance for their work more easily than if they had not had the association. Again, this was evident in the findings of this project, with participants (I17P and I14NP) admitting being more willing to accept work if it was from a 'good' lab or if the author was supervised by a reputable scientist, as well as making explicit reference to those with the greatest reputations having too much influence and having a negative impact on the field.

The analysis conducted in this project has highlighted that reputation and competition are intricately linked with those scientists who perceive themselves as 'winning' the competition often seen as having the greatest reputations. Having a strong reputation puts scientists at an advantage in the competition as they can attract more resources and have a disproportionately high probability of their findings being accepted over those in less-established positions.

Impact on the Impasse

In the schistosomiasis case, competition is restricting progress in the development of an efficacious vaccine and in replacing primates. The competition evident in this field both explicitly described by participants and implied through their concerns about being anticipated, has led to secrecy and a reluctance to cooperate, resulting in there being very little collaboration within or external to the field. This is compounded by the 'Matthew Effect', with those scientists with the greatest reputations seemingly driving the field and limiting which areas are explored and/or accepted.

These two factors have contributed to explicit conflict about which research aims to pursue in schistosomiasis, with different aims all being explored independently with little, if any, within-field or external interaction. This means that alternative methods and the limitations of the existing models and/or research aims are not being explored or addressed, as researchers will not share information and are reluctant to collaborate or explore different avenues or aims. The multiple aims appear to be an influencing factor in the continued use of primates and a reluctance to replace them. These consequences are not surprising; Barber *et al*. (1979) and Hagstrom (1974) both noted that those who are relatively successful in the competition are more likely to follow strict patterns of behaviour and are less likely to seek new ways to solve problems. The dominance of the view that primates are necessary in this field is likely also to be related to the non-primate users' perception that their reputation and consequent influence on the field is very low. This will add to reluctance by the more dominant scientists within the field to engage with alternative methods and/or accept them.

In PD, competition was much less of a factor in determining progress in the field, which has provided insight into how competition functions and how countering it can help to overcome the impasse. Participants in the PD case placed much less explicit emphasis on competition. Instead, they focused on the relatively high level of collaboration that occurs within the field, which indicated that, in this case, this was a means by which the negative influence of competition seen in schistosomiasis was being overcome. Reputation was also viewed slightly differently, with participants placing more emphasis on group or institutional reputation rather than individual reputation and non-primate users not seeing themselves as having less of a reputation

than primate-users. This has resulted in the general agreement that several research aims need to be explored in parallel and in conjunction with each other rather than any one being seen as more important than the others. It has given rise to broader collaboration whereby several models are utilised, and as such there is more willingness to discuss the possibility of replacing primates even if at present they remain in use.

This higher level of collaboration in PD appears to be explained by several interrelated elements. The reduced negative impact of reputation is most likely to be a consequence of there being relatively more research questions to solve in this field which, as Hagstrom (1974) noted, leads to less intense competition. Therefore, it may have been easier for scientists in this field to establish reputations, but as a consequence no single individual or group has a greater influence on the direction of the field than another. This could also explain why in this case it was felt that when those with specific expertise were cooperating, the discussions were more open and honest; the fear of losing the competitive edge or being anticipated is diminished, as there is less focus on one breakthrough being the final answer to effective treatment in this field. It supports Hagstrom's (1974) view that those who cooperate are less secretive and communicate more. The ability to communicate both within the field and to wider audiences is, as Merton (1968) argued, important for science to advance. One PD participant (I20NP) was particularly aware of this and noted that to fully benefit from a good reputation, a scientist needed to actively engage with the scientific community. This appears to be happening a great deal within PD research, as opposed to the situation in the field of schistosomiasis.

Another contributing and perhaps more unusual influence appears to be the PD scientists' relative closeness to their patients. While Barber *et al*. (1979) discussed how competition can affect researcher behaviour in a clinical setting, making those less successful more likely to take advantage of patients, there is, as far as I am aware, no literature on the influence that the clinic can have on competition. The findings from this case lead me to propose that when researchers either work as clinicians or are more focused on the final translation of their research into the clinic, they are more inclined to cooperate to reach a solution more quickly, in order to benefit the patients as soon as possible – and so are less competitive. I would argue that the pressure from a well-established patient support group (Parkinson's UK) is contributing to this effect, as scientists are more routinely faced with the impact of PD and thus feel more obliged to find and develop effective robust treatments efficiently, to satisfy the support they receive. Stilgoe and Wilsdon (2009) noted that questions raised by the Alzheimer's Society patient group, '*…make a real difference to research. And a growing number of scientists are rising to the challenge'* (p.24). This proposition is strengthened by the finding that schistosomiasis is largely a disease of the Developing world, so participants noted that it has a low public profile in the western world and there is no patient support network to speak of. Therefore, although some researchers described visiting patients suffering with the disease, in general the research community in this field, in Europe, is much further removed from the translation of their research into effective therapy, and comes into contact with the effects of the disease much more irregularly than PD scientists do.

Consequences for Existing Social Scientific Thinking

This project has revealed several interesting and important observations that could influence existing knowledge in the area of competition in science. In general, although studying competition in science has fallen out of favour, I believe it should play a more significant role than presently in STS. This is particularly true for those studies investigating controversial areas, and for aiming to understand if and how they might be resolved.

However, the findings indicate that care should be taken when applying the existing competition framework, and that it may need to be augmented or changed in response to changes occurring in modern scientific practice. From the discussion above it is clear that some of the tenets of existing competition theory are supported by this project, particularly those of Hagstrom (1974). However, I feel that there are several aspects of the accepted thinking that need re-examining. To illustrate these I will focus on areas of my research which seem to contradict or at least question some of the statements and conclusions in Hagstrom's (1974) work. Hagstrom (1974) identified that there may be some questions about the adequacy of the functional theory that:

> …the incidence of competition and concern about it will be greatest in specialities perceived to be most important for further developments in science because the number of competent researchers relative to the number of known research problems will be greatest there. (p.12).

But he felt that it was more likely a result of a difficulty in measuring the importance of the speciality within a discipline rather than the theory *per se*. The findings of this project indicate that it may be just as important to consider the perceived importance

of the discipline as whole. If the theory is applied to the two cases investigated here then competition should not be an issue within schistosomiasis, because there is disagreement about which research aim (i.e. speciality) within the field is the most important, and there are also relatively few scientists within the field. Yet, in PD, there is agreement that all of the current research aims are important but there is a much larger pool of scientists working towards them, meaning that, theoretically, competition should be more acute in this field. However, the opposite situations seem to exist. Instead, it appears that the importance of the field in the eyes of the scientific community as a whole and to the wider public is a much greater determinant than the within-field speciality importance. I believe this is linked to the availability of resources and, to some extent, to accountability to succeed quickly. In fields such as PD, which have a high public profile and are perceived as being highly regarded among other scientists and scientific funding bodies, there are more resources available, so competition is less intense. The high visibility of the research makes scientists more willing to cooperate in order to meet the research aims more quickly and robustly, which again diminishes competition. In contrast, in fields such as schistosomiasis in which profile is much lower, there are relatively few resources available, making competition greater and resulting in scientists being possessive about their research and not wanting to share the limited spoils with others.

Hagstrom (1974) found that competition should increase productivity and allow for greater flexibility and increased acceptance of findings, because when competition is high scientists are more likely to be more open to exploring alternative strategies and questions. In addition, as Merton (1968) pointed out, in competitive situations there is increased chance of more than one group/individual independently making a

discovery. This functions to make the finding more acceptable as it has been produced more than once. Hagstrom (1974) concluded that the positive functions of competition in science are more important than the dysfunctions. My analysis indicates that this is not true of every case, with the dysfunctions due to competition apparently being much more significant in determining progress in schistosomiasis, and from the PD case that overcoming these by collaborating actually has a bigger positive influence on a field than the above-outlined functions of competition do. Therefore, I suggest that social scientists should undertake detailed work on different cases when investigating the influence of competition in science, rather than assuming that all science will be affected in the same way.

These findings indicate that perhaps changes in the function of competition over the past 40 years, due to the impact of increasing public awareness, accountability and emphasis on applied research in science, mean that it is time to re-examine the existing competition in science framework. For example, Rödder's (2009) analysis of the medialization of science suggested that scientists may attempt to exploit the media in order to secure priority, particularly in situations characterised by competition or controversy. In addition, Holliman and Scanlon (2009) note that controversial, contested science has more potential to be the subject of media reporting. Therefore, increasing media attention on scientific issues and the increasing orientation of science towards the media recently documented in the sociological literature (see Rödder 2009 for examples) may be another dimension which needs to be incorporated into the dynamics of competition, and how it functions within the scientific institution.

6.2.2 Expectations, Core Sets and Publication

The documentary analysis (Chapter 3) suggested that the theory of expectations can help to explain why some of the arguments in the primate debate are presented as they are, including how the primate proponents' views dominate. It indicated that 'core sets' could be an influencing factor in the existence of the impasse in moving towards replacing primates. The interviews (Chapters 4 and 5) provided more detailed insight, revealing that the social dynamics involved in expectation building, core sets and scientific publication intersect with two of my analytical themes, 'Scientific Institution' and 'Health and Ethics'. In addition, the analysis has shown that these factors are interrelated, and together they can be used to interpret why nuanced differences in the impasse exists between the two cases. Also, they provide a means to resolve some of the restrictions placed on the research and primate replacement by the dominance of some models/methods and/or particular specialists.

Individually, the concepts of the 'core set' and the 'theory of expectations' have become robust but, in general, distinct tools in the sociological analysis of a variety of areas in science and technology. Collins (1981) conceived the concept of 'core sets' to explain how scientific communities respond to experiments, controversy and outside influence, and many scholars have since implemented it successfully. A notable example in the context of this project is Michael and Birke's (1994a) use of the idea to investigate animal experimentation. They found that animal experimenters attempt to exclude 'irrational' others such as anti-vivisectionists from their core set and, as a result, exclude their voices from the discussions about animal studies. Borup *et al*. (2006) provide a nice synopsis of the value of the theory of expectation: ' *a number of studies have shown the decisive role of expectations in establishing new scientific and*

technological fields' and '*…hype and disappointment dynamics have surfaced as an important element in studies of specific scientific or technological fields*' (p.287). Interestingly, the two concepts have rarely been combined, yet the work of Hedgecoe (2006) indicates that this may be a particularly productive way to examine controversy and dispute within science, and the findings of this project support this theoretical approach. Participants in both cases show evidence of constructing 'core sets' but these appear to be functioning in slightly different ways, with a 'core group' of primate users apparently dominating in schistosomiasis but a wider core set including non-primate users being present in PD. This appears to be partially explained by the ability of the different specialists, i.e. primate and non-primate users, to build expectations about their research.

Hedgecoe (2006) also noted that Collins' (1999) view of the different groups outside the core set as consumers of scientific papers glossed over the variations that exist in genres of scientific writing. He argued that different types of scientific publication influence how the science is communicated between those groups. This was evident in the documentary analysis, and in the interviews it was clear that publication was important to the majority of the participants for gaining acceptance of their scientific claims, particularly by their peers. Gilbert (1976) noted that scientific knowledge was constructed within research papers and that citations were used to establish the authority of the author's arguments. He proposed that this method of construction made it extremely difficult for a scientist to achieve recognition when proposing an alternative to an established model. This view was supported by my findings, with participants describing practical difficulties with getting new ideas published. However, they often commented that novelty was necessary in order for a finding to

be noticed and publishable, seemingly creating a dichotomy whereby novelty is both a barrier and facilitator to creating scientific knowledge claims. The analysis showed that different emphasis was placed on the validity of a claim as a result of how and where the information was disseminated. This led me to view scientific publication as a consideration in combination with core set and expectation theory. The findings showed that the lack of publication of negative data; media hype; and the dichotomy of novelty were all influential in how the core set and expectations functioned in schistosomiasis and PD, and could impact on overcoming the primate replacement impasse.

Impact on the Impasse

In schistosomiasis, a combination of the influence of a faction within the core set and an inequality in how the different specialists are creating expectations about their research is maintaining the impasse, slowing progress towards replacing primate models and creating conflict about which research aims to pursue.

The existence of a core set in schistosomiasis research is a factor in the slow progress of the field in general, and more particularly in the adoption and use of non-primate alternatives. Participants indicated that only the specialist group, that is, the 'core set' (Collins 1981 and 1988), can move the field forward and that those outside had to be, by their definition, rational, informed and accurate for their input to be valid. As a consequence, scientists in this field are very reluctant to engage with the public, particularly with anti-vivisectionists, and have a low opinion of their respective views and perception. This has contributed to the low profile of the research and the disease,

and the associated negative impact this has on cooperation to discuss alternatives highlighted in the previous competition and reputation section. However, the findings show that within this field 'outsiders' are not limited to the public or non-scientists but also to the researchers within the field. A 'core group' (Collins 1999) of primate users appears to have formed within the 'core set'. Collins (1999) argued that the core group holds the dominant view within a field and the remaining members of the core set become marginalised because the core group ignore their claims even if they are potentially very important for the field. In schistosomiasis this has led to a delay in the acceptance of non-primate methods and findings, via the core group blocking publication through peer review and because of a possible influence of 'enchantment' on the core group. Hedgecoe (2006), interpreted 'enchantment' as when people outside the core set are certain about results produced within it, but within the core set there is always doubt. I think this functions in this case to make those in the core group and to some extent those in the remaining core set unwilling to dismiss the primate models completely, just in case they are wrong in maintaining that they will not provide useful results.

The impact of the core group has been compounded by the dichotomy of novelty described above and by the relationship between publication and the building of expectations. In schistosomiasis it seems that the non-primate users are much less adept at building expectations about their research to attract resources and acceptance for it than the primate users are, making it more difficult for alternative methods to outshine or even become as mainstream as primate models. Unlike non-primate users, primate users extensively use sickness narratives in their responses, which is a classic mechanism for justifying morally challenging research with visions of future benefits

that might accrue from that research (Brown 2003). In creating those visions the primate users are committing to that specific type of research (Hedgecoe and Martin 2003), making them even more reluctant to deviate from it. Expectations are an established means of channelling, '*efforts into certain directions and contribut*[ing] *to the emergence and stabilisation of socio-technical structures*' meaning that, '*other viable options may then be neglected*' (Konrad 2006, p.430). Therefore, it makes sense that the benefits of the non-primate users' novel techniques and findings are not being realised.

This is exacerbated by two interrelated factors: the negative view of media reporting and hype that the majority of participants voiced, and the problems they identified with being unable to publish negative data. Collins (1999) argues that relying on literature rather than engaging with members of the research community can result in outsiders, such as sociologists, producing a representation of results unrecognizable to those who specialise in the topic, that is, the 'core set'. Hedgecoe (2006) felt that this could be extended to scientists within a field making the research of others in that field unrecognizable. Given the lack of collaboration in this field I would say that not only is a lack of engagement between primate and non-primate users enabling the primate users to dismiss the alternatives, but also that only having a biased literature base to rely on, that is, one which does not report limitations of studies or negative/neutral findings, makes this easier. Additionally, even though some of them acknowledge that it is necessary, the reluctance by participants to engage with mass media or to 'sex up' their research is limiting the acceptance of alternative models and to some extent the primate ones as well. This is because, although it can have negative

consequences (see example in PD below), hype functions to enrol necessary allies and secure investment (Brown 2003).

In PD there were some parallels with the issues in schistosomiasis, such as the presence of the dichotomy of novelty, problems with publishing negative data and negativity towards media reporting, which participants see as overly optimistic and dishonest, leading to false hope that can and has been detrimental for the field. This is restricting the development and acceptance of alternatives that might completely replace primates, and preventing non-primate users from having some success with the methods already available. However, there is no evidence of a core group and the core set appears to be less influential due to a number of factors: more generally, dominance by any particular group is less pronounced because, unlike in schistosomiasis, there is a relatively large pool of specialists, much wider availability of resources and higher disease profile.

While there was evidence that the participants in PD were constructing a core set and viewed those outside as irrational, there was more general respect for the public, with the acknowledgement that public support was important for accountability and for recruiting volunteers to help with the research. This seemed to stem from a drive by funders (particularly Parkinson's UK) to increase public engagement, but was also viewed by the scientists, particularly non-primate users, as a mechanism to increase awareness and understanding of certain models and methods. Therefore, this could be stopping the establishment of a core group, as members of the core set have more avenues for validating their work than just traditional publication, making it more difficult for one group of specialists to hinder dissemination. The PD participants were

more positive about media hype, showing more willingness to engage in that type of communication. There was still some caution about creating false hope, and an example mentioned by I16NP, of the cell transplantation field being halted by too-rapid progression leading to side effects and subsequent adverse publicity, illustrated that hype/disappointment cycles function in scientific change as well as in the technological change described by (Brown 2003). However, the positive value of having more outlets to create expectations about, and gain resources for, research seems to be reducing the relative dominance of primate use in this field.

The findings highlighted a very interesting difference in how schistosomiasis researchers and PD researchers constructed expectations. As noted above, schistosomiasis participants extensively used sickness narratives, but in the PD case, these were replaced by health benefit narratives, with primate users in particular emphasising the therapeutic benefits that would accrue from their research rather than how ill the disease makes the patients. This is most likely because the high profile of PD leads to the assumption that people do not need to be told the impact of it as it is widely understood. Additionally, I think that it is possibly a more effective means of garnering support, evidenced by the increased amount of resources and number of researchers that are attracted to the field, and may again be contributing to the reduced impact of the core set. Several authors have commented on the dynamics of a rhetoric of hope and the benefits that derive from it (e.g. Brown 2003; Borup *et al*. 2006), and although it is acknowledged that the telling of sickness narratives can be a powerful means of creating space, attracting investment and justifying morally challenging research (Brown 2003) there is much less reference to it as a positive force in the theory of expectations. Indeed, indications from these interviews and the documentary

analysis (Chapter 3) suggest that it has more of a negative influence, as it is viewed by some as mean to justify research when the science might not be so good, possibly contributing to the slow progress in schistosomiasis research.

Although non-primate users do not appear to be as marginalised in PD as they are in schistosomiasis there is still resistance to replacing primates, including consideration of how alternatives might be developed. The main contributing factors in the context of this section appear to be a more acute impact of the dichotomy of novelty problem and a difference in how expectations are constructed by the two types of user. Primate users view their work as established, meaning that they are not troubled by the problems of needing to be novel to be published. In contrast, the dichotomy is more acute for the non-primate users who acknowledge that although novelty is important they need to put their research in the context of what has gone before. This makes getting their newer models accepted much more difficult as the historical background is absent, particularly if they propose replacing a long-established method such as a primate study. Additionally, all of the primate users emphasise the health benefits of their research, whereas only a minority of the non-primate users do. This is probably related to the more morally challenging nature of primate research requiring more overt justification, but indicates that the primate users are more adept at constructing expectations, and so are gaining more resources and acceptance for their research relative to the non-primate users.

Consequences for Existing Social Scientific Thinking

This project provides support for several of the existing concepts of the theory of expectations and core sets. For example, it gives additional evidence for Michael and Birke's (1994a) observation that scientists place criteria on who should be legitimate members of the core set and that enchantment does occur (Hedgecoe 2006). There are several instances, in the interviews and the documentary analysis, of expectation-building to gain resources for certain aspects of research, and examples of hype having both a positive and negative role in the social dynamics of science that are in accordance with authors such as: Brown and Michael (2003), Pollock and Williams (2010), Hedgecoe and Martin (2003) and Brown (2003). However, it raises some important questions that are either not addressed sufficiently by the existing literature or may need to be incorporated into it, which are now explored.

Although Brown and Michael (2003) suggest that one approach to the relationship between forms of expectations and innovation change is to think about the relationship between different actors' proximity to the actual scientific work (i.e. those closest are more uncertain than those 'outside'), there is very little existing literature that combines 'core set' thinking with the theory of expectations as an analytical tool. The findings herein lead me to suggest that combining the theory of expectations with the concept of core sets, in a similar way to Hedgecoe (2006), is a fruitful means by which to more subtly analyse scientific controversy and practice. I would add a third dynamic of publication to the combination, because as shown in these findings and noted by Hedgecoe and Martin (2003) and more recently by Wainwright *et al*. (2009) '*…a key focus of the sociology of expectations is in the practices by which such* [hope

and hype] *discourses are put into circulation, for example, the material form statements take, the routes of their dissemination, their timing*' (p.962).

Additionally, these dynamics were involved in my analytic theme of 'Health and Ethics' as well as 'Scientific Practice' and the ethics of using primates have been examined on a number of occasions (e.g. Sauer 2004; Willemsen 2007). Therefore, in terms of future work, I would suggest that the primate debate could be a pertinent example to examine in the context of Hedgecoe's (2010) recent research on bioethics and the reinforcement of sociotechnical expectations, and to investigate how the bioethicist's role might alter the dynamics of the debate.

This project indicates that when using the theory of expectations to examine biomedical science, care should be taken regarding the impact attributed to sickness narratives, as they may not be as beneficial as they first seem. In much the same way as hype has been carefully examined as both beneficial and disruptive to scientific advancement (e.g. Brown 2003), more emphasis should be placed on establishing if, as the present study indicates, sickness narratives can be detrimental to a field rather than simply assuming they are beneficial. This should be supplemented by an appraisal of what influences how sickness narratives function within the scientific dynamics of that field, such as public profile or disease complexity.

The documentary analysis (Chapter 3) revealed an interesting and somewhat unusual approach to citation by some report authors (Hampson *et al*. 1990; Bottrill 2000), which could not have been predicted by existing theoretical thinking. They appeared to be using what I termed 'balanced' rather than persuasive referencing and, although

this was not explicit in the interviews, the participants' discussions around the honesty/dishonesty in media hype and the limitations of their research did indicate a more balanced approach than is normally taken when they publish findings. Although this was not sufficiently influential in this study to warrant inclusion in the discussion above, I feel that it may be an aspect for STS scholars to consider when they examine science in the context of core sets and theory of expectations. It could have implications for the transformation of knowledge and for who is admitted into the core set.

The findings in this project do support Gilbert's (1976; 1977) and more recent work (e.g. Golinski 1990) on transformation of scientific knowledge claims into accepted knowledge through persuasive referencing. However, as noted above, another dimension, 'balanced referencing' may need to be considered when examining how authors utilise citations. As Michael and Birke (1994a) noted, scientists in the animal experimentation controversy place criteria upon who can be a member of the core set. So, attempting to present a more balanced account could be a means to being accepted into the core set, and being seen by scientists as a credible voice in the debate. Scott (1990) argues that readers must assess the credibility and sincerity of a document by trying to determine any prejudices that led the author to adopt a certain stance toward what is being reported. Therefore, 'balanced referencing' could be a means to diminish bias by presenting matters in a neutral format rather than as favourable or unfavourable, perhaps with the aim of increasing the sincerity and credibility of the work. Balanced reporting or 'false balance' appears to be a consideration in media reporting of science (see for example Tom Chivers' [2012] Telegraph blog or the

Understanding Science [2013] education website), but as yet it does not appear to have been considered in any depth in the social dynamics of science.

Another interpretation could be, as noted in the documentary analysis, that the anti-primate participants in the debate are moving toward a more 'scientific' way of making and presenting their arguments, making it more difficult for scientists to refute or dismiss their claims. This would support existing literature on social movements becoming more 'scientific'. For example, Eden *et al*. (2006) noted that increasingly in environmental and health lobbies '*...critics of the results of science use scientific techniques to research and argue their case...*' (p.1063) and Epstein (1995) described how AIDS activists have learned the language and culture of medical science in order to establish their credibility as people who might legitimately speak on biomedical matters.

6.2.3 Entrenchment and Policy

Examination of participants' responses analysed under the theme of 'Practical Science' revealed that there are many comments that express an inevitability about issues around model choice, policy and alternatives that they are somehow ingrained and unchangeable. Therefore, it appears that the concept of 'entrenchment' may be a key factor in restricting the development and use of alternatives, and in the resistance to adopting change in the fields studied. However, there is an interesting contrast in flexibility between the schistosomiasis and PD cases, which provides important insight into how to overcome the impasse. It seems that this might be influenced to

differing degrees by the participants' experiences of policy, in terms of research agendas and legislation.

Collingridge (1980) introduced the concept of the entrenchment of technology as '*...the adjustment of other technologies to one which is developing, so that eventually control of the latter is only possible at the cost of re-adjusting the technologies surrounding it.*' (p.47). He argued that this leads to inflexibility in controlling or changing a technology. This is evident in the findings of this project, particularly in the schistosomiasis case; when scientists were directly asked, they could not even imagine that primates could be replaced. There are several of the nuanced consequences of entrenchment present in the data, such as change being hotly debated and the status quo (primate research) having an unfair advantage in the debate.

More recently, Knot *et al*. (2001) describe a series of flexibility strategies that aim '*...at diminishing the entrenchment of existing technologies or at stimulating the entrenchment of alternative technologies...*' (p.342). Data supporting some aspects of these strategies are present in the current analysis and may explain the observed differences between the cases and different users, in their certainty that primates cannot be completely replaced.

Additionally, Knot *et al*. (2001) argue that their flexibility strategies could be enhanced by Government policies, which consider the problems associated with entrenched technologies and try to foster flexibility and the creation of more options. Salomon (1977) defined science policy as '*collective measures taken by government in order, on the one hand, to encourage the development of scientific and technical*

research, and, on the other, to exploit the results of this research for general political objectives' (pp.45-46). In the context of this thesis I have broadened this definition to include funding and scientific bodies that set priorities for research. While it is beyond the scope of this thesis to conduct a detailed review and analysis of the policies related to primate experimentation, it is apparent that they are taken into consideration by the interview participants. Legislative, funding and research agenda policy can exacerbate the perception of inevitability that a particular area of research will go in a particular direction, such as primates having to be used before therapies can be translated into humans. These policy implications are dealt with in Chapter 7.

Impact on the Impasse

In schistosomiasis, entrenchment is making it extremely difficult for the field as a whole to move away from using the primate model. It has a role in the creation and maintenance of the primate debate, and so is a challenge to overcoming the impasse. To a lesser extent there is evidence that policy is viewed by some of the participants as influencing the direction of research in the field, and that this may be a positive way to move the field forward and to drive the replacement of primates; so overcoming some of the negative consequences of the entrenchment.

When asked directly, both types of user were adamant that it was impossible to completely replace primates in schistosomiasis research, even when asked to theorise a situation where primates were unavailable. Yet despite this, at other times in the interviews, there were suggestions of possible alternatives to primates, such as pigs, and comments by I8P and I9P about precedence in other similar fields, such as

hookworm research, to bypass pre-clinical studies in primates. Therefore it seems that, while some participants could contemplate replacing primates, they were unwilling or unable to say overtly that it could be done. This inability to change from a default position of primate experiments being the only way to conduct the research appears to be a classic example of Collingridge's (1980) 'entrenchment', but in the context of scientific rather than technological developments.

Several of the consequences of entrenchment that Collingridge (1980) described are evident in the data, and help to explain why the impasse remains. For example, entrenchment means that change is expensive and, in this case, participants noted that primates and the specialised infrastructure needed to house and use them was very expensive. Given this investment, there would be financial implications for changing housing systems, investing in new laboratory equipment/animals and retraining staff to work with alternative models. There would be an additional expense of re-housing the animals or if this was not possible the ethical cost of euthanizing them. Additionally, entrenchment means that change is hotly debated. So in the case of schistosomiasis, because it would be difficult to move to other models given the academic as well as financial investment in primate models, the arguments about whether or not to use primates continue.

Collingridge (1980) noted that entrenchment means that, in the debate about change, the status quo has an unfair advantage. In this case, participants provide scientific reasons for the non-primate models they use and suggest other models that might supplant primates, but the associated costs and protracted timeframe for making the shift, mean that the scientific case for the alternatives has to be made much stronger

than it would otherwise have to be. This could account for the reluctance to explicitly state that alternatives could be used. In addition, when entrenchment occurs, 'fixes' are strongly favoured. That is, if a way to alleviate the problems which give rise to the call for change without actually making the change is proposed, it is received more favourably. In the primate context this might account for the emphasis in the interviews on the welfare of the primates, and on suggestions of how to reduce their use – for instance only using them when absolutely necessary at the end-stages of research.

Finally, entrenchment is particularly severe for highly valuable, low variety systems; that is, where the operation of the system depends heavily on one technology and where its failure is very costly. This is certainly true of primate research in schistosomiasis, which generally involves one or two specific species models, the cost of which is extremely high. If the research is not successful, not only is there a financial loss as outlined above, but there is also a high ethical cost.

Furthermore, David (1985) noted that expectations can contribute to 'lock in' (i.e. once led down a particular technological path, the barriers to switching to another, possibly more efficient, one may be prohibitive). Therefore, because the primate users in schistosomiasis are more adept at building expectations this may be compounding the entrenchment. As Knot *et al.* (2001) note and the interview findings indicate, policy may be a way to ameliorate some of the effects of this entrenchment. Participants indicated that changes in funding body policy and external health care agendas were making primate work more difficult and redirecting the research programme respectively. Participant I10P commented that engagement with policy

makers was essential for moving the field forward. These influences are not surprising as Huang and Murray (2010) note in their succinct overview of the role of science policy: '*The traditional role of science policy has been to establish and allocate government funding of science research. Policy makers within the key funding agencies serve as investors in the scientific community. Rather than simply responding to the supply of scientific projects, they use a variety of programmatic structures and research themes to shape both the level and direction of scientific progress*' (p.567). This has been observed in other fields with Peters *et al*. (2012) noting that policy support is crucial in fostering technical changes, particularly for environmental innovations. However, there was also suggestion that policy, particularly if influenced by the public or lobbyists, can have negative or less effective consequences for research. This could exacerbate the entrenchment problem rather than help diminish it. Indeed, despite some arguing that 'public engagement' in policy decisions has several benefits, such as improving trust in policy makers and better compliance and decisions, there is also evidence that in many situations it may not lead to such benefits (see Rowe *et al*. [2010] for references). The participants indicated that legislation prevents the replacement of primates, as the studies on them are required before permission to conduct clinical trials is given. This could be a perception rather than reality, but it also has implications in the next section on Ethics, Speciesism and 'Others'.

The PD interview findings indicate that while there is some entrenchment, in that there is still initial resistance to acknowledging even the possibility of replacing primates, there is much more flexibility to discuss potential alternatives than there was in schistosomiasis. This seems to have been helped by an apparent lesser impact of

policy on participants' decisions and justifications, making the potential for overcoming the impasse in this field much greater. There are caveats to this, with certain areas such as surgical therapies appearing to be more resistant to change than others, but the data provide some indications of how perhaps to begin moving toward primate replacements in those areas by adopting the flexibility seen in others.

Some PD interview participants noted a lack of historical data relating to alternatives to primates, which could be a contributing factor to the reduced but still noticeable entrenchment in this case. Knot *et al*. (2001) highlight that users choose technology, or in this case the primate model, because '*...many others do; this offers the possibility of comparing and exchanging experiences, the benefits of the availability of literature and documentation, and certainty about the availability of the technology or complementary technologies…*' (p.337). However, unlike in schistosomiasis, more PD participants indicated that replacement was or could be possible. They gave examples of alternative models such as pigs, rats, sheep, post mortem human tissue, non-invasive human imaging and mice, and they indicated a precedent within the field of moving directly to clinical trials without primate studies. One participant (I19NP) noted that developments in some alternatives have not been widely disseminated yet. The collaboration identified in this field, the lack of evidence for influential policy and the apparent flexibility of the field are likely to account for this increased amenability to replacing primates.

Actors, in this case scientists, that are closely linked to a technology are not likely to contribute to the flexibility for a substitute (Knot *et al*. 2001). This could account for the PD primate users in particular being adamant that primates cannot be replaced.

However, Knot *et al*. (2001) also argue that collaboration through multi-stakeholder alliances can create new options and increase variety and flexibility for choice. Thus, the higher level of collaboration in PD is probably able to ameliorate the impact of the low level of entrenchment, through the development and use of a variety of models to investigate several, parallel research aims. In conjunction with an apparent lack of restriction in having to follow a specific research path dictated by national policy, this enables them to adopt flexible strategies. There was some evidence that funding policy may be having some influence on primate use, but this is more in the context of ethics speciesism and 'others', and so is discussed in the next section. Of the flexibility strategies that Knot *et al*. (2001) discuss, two are particularly relevant to the PD situation. First, have 'robust options' – that is, technologies which would be appropriate in several relevant futures. In PD, several models are used to investigate a wide variety of research aims with some of them being relevant to more than one area of research, meaning that they can be applied to a variety of scenarios. The scientists should ensure that any expectations they create about alternatives (as recommended in the previous section) provide options for benefits in the distant, as well as the near, future – so that they continue to be viewed as being as robust as the present primate models. Second, have flexibility by variety – that is, the development and maintenance of different technologies that can serve the same function. As noted above, PD participants identified the need to use several different models in their research. Some of these can give the same or similar information as each other and as the primate models, which enables the scientists to switch between the alternatives when necessary. These options should be accompanied by conditions that make it easy and relatively cheap to make the switch, which collaboration can and probably is

facilitating, as each individual scientists does not have to own all the equipment etc. for using and analysing each of the models they can share the data.

Consequences for Existing Social Scientific Thinking

This project has provided findings which have interesting analytical consequences for STS. They imply that the concept of entrenchment is not restricted to technological development (Collingridge 1980) but can be applicable to scientific practice and progression. It can be used to analyse and understand controversies and impasses. In the case of the primate debate, entrenchment is not only a problem because of the animals' high economic value and historical academic investment, but also because its failure has ethical costs as well. Koch and Stemerding (1994) note that '*...application of a new technology requires the creation of an environment in which such applications can actually be realized, in which technology can be "entrenched"* (p.1212) and Knot *et al*. (2001) admit that '*...entrenchment is not problematic as such*' (p.336). Hence, one might argue that entrenchment is necessary for getting alternatives engrained within scientific practice, but in the cases studied here it appears to serve a more negative function. Therefore, when interpreting debates and conflicts within biomedical science, it may be advisable to focus on how flexibility within the scientific practice is functioning and can be increased, rather than how entrenched a new method, model or research aim is or should be. This is particularly true if the arguments that flexibility strategies also offer a way out of controversy (Knot *et al*. 2001) are elucidated further.

6.2.4 Ethics, Speciesism and 'Others'

Findings from the final analytical themes, Animals and Ethics and Health and Ethics, revealed aspects that involved moral considerations that participants identified as influencing their decisions about animal experimentation. These aspects provide some explanation as to why primate use persists, and give some insight into how to make replacement more plausible to the scientists in the two fields. These data indicate an intricate link between scientists' views on ethics, what they report or demonstrate as speciesism, and how they describe the ethical decisions about primate use made by 'others'.

Chapter 1 notes that an emphasis on ethics in science is not unexpected in studies of this kind. The findings of this project support Wainwright *et al.*'s (2006) suggestion that '*…"ethics", is becoming an integral part of maintaining the image of science*' (p.375), as many participants justified their research by talking about the ethical decisions made by themselves and others. This is particularly pertinent in the primate debate as there have been specific discussions about the ethical considerations regarding experimental primates, which some regard as meriting '*special consideration'* and having '*special ethical problems*' (Sauer 2004, p.312). This viewpoint is borne out by participants' comments about work on primates requiring extra justification and prior evidence from other models, and only being conducted when the scientific questions are extremely important. This special consideration for primates is restricting the replacement of primates; the scientists feel that the extra precautions and justification for their use means that ethically the studies are sound, as the benefits in their opinion will far outweigh the costs to the primates due to the extra measures.

Peter Singer (1995) argued that, like racists, '*…speciesists allow the interests of their own species to override the greater interests of members of other species*' and that '*Most human beings are speciesists*' (p.9). In the context of this project, in both cases, participants commented on their personal restrictions as to which experimental models they would use and, in schistosomiasis, specifically related this to being speciesists. Indeed, Hobson-West (2012) noted this kind of response from scientists, but in the present research these comments were in relation to certain species, rather than all experimental animals. Thus, as detailed in the next section, the special consideration given to primates over other animals, and the general consensus from the interviewees that working with rodents and livestock is easier does not completely fit with Singer's definition of speciesism, and suggests that the capacity-based model of moral evaluation (Walker 2006) could be more applicable here.

These data indicate that participants are using the actions or decisions of 'others' to place the responsibility for their own choices of experimental model with other parties. Birke *et al*. (2007) note that '*People come to define themselves and their identities, in short, by differentiating themselves from various others*' and that '*it is a widespread habit that can serve to present one's own practices in a positive moral light*' (p.158). In doing so they provide examples of scientists' interview responses that paint 'others' both inside and outside science as doing things improperly. Participants in the two cases described in this thesis discussed 'others' in a slightly different context. Rather than paint 'others' such as other scientists, regulators and society as doing things incorrectly or immorally to justify their own choices as appropriate, participants described how their choices were dictated or excused by the role the 'others' have in the decision process.

It is worth noting here that scholars taking a more constructivist approach might give an alternative interpretation of these findings in the context of 'boundary-work' or in light of emerging studies, more specifically 'ethical boundary-work'. Gieryn (1983) argued that '*...boundary work exempts members from responsibility for consequences of their work by putting the blame on scapegoats from outside'* (p.792). Hobson-West (2012) interpreted ethical boundary-work as '*...in contrast to boundary-work between science and non-science, ethical boundary-work concerns the distinction between what is ethically legitimate research activity and what is not*' (p.651). This approach is not particularly compatible with the objectivist approach adopted here, of taking the participants' responses as giving direct access to their experiences and views. The concept of boundary-work requires taking participants' responses as narrative accounts and interpreting the data as participants deliberately engaging in boundary-work to convince the interviewer of the moral legitimacy of their activities, which is not how this analysis is framed.

Overall, however, the influence of ethics in terms of scientists' choices is very apparent in this project, and has consequences regarding who else in each field, in addition to the scientists, will need to be consulted if the impasse in replacing primates is to be overcome. Of particular interest in this project was the impact of regulators and regulations, which appeared to have both negative and positive consequences for primate replacement and led to an interesting observation about primate use moving abroad.

Impact on the Impasse

The findings from the schistosomiasis case indicate participants' personal ethical choices, based on what some of them see as speciesism and the deference to the decisions of 'others', are restricting the replacement of primate experiments. However, there is some indication that, if utilised in a slightly different manner, these dynamics could, in fact, act as opportunities to overcome the impasse. While the participants often see these personal choices as somewhat emotional or irrational they may function to make replacing primate experiments easier, as even primate users have expressed discomfort about some of the primate models they have or are using.

In schistosomiasis, the participants' personal ethical boundaries indicated a reluctance to use primate models, even by primate users, with two participants (I5P and I6P) saying that although they had used chimpanzees in the past they would no longer feel comfortable using them. Importantly, this illustrated that scientific utility could be overcome by these personal preferences. Several participants indicated that they were much more comfortable working with rodents and livestock as opposed to primates and companion animals. Alone, this might prove to be beneficial for replacing primates as it could mean that schistosomiasis scientists were happy to adopt alternative models. However, both types of user indicated that they gave more consideration to the decision to use primates than for other models. In conjunction with participants expressing that their personal choices were irrational (i.e. not scientific), the extra measures they note in regard to only using primates when absolutely necessary could account for their continued use.

Theoretically, this emphasis on the moral aspect of the participants' model choice is to be expected because, as Singer (1995) would argue, the scientists are speciesists, in that they are putting human interests above those of the experimental animals. Indeed, one participant (I2NP) specifically mentioned speciesism. However, the emphasis on more consideration for primates indicates that this is not speciesism as defined by Singer but is more nuanced. This is because while the researchers are still putting their own human interest above those of the primates, they are putting the primates' interests above those of other species. Therefore, this is better explained by the capacities-based model of moral status (also known as the sliding scale model) which Walker (2006) describes as '*beings with greater or more complex ["higher"] morally relevant capacities have higher moral status than those with fewer or less complex ["lower"] capacities*' (p.315). She defines capacities as cognitive, sensory, emotional and social abilities. Primates are generally regarded as having greater cognitive capacity than other mammals, although this is not universally agreed (see for example Nuffield Council on Bioethics 2005 pp.41-44), hence the greater consideration and legislative protection they are afforded in biomedical science.

Compounding the effect of these personal boundaries, it appears that schistosomiasis participants are referring to the ethical decisions made by 'others' that are beyond their control, which is enabling them to transfer the responsibility for their choices of experimental model on to other parties. This allows the continued use of primates to persist, although it also provides some opportunities for driving their replacement. Both types of user deferred the choices about experimental models to others. This included I7NP saying that, while they did not want to use primates, they were happy for others to, or I5P commenting that the research had been accepted by the scientific

community (via peer-review) and therefore must be justified. Indirectly, however, the participants indicated that the research decisions were the responsibility of society, via the views about research that communities suffering from the disease held. The greatest emphasis was on describing the role played by regulators and regulation in ethical decisions, with both types of user arguing that the rules governing primate research are very strict, so work deemed to satisfy the requirements must be justified. They also expressed this in the context of regulators requiring primate studies to progress clinical trials and so they would have to be done. Most significantly there were concerns that as the rules tighten, and if they go as far as banning primate use, the research would move abroad. This focus on careful regulation serves to tip the ethical balance in favour of experiments, because as Walker (2006) notes it can lead to the impression that the animals are protected by requirements of justice.

However, when describing the ethical decision made by funders, some schistosomiasis participants (I8P and I7NP) noted that there had been a shift from experiments on primates being used to attract funding to funding agencies now expressing a preference for them not to be included in grants. This indicates that engagement with funding bodies will be particularly important for driving research towards non-primate alternatives in this field.

In PD there was a very similar response in terms of the participants' personal ethical choices about which models to use, particularly in seeing this choice as generally irrational or emotional, rather than scientific *per se*. There were examples where the scientific utility of a model had been overcome by the associated ethical concerns. Unique to this case, one participant (I18NP) described how the opposite had occurred

and they had overcome a previous personal limitation about using mice because the scientific case was too strong not to conduct the research. This suggests that it could be important to make the scientific rationale for using non-primate models stronger and more visible so that they are not seen as the 'irrational choice', which in conjunction with the general personal unease about primates could make replacing primate experiments less problematic.

However, as was the case in schistosomiasis, in PD there was strong evidence that primates are given greater consideration than other species when it comes to making decisions about using them, which could partially explain why they continue to be used despite there being obvious reluctance to do so. There was more discussion about the ethical difficulties of using other species in this case, with no overt indication that some species were favoured over others or any explicit mention of speciesism. This indicates that it may be slightly easier to overcome the problem of primates being justified by the extra measures taken in making the decisions about them in the case of PD than in the case of schistosomiasis.

Similar to schistosomiasis, there is evidence that the PD participants refer to the ethical decisions of 'others' to legitimise and justify their research, and that this could be contributing to the primate impasse, as it enables primate experiments to continue even when the scientists themselves do not really think they are necessary. Although some of the parties that PD participants defer the ethical decision to are the same as in schistosomiasis, such as other scientists, funders and regulators, there is an important contrast between how and where the participants in PD place many of their boundaries.

As noted PD participants do talk about the decisions of other scientists as justification for research, in that others do the work, the scientific community as a whole accepts the studies or that peer review means the work must be justified. In particular, where primates are concerned some participants (I17P and I14NP) felt that the validity of the primate models should be decided by the scientific community as a whole rather than by individuals. However, in PD, unlike in schistosomiasis, it was relatively common for participants to explicitly refer to the ethical decisions of society. This could be understood as an example of Brown and Michael's (2001) 'switching' in which scientists can be seen to swap between science and culture as they go from scientific reasoning for their choices to being part of societal decisions. This indicates, that the PD scientists are more 'sociologically sophisticated', as Brown and Michael (2001) would term it, than the schistosomiasis researchers. They use the cultural/ethical case to add strength to the scientific case they make by utilising both sides of the boundary, i.e. scientists '*pragmatically traverse the boundaries between scientific and social reasoning*' (Brown and Michael 2001, p.7). This may not be surprising given that PD has a much greater public profile than schistosomiasis, so this angle can be exploited more. This also links to comments about funders, with PD participants seeing Parkinson's UK as particularly influential in directing research in this field, whereas there is no such patient advocacy group for schistosomiasis. There was no indication that funding bodies were shying away from funding primate work in this field, and indeed a non-primate user (I14NP) felt that they actually place emphasis on animal research, which could contribute to the difficulty in getting newer alternatives developed.

As in the first case, in PD there was great emphasis on the difference in decisions between the scientists and the regulators/regulations. In a similar way to schistosomiasis this was framed in the context that the research is so highly legislated that it prevents inappropriate studies from occurring. Indeed, some participants went as far as to say that it was more heavily regulated than human research. In stark contrast to schistosomiasis, the PD participants rarely asserted that using primates was a regulatory requirement, which probably accounts for the greater willingness to give examples of alternatives to primates, as they do not perceive legislation as an immediate barrier. Instead, they saw regulation as a challenge to conducting primate research because of increasing associated costs etc. There was particular emphasis (similar to the first case) that, if there was a ban on primate use or if the current legislation became even stricter, research would move abroad to countries such as China which are more permissive, but where conditions and animal welfare are not as good as they are in the UK and Europe. The focus on this aspect of regulation could make it more difficult for scientists in this and other fields to envisage not using primates. Although it was beyond the scope of this project to investigate the validity of these claims, it is clear it contributes to the impasse in the primate debate. In short, it raises serious ethical questions about whether the knowledge claims that are produced in these less stringent countries should be accepted by the scientific community, which the scientists in these two fields need to address.

Consequences for Existing Social Scientific Thinking

The interview findings from this project will be of significant interest to those involved in the discourse about the ethics of animal experimentation, including

sociologists and philosophers. Rollin (2007) argues that '*...little morally sound discussion has come from the research community. If one presses scientists for a response, it usually takes one of two forms: we are "superior" to animals and can do as we wish; or invasive animal research is justified because it produces more benefits to humans and/or animals than harm to animals*' (p.523). This sentiment is echoed in many texts that focus on animal rights and animal ethics, with scientists being portrayed as morally corrupt or as not caring about or dealing with the ethical ramifications of their work.

The data from this study indicates that while there was some evidence of the cost-benefit argument noted by Rollin, the participants in both cases showed a far more nuanced approach to the ethics related to their work and did not need to be pushed to discuss it. Although it could be the case that those who agreed to be interviewed tended to be more ethically aware, it was clear that these scientists had discussions in their own minds and with others in the community about the ethical implications of their choices. In some cases this has prevented them from conducting certain types of research or from using certain animals. Therefore, I believe it would be more fruitful to try to understand why scientists do not make these deliberations more public, despite it being evident that they are privately concerned about it. This could be related to the emotion versus scientific rationality which appears to restrict scientists from being more open about this. This might be eased by focusing more on the capacities-based model of moral status, as scientists in this study already think more in terms of this than animal rights.

Although, Walker (2006) makes a good point that the capacities-based model fails to justify any categorically different treatment of humans versus nonhuman animals, it does give rise to a more 'scientifically' measurable concept (animal capacity), which could work to diminish the irrationality scientists attribute to some ethical decisions. As illustrated by Walker (2006), it offers a means to explore the link between ethics and animal research regulation. The findings indicate that conducting interviews with scientists engaged in research is a useful means to bringing a new dimension to theoretical discussion about animal experimentation ethics. It provides rich data and insight into how animal users discuss, separate and implement moral considerations in their everyday doing of science. Methodologically, this project also provides insightful information into who else should be considered when examining controversial debates and impasses, by identifying who the scientists refer to when describing the impacts that the decisions of 'others' have on their area of research.

6.3 Conclusion

In bringing together the findings from the documentary analysis (Chapter 3) and the case study interviews (Chapters 4 and 5) this chapter has illustrated how the methodological approach taken (Chapter 2) has enabled me to address the research questions posed within the main aim of the project. Of the four research questions posed in Chapter 1 (and highlighted at the beginning of this chapter), the data in Chapters 3-5 have provided many examples of the arguments and justifications given for and against primate use in biomedical science, which are summarised within this discussion. The interview data in particular have revealed that there are differences in

those arguments between the different fields of research and between the different specialists. However, as the discussion presented here reveals, there are also areas of consensus.

Despite much of the public and published debate about primate research revolving around their scientific utility and, to some extent, the ethical implications, this project has uniquely shown that in order to fully understand why the impasse exists and be able to find ways to overcome it, the social dynamics of science need to be examined. So in answer to question three the social dynamics of science are required to fully explain the continued impasse about primate use. They allowed much greater understanding of the primate debate and enabled me to suggest ways to overcome it. This project also illustrates that there is not a singular explanation, but rather several social dynamics that are interrelated in complex and important ways, resulting in this being a multifaceted problem requiring a multi-pronged and adaptable solution. It shows that while the use of primates in biomedical science is often portrayed as a special case in terms of the ethical and scientific justifications for and against it, which requires particular attention within the more general animal research debate, in many circumstances the social dynamics affect it in much the same way as other areas of science.

Therefore, in outlining how this research examines the opportunities and challenges of primate use, this chapter shows that the impasse in moving towards replacing primates illustrated in publications is echoed by scientists in their conversations and practice. It also goes further, to explain why the polarisation continues and why challenges exist to moving beyond the well-documented and repeated arguments. These explanations

are strongly influenced by the social dynamics of science, such as competition, entrenchment and expectations.

This deeper understanding enables the conclusion that the primate impasse can be overcome, by identifying the social dynamics of science that are involved and by harnessing those dynamics to overcome or enhance aspects of the scientific practice. The final chapter now moves on to consider the last research question regarding the implications for primate use policy and good practice. It also considers opportunities for future research that arise from this project and discusses the key limitations of the research.

Chapter 7: Conclusion – Overcoming the Impasse: Policy and Practice Implications

7.1 Introduction

The aim of this project was to gain a deeper understanding of the primate debate to decide if it was possible to overcome the long term impasse which exists. That is, the two sides in the debate aspire to achieve the same aim of finding effective therapies and cures for disease without using primates, but neither side seems able to move beyond the arguments and work towards this goal. The findings revealed that this characterisation of the debate as paralysed by the pro vs. anti-campaigns may be too simplistic. The interviews pointed toward a more complex situation with numerous tensions existing both within and between scientists involved in animal experimentation including primate users. As the discussion in Chapter 6 illustrates, exploring the social dynamics of science, and how they function has shown why the deadlock persists. This resulted in the conclusion that, the impasse in the primate use debate can be overcome in the cases studied. This chapter presents the details of that conclusion, and describes how it might be achieved.

The findings from this research (discussed in Chapter 6) provided the means to make recommendations for how the two fields of research studied, schistosomiasis and PD, can move towards replacing primates. The long term history of the impasse and the ingrained nature of scientific practice identified in this research mean that it must be

acknowledged that implementing these recommendations will not be straightforward, but they represent the ideal situation and where difficulties might arise, these are considered. However, the recommendations cannot be implemented in isolation. They have implications for current policy and practice and will require input from various stakeholders if they are to be successful. Therefore, how the recommendations might be implemented and who and what will influence that are described. The multi-method design of the project enabled a unique vantage point from which to investigate the research aim and questions, and reflections on the nature of the findings and approaches used are discussed. Throughout this thesis, areas of further research have been identified and the limitations of the work noted, so this chapter closes with suggestions of how the findings from this project could be strengthened, how their applicability could be broadened and how they might be used as a basis to enrich current STS research.

7.2 Recommendations for Overcoming the Impasse

The aim of this section is to present the recommendations for overcoming the primate use impasse in schistosomiasis and Parkinson's disease research. These recommendations are based on the understanding gained from this project about the functions of the social dynamics of science and the arguments for and against primate use in these two fields. In general, the suggestions revolve around illustrating how the functions of the identified social dynamics of science can be utilised to overcome or enhance various aspects of scientific practice. There are no time scales indicated as this will be an evolving and dynamic process, dependent on when and how each of the

recommendations is implemented and how they might impact on each other. The section is divided by social dynamic to reflect the discussion in Chapter 6, with field specific recommendations made under each dynamic. A summary of all the recommendations can be found in Appendix 4.

Competition and Reputation

Improving collaboration in schistosomiasis research and maintaining and expanding it in PD research should be attempted. In general terms, increasing cooperation within the fields will reduce secretive and possessive behaviour and enable researchers to discuss more openly the limitations of their current research aims and models, what the alternatives are and how best to proceed. It may enable better allocation of resources and better distribution of research effort which, consequently, could improve productivity and progress towards meeting research aims. It should improve the acceptance of methods and findings that have been used or discovered by a wider variety of the scientists working in the field, with the consequence that the *status quo* and dominant views about the use of primate models are reconsidered and alternatives more readily tried. As noted in the previous chapter, this is a bigger issue in the schistosomiasis case, so field-specific recommendations of how enhanced cooperation might be achieved are given.

Recommendation: Improve the level of collaboration in schistosomiasis research to diminish the negative effects that competition is currently having on delaying general progress in the field, and on the possibility of replacing primates. In order to do this I recommend that the schistosomiasis community consider how they can

actively implement the following concepts and actions, none of which are mutually exclusive and will require a coordinated approach.

a) Improve the profile of the disease within the scientific community and increase public awareness; some possibilities for doing this are outlined in the expectations section below (from p.282)
b) Increase engagement with schistosomiasis patients and with clinical application of vaccines/treatments, perhaps by visiting areas with high disease incidence or establishing patient groups within those countries that can regularly be updated about research and can feedback their experiences to the researchers.
c) Increase the non-primate users' reputation or perception of their reputation by improving the communication of their work. This might initially be through involvement with media outlets through individuals such as journalists or communication professionals, and including social media, creating expectations about it (from p.282) or engagement with patient groups or the public.
d) Where collaborations do exist, attempt to build on these to discuss the conflict surrounding which research aims in the field are the most important to pursue, and try to reach a consensus as to whether it is important to continue with all the aims, or whether any can be abandoned. This might require the facilitation of an external body such as the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs)[8] or a funding

[8] The NC3Rs was launched in 2004 in response to the House of Lords Select Committee report on Animals in Scientific Procedures 2002, available at: http://www.publications.parliament.uk/pa/ld200102/ldselect/ldanimal/150/15001.htm (accessed 12/03/15), which recommended the establishment of a national centre to increase the focus on the 3Rs.

agency, and should include as many specialists in the field as possible.

e) Investigate ways that the limited resources that are currently available can be cooperatively used to address more efficiently as many research questions as possible, by pooling expertise within the field and in some cases, externally. Despite currently being a contentious subject (see the discussion below), the emphasis should be on co-authorship to achieve an end rather than involvement in a race to be the first. This should become easier as the disease profile increases, more resources become available, and all scientists view what they contribute, as being of equal importance.

Given the findings in PD research, these recommendations should improve the impetus to cooperate in schistosomiasis research by diminishing the competitive edge that some researchers have in the field, and emphasising the joint responsibility of the field as a whole to discover an efficacious vaccine. Improving the profile of the disease, increasing collaboration and reducing the explicit conflict regarding research aims should hopefully function to attract resources, and other researchers, to the field to expand what can be achieved in a shorter timeframe than currently seems possible. Cooperation should lead to a more open dialogue about the limitations of current methods, how they might be overcome and what alternatives exist or could be developed, including those that could replace primates.

As noted above, some of these recommendations could be seen as problematic. For instance, here and in further recommendations, a case has been made for increasing public engagement in one form or another. That is, dialogue-informed engagement '*seeking to foster productive exchange between scientists and other stakeholders*

(including members of the general public)' (Jensen and Holliman 2009 p.56). This requires an element of expertise to perform it effectively and may have financial implications for scientists, both in terms of additional training for and, for participating in, the public engagement. This is particularly true in schistosomiasis research for which many of the people they would ideally like to engage with are based in developing countries where language and distance are significant factors. This may be ameliorated somewhat with the emerging digital online forms of communication which Holliman (2011a), notes can afford '*…audiences and users greater opportunities on occasion to respond, participate and contribute to the sciences, e.g. through data collection and analysis as part of citizen science initiatives and via online debates and consultations about scientific developments*' (p.3).

There is also literature questioning the value of engagement and whether the benefits proposed by its proponents can ever be realised (see Delli Carpini *et al*. 2004; Rowe *et al*. 2010 for examples). This includes the dangers of over-hyping research which can damage the legitimacy of, or trust in, a field (Porter *et al*. 2012); this is discussed in more detail in the next section on expectations. However, increasing discourse on the concept of involving the public in research-funding decisions (Rowe *et al*. 2010), and in increasing participation by scientists in the public understanding of science (Pearson 2001), has given greater emphasis to public engagement over recent years. Consequently, funders are actively encouraging researchers to undertake public engagement activities and, in some cases, making this a requirement of receiving support. For example, the Government's Science and Innovation Framework 2004-2014 (HM Treasury 2004) states:

> Over recent years the focus of the Government's Science and Society public engagement activities has moved forward from simply promoting public understanding of science to the wider agenda of facilitating public engagement with science and its application…
>
> The office of Science and Technology's Public Engagement work programme addresses these issues through: offering public engagement grants to widen participation to include people from across the diverse spectrum of social groups in the UK… (pp.103-104).

The Government pursues this agenda through the Research Councils UK and the British Science Association amongst others. The Councils have developed four specific initiatives to involve their funded researchers in public understanding activities/public engagement, two of which are particularly relevant here: offering financial inducements in grant schemes and providing training in communication skills. The experiences of some of the PD participants in being incentivised by Parkinson's UK to participate in public engagement also indicate that this is not limited to traditional funders. Together, this suggests that the financial limitations indicated above could be eased by training and specific funds being made available for scientists to become involved with the public in this way.

Based on the analysis in the previous chapter it is recommended that schistosomiasis researchers should focus on co-authorship. However, some critics of the Research Excellence Framework (REF) system for assessing the quality of research in UK higher education institutions believe that REF acts as a disincentive to collaboration within institutions (Wells 2012) or that it may incentivise dishonest co-authorship (Shaw 2012). For example, on the LSE blog, Dr Peter Wells (2012) argues that because '*...only one author within an institutional unit is able to take credit for a given paper*' then '*...the logical response is to collaborate only with authors outside*', which would encourage external collaboration but discourage the internal cooperation

that is urgently needed in the first instance in schistosomiasis research. However, others question the real impact that this has on scientific practice (Adam 2012) and evidence from funding bodies and some governments indicates that collaboration is actively being encouraged, and can be used as an asset to attract researchers. For example: the *EU Framework Programme for Research and Innovation – Horizon 2020* has international cooperation as an important cross cutting priority (European Commission 2013b); the UK Government's *Strategy for the Life Sciences* (Department for Business, Innovation and Skills 2011) reports that in their forthcoming strategy on innovation and research they will attach considerable significance to international collaboration; and the Government of the Netherlands says in its *2025 choices for the future Vision for Science* report '*We shall strive to facilitate international cooperation*' (Ministry of Education, Culture and Science 2014, p.23) and '*Cooperation is essential both within the scientific field itself, and between science and private sector organisations and civil society*' (p.17). There are also examples of initiatives within institutions to encourage collaboration such as the University of Sheffield's *Sheffield Science Gateway* (University of Sheffield 2015). In conjunction with the experiences of Parkinson's disease researchers, these examples indicate that co-authorship and collaboration are generally achievable and desirable.

Recommendation: Expand the collaborations in PD research to include more incidences of different primate users working together and working with non-primate users to increase dialogue about the limitations that both types of user face, and discern whether some of the dominant views regarding what is and is not necessary in terms of using primates are perceived, regulatory-related or actual. In the long term, this should help with realistic exploration of alternatives to primate use. In the shorter term, it should enable the identification of instances where primate

numbers can be reduced by primate users collaborating rather than duplicating similar studies. It might also reveal that some of the non-primate research can already, or with modification, completely or partially remove the need for primates.

Recommendation: Increase the number of interdisciplinary collaborations in PD research to increase the likelihood of moving toward non-primate methods. If discussions occur across disciplines and institutions that do not normally communicate, it may reveal that it is possible to ask a slightly different question or use a completely novel (in the field of PD research) methodology to investigate PD that will replace the need for certain primate models. For example, advances in non-invasive imaging of humans and small animals that might allow for different avenues to be explored, studies in fish or small mammals, or invertebrate models such as the yeast and fruit fly models used by some participants.

Maintaining the impetus to collaborate in PD research should help progress within the field. Expanding it could see new innovations and resources becoming available to help to more quickly develop effective therapeutics without using primates. It should mean that the currently available resources are used to their maximum potential.

Expectations, Core Sets and Publication

With the above in mind, it is suggested that, to make more progress towards replacing primates, both fields need to overcome, or at least diminish the impact of the dichotomy of novelty through changes in publication practice. Researchers must also address how the non-primate users, in particular, communicate their work to attract support and resources for their research. Scientists should work to diminish the

influence of the core group of primate users in schistosomiasis, and prevent one from forming in PD research. In general this will enable alternatives to primate disease models to become more easily accepted by the scientific communities in each field and, as a consequence, hopefully speed up progress in overcoming the impasse. It should improve communication and acceptance of alternative viewpoints, and may even go so far as to make the alternatives users the core group within the field, making it easier for the field in general to progress and making it more likely that primates will be replaced. As noted in the previous section, some of the recommendations made here could provide a further means to reduce the impact of competition and improve collaboration. Brown (2003) noted that the most vociferous group are the most likely to have their expectations disseminated widely enough to win the competition for their work to be accepted, so in the context of this discussion this is the core set or, in the context of the previous section, those with the greatest reputation. So, as some of the recommendations here aim to diminish the influence of the core set to enable wider dissemination of expectations about alternatives, they will also be useful for improving the reputations of non-primate-using scientists.

Once again, there are differences in how the social dynamics discussed here affect the two fields, so some field-specific suggestions are given. However, it should be noted that some of the dynamics affect the two fields in the same way, so some of the suggestions are repeated in both cases but the emphasis may be slightly different.

Recommendation: Reduce the dominance of the core group of primate researchers in schistosomiasis to enable information and claims about alternative, non-primate research to be more widely disseminated and accepted and to allow the dominant view that primates are necessary to be questioned more readily. This could

be achieved by improving how and by whom expectations are created, and by changing practice in regard to communicating research by implementing the following recommendations.

a) Non-primate users should construct expectations about alternatives by focusing on the health benefits of the research, and discussing their methods in the context of what has already been found, and by emphasising the novel contribution they will make. This will require the writing of review papers and/or more engagement with the public and press (see below).
b) Increase overall engagement with the public by being more willing to address their views and talk to them about the research to increase the public profile of the diseases. This may require some impetus from funding bodies and the development of a patient group could help with this.
c) Increase engagement with media outlets including social media to disseminate expectations about alternatives and the research aims, using the 'hype' to initially raise the profile of the alternatives and the field to attract resources for them.
d) Increase the publication of negative data. This will require dialogue with journal editors and/or funders.

Each of these recommendations should function to draw researchers and resources to the schistosomiasis field to increase the pool of scientists available to form a core set, and reduce the marginalisation of the non-primate users, as has been the case in PD research. By identifying and utilising different outputs for their research in combination with 'selling' their research more effectively, non-primate users should

be able to overcome the negative implications of the dichotomy of novelty and improve their reputation and standing within the core set. This will hopefully lead to greater acceptance of the alternatives to primates, and help to reduce the conflicts about research aims evident in the field, making progress towards effective vaccines more rapid.

Recommendation: Prevent the establishment of a core group of primate researchers in PD to ensure that non-primate alternatives continue to develop and that the collaborative nature of the field is not disrupted, enabling progress toward overcoming the impasse to occur. Once again, how the research is communicated will determine whether this is achievable and the following are suggestions for a multipronged approach to changing and improving current.

a) Continue to engage with the public and, in the case of non-primate users, increase that engagement.
b) Non-primate users should construct more expectations about their research, focusing on the health benefits that will accrue from it and placing it in the context of the research that has already been done while emphasising its novel contribution. This could be facilitated by using existing collaborations to further validate non-primate research in different labs or models.
c) Increase engagement with media outlets including social media, in particular the non-primate users. However, caution should be used to ensure that the 'hype' does not entirely overestimate the short-medium term potential of the research as the costs of hype could be more detrimental in this field. This is because there is much wider public awareness that could lead to more

exaggerated false hope and disappointment and, although there is some necessity to attract resources and acceptance to non-primate studies, it is not as acute as it is schistosomiasis.

d) Increase the publication of negative data. This will require dialogue with journal editors and/or funders.

Implementing these actions should enable non-primate using researchers to overcome the dichotomy of novelty, where, as detailed in Chapters 6, novelty is both a necessity and a hindrance to getting findings accepted, and build upon the successes they have already achieved in gaining acceptance for their research. They should help the field as a whole to reassess the dominant view that primates are essential to certain aspects of the PD research and can never be replaced, as well as, helping to make practical progress towards primate replacements in areas of research where the community seems to agree that it is more feasible.

The problem of negative data publication was raised by participants in both cases and is recognised in the literature on medical research in humans, in which it has been shown that studies are more likely to be published if they report significant or positive results, which can overestimate the effectiveness of a treatment (Dwan *et al*. 2008). More recently, attention has begun to focus on the important consequences that such publication bias can have in laboratory animal research (ter Riet *et al*. 2012). As noted above, this problem will require action by journal editors and/or funders but there is a movement towards making publication of negative or neutral data a more readily available option, with the introduction of journals such as *The All Results Journals: Biol* and the *Journal of Negative Results in Biomedicine*, as well as negative results

sections in other journals such as *Neurobiology of Aging*. This is discussed in more detail in the Policy and Practice section.

As well as the economic issues related to public engagement noted above (p.278), increasing public engagement, in the ways proposed in these recommendations, can be problematic from a professional reputation point of view. Porter *et al*. (2012) found that '*a strongly held perception that communicating science is not institutionally rewarded or perhaps valued in the same way as more traditional research outputs (e.g. publications and grants) has meant engaging the public carries the risk of not being seen as a "serious" scientist by peers*' (p.420). However, this is likely to be less of an issue in the future because, as noted above, funders continue to incentivise scientists to take part in public engagement. Perhaps more importantly in this context, the 2015 REF will include some form of assessment of public engagement in addition to the evaluation of scholarly impact, which represents a significant step towards institutionalising the governmental and scientific commitment to developing a closer relationship between science and the public (Burchell *et al*. 2009).

Entrenchment and Policy

Taking the findings detailed in the previous chapter, it is suggested that overcoming the impact of any existing entrenchment and improving, the flexibility of available methods will reduce the evident restrictions on contemplating primate replacement. This should lead to alternative models being more routinely used and prevent the need for primate use being automatically assumed, thus helping to overcome the impasse. Science policy, as defined in the previous chapter, if properly developed, could assist

with the creation of flexible scientific practice. As well as the field-specific recommendations described below, it should be considered that Knot *et al*. (2001) noted that competition can hamper flexibility because it restricts the free flow of information about the different possibilities or alternative options. Therefore, the recommendation made in the Competition and Reputation section (pp.275-282) will also contribute to a reduction in entrenchment, as will recommendations to increase the expectations regarding alternatives.

Recommendation: Overcome the entrenchment of primate models in schistosomiasis research to enable alternative methods to be considered and become more widespread throughout the field. In order to do this the schistosomiasis community should considers the following to improve flexibility within their scientific practice and to provide an impetus to embrace change.

a) Implement flexibility strategies by: conducting more research on the alternative models proposed in this project (i.e. pigs) to establish a strong bank of background literature; disseminating information more widely on the non-primate models already used, including information on how they can be used in different circumstances, thus improving collaboration and expectations about alternatives.
b) Engage with funders to discuss the possibility of making funds available to implement the logistical changes needed to switch to other methods and to encourage them to provide an impetus to collaborate by offering multi-centre grants
c) Engage with policy makers to determine what is required in terms of scientific evidence to remove the necessity for primate studies. In addition, discuss the

limitations of current research agendas and how more progress could be made. This could be facilitated by involving funders and could also require an element of public engagement.

Recommendation: Maintain and enhance the flexibility in PD research to overcome the persistent but relatively less influential entrenchment of primate use. This should enable PD researchers to move beyond simply a willingness to discuss the potential for replacing primates, to actually conducting their research without them. They can do this by considering the following actions.

a) Conduct studies to establish the applicability of the suggested alternatives (i.e. pigs, mice, rats, sheep, post-mortem human tissue, and non-invasive human imaging) and the existing primate research (e.g. through systematic review and/or meta-analysis) to create and expand the available literature to reduce the reliance on historical data from primate studies and increase the validity of the alternatives.
b) Increase the dissemination of findings from the non-primate alternative models already in existence and being developed through publication and conferences.
c) Maintain and increase collaboration within and external to the PD field.
d) Engage with policy makers and primary legislators to determine how previous studies (such as those in hookworm identified by interview participants) have been able to by-pass primate experiments and how future studies can do the same. Research agendas will then need to be modified to enable the appropriate studies to be conducted, which may require input from the funding agencies.

Implementing these proposals should help to curtail the automatic response that primates definitely cannot be replaced. They should enable the non-primate methods to be more widely considered, accepted and used, and a move away from primate models to occur.

Whilst proposing overcoming entrenchment, it is important to acknowledge that recognition of the concept by scientists will be key to achieving this recommendation. This will require work by Three Rs organisations and professional scientific societies to highlight the areas of research that have become stagnated and facilitate opportunities to refresh and reinvigorate thinking in the field. A recent report detailing the Government's Delivery Plan to reduce the use of animals in scientific research does not quite go as far as describing entrenchment, but it does note that some of the challenges to rapid progress in the Three Rs '*...may relate to conservatism and a risk-averse approach to adopting change*'(Home Office *et al*. 2014, p.17). Therefore, this offers hope that the concept would not be entirely alien to the scientists and associated stakeholders so could be introduced, particularly with support from STS scholars via better dissemination of their work to the scientific communities that they study; something which the present author aims to do.

Engaging with regulators could be seen by some as potentially difficult given the entrenched views about legal requirements and resistance to adopt change. However, recent developments regarding increased openness and transparency about animal experiments (e.g. the *Concordat on Openness on Animal Research in the UK* [Anonymous 2014]) and the scale of consultation regarding the revision and adoption of *Directive 2010/63/EU* and then ASPA, indicate that engagement with regulators such as the Animal Science Regulation Unit (ASRU) is possible. Indeed, (as noted

below in the Policy and Practice Implications section) the Government are now actively pursuing engagement between stakeholders, scientists, government departments and regulators on a domestic and international scale (Home Office *et al*. 2014).

Another potential but significant problem with implementing more flexibility by conducting new studies and exploring alternative models is how the work can be funded in austere economic times. The recent emphasis in Europe and particularly in the UK regarding the importance of the Three Rs and consequent changes/additions to funding research priorities both by the Government and some of the major funding bodies could alleviate this restriction. Indeed, one of the Governments key objectives in their Delivery Plan is to '*Support the NC3Rs and other funders in delivering high quality programmes to develop engagement, uptake and understanding of 3Rs approaches*' (Home Office *et al*. 2014, p.20).

The Government acknowledge that the funding given towards alternatives research is very small in relation to other areas of research but it has increased the amount to just over £8 million in 2014/15 when other areas are undergoing cuts. Initiatives such as the NC3Rs CRACK IT challenge (NC3Rs 2015a) and Innovate UK's feasibility study and SMART funding competitions (Innovate UK 2015), offer opportunities for some of the studies recommended above to be conducted. In addition, five of the major scientific research funding bodies in the UK (Biotechnology and Biological Sciences Research Council [BBSRC], Department for Environment, Food and Rural Affairs [Defra], Medical Research Council [MRC], Natural Environment Research Council [NERC] and the Wellcome Trust) have coordinated with NC3Rs to clarify their expectations regarding animal use in the biosciences. In doing so they '…*encourage*

researchers to look for opportunities for developing new 3Rs techniques as part of larger programmes of work' (NC3Rs *et al*. 2014, pg.13), so some of these recommendations may initially need to be implemented as adjuncts to larger programmes of work. It appears that there is much more impetus for funders to provide resources for alternatives research than ever before and as detailed in the previous section, attracting alternatives funding and resources should become easier as improvements in dissemination, disease profile, collaboration and expectations occur. Further discussion of the impact funding bodies will have in terms of policy and practice is presented below (p.302).

Ethics, Speciesism and 'Others'

In order to overcome the primate impasse in both fields studied it is suggested that the scientists involved need to address the ethical considerations and their views about them directly and as a community. In addition, schistosomiasis and PD scientists identified several parties whom they referred to as justification for certain aspects of research. This has served to highlight the parties that could be particularly important in facilitating many of the recommendations made in this chapter, as such the scientists should engage with these parties. This should further a move away from using 'others' as justification for the continuation of primate research and allow a more constructive dialogue about the moral capacity and scientific validity of all the models used. As noted above, there were some differences in how the ethical dynamics affected the research and participants in the two fields, and these are reflected in the recommendations that follow.

Recommendation: Address the ethical considerations of experimental model choice in schistosomiasis research to enable scientists to move beyond seeing their own choices as irrational and unscientific, and to prevent the decisions of others being used to justify existing primate use even when the scientific case might be questionable. This could be best achieved by implementing the following suggestions and engaging with various interested and involved parties.

a) Non-primate users should increase their sociological sophistication by considering how they can better address the cultural or social implications of their work and in so doing add strength to their scientific case by switching between the social and the scientific justifications. This will no doubt become more important, and perhaps easier if, as suggested in previous sections, the public profile of schistosomiasis disease and research improves. The requirement to report the impact of research in the most recent REF may also prompt more consideration toward this recommendation as its definition of impact includes *'...an effect on, change or benefit to: the activity, attitude, awareness, behaviour, capacity, opportunity, performance, policy, practice, process or understanding of an audience, beneficiary, community, constituency, organisation or individuals*' (HEFCE 2012, p.26).
b) Explore the ethical considerations and moral capacities associated with all the experimental models used and proposed for schistosomiasis more explicitly and directly. This should be done as a community, and the Animal Welfare and Ethical Review Bodies (AWERBs) will have a role to play. It may also need to be facilitated by an external party such as a Three Rs organisation or a specialist group such as the Boyd Group or the Nuffield Council on Bioethics.

c) Strengthen the scientific rationale for the non-primate alternatives by implementing some of the recommendations from previous sections and emphasising each model's scientific advantages to make it more difficult for scientists to see their model choice as irrational or unscientific.

d) Researchers should continue to engage with funders to continue to move away from funding primate experiments and providing more resources for the alternative models. This will be especially important if a patient advocacy group develops with its own capability to fund research in this field.

e) Researchers should consider how to improve dialogue with regulators in this field to remove the presumption that certain studies must be done. The scientists and regulators should also engage in discussions about research moving abroad and how this has and could impact on UK and European schistosomiasis research. This should be realistically based on evidence rather than anecdote. This could also be extended to journal editors to develop and adopt guidelines such as the ARRIVE guidelines (Kilkenny *et al*. 2010) to prevent any ethically questionable research done in more permissive countries from being accepted for publication.

f) Engage with welfare experts, industry and regulators to determine how to improve conditions abroad so that experiments are subjected to the same ethical, welfare and scientific rigor that scientists argue is the case in the UK and other parts of Europe.

Recommendation: Build on the existing ethical consideration given to the models used in PD research to remove the scientists' perception that their model choice (in terms of which species they are willing to use) is irrational and enable the alternatives

to primates to be viewed as scientific and justified. Directly addressing and engaging with the parties they indicate are influential in PD research will enable them to stop being used only as a reason to prevent replacing primates and instead as an opportunity for the change, which some participants have already identified as being a possibility. Achieving this will require input from several parties, but also a slightly different approach by the PD scientists themselves as suggested below.

a) Explore the ethical considerations and moral capacities associated with all the experimental models used and proposed for PD more explicitly and directly. This should be done as a community and the AWERBs will have a role to play. It may also need to be facilitated by an external party such as a Three Rs organisation or a specialist group such as the Boyd Group or the Nuffield Council on Bioethics.
b) Continue to strengthen the scientific rationale for the non-primate alternatives by implementing some of the recommendations from previous sections and emphasising each model's scientific advantages to make it more difficult for scientists to see their model choice as irrational or unscientific.
c) Engage with funders, in particular Parkinson's UK, to discuss how to create and inject more resources into non-primate and also non-animal alternatives for researching PD.
d) Scientists and regulators should engage in discussions about research moving abroad and how this has and could impact on UK and European PD research. This should be realistically based on evidence rather than anecdote This could also be broadened to persuade journal editors to develop and adopt guidelines such as the ARRIVE guidelines (Kilkenny *et al*. 2010) to prevent any ethically

questionable research done in less regulated countries from being accepted for publication.

e) Engage with welfare experts, industry and regulators to determine how to improve conditions abroad so that experiments are subjected to the same ethical, welfare and scientific rigor as scientists argue is the case in the UK and other parts of Europe.

This final series of recommendations have two specific challenges associated with them that must be taken into consideration. First, creating the space and opportunity for researchers to explore the ethical considerations and moral capacities associated with all their experimental models more explicitly and as a community. In the UK the AWERBs could play a significant role in encouraging researchers to discuss these issues more openly as one of the bodies' additional tasks is to '*provide a forum for discussion and development of ethical advice to the establishment licence holder on all matters related to animal welfare, care and use at their establishment*' (Home Office 2014b, p.89). However, in order to broaden dialogue beyond individual research groups and institutions there will probably need to be facilitation by external organisations. In particular, specialist groups such as the Boyd Group could provide the necessary platform for discussions of this nature. For instance, one of the Boyd Group's objectives is to promote dialogue between a diverse set of people and organisations, such as veterinarians, scientists using animals (from industry and academia), members of animal welfare organisations, anti-vivisectionists, members of government and charitable bodies funding or directly engaged in research, philosophers and others. The group has successfully achieved this for several areas of

concern related to the use of animals in science, including the use of primates (Boyd Group 2008).

Second, the question of research moving abroad was identified as important in both case studies, and overcoming it will again require engagement and dialogue between several parties. The Government's delivery Plan (Home Office *et al*. 2014) has recently provided positive indications that the recommendations set out here are achievable. Echoing the responses of participant's the Government notes that *'...if the UK reacts unilaterally in banning the animal tests* [legally required]*, the work is likely to move overseas where welfare standards may be lower*' (p.17). In order to counter this they have committed to several actions related to international harmonisation of regulations and welfare standards, including supporting the NC3Rs' international initiatives and engaging with other countries, especially through the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and the Organisation for Economic Co-operation and Development (OECD). They will also work with the Foreign and Commonwealth Office to support a Chinese initiative to develop standards for research animal welfare and ethical use. This is an ideal platform from which to drive the collaboration and engagement suggested in the recommendations above, but it is my belief that it will require the cooperation and assistance of as many stakeholders and organisations as possible to really press for international change. For example, organisations such as RSPCA International have run training events for several years on topics such as, legislation, ethical review, training for personnel, the Three Rs and animal care in countries such as China, South Korea and Taiwan. They have a history of collaborating with other animal and science organisations and groups (RSPCA

2015), so could contribute a great deal to realising the overall goal of harmonisation of standards and regulations.

Putting these recommendations into practice will require a lot of collaboration between different interested parties, and a great deal of dialogue that would not traditionally occur. However, if effort is put into addressing these ethics-related issues it should make overcoming the primate impasse easier and, in the long term, more rapid. It will enable scientists to discuss more openly the limitations of the models that they are aware of, but which are generally not expressed in the everyday pursuit of science and to fully evaluate the moral standing of all the proposed models. It should also create greater awareness about the impact that those outside of the laboratory have, and how they can contribute to overcoming the primate impasse. It could have a positive impact on the international acceptance of the Three Rs and alternatives more generally.

7.3 Policy and Practice Implications

The discussion above illustrates that exploring the social dynamics of science and the roles of the various functions, should help to overcome the primate impasse, where the polarisation has prevented the two sides from achieving their joint aspiration of finding effective therapies and cures for diseases without using primates. It has provided a framework of recommendations for how the two fields of research under study, schistosomiasis and PD, can move beyond the established arguments, towards primate replacements. However, the recommendations (see Appendix 4 for a

summary) cannot be implemented in isolation, they have implications for current policy and practice and will require input from various stakeholders if they are to be successful. The aim of this section is to outline how the recommendations might be put into operation and who and what will influence that, so the section is divided to consider current policies and the stakeholders involved.

Regulators, Government and Legislation

In the two case studies undertaken, it was clear that legislation and the perception of what regulators require is important to the scientists in both validating and directing their research, and that their responses go deeper than just the fact that they can only perform studies sanctioned by legislation. As noted in the introduction (Chapter 1), recent changes to the European and UK legislation controlling animal experiments have included a greater emphasis on the Three Rs and on protecting primates, theoretically making it more difficult to use them. As the majority of the participants in this study were based in the UK the focus will be on the amended *Animals (Scientific Procedures) Act 1986* (ASPA), the role of the Home Office and UK Government and the Medicines and Healthcare Regulatory Agency (MHRA).

Under ASPA, all projects using primates must be retrospectively reviewed, which will include assessing if the objectives of the programme have been achieved, the amount of harm caused to the animals and whether any lessons can be learnt that will contribute to further implementation of the Three Rs. There is also a requirement for scientists to publish non-technical summaries of their projects that must include information on the harms and benefits associated with the work. These two aspects

present an opportunity to increase transparency around how scientists make their decisions about model choice and give them an opportunity to properly address the limitations of their models, which, at present, they are willing to talk about but are rarely able or prepared to publish. The Home Office should ensure that the retrospective reviews are rigorous in order to facilitate progress towards overcoming the primate impasse. The advisory role that the Home Office Inspectors have in the legislative process provides great scope for the dissemination of information on alternatives which will give scientists another outlet through which to strengthen the scientific case and expectations for their use. The Home Office Inspectors are also ideally placed to disseminate the recommendations made in this thesis, through their establishment visits, conferences and electronic newsletters. This is particularly important given the regard in which the scientists in this study hold the Inspectors and their advice, and is bolstered by the Government plan to enhance the role of Home Office Inspectors and other regulators in disseminating Three Rs advances within the regulatory framework (Home Office *et al*. 2014).

On the 18 July 2011, the Coalition Government pledged to reduce animal experimentation (Featherstone 2011), and the existence of Parliamentary Groups such as the Associate Parliamentary Group for Animal Welfare and the All-Party Parliamentary Group for the Replacement of Animals in Medical Experimentation indicates that, while not a top priority, animal experimentation and welfare are on the political agenda. If the concerns expressed by my participants, that large amounts of scientific research will move abroad become a reality, it may well move up that agenda. While the Government has acknowledged that this could be a problem and it has initiated some counter steps, it needs to consult further with scientists, the Home

Office and funding agencies to determine the current level of movement abroad, how this is predicted to change and what impact it will have on the UK economy, scientific reputation, animal welfare reputation and healthcare. They may then need to work with the various stakeholders to provide incentives for researchers to remain in the UK and to address how to continue to improve international standards, perhaps through accreditation and collaborative funding schemes as well as legislative harmonisation

The MHRA controls whether medicines and medical devices are licenced for market and use. It is these controls that many of the interview participants refer to when they defer back to regulators requiring pre-clinical studies in primates before clinical studies in humans can proceed. However, this may be a perception held by the majority of scientists that needs to be clarified by the MHRA rather than a strict reality. Indeed, personal communications with MHRA staff and the responses of some of the participants indicate that primate evidence is not always a requirement.

It appears from their website (MHRA 2015) and from the presence of staff members on various working groups associated with animal experimentation, that the MHRA are very willing to engage with stakeholders about how they regulate and what their role is. Nevertheless, the scientists' perceptions about the inflexibility of the system remain, so it may now be necessary for the MHRA to be more overt and explicit about their willingness to discuss with scientists what they will and will not accept, in terms of pre-clinical data and to perhaps specifically invite them to submit data from novel methods. They should build upon: their work with the Home Office to push manufacturers and overseas regulators to adopt refinements in the batch testing of

Botulinum toxin. In addition the MHRA should conduct further collaboration with NC3Rs to investigate how to reduce the use of recovery animals in pharmaceutical development and using human tissue instead of animals for pharmacology safety studies (Home Office *et al*. 2014), and engage with other stakeholders and scientists to ensure that the established tests are reviewed and updated as new information and scientific developments, particularly in the field of alternatives, become available.

Funders and Patient Groups

The findings in this study have shown funding priorities to be a factor in driving research in schistosomiasis and PD, and a means to justify the research. Therefore, funding agencies could have a significant impact on progress towards replacing and reducing the number of primate models used in several ways. This is especially so given the present political will to improve Three Rs funding and the recent impetus by the major funding bodies to facilitate greater collaboration and research related to alternatives to animal experiments noted above.

As hinted at by schistosomiasis participants, the funding bodies can refuse or dissuade researchers from using primates by providing funding for alternative models and requiring very strict justification for primate work, which could include making reviews such as the Bateson review (Bateson 2011) mandatory. The Bateson review was commissioned and funded by the BBSRC, MRC and Wellcome Trust in response to a Weatherall Group recommendation (see primate report [17]). The aim of the review was: to assess the quality, outputs and impacts of research using primates supported by them over the last decade, on advancing knowledge in human and

animal health; to identify the strengths and weaknesses of the funded science in this field; to inform their future science and funding strategies; and to feed the outcomes of the review into any Government strategy on primate use. In addition, funders can provide more collaborative funding programmes in a similar vein to the European Framework programmes, such as Horizon 2020 (European Commission 2013b) in which multicentre participation is mandatory for getting the funding. Funding bodies should also work together with industry to create funding opportunities that inspire innovation and development in alternatives such as the NC3Rs CRACK IT challenges (NC3Rs 2015a).

Patient groups or medical charities can also contribute significant funds for researching treatments and cures for their respective diseases as illustrated by the £65 million investment by Parkinson's UK. Therefore, they have the potential to influence the direction of research in much the same way as any of the other major funders. Perhaps, just as importantly, they can help scientists to be more widely exposed to the sufferers of the disease and push for more public engagement, as PD participants indicated was the case with Parkinson's UK. This encourages greater cooperation and more accountability that, as discussed previously, will aid better acceptance of alternatives to primates and improve progress in both fields of research. Patient groups should help to disseminate realistic and responsible expectations and help scientists to communicate their work more effectively to audiences other than their peers. This is a role that Parkinson's UK appears to be adopting as evidenced by the participants' responses about the charity and also by news articles on their website, such as *Bulgarian Yogurt: A Cure for Parkinson's?* (Parkinson's UK 2014), which gives a more realistic explanation of work described in a national newspaper as being a new

treatment for PD. Parkinson's UK Research Communications Manager, Claire Bale, commented that, '*There's no evidence that eating yoghurt benefits people with Parkinson's*' and '*This study was carried out in microscopic worms, so there's a huge amount of work to do before these early findings could lead to a treatment for people with Parkinson's*'.

Scientists and Scientific Progress

Many of the recommendations made here have implications for established scientific practice; therefore, scientists will need to be open-minded and willing to make some changes to their current behaviour. However, the incentives and support from the other parties discussed here should make this transition easier. Indeed, many of the participants acknowledged that things needed to change, so, if provided with the impetus and opportunity, they should be willing and able to adapt.

The scientific community needs to come to a consensus about not accepting findings coming from what they describe as sub-standard labs in Europe or elsewhere in the world. Researchers will need to work with many of the stakeholders and international parties to develop guidelines on what will be accepted, and disseminate these widely through journals and international conferences. Examples of similar consensus being achieved include the ARRIVE guidelines for journals and, more recently, the European Cosmetic testing ban which is being adopted by India (Dhar 2013) and, in part, by China (Iaccino 2014). This should be very productive if the Government support in this area continues and is widened as suggested above (p.297).

As well as implications for the scientists, there will be important considerations for the progress of the two fields. There may be an initial slowing of progress as data are accumulated for non-primate models and new methods are developed. Changes in funding etc. will not be instantaneous, and it will take time to set up the networks necessary, and for scientists to identify and form collaborations, either new or beyond what already exists. However, there will be long- to medium-term gains and, as more interest in the two fields (particularly schistosomiasis) is generated, more resources will become available. Coupled with movement away from expensive primate models and increased collaboration, those resources will ultimately go further, enabling more candidate treatments to be developed leading to an increased chance of an effective one being identified and more quickly progressed through clinical trials. If non-animal or invertebrate methods are utilised, this could further improve the speed of progression as the administrative burden of needing a licence would be removed (indeed some participants highlighted this as a reason for using fruit flies and yeast in their research). This may be hindered by the timescale required to build the necessary evidence base to make the switch to alternatives, although, if the improvements in dissemination and collaboration suggested in the recommendations above are made, this could mitigate the delay somewhat.

Journal Editors, Science Communication and Public Engagement

As noted in this study and by others (ter Riet *et al*. 2012), publication bias due to the non-reporting of negative data is an important problem that can hamper progress in laboratory animal research. Journal editors and, to some extent, funders need to address this. This presents a relatively short-term and efficient way to improve progress in both of the fields studied here and in science more generally as it will

prevent unnecessary duplication of studies and use of animals, provide additional evidence to strengthen knowledge claims and enable better estimation of the potential for novel therapies in clinical trials. The paper by ter Riet *et al*. (2012) provides some useful suggestions for overcoming this problem, which editors, funders and scientists should investigate and consider implementing, such as developing a registration system for all animal experiments similar to that for clinical trials. This would be difficult due to the need to ensure security and minimise bureaucracy but they argue modern information technology should help. Indeed, Holliman (2011b) notes that '*Scientific information is now routinely stored, shared, archived and retrieved over digital networks*' (p. 839). A second idea is to submit manuscripts without any results initially so that acceptance is not reliant on them and the value of the work can be judged on the other aspects of the manuscript. However, this would require consensus within the scientific community in order for peer-reviewers to be willing to work in this way. Alternatively or additionally, there could be more dedicated journals similar to the *Journal of Negative Results in Biomedicine*, and dedicated journal sections or repositories for negative results.

The dichotomy of novelty is a problem in terms of publication and this has been recognised in part by the Government who note '*A challenge for academia is conservatism on the part of journal editors and peer-review panels to accept publications based on non-animal techniques in lieu of the "traditional" animal model*' (Home Office *et al*. 2014, p.17). They suggest that this is being ameliorated by the widespread adoption of the ARRIVE guidelines by a significant portion of international journals. While I agree that this is helpful, further work needs to be done to address the problems associated with peer-review, reputation and core sets etc. that

are noted in this study. This may involve guidelines for peer-reviewers, paid reviewers or an element of continued professional development training for scientists for example. Researchers and journal editors should work together to devise additional ways to address this issue.

Many of the observations and recommendations made in this project will require scientists to improve their scientific communication skills particularly in terms of public engagement. This could be problematic as it has been shown that scientists are concerned that they will not receive professional recognition for undertaking public engagement. For example, Stilgoe and Wilsdon (2009) note that '*Scientists on the whole feel the expectations from funders, colleagues and those who judge quality systematically ignore social aspects, so public engagement becomes a hobby rather than part of everyday work*' (p.23). As noted above, scientists willingness to engage can be driven by funders, but the Government can also influence this. Rodgers-Haydon and Pidgeon (2007) note that sectors of the Government, as well as civil society groups and science policy communities, are increasingly supporting early public engagement to consider technology, and any potential social or ethical issues before significant research decisions are made. In the context of this thesis this is particularly pertinent as they argue that early public engagement can avoid polarization of opinion. This would seem to be a reasonable and effective approach for Government and scientists to take in this case.

Although this thesis provides support for increased public engagement, there is a broad range of existing literature which indicates that, for some areas of research as noted above, scientists will need to be cautious of the impact this could have on

policy. Well-established techniques such as consensus conferences (Einsiedel *et al*. 2001) may need to be employed to ensure there are no unnecessary negative consequences.

Three Rs Organisations and Scientific Societies

As described above, it is envisaged that Three Rs organisations such as FRAME and the NC3Rs, as well as scientific societies such as the Society of Biology and professional bodies such as the Institute of Biomedical Science will play a pivotal role in developing, implementing and disseminating the recommendations made as a result of this project. Societies and professional bodies have the infrastructure to disseminate best practice widely to their members within the scientific community, so are well placed to encourage more emphasis on alternatives and the recommendations in this thesis, particularly those around public engagement and science communication. For example, on its website, the Society of Biology describes itself as '*a single unified voice for biology: advising Government and influencing policy; advancing education and professional development; supporting our members, and engaging and encouraging public interest in the life sciences'* (Society of Biology 2015). Similarly, the Institute of Biomedical Science (IBMS) has among its principal aims 'setting standards of behaviour for its members, educating its members and promoting biomedical science to the public' (IBMS 2013).

In addition to the funding opportunities that Three Rs organisations can provide, they will also play a key role in facilitating collaboration, educating scientists about alternatives and disseminating and directly developing the recommendations made in

this thesis. I have noted some of the collaborations that the NC3Rs have already facilitated and its 2013 annual report provides more details about these (NC3Rs 2013). It could build on the proposals in the Governments delivery plan to help foster the collaborations recommended for PD and schistosomiasis in this project.

Education initiatives such as the FRAME Training Schools (Howard *et al*. 2009) and the RSPCA's international training events and work with AWERBs (RSPCA 2014) could also provide a platform for bringing scientists together to discuss the issues raised by this research and facilitate changes in scientific practice.

As outlined in Chapter 1 'Phasing Out' primate use or the 'Zero Option' as it was termed when first conceived (Balls 1995) has been suggested on several occasions as a means to move towards replacing primates in biomedical research. However, the limited proposals for how to achieve it have never been adopted into practice or meaningfully pursued by scientists. By viewing the impasse through the lens of social dynamics I can more accurately and sensitively suggest how the phasing out process could occur. Therefore, a further step could be to use the recommendations made here as the basis for a 'phasing out' strategy with further practical actions regarding the scientific reasoning to implement it. This will require support from those organisations and societies who can help to validate and refine any such strategies through their links with the scientific community, regulators and other interested stakeholders.

While reducing or even completely replacing primates in some instances, the recommendations arising from this project will undoubtedly lead to increases in the

use of other animals such as livestock and rodents in these two fields of research. This is not without ethical or scientific problems and, in the same way that the validity of the primate models should be examined, so should these other models. While, generally, it is accepted within the scientific community (of these two fields at least) and to some extent by the public (Ormandy and Schuppli 2014) that it is more acceptable to use 'lower' or 'food' animals for research, it is questionable whether this is ethically preferable to using primates (which was noted by one participant). The scientific case also needs to be examined. Examining the consequences of alternatives could be greatly facilitated or even conducted directly by Three Rs organisations given their history of engagement with scientists as well as their experience and expertise in a wide variety of related factors such as, biomedicine, toxicology, ethics, animal welfare and alternative non-animal approaches. Indeed, there is precedence such as the recent FRAME/BUAV report on the use of dogs in pharmaceutical research and development (Bailey *et al*. 2013) and the NC3Rs ongoing work on mammalian models of epilepsy (NC3Rs 2015b).

The successful implementation of the recommendations outlined in this chapter through the parties and policies detailed above is reliant on the effective dissemination of the proposals. This study has highlighted many of the difficulties of communicating novel findings, but the solutions that it has also revealed in terms of public engagement and publication will be applicable. Taking this into consideration the intention is to publish the recommendations in this thesis via the traditional route of peer-reviewed journal and conference presentation, aiming at those relevant to the two fields of research initially. In addition, my position at FRAME will enable me to utilise the findings from this project regarding effective science communication to

publicise the recommendations more widely through various outlets such as, news media, social media and direct engagement with many of the parties highlighted in this chapter.

7.4 Reflections on the Methodology

As outlined in Chapters 1 and 2 the multi-method design of this project is somewhat unusual in this particular area of research into the animal experimentation debate. However, it has enabled the successful elucidation of the non-scientific dimensions which drive the continued impasse in replacing primate studies and given a practical means by which to understand and explore how to overcome it. The resulting analysis and recommendations are more in-depth than would have been possible if the focus had been on one particular phase of this study or with a single methodology. Reflections on taking this multi-method, STS informed approach and the resulting nature of the findings are discussed in this section.

When approaching a qualitative study involving direct access to scientists this investigation has shown there is great benefit in having some prior experience with scientific practices and conducting a literature review of the research areas of the target population. It provides a knowledge base which helps to make the interviews successful, as it gives the interviewer an appreciation of the context and an understanding of the vocabulary which improves the rapport and flexibility.

I felt that having a personal association with the topic, appreciation of the field and at least a basic understanding of the scientific aspects of each case study was invaluable

in gaining access to and building a rapport with the scientific participants. Although my role at FRAME might have been problematic in terms of the participants being reticent to give full and honest answers I found the opposite to be true. I believe that this was in part due to me showing an appreciation for the safety concerns of participants, and FRAME's reputation as a nonthreatening scientific organisation with long standing associations in academia and industry. Having a scientific background but approaching this project as a social scientists gave me as an analyst a different perspective of what the scientists views meant for scientific practice and perhaps a better understanding of the challenges and opportunities discussed in the interviews than perhaps I would have as purely a social science researcher.

Collecting data in a semi-inductive way and using multiple methods, namely documentary analysis, literature review and a multiple-case study comparing semi-structured interviews gave the project the flexibility and roundness to identify important aspects that might not otherwise have been revealed. For example, if from the outset the data had been analysed with preconceived theoretical categories then the impact that social dynamic such as entrenchment and ethics were having could have been missed. If different cases had not been compared then the interplay between different social dynamics may not have been clear, which would have made constructing the recommendations for how to overcome the impasses more difficult and may even have meant that the possibility for doing so was not supported.

In her discussion of the use of qualitative methods within health psychology, Yardley (2007) proposes four characteristics for assessing the validity of qualitative analysis: sensitivity to context; commitment and rigour; transparency and coherence; and

impact and importance, which make a useful reference point from which to summarise these reflections on the design and analysis of this study. In terms of context my role at FRAME and my scientific background gave me a broader view of the topic in which to place the findings and asses their impact and meaning. My commitment to the topic comes from my previous experience with the debate and exploring the views of scientists enabled me to become immersed in new information and to develop new methodological skills. The multi-method approach provided rigour as it resulted in rich data, and the thematic analysis of full transcripts gave plentiful information to address the research questions. Tackling the research in phases using appropriate methods gave coherence. Meanwhile, giving a detailed account of the methodological design and process as well as thick descriptions, including examples of contradictory or unexpected findings, was done to increase the transparency. Finally, in terms of impact this project set out to give a novel and challenging perspective to the primate debate to open up new ways to understand the topic. It has resulted in important recommendations that have practical implications for primate researchers and related stakeholders to enable a culture change to overcome the deadlock in replacing primate experiments.

As with all research projects there are limitations and the next section aims to suggest how some of these might be overcome in future work.

7.5 Future Research

Throughout this thesis, areas for further research have been identified and attempts made to note the limitations of the work undertaken. The purpose of this section is to

draw all of these together to suggest how the findings from this project could be strengthened further, how their applicability could be broadened and how they might be used as a basis to enrich current STS knowledge.

Next Steps and Broader Applicability

While this thesis outlines how it might be possible to overcome the impasse on primate use in these two specific cases, the broader applicability of these findings to all primate research is less certain due to the complex and specialised nuances of each field of research. However, examining the debate through a social dynamics of science lens indicates that there are many common factors related to the impasse that should be applicable to other areas, or at least provide an analytical starting point from which to examine them within Europe. Therefore, to check the wider relevance of the findings in this study an investigation of related fields such as Alzheimer's disease and malaria could be conducted to determine whether this is the case. This could then be broadened out to other diseases such as, HIV/AIDs. It would be important to look at other countries such as the US and China to identify if differences in legislation, culture and/or attitudes towards animals impact on the effects of the social dynamics of science highlighted in this study and, thus, the recommendations needed to overcome the impasse.

The approach taken in this study of speaking to scientists, rather than other stakeholders and/or the public, gave the perspectives of those intimately involved in the impasse, resulting in a richer understanding of the scientific and social aspects of

the debate. However, the findings regarding 'others' indicate that this could be limiting in terms of thoroughly evaluating how effective the recommendations to overcome the impasse can be. Therefore, to ensure the recommendations are as robust as possible it would be useful to investigate the views of some of these key parties such as funding agencies, journalists and journal editors. For example, as a next step it would be very useful to conduct interviews with regulators/policy makers to get their views on dilemmas they face in developing the related policy, and on what is true and perceived in terms of current legislation and willingness to consult with others. Another interesting aspect to investigate would be the medialization of science by comparing news coverage of PD, schistosomiasis and perhaps other fields to see what impact it is having on the 'scientific institution' and whether it will become a more significant factor in overcoming or even exacerbating the impasse.

While the advantages and disadvantages of the adopted methodology are discussed in Chapter 2, it is perhaps useful to reflect that given the nature of the problem under study, another productive way of investigating the primate impasse could be using action research methodology. Jenson and Holliman (2009) note that this methodology is based on the dual aim of:

i. Increasing knowledge or understanding about a particular field or practice
ii. Acting on the basis of that newly produced knowledge to effect positive change within this field

This approach could be extremely useful for examining how to implement the recommendations or even refine them, incorporating more of the identified stakeholders than the present study does.

While this study generated many findings related to expectations and their role in the debate, the time constraints associated with a PhD project and the scope of this particular investigation prevented further investigation into the relationship between bioethics and expectations. Looking at this in more depth, perhaps via AWERBs and/or interviews with bioethicists could give an even deeper understanding of the impasse and why it persists. Another ethical aspect which deserves more attention is the movement of research abroad to countries and laboratories with levels of welfare and scientific practices that are of concern to the scientific community in the UK in particular. Reviewing to what extent this is occurring and deciding how to combat it would provide a timely project that could inform the Government's efforts in this area.

Finally, this thesis presents recommendations for changes in scientific practice and policy with regards to replacing primate experiments and identifies the main stakeholders that will be involved in implementing those recommendations. Further work is required to operationalise the recommendations and mobilise the stakeholders to effect the changes necessary. This could involve prioritising the recommendations in order to maximise their effectiveness. One way to do this would be to return to the case study participants and ask for their views on which recommendations could or should be tackled first. Conducting focus groups involving several of the stakeholders could also be a practical way to do this. It will also be necessary to give further consideration to identifying who among the stakeholders are the leaders and key agents of change and to develop mechanisms to incentivise them to adopt the recommendations and participate in the necessary actions to gain widespread acceptance and implementation of the proposals. In this context it might be useful to

explore the recommendations using Michael's (2009) concept of Publics in General (PiGs) and Publics in Particular (PiPs), which examines the complexity of how different stakeholder groups might emerge over time and indicates that implementing engagement with these 'publics' may require different approaches. For example, in the context of the present research the PiGs strategy might require a sophisticated science communication scheme to inform more broadly about the primate debate or alternatives research. Whereas the PiPs strategy may need to involve a more targeted engagement approach with particular publics, for example patient groups or regulators, for particular purposes such as identifying key research aims or changing funding priorities.

Science and Technology Studies

Chapter 6 describes in detail where this study has revealed areas of interest to STS scholars and discusses how the present study is placed within the context of current thinking/literature. This section highlights the areas which have particularly significant or interesting consequences for existing STS practice and understanding, and suggests future research avenues.

The role of competition in science has been largely neglected by academics in recent years. Further research should be done to address the relevance of the established functions of competition in science, to examine if changes in scientific practice have altered them or whether they can still be applied to science or explain how it is done. Additionally, work should be done on the influence of the clinical setting and patient

groups on competition, as competition may no longer be driving how scientists conduct research in this setting, but instead the clinic may be reducing competition.

An aspect that would greatly help with understanding the 'scientific institution', particularly the primate impasse, would be to investigate further why scientists are willing to talk about limitations of research but will not publish them, and if this is a symptom of the current scientific reward system.

In terms of the theory of expectations, this project has indicated that some of the established thinking may need to be adapted and further work will need to be done to determine if this is the case. For example, looking at the role of hype; is it more positive than negative or becoming increasingly so, as demand for more public engagement increase? There needs to be a more nuanced approach to sickness narratives to determine if they are particularly important for certain classes of disease and if their role is influenced by outside factors such as organised patient interest.

Finally, this project has methodological implications. It shows that it is possible to work with scientists in controversial areas, and that interviews provide rich data that cannot be found in any traditional literature, but that have significant implications for understanding science and controversies within it. It illustrates that, when looking at the social dynamics of science, there are case-by-case factors that make sweeping inferences about the doing and understanding of science problematic. The analysis shows that combining social dynamics of science such as expectations and core sets, is a productive approach for understanding scientific practices and contentious scientific research. Therefore, it is recommend that more in-depth interdisciplinary

studies of this nature are conducted when investigating controversial areas of science and that more focus be placed on how they might be overcome as well as the more common discussion of why they exist.

7.6 Conclusion

The animal experimentation debate and, in particular, the polarisation arising around the use of primates in scientific research has persisted for decades. Using an unusual multi-method approach, this project has identified the arguments involved, explained the differences in the justifications given between different fields of research and different specialists within those fields and, importantly, identified that the social dynamics of science are essential to explaining the continued impasse in the primate debate and how to overcome it. This led to the conclusion that, in certain circumstances, the impasse can be overcome. This thesis offers constructive recommendations for how this might be achieved, involving improved collaboration and communication, increasing flexibility in scientific practices and by addressing ethical considerations surrounding experimental models. Implementing these recommendations involves various stakeholders and has important consequences for primate and alternatives research practices, and science communication. The conclusions of the study have implications for sociological thinking regarding scientific controversy, including the need to increase attention on competition, combine expectation and 'core set' theory, and highlight the applicability of the entrenchment concept to scientific practice. This is just the beginning of what will be

an interesting and important journey for those involved in the primate experimentation debate.

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Appendix 1: Primate Reports Analysed in the Documentary Analysis (originally collated October 2007)

Number	Author	Year	Title	Place published	Publisher	Pages	URL[9]	ISBN
1	Anonymous	1987	The Use of Non-Human Primates as Laboratory Animals in Great Britain	UK	FRAME and Committee for the Reform of Animal Experimentation (CRAE)	16	N/A	N/A
2	Hampson, J., Southee, J., Howell, D. and Balls, M	1990	An RSPCA/FRAME Survey of the Use of Non-Human Primates as Laboratory Animals in Great Britain 1984-1988	UK: ATLA 17: 335-400	FRAME	68	N/A	N/A
3	Crawford, D.	1994	Paradise Lost: A review of UK Primate Research	UK: London	BUAV	141	N/A	N/A
4	Ruhdel, I.W. and Sauer, U.H.	1997c.	Primate Experimentation a Report on the Use, Supply and Housing Conditions of Primates used for Scientific Purposes Within the European Union	Unknown	European Coalition to End Animal Experiments	80	N/A	N/A
5	Bottrill, K.	2000	A Report on the Use of Non-Human Primates in the European Union	EU	Unknown	104	N/A	Technical Assistance Contract no: B4-3040/98/000614/MAR/E2
6	Langley, G.	2002	Phasing Out Primate Use in Belgian Laboratories	Belgium: Brussels	Global Action in the Interest of Animals (GAIA)	85	http://www.gaia.be/ned/downloads/rapport_langley_eng.pdf [10]	N/A

[9] Last accessed 12/01/15

Number	Author	Year	Title	Place published	Publisher	Pages	URL[9]	ISBN
7	Smith, J.A. and Boyd, K.M. (Eds)	2002	The Use of Non-Human Primates in Research and Testing	UK: Leicester	The British Psychological Society	59	http://www.boyd-group.demon.co.uk/Prefaceandsummary.pdf	1 85433 371 2
8	Scientific Committee on Animal Health and Animal Welfare	2002	The Welfare of Non-Human Primates Used in Research	EU	European Commission	135	http://ec.europa.eu/food/fs/sc/scah/out83_en.pdf	N/A
9	Animal Procedures Committee	2002	The Use of Primates Under the Animals (Scientific Procedures) Act (1986) Analysis of Current Trends with Particular Reference to Regulatory Toxicology	UK	Animal Procedures Committee	39	https://www.gov.uk/government/publications/use-of-primates-in-scientific-reseach-2002-report	N/A
10	Creamer, J. and Phillips, T. (Eds)	2005	My Mate's a Primate Evaluating our Relationship and Behaviour Towards our Fellow Primates	UK: London	Animal Defenders International	52	http://www.ad-international.org/admin/downloads/mmap_report_-_complete.pdf	0 905225 16 3
11	Chapman, K.	2006	Opportunities for Reducing the use of Non-Human Primates in the Development of Monoclonal Antibodies a Workshop Report	UK: London	NC3Rs	30	https://www.nc3rs.org.uk/sites/default/files/documents/Workshop_reports/Opportunities_for_reducing_the_use_of_non-human_primates_in_the_development_of_monoclonal_antibodies_(Workshop_report).	N/A

[10] No longer available online as of 12/01/15

Number	Author	Year	Title	Place published	Publisher	Pages	URL[9]	ISBN
							pdf	
12	Langley, G.	2006	Next of Kin a Report on the Use of Primates in Experiments	UK: London	BUAV	98	http://www.buav.org/primates/downloads/BUAVNextofKinreport.pdf[11]	N/A
13	Taylor, K.	2006	Still Dying of Ignorance? 25 Years of Failed Primate AIDS Research	UK: London	BUAV	15	www.buav.org/.../files/Science_Reports/HIV_**Research**.pdf	N/A
14	Anonymous	2006	The Case for an EU Ban on Primate Experiments	UK: Tonbridge	Animal Aid	6	http://www.animalaid.org.uk/images/pdf/euban.pdf	1 905327 20 X
15	Creamer, J. and Phillips, T. (Eds)	2006	The Primate Nations the Case Against Laboratory Research on Primates	UK	Animal Defenders International	20	http://www.ad-international.org/admin/downloads/primate_nations_fin2_(low).pdf	0 905225 17 1
16	Anonymous	2006	Primates in Medical Research	UK	Medical Research Council and Wellcome Trust	21	http://www.mrc.ac.uk/news-events/publications/primates-in-medical-research/	N/A
17	Weatherall, D.	2006	The Use of Non-Human Primates in Research A Working Group Report Chaired by Sir David Weatherall FRS FmedSci [*The Weatherall Report*]	UK: London	The Academy of Medical Sciences, Medical Research Council, The Royal Society, Wellcome Trust	147	https://royalsociety.org/policy/publications/2006/weatherall-report/	N/A
18	Anonymous	2007	Response to the Statement of the EU Scientific Steering Committee on the	UK: London	Animal Defenders International	19	http://www.ad-international.org/admin/downloads/ssc_resp	N/A

[11] No longer available online as of 12/01/15

Number	Author	Year	Title	Place published	Publisher	Pages	URL[9]	ISBN
			Use of Non-Human Primates (NHP) in Biomedical Research				onse_english.pdf	

Appendix 2: Schistosomiasis Interview Schedule

Background

1. What is your position within the department/facility?
2. How long have you worked on schistosomiasis?
3. Which models/methods have you used in that time?
4. What made you decide to work in this area?
5. Is this something that you see yourself continuing to work on for the foreseeable future?
6. Was the primary focus of the research to develop a vaccine? If not, could it have consequences for vaccine development?

Theme 1: Expectations and justification used in biomedical research

1. Is the development of a schistosomiasis vaccine feasible and how long do you think it will take from now?
2. What are your main reasons for using [animals/in vitro models/human studies]?
3. Do you find that you emphasise these reasons in grant applications and/or when publishing the work?
4. What do you consider to be your own most important findings towards the development of an effective vaccine? Which models did this involve?
5. How do you personally measure/judge the success of your work?

Theme 2: Scientific controversies and misunderstandings

1. There seem to be three main vaccine strategies: a) the attenuated vaccine model, b) the self cure model and c) naturally occurring infection in wild pops. What are your thoughts on these in terms of their relevance and likelihood of being successful for identifying and developing an effective human schistosomiasis vaccine?
2. How likely do you think it is that knowledge from animal models will ever translate into an effective human vaccine?
3. Of the animal models utilised in this field, which do you feel are the most relevant to the human condition?
4. Considering the non-animal models (human studies/*in vitro*/omics), what impact do you believe they have had on the development of a vaccine and how important do you think they will be in the future?
5. What do you see as the limitations of the model(s) you have used and what further developments do you see on the horizon?

Theme 3: Perceptions of biomedical research

1. Biomedical research is sometimes seen as morally challenging. How do you think scientists generally deal with this?
2. Are there any models or methods that you would personally not use for your research and why?
3. When you read papers or listen to presentations at conferences, what are the things that tend to lead you to trust what is being said?
4. In your opinion what factors help a scientist to gain a professional reputation within this field? What influence can these have on the field in general?

5. How important is the public's perception of your work to you personally and to the field in general?

Theme 4: Shaping biomedical research, barriers and facilitators

1. ~~Is there anything that would or has ever led you to change the emphasis of your work or the models that you use?~~ (This question was removed after the first couple of interviews as participants found it confusing)
2. In your experience do previous findings in the field shape how you decide to conduct your research and if so in what ways?
3. Have you ever experienced any difficulties with disseminating or gaining acceptance of your work and were you able to overcome these?
4. Workshops/working groups with invited participants/members have been used to encourage dialogue between those holding different viewpoints within a field in order to determine the best ways forward. What are your thoughts on the types of outcomes that might result from these meetings and if you were invited to participate, what would your reaction be?
5. Say you were asked to report on how best to move the field of schistosomiasis nearer to its vaccine goal and that stakeholders needed to be involved how would you approach the task?

Theme 5: Views on implications for primate use policy and regulations

1. It seems that unlike in other fields of research, with schistosomiasis investigators tend to work with a range of species and models. Do you have any ideas as to why this is?

2. In your opinion to what extent is the development of a schistosomiasis vaccine possible without using primates?
3. a) Theoretically if primate use was banned tomorrow could your work continue via other means of enquiry

   b) Thinking about colleagues who use primates, if primate use was banned tomorrow could their work proceed via other means of enquiry?
4. Some people have suggested that it might be better to develop a tiered strategy to minimise primate use in schistosomiasis vaccine research. For example, using alternative models for basic research and initial development of vaccines then only using primates for the safety testing if this is deemed necessary. How feasible do you think this is?
5. What existing models could be utilised for this and what methods would need to be developed or improved?
6. If someone at the EU decided to act on the calls for primate use to be gradually phased out and appropriate legislation to that effect was put in place, how long would be needed to remove the need for primates in your particular research and in the field in general?

Appendix 3: Parkinson's Disease Interview Schedule

Background

1. What is your position within the department/facility?
2. How long have you worked on Parkinson's disease?
3. What made you decide to work in this area?
4. Which models/methods have you used in that time?
5. Is this something that you see yourself continuing to work on for the foreseeable future?

Theme 1: Expectations and justification used in biomedical research

1. What are your main reasons for using [animals/in vitro models/human studies]?
2. Do you find that you emphasise these reasons in grant applications and/or when publishing the work?
3. What do you consider to be your own most important findings towards the development of an effective treatment? Which models did this involve?
4. How do you personally measure/judge the success of your work?
5. How far away do you think a completely effective treatment/cure is?

Theme 2: Scientific controversies and misunderstandings

1. There seem to be 2 main strategies: Surgical approaches such as DBS and neural transplant and chemical, either systemic of targeted, would you agree?
2. Which approach do you believe will be the most effective?

3. What do you think is the key piece of knowledge that has been gained from the animal models of PD?
4. Of the animal models utilised in this field, which do you feel are the most relevant to the human condition?
5. What do you see as the limitations of the model(s) you have used and what further developments do you see on the horizon?
6. Considering the non-animal models (human studies/*in vitro*/omics), what impact do you believe they have had on the development of treatments and understanding of PD and how important do you think they will be in the future?

Theme 3: Perceptions of biomedical research

1. Biomedical research is sometimes seen as morally challenging. How do you think scientists generally deal with this?
2. Are there any models or methods that you would personally not use for your research and why?
3. When you read papers or listen to presentations at conferences, what are the things that tend to lead you to trust what is being said?
4. What factors help a scientist to gain a professional reputation within this field? What influence can these have on the field in general?
5. How important is the public's perception of your work to you personally - and to the field in general?

Theme 4: Shaping biomedical research, barriers and facilitators

1. Do previous findings in the field shape how you personally decide to conduct your research and if so in what ways?

2. Have you ever experienced any difficulties with disseminating or gaining acceptance of your work and were you able to overcome these?
3. How effective do you think workshops/working groups with invited participants/members are at encouraging dialogue to determine the best ways forward in a field?
4. Have you or would you participate in such events?
5. Say you were asked to report on how best to move the field of PD treatment forward and that stakeholders needed to be involved how would you approach the task?

Theme 5: Views on implications for primate use policy and regulations

1. To what extent is the development of a treatment or cure for PD possible without using primates?
2. a) Theoretically if primate use was banned tomorrow could your work continue via other means of enquiry
   b) Thinking about colleagues who use primates, if primate use was banned tomorrow could their work proceed via other means of enquiry?
3. What existing models could be utilised for this and what methods would need to be developed or improved?
4. If phasing out primates became law in the EU what time frame would be needed to make the necessary developments to remove the need for primates in your particular research and in PD in general?
5. As well as the possibility of legislation do you see any other pressures that are or might force the replacement or reduction of primate use in PD research? (e.g.

financial, public perception, availability of animals, new technological developments)

Appendix 4: Summary of the recommendations for overcoming the current impasse about replacing primates in biomedical research for the two case studies explored in this project, schistosomiasis and Parkinson's disease.

Schistosomiasis Recommendations
1. Increase the amount of collaboration initially within the field and then externally by: a. Improving the disease profile b. Increasing engagement with schistosomiasis patients possibly by establishing patient groups c. Increasing non-primate users reputations d. Addressing the conflict surrounding the research aims e. Using available resources cooperatively 2. Reduce the dominance of the core group by: a. Constructing expectations about alternatives based on their health benefits b. Increasing public engagement c. Increasing engagement with media outlets and utilising hype d. Publishing negative data 3. Overcome the entrenchment of primate models by: a. Implementing flexibility strategies b. Engaging with funders

c. Engaging with policy makers

4. Address the ethical considerations of experimental model choice by:
    a. Increasing sociological sophistication of non-primate using scientists
    b. Exploring the moral capacities and ethical considerations of experimental models explicitly
    c. Strengthen the scientific rational for non-primate alternatives
    d. Engage with funders and patient groups
    e. Developing a dialogue with regulators
    f. Engaging with various parties to identify ways to ensure ethical, welfare and scientific rigor in countries outside UK and Europe

Parkinson's Disease Recommendations

1. Continue, but expand collaboration by including increased numbers of:
    a. Different primate users cooperating with each other and with non-primate users
    b. Interdisciplinary collaborations including across institutions
2. Prevent the establishment of a core group of primate users by:
    a. Continuing public engagement and increasing it for non-primate users
    b. Non-primate users constructing more expectations about the health benefits of their research
    c. Increasing engagement with media outlets but being cautious about over hyping the research
    d. Publishing negative data
3. Maintain and enhance the flexibility by:
    a. Conducting further studies on alternatives
    b. Increasing dissemination of non-primate findings

c. Maintain and increase collaboration

d. Engage with policy makers

4. Build on existing ethical consideration given to experimental models and utilise ethical boundaries by:

    a. Explicitly exploring the ethical considerations and moral capacities for experimental models

    b. Continuing to strengthen the scientific rationale for non-primate alternatives

    c. Engaging with funders, particularly Parkinson's UK

    d. Developing a dialogue with regulators to address movement of research abroad

    e. Engaging with various parties to identify ways to ensure ethical, welfare and scientific rigor in countries outside UK and Europe

Appendix 5: Presentations and Posters Related to the PhD

2008

- Presentation: *Revealing Rhetoric: What do primate reports really say about primate use in biomedical research?* Hudson M. IPS 22nd Congress, 08/08/08.

2009

- Poster: *Can the Worm be Turned? Schistosomiasis vaccine research in men, mice and monkeys*. Hudson M. 7th World Congress, 08/2009.
- Poster: *Schistosomiasis Vaccine Research: Scientists' Views on Replacing Primate Models.* Hudson M. LASA Winter Meeting 2009, 12/2009.

2010

- Conference: Invited to speak at LASA Winter Meeting - The Use of Non-Human Primates in Biomedical Science Could not attend due to adverse weather
- Schools Outreach: *I'm a Scientist Get Me Out of Here Competition* -3rd place in my group

2011

- Presentation: *A New Approach to Replacing Primates in Biomedical Science: Accessing the Views of Scientists*, 8th World Congress, Montreal, Canada
- Poster: *Primate Experimentation A New Perspective on an Old Problem*, LASA Winter Meeting, London and STS Priority Group Launch Event, University of Nottingham. This won: Best Postgraduate Research Student Poster (Year 3), Vet School, University of Nottingham

2012

- Presentation: *A New Approach to Replacing Primates in Biomedical Science: Accessing the Views of Scientists*, Animal Use in Research and the New EU Directive Conference , Newcastle

2013

- Presentation: *Social Dynamics of Biomedical Science: An explanation for the impasse in the animal experimentation debate about primate use?* Science in Public, University of Nottingham