Anticipatory Governance: Bioethical Expertise for Human/Animal Chimeras

ALISON HARVEY* & BRIAN SALTER**

*King’s College London, CBAS, London, UK, **King’s College London, Strand, London, UK

ABSTRACT The governance demands generated by the use of human/animal chimeras in scientific research offer both a challenge and an opportunity for the development of new forms of anticipatory governance through the novel application of bioethical expertise. Anticipatory governance can be seen to have three stages of development whereby bioethical experts move from a reactive to a proactive stance at the edge of what is scientifically possible. In the process, the ethicists move upstream in their engagement with the science of human-to-animal chimeras. To what extent is the anticipatory co-establishment of the principles and operational rules of governance at this early stage in the development of the human-to-animal research field likely to result in a framework for bioethical decision making that is in support of science? The process of anticipatory governance is characterised by the entwining of the scientific and the philosophical so that judgements against science are also found to be philosophically unfounded, and conversely, those activities that are permissible are deemed so on both scientific and ethical grounds. Through what is presented as an organic process, the emerging bioethical framework for human-to-animal chimera research becomes a legitimating framework within which ‘good’ science can safely progress. Science gives bioethical expertise access to new governance territory; bioethical expertise gives science access to political acceptability.

KEY WORDS: Bioethical expertise, good science, anticipatory governance, human/animal chimeras

Introduction

When biologist Irving Weissman had the idea of creating a ‘human neuron mouse’ — a mouse in which the brain neurons were replace with human neural
stem cells—he turned to his colleague at Stanford University, Henry Greely, a lawyer and bioethicist, for advice on whether such an experiment should proceed. Although the experiment remains undone, Greely and the panel he convened concluded that the research ‘could be performed ethically, subject to some guidelines’ (Greely et al., 2007, p. 27). That bioethical input on this ‘thought experiment’ was asked for, and given, before the research actually took place is suggestive of a new phase in the burgeoning relationship between bioethical and scientific experts, manifest through the proactive anticipation of the potential governance issues emerging from new scientific developments. Of itself, the demand for the production of new forms of governance in parallel to novel forms of scientific research is a recognised feature of the political landscape. Technoscientific developments continually generate new activities that have the potential to become contentious as they enter the public domain. The potentiality lies in the tension between the proposed technoscientific developments and prevailing cultural values that ‘may be more or less sympathetic to the new science and may or may not resonate positively with values supportive of the science such as those of “scientific progress” and “population health gain”’ (Salter and Salter, 2007, pp. 554–555).

With increasing frequency, the management of this tension has relied on bioethical expertise as an authoritative source capable of legitimating the regulation of contentious issues in bioscience and, through its political operation, acting as ‘a device for bridging potentially troublesome divides: among disciplines, professions, and institutions; and increasingly also among science, state and society’ (Jasanoff, 2005, p. 188). The deployment of bioethical expertise is considered ‘an appropriate strategy for engaging public disputes about science in pluralist democracies in that it provides a predominantly secular, rational, and “neutral” discourse, not unlike the law or science itself, for negotiating the competing value complexes of various public interests’ (Kelly, 2003, p. 342). There is an increasing demand from national and international policymakers for the visible demonstrations of such anticipatory governance of technoscientific developments, as ‘a kind of assurance that potential or actual ethical problems have been identified, attended to and resolved. Thereby, no matter how ambitious or controversial, biomedical research is then able to progress’ (Hoeyer and Tutton, 2005, p. 386). The objective of this anticipatory mode of governance is to pre-empt potential conflict through an earlier and more proactive use of bioethical expertise.

If this is the case, then it can be hypothesised that the anticipatory governance represented by the engagement between bioethical and scientific expertise has been moving ‘upstream’, whereby bioethicists take the initiative to problematise aspects of emerging technoscience as ‘ethical issues’ in order to facilitate the preemptive deployment of their bioethical expertise. On the one hand, Greely suggests that the role his committee took in considering Weissman’s ‘human neuron mouse’ was that of providing a ‘“benchside consult”, an effort to provide ethics-based advice on research in progress’ (Greely et al., 2007,
p. 27). This model suggests a possible role for bioethical expertise as a mechanism to pre-authorise technoscientific developments with the legitimating stamp of bioethical approval, a kind of ‘embedded’ Research Ethics Committee or Institutional Review Board function to deal with proposed science that raises novel ethical problems (rather than to ensure that planned science conforms to pre-established procedures that define what is ethical). On the other hand, there have been calls for a ‘closer collaboration between scientists and philosophers’ (O’Malley and Dupré, 2005, p. 1271) in the form of ‘socio-ethical’ research that ‘does not merely follow scientific transitions but accompanies and interacts with them’ and as such ‘helps anticipate (and to some extent shape) the emerging social issues’ (O’Malley et al., 2007, pp. 67, 74). The ‘socio-ethical’ model suggests something deeper than a ‘benchside consult’; that is, the symbiotic deployment of scientific and bioethical expertise to ensure that only ‘good’ (i.e. ethical) science gets done. General prospects for anticipatory governance will be explored here through the case of human/animal chimeras, i.e. the production of animals containing human biological material in bioscience research.

In this context the social science task is to follow the bioethicists upstream in their engagement with the technoscience of human-to-animal chimera production to analyse the changing relationship between bioethical and scientific expertise: a relationship that acts as a vehicle for the ‘anticipatory governance’ necessary for the production of ‘good science’. The focus is on developing an understanding of what constitutes bioethical expertise in this arena and how that expertise may operate as a form of power, a topic that has received little empirical attention (Haimes, 2002, p. 110; Salter and Jones, 2005, p. 715).

Questions to be explored in this paper are as follows. How does bioethical expertise make judgements about good science and ethical science? And how are these judgements linked to ensure a mutually pleasing form of knowledge production (Hurwitz, 2002)? How has bioethical involvement facilitated and/or hindered scientific research in this area of human/animal mixtures? What are the strategies for enhancing the authority of bioethical expertise?

**Bioethical Expertise and the Construction of Anticipatory Governance**

The role of bioethical expertise in technoscientific governance forms part of the political response to the inadequacies of the technocratic mode of science policy formation with its heavy reliance on the input of expert advisory committees and limited public scrutiny (Irwin and Michael, 2003, p. 44). A more inclusive approach to science policymaking was spurred, in the UK case, by a spate of very public controversies over science in the 1980s and 1990s, such as the crisis over bovine spongiform encephalopathy (BSE) (where a conflicting scientific advice was withheld from the public, prompting a questioning of the validity of scientific knowledge claims) and the reaction to genetically modified (GM) crops (where there has been widespread opposition to their proposed development). The initial response
from scientists and policymakers was to consider such reactions as a dispute over facts, with the public, in a ‘deficit model’, seen as lacking requisite understanding of the science, such that disputes could be alleviated through education (The Royal Society, 1985, p. 10). This public deficit model has been challenged by sociologists of science, who have argued that all knowledge is situated, perspectival and contingent (e.g. Irwin, 1995; Irwin and Wynne, 1996; Jasanoff, 2005). Such claims for the symmetry of knowledge are used to support arguments that ‘lay expertise’ be brought into the decision-making process on an equal footing with the expertise of scientific authorities. The means to resolve tensions, in this case, are considered to be not education of the (deficient) public, but engaging the (expert) public in dialogue with other experts so that a consensus can be achieved.

In some cases, this engagement is moving ‘upstream’ (Rogers-Hayden and Pidgeon, 2007), so that rather than public input being sought on how best to regulate technoscience after development in order to minimise adverse societal impacts, engagement is enrolled as a tool that can ensure the development of a ‘socially robust science’ (Kearnes and Macnaghten, 2006). Governance problems are anticipated through the diagnostic and facilitative skills of social scientists. This ‘upstream’ shift gives social scientists the opportunity to take an active role in the mutual development of science and society, rather than simply acting as chroniclers of this development (Macnaghten et al., 2005). The role of social scientists is two-fold (Barben et al., 2008, p. 984): their expertise is seen to be of value in giving the public a voice and their skills also allow them to take a place in the laboratory as active participants in the process of knowledge production (Macnaghten et al., 2005; Guston, 2008).

To the extent that the ‘upstream’ engagement between science and social science is encouraged by policymakers, it has been conceptualised as a form of ‘anticipatory governance’ that ensures that the science that gets done is socially acceptable science by integrating social science research into the process of scientific research and development so that social perspectives have an influence on the conduct of the science (Barben et al., 2008). To the extent that the state has adopted this approach across a number of policy domains, not just with science, the concept of the ‘anticipatory state’ is beginning to be used to indicate a general shift in its approach to governance (Nelson et al., 2008). In this context one interesting political question is what form of expertise is most attractive to the state as the provider of a legitimating function. Approaches to science governance founded on the ‘dialogic turn’ (Irwin and Michael, 2003, p. x) in public understanding of science resonate positively with the wider ‘deliberative turn’ in democratic modes of governance. As such, it is unsurprising that engagement of the public in dialogue over science was readily taken up by governments in the form of initiatives such as citizens’ juries, consensus conferences and public debates (for example the GM Nation? debate in the UK). However, while such initiatives might be attractive in principle to governments searching for new ways to engender trust in their activities through ‘openness’ and ‘transparency’,
in terms of political practice they have proved rather less appealing. Not only are they ‘difficult to operationalize with any consistency and regarded with suspicion and hostility by the established culture of the UK’s scientific and advisory system’ but they also have the potential to politicise previously uninvolved constituencies, thereby generating controversy where there was none before (Salter and Jones, 2005, p. 713). From the perspective of the pragmatic policymaker, ‘power to the people’ constitutes a cumbersome and unpredictable form of science governance.

In contrast to the uncertain path and products of democratic dialogue with the public, bioethical expertise offers a form of anticipatory governance based on a proven relationship with science and a known utility to policy. It also deals with knowledge in a manner quite different from the style of the deliberative approach. As an alternative to understanding scientific controversies as disputes over facts, the more recent ‘ethical turn’ in science governance frames tensions as due to a conflict of values between science and ‘the public’. It is in this context that the development of the role of bioethical experts in legitimating the governance of science has assumed political salience. Scientific expertise in policymaking is complemented and, in some cases, replaced with a new form of expertise—bioethical expertise—that ostensibly provides ‘a formalized procedure to define public values for policy purposes’ (Tallacchini, 2009, p. 283). At the same time, from the point of view of functional politics, bioethical expertise ‘offers interpretations of political reality which provide policy-makers with a means for defining and codifying their interests, providing orientation and dealing with conflict’ (Salter and Jones, 2005, p. 712).

A major attraction of bioethical expertise as a knowledge base for science governance is that its method of rule creation provides it with a modus operandi that is highly adaptable. As each new territory of bioscience emerges, so bioethical expertise can be deployed to maintain not only its expert reputation, but also as a contributor to cutting edge governance by negotiating a particular way forward that will provide legitimacy for technoscientific developments. Through this engagement, bioethical expertise is absorbed by technoscientific experts in an effortless communion of self-interest. Like any group, bioethical experts have a natural interest in maintaining their knowledge base and expanding their authority over new territories. Over time, bioethical experts have refined the strategies used to achieve this political end. Appearing in the 1960s and 1970s as a replacement for ‘medical ethics’, which had been discredited through its paternalist approach, bioethical expertise was initially concerned with issues in biomedical. Now, as a mature and increasingly self-confident discipline, bioethical experts have assumed the authority to pronounce on any aspect of the biosciences, whatever their application. For example, the fortieth anniversary issue of the influential bioethics publication The Hastings Center Report contains articles on the ethics of ‘bioprospecting’ and of biological weapons. The editor notes: ‘both topics are unusual enough for bioethics that when we first received the
manuscripts, we wondered a little whether they quite fit within our scope. [But] it’s always good to be stretched’ (Kaebnick, 2010). Certainly, from a disciplinary perspective, it is ‘good’ to be stretched if this means accepting the opportunity to expand one’s territory to encompass new bodies of knowledge over which authority can be asserted.

**Demand for Anticipatory Governance in Human/Animal Chimera Research**

From one perspective, the production of animals containing human biological material is not a new scientific or governance domain so it is important to explore why there has been a demand for new forms of governance in this domain, and particularly anticipatory governance (Behringer, 2007, p. 262). For example, cancer research uses chimeric mice produced by xenografting human tumours and transgenic mice containing human oncogenes, both to develop new understandings of disease processes and as tools to screen new therapies. These technologies have become an accepted and, for scientists, essential part of scientific practice with very little in the way of open controversy or ethical debate. This unproblematic acceptance is in contrast to much of the science that uses the converse approach, putting animal material into humans, where the development of xenotransplantation of animal organs into humans as a potential therapeutic tool has received a good deal of scrutiny (NCoB, 1996). Such technoscience raises ethical issues around human identity, challenging the way we intuitively think about what it means to be human (Birke and Michael, 1998, p. 247) and potentially violating the sanctity of human entities (Robert and Baylis, 2003, p. 7).

![Figure 1. Chimeric mouse. Credit: Jenny Nichols, Wellcome Library, London.](image)
In the UK, the recent debate over the ethical permissibility of producing interspecies embryos through Somatic Cell Nuclear Transfer of the nucleus from a human cell into an enucleated animal oocyte, as the first step in the generation of stem cells for research, opened a Pandora’s Box of human-to-animal biological mixing. For example, in its report on interspecies embryos, the Academy of Medical Sciences (AMS) notes:

Whilst much of the current debate focuses on human embryos incorporating animal material, we consider that discussion of the converse situation—already an active and productive field of research—is helpful for a full appreciation of the issues involved. We think it possible that this area of research will generate more active discussion as the science progresses over the coming years. (AMS, 2007, p. 33, their stress)

Furthermore, it is not just mixing of human material into animal embryos that is becoming an issue. The AMS is currently undertaking a project to examine the ‘scientific, social, ethical, safety and regulatory aspects of the creation and use of non-human animals and embryos incorporating human material’, noting in its press release announcing the project that this is a ‘burgeoning area of research’ (AMS, 2009).

What is significant from an ethical and political perspective, is not that the area of research is expanding but that it is moving to produce forms of animal containing human material that are seen to be potentially problematic through the raising of new ethical issues and the stimulation of disquiet among the public. According to Greely, when Irving Weissman approached him with his ‘thought experiment’ for producing a ‘human neuron mouse’, he was ‘aware of the sensitivity of these planned experiments, both ethically and in terms of public reaction’ (Greely et al., 2007, p. 32). Weissman’s hesitancy suggests a concern with mixing of neural material between human and animal—although such mixing had been performed prior to his proposal in 2000, and has continued and expanded since. Why the concern? Such concern may be due to the expansion of the field of stem cell science, particularly the opening up of the field of human embryonic stem cell (hESC) science following the passing of the Human Fertilisation and Embryology Act 2008 in the UK and Obama’s rescinding of Bush’s ban on federal funding of hESC research in the USA in 2009. These seem to have been significant motivating factors encouraging ethicists and policymakers to consider human-to-animal mixing as a potential issue, and much of the current ethical debate on human/animal chimeras focuses exclusively on those chimeras produced using human pluripotent stem cells [see for example the Stanford Encyclopaedia of Philosophy entry on ‘human/non-human chimeras’ (Streiffer, 2009)].

A second factor contributing to the emerging political profile of this governance domain is the use of non-human primates (NHPs) in scientific research. In the UK,
use of NHPs has been considered to raise particular ethical concerns (Boyd Group, 2002; Wetherall, 2006). At the EU level, the European Parliament has adopted a declaration (0040/2007) urging the Commission to establish a timetable for replacing all NHPs in scientific experiments with alternatives. However, the demands of scientists, particularly neuroscientists, for an efficient supply chain of research materials fit for scientific purpose militate against the aspiration to reduce NHP use. For neuroscientists,

the development of effective stem cell therapies will need to ensure that the cells differentiate into specific neural cell phenotypes and generate appropriate synaptic connections. This can only be carried out in a living system of neural complexity comparable to humans. (Wetherall, 2006, p. 75)

The demand from scientists for the essential use of NHPs in research is politically supported by the pharmaceutical industry:

The [pharmaceutical] industry’s view is that its future lies in developing entirely new classes of neuroactive drugs to combat the increasingly important neurological diseases of old age. […] The existence and availability of an effective non-human model with similar neuroanatomical and biochemical properties to humans, both for basic research in the neurosciences and subsequent pharmaceutical development, is considered by the pharmaceutical industry to be paramount to the success of this endeavour. […] It is industry’s view that this may well mean that primates will become the only species, rather than merely the preferred option, both for fundamental research into these conditions and for the regulatory toxicology associated with product development. (APC, 2002, p. 29)

With two such powerful players insisting that the enhanced production of animals, specifically NHPs, containing human biological material is a necessary condition for scientific and industrial advances in important new fields of medical research, it naturally behoves a body such as the Academy of Medical Sciences (AMS) to reflect and respond. This they have done with the view that: ‘The increasing power and sophistication of methods for introducing human material into animals, including new stem cell technologies, is likely to present new opportunities and significant regulatory and ethical challenges in the future’ (AMS, 2009).

The AMS brackets together the ‘regulatory and ethical’ as challenges emanating from new scientific ‘opportunities’. Other bodies with an interest in biomedical governance have also recognised and responded to the emerging governance demands of this domain. In Denmark, the Council of Ethics and the Ethical Council for Animals have already produced a report: Man or Mouse? Ethical Aspects of Chimaera Research (Danish Council of Ethics, 2008). In Germany,
The National Ethics Council, which can choose its own topics, has listed ‘Research on genetic chimeras’ as one of the areas it will be examining (German Ethics Council, 2008). The Swedish National Council on Medical Ethics, which requires a remit from its government to undertake projects, ‘requests that the Government addresses ethical and legal aspects of research with human–animal mixtures’ (Swedish National Council on Medical Ethics, 2008). In addition, the EU commissioned research into ‘fundamental problems in research with mixing creatures between human beings and animals in Europe and abroad’ (Chimbrids project, undated).

The ethical issues raised by human-to-animal chimeras has received considerable attention in articles and debates in bioethics journals, scientific journals, and in reports such as that by the ‘Ethics and Public Policy Committee’ of the International Society for Stem Cell Research (ISSCR) (Hyun et al., 2007). It is this material that provides the main data analysed in this paper. Documentary data are complemented by material from six semi-structured interviews with key players in the human/animal chimera debate. These individuals were identified as key players because of their membership of working groups which have produced or are producing reports on human/animal chimeras designed to feed into policymaking. The membership of such working groups is varied, including academic ethicists, scientists, lawyers, members of animal welfare groups, etc. However, as members of the working groups they are all involved in policy-relevant ethical debates, and as such for the purposes of this paper they are considered as bioethical experts. Interviews were designed to allow refinement of the analysis produced from the main phase of documentary data analysis. Our analysis explores the engagement between bioethical and scientific experts, and investigates the extent to which ‘good’ science may be guaranteed through ‘anticipatory governance’.

Bioethical Power and Human/Animal Chimeras: A Case Study of Anticipatory Governance

If the analysis of the power and political capacity of bioethical expertise is correct, its components should be manifest in the methods and ideas used to deal with the potential governance issues raised by the creation of human/animal chimeras. To what extent are bioethical experts anticipating these governance issues? How is the bioethical discourse on human/animal chimeras establishing the principles to be applied in governance of this domain? And how is this contribution reinforcing the legitimating role of bioethical expertise in the anticipatory governance of science? In addressing these questions we argue that the concept of anticipatory governance helps to explain three phases of deployment of bioethical expertise in human/animal chimera research. These include: agenda setting; exclusion of operating principles; and inclusion and implementation of operating principles.
Defining the Governance Agenda

In their study of the stem cell discourse in the United States, Wolpe and McGee (2001, p. 185) note that in public policy debates

the first battle is often a struggle about definitions, and the winning side is usually the one most able to capture rhetorical primacy by having its definitions of the situation accepted as the taken-for-granted landscape on which the rest of the game must be staged.

In relation to hESC science, bioethical experts established their authority by defining a limited set of components—embryo source, embryo age, embryo creation date, and so on—as the matters that were relevant for the debate and hence appropriate for the policy agenda. These components, ‘simultaneously scientific and ethical objects’ (Salter and Salter, 2007, p. 568), became the counters that were valid for use in the ethical trading game of governance formation.

Similarly, in the field of the production of animals containing human biological material, the first task for bioethical experts is the identification of the principles that can be used to draw the line between ethically unproblematic and ethically contentious technoscience. When applied, such principles anticipate where ethical governance is needed and where not. In their Ethical Standards for Human-to-Animal Chimera Experiments in Stem Cell Research, the International Society for Stem Cell Research (ISSCR) achieves this division by the simple expedient of stating:

One common type of human-to-animal chimera study is the use of human embryonic stem cells (hES cells) to form teratomas in immunodeficient mice to assess stem cell quality and developmental potential. While this routine practice raises no ethical difficulties, other forms of chimera research may—such as preimplantation studies resulting in high but transient levels of human-to-animal chimerism in vitro, and the transfer of differentiated human stem cells into the central nervous systems of higher-order animals. (Hyun et al., 2007, p. 159)

The dividing line thus becomes a temporal one, i.e. those chimeras currently produced as ‘routine practice’ in bioscientific research are ‘ethically unproblematic’, while those that are novel are ‘potentially ethically challenging’.

The ISSCR then considers the specific issues raised by chimeras produced using hESCs. It argues ‘that fears are directly related to the degree of deterministic biological agency that is attributed to the “fundamental units” that get mixed’ (Hyun et al., 2007, p. 159). Genes and stem cells, it suggests, are considered (by the public who potentially have ethical concerns) to contain the essence of the organism, such that putting a human gene or stem cell into another animal confers a
fundamental ‘humanness’ on that animal (such ‘humanisation’ of the animal being constructed as problematic in ways that we discuss in the next section). One key element then is the type of human biological material that is transferred to the non-human. Elsewhere, the other criteria that come into play once the material has been defined as a ‘fundamental unit’ have been considered. Focusing on human/non-human neural grafting, particularly grafting of human stem cells into non-human primates, Greene et al. (2005, p. 386) propose six elements that should comprise the starting framework: (i) proportion of engrafted human cells; (ii) neural development of the animal recipient (neonatal vs postnatal); (iii) NHP species; (iv) NHP brain size; (v) site of integration of donor material within the recipient brain (e.g. whether introduced into the cerebellum, which is the site of higher brain functions, or elsewhere); and (vi) brain pathology (whether the recipient is a NHP model of human neurodegenerative disease and thus has a different level of cognition from a ‘normal’ member of the species prior to introduction of human neural material).

Many of these ‘criteria for concern’ are also ones identified by Henry Greely (2003) in his comprehensive discussion of human/animal mixing. Starting with a broad definition of ‘chimera’ as ‘a single biological entity that is composed of a mixing of materials from two or more different organisms’ (Greely, 2003, p. 17), Greely produces a detailed exposition of the issues, summarising the concerns over human-to-animal transfer thus:

Creating a mouse with a brain made from human neurons, as proposed by at least one researcher, has attracted some press attention and does raise some concern. Putting human brain tissue into nonhuman primates can be even more problematic. . . . Chimeras made by moving human parts into nonhuman beings would raise concerns when they are significant enough to raise the question of the possible humanity of the recipient. In both cases the ‘importance’ of the parts—brains and gametes are more important than heart valves or skin—and the number of parts moved—transplanting five visceral organs would be more troubling than transplanting one—seem significant. So do the uses of such part-human, part-nonhuman chimeras. Making a chimera of a human and a nonhuman is much less controversial when done for medical purposes than if such a creature were made for entertainment or ‘art’. (Greely, 2003, p. 19)

Alongside the nature of the donor (human) material (whether it contains a fundamental essence of humanness), the recipient species is a criterion for concern. Transfer into a species such as a non-human primate, which is already more like a human than, say, a mouse, is regarded as problematic because there is less leeway for adding human material before the creature becomes too human for (human’s) comfort. Relatedly, the greater the amount of human material introduced into the animal, the greater the potential for problems. The stage of
development of the recipient species is a further criterion for concern because introduction early in development (into the foetus rather than an adult animal) gives greater opportunity for the animal material to integrate and proliferate.

In all cases, the definition of the criteria for concern is derived from the principle that it is culturally inappropriate to create an animal that is ‘too human’. As Greely puts it in the quotation above ‘chimeras made by moving human parts into nonhuman beings would raise concerns when they are significant enough to raise the question of the possible humanity of the recipient’ (2003, p. 19). What particular features are salient in determining ‘humanness’ and the degree to which they would have to be altered to be uncomfortably ‘too human’ are matters of continuing debate. Language is a prominent concern, as one UK bioethical expert explained:

There is a gene [...] that seems to underlie some of the human propensity for language. Now if the experiment were to introduce that into a non-human primate, such that the animal [...] started making noises that in some identifiable way were more humanised, you might feel that we’d strayed into areas that we should have steered clear of. (Neuroscientist, 8 July 2010).

In another interview, a US bioethical expert suggested that salient features could be summed up as ‘brains, balls or beauty’ (Lawyer, 27 July 2010): that is the conferring of human cognitive capacities or human appearance on a non-human animal or the mixing of gametes between human and non-human animals. There is political utility in keeping the terms loosely defined—not explicating definitively what features are relevant or what change counts as ‘too human’—at this early stage, so allowing for the negotiations that are necessary for the governance function to occur. In parallel to the definition of the governance agenda through the identification of the criteria for concern, there is also a governance need for the definition and development of the principle that can be used to adjudicate on the implementation of this agenda. How far and in what ways is ‘humanness’ articulated through the promulgation of ‘human dignity’ as the appropriate adjudicating principle?

Defining the Operating Principle of Governance: Exclusion of Principles

Having established the parameters of the anticipated governance problem, bioethical experts then move to define the principle that should guide the operation of the governance mechanism through a process of adjudication. In so doing, and as is customary, the bioethical experts are guided by an internal operating principle of ‘utility to science’. A number of possible candidates for principles that can be used to adjudicate on the permissibility of human/animal mixing have been put forward for discussion. ‘(Un)naturalness’ has been considered, but firmly discarded; it is described as the argument most often considered and also most often rejected (Streiffer, 2009).
The concern that scientists are tampering with nature in ways that are impermissible has been put forward as central to public disquiet over biological mixing in agricultural biotechnology (NCoB, 1999, p. 7; Shaw, 2002; Macnaghten, 2004). However, most scientists and philosophers find themselves unable to make sense of this distinction between ‘natural’ = good and ‘unnatural’ = bad. From their perspective, humankind has been acting on nature for millennia, making it hard to distinguish between ‘natural’ and ‘unnatural’. Further, many such interventions have met with approbation. As Greene et al. (2005, p. 385) forthrightly state:

Stipulating that research is ‘unnatural’ says nothing about its ethics. Much of modern medical practice involves tools, materials, and behaviors that cannot be found in nature but are not unethical as a consequence. (see also Karpowicz et al., 2005, pp. 113–115).

As such, for these bioethical experts (un)naturalness cannot be supported as a principle for deciding what mixing between species should be allowed because there is no firm link between the naturalness of an action and its ethical acceptability.

Related to (un)naturalness, the specific unnaturalness of crossing species boundaries has also been discussed as a potential evaluative principle (Robert and Baylis, 2003 and responses; Karpowicz et al., 2005, pp. 115–118). Again, for scientists and philosophers of biology the concept of ‘species boundary’ is problematic:

Biologists are unsure about the extent and even the definition of ‘natural species boundaries’. Indeed the meaning of the term ‘species’ is itself far from clearcut, depending very much on the context in which it occurs. (BBSRC, 2000, p. 14)

Or, as a US bioethical expert explained when interviewed:

A lot of my colleagues are keen to talk as though there probably is a genetic essence [...] They had a view of species as an example of things like gold—so gold has the atomic number of 79 and that’s its essence, right? All possible gold has that, and everything that has that atomic number is gold. And they kind of view species as something like that. But it really is nothing like that. There is no GT or GGT[T [genetic code] that defines ‘human’ or anything like that. (Philosopher, 20 July 2010)

For this interviewee, there is no ‘essence’ that defines a species. Similarly, for the majority of scientists, species are not fixed entities with immutable boundaries; for example, they change over time with evolution (Boyd Group, 1999, Section 2). Further, biological science is increasingly recognising that any boundary between species is fluid; for example, gene transfer occurs between species (APC, 2001, p. 18).
Against this scientific and philosophical view that species boundaries do not exist and so cannot be used to adjudicate on the permissibility of human-to-animal mixing, some bioethicists acknowledge that,

... fixed species exist independently as moral constructs. That is, notwithstanding the claim that biologically species are fluid, people believe that species identities and boundaries are indeed fixed and in fact make everyday moral decisions on the basis of this belief. (Robert and Baylis, 2003, p. 6)

The transgression of culturally prescribed boundaries involved in interspecies mixing, Robert and Baylis argue, would cause a ‘moral confusion’ about how the resulting part-human entities should be treated, and as such the argument against boundary crossing deserves at the least consideration.

However, such an emphasis on the importance of the social construction of species definition is a minority and isolated strand in the debate within bioethics. The consensus is that the culturally perceived inviolability of species boundaries cannot form the bases for moral judgement on production of chimeras because it lacks both scientific and ethical foundation. One ethicist has claimed that while species typologies might be ‘useful for responding to animals with stripes and big teeth when strolling in the Bengali forest’, when it comes to making moral judgements ‘arguments using typological thinking [...] are so weak they can be toppled with pea shooters’ (Castle, 2003, p. 29). Specifically:

... the species integrity argument provides no reliable criteria for assessing when the lines between species have been crossed, and, were it to do so, no clear argument about when and why crossing them would be ethically unacceptable. It offers no reasons why society should not accommodate new ways of classifying living organisms. [...] That one is used to thinking about things a certain way is not a strong reason to argue against the development of new ways of thinking. (Karpowicz et al., 2005, p. 118)

So, while the species concept might provide a useful way of ordering and making sense of the world, the fluidity of the concept means that it is impossible to use it to determine which crossings are legitimate and which illegitimate. Further, for bioethical experts, just because we do use the species concept to make moral sense of the world, does not mean that it should be used to govern our actions.²

A third candidate for an ethical principle to be used in adjudicating on relevant arguments about chimera production is that of ‘moral status’ (Greene et al., 2005; Munzer, 2008; Fiester and Düwell, 2009). This principle is premised on an understanding that a distinction can be made between humans and other animals. In contemporary understandings, people are considered to have equivalent moral status by virtue of being human, such that we have a moral obligation to treat other human beings as the same kind of being as ourselves. Animals are considered
to be ‘not persons’ in this sense although the argument as to whether non-human primates, in particular Great Apes, do have moral status is prominent in discussion over the use of such animals in research. Here there is considerable debate as to ‘whether they have properties or characteristics which make them sufficiently similar, in morally relevant ways, to humans’ that their use as means to human ends should become untenable [Boyd Group, 2002, p. 33; for discussion see reports on the use of NHPs in research (Boyd Group, 2002; Wetherall, 2006)].

The issue for chimera research is whether the introduction of human biological material into non-humans would alter the recipient animal’s morally relevant capacities in such a way as to confer on them the moral status of persons. Again, both scientific (practical) and philosophical objections to the principle of moral status have been advanced. Scientifically, there is difficulty in agreeing on what constitutes morally relevant capacities (Savulescu, 2003; Fiester and Düwell, 2009), and how to determine experimentally if they have been enhanced (Greene et al., 2005). Philosophically, a drive to maintain the distinction between humans and other animals on the basis that the former have moral status while the latter do not is problematic when assessed on a social cost–benefits basis:

We might be confused about the status of such interspecies beings, and this might create social disorder. [However] many people are confused about many things [children produced by surrogacy, clones, hESC and ‘racists were confused about the moral status of race’]. We should not base social policy and law on such confusions. […] The social costs of acceding to irrational confusion are, at least historically, much greater than the costs of clearing it up and reforming society. (Savulescu, 2003, p. 25)

That is, historically those entities classified as having moral status have been open to change. In the past, various categories of human (women, slaves, other races etc.) have been adjudged of lesser moral status and hence not entitled to full rights of personhood. Today, the personhood of, for example, the foetus or embryos, or those in a persistent vegetative state, or (as previously noted) Great Apes, has been opened to philosophical questioning. In debates among bioethical experts, the very fluidity of the boundaries based on the concept of ‘moral status’ is used as an argument against its utility as a principle to adjudicate on disputes over the permissibility of creating human/animal chimeras. It is not valid because it is not practical.

**Defining the Operating Principle of Governance: Inclusion and Implementation of Principles**

In debates among bioethical experts, the emerging front runner for a principle to be used in adjudicating on ethical issues in human-to-animal chimera production is that of ‘human dignity’ (Johnston and Eliot, 2003; Karpowicz et al., 2004, 2005;
National Research Council, 2005; Baylis and Fenton, 2007; deGrazia, 2007; Hyun et al., 2007; de Melo-Martin, 2008). ‘Human dignity’ is related to ‘moral status’. Both concentrate on the human-like capacities that might be developed in chimeric entities, but the human dignity principle focuses attention on how this mixing creates problems for humans:

By giving nonhumans some of the physical components necessary for development of the capacities associate with human dignity, and encasing these components in a nonhuman body where they would either not be able to function at all or function only to a highly diminished degree, those who would create human–nonhuman chimeras would denigrate human dignity. (Karpowicz et al., 2005, p. 121)

This is the spectre of a human being trapped inside the body of a mouse (Ahuja, 2006). In this creature, it is argued, the principle of ‘human dignity’ is violated because it is unable to realise the full potential of its dignity-associated capacities—either in the sense of offending against the dignity of the creature, as a human individual, or in the sense of diminishing the dignity of humanity as a species (Johnston and Eliot, 2003).

Given that ‘human dignity’ is becoming increasingly prevalent in the policy discourse of bioscience more widely, it is perhaps unsurprising that it also has a dominant place in the bioethical literature on human-to-animal mixing. Linked closely to the established discourse on human rights, the concept of human dignity has considerable rhetorical power (Andorno, 2009; Jordan, 2010). Enshrined in the 1948 United Nations’ Universal Declaration of Human Rights through the ‘recognition of the inherent dignity and of the equal and inalienable rights of all members of the human family’, the principle of human dignity is the foundation of much human rights policy and legislation. Over the last two decades, it ‘has emerged as a key point of reference for the regulation of modern science and technology’ (Caulfield and Brownsword, 2006, p. 72). Thus, for example, the Council of Europe Convention on Human Rights and Biomedicine (1997) resolved ‘to take such measures as are necessary to safeguard human dignity and the fundamental rights and freedoms of the individual with regard to the application of biology and medicine’. Similarly, the UNESCO Universal Declaration on Bioethics and Human Rights (2005) recognises that ‘ethical issues raised by the rapid advances in science and their technological applications should be examined with due respect to the dignity of the human person and universal respect for, and observance of, human rights and fundamental freedoms’. Human dignity has also begun to feature prominently in bioethics discourse in the USA; for example, the first report of the President’s Council on Bioethics (2002) was entitled Human Cloning and Human Dignity.

The rise of ‘human dignity’ as a principle is not undisputed. For academic ethicists, it is a ‘useless concept’ (Macklin, 2003) that is ‘notoriously slippery, [...]
confounding and contentious, and, as such, its utility as an action-guiding tool’ is limited (Harmon, 2009, p. 946; see also Caulfield and Brownsword, 2006). However, while its ill-defined character might restrict its appeal to academic ethicists seeking an absolute philosophical resolution of its conceptual ambiguities, for bioethical experts whose contribution is directed to the formulation of science policy the criteria of worth are different and here the very vagueness of human dignity is undoubtedly viewed as a governance asset—at least from a political perspective. Human dignity, ‘precisely because it is understood in so many ways, facilitates the drafting of international aspirational statements’ (Caulfield and Brownsword, 2006, p. 75).

The emerging dominance of the principle of human dignity in the area of human-to-animal mixing is attested to by the way that discussion has developed in the bioethics literature on the subject. In early papers where human dignity is considered it is put forward as one possible principle for evaluation (e.g. Karpowicz et al., 2005). Latterly, it is the principle itself that has become the topic for debate (Hyun et al., 2007; de Melo-Martin, 2008). Bioethical experts are no longer debating whether human dignity is a suitable principle for use in considering the subject of human-to-animal mixing. It has been agreed that it is, and the discussion now centres on how that principle can be applied to evaluate the permissibility of chimera production. In governance terms, the discussion has moved from whether the principle should form part of the governance agenda (it should) to how best can it be operationally implemented. Here, as noted earlier, the ambiguity of the concept of ‘human dignity’ has political utility, making space for the relative stabilisation of its meaning as a product of power relations in the policymaking process.

We have shown how work is carried out among bioethical experts to negotiate a consensus position on the elements that are to be allowed entry for consideration in the debate over the permissibility of creating human/animal chimeras (the type and amount of human material used, the recipient species and its stage of gestation) and the principle to be used in adjudication (by reference to whether the proposed chimera infringes human dignity). We should be clear here that the principle for adjudication and the elements allowed into the debate are being co-established as the constituent elements of the debate agenda. Notably, the elements that are considered valid for inclusion are those that relate to the issue of introducing a problematic degree of humanness into the non-human animal, and in synergy with this the principle for adjudication that is being settled on is that of ‘human dignity’.

At the same time, the animal perspective is excluded from both the governance agenda and its operational implementation. No attention is paid to any problems for the animal that is modified to be more like a human. The focus is entirely on the problems for humans of creating human-like animals. Commenting on the 2005 US National Academy of Sciences Guidelines for Human Embryonic Stem Cell Research recommendation that experiments introducing hESC into an NHP
blastocyst should not be permitted, Alta Charo, one of the report’s authors, commented that such research ‘might humanize animals in ways that are unnerving’ (quoted in Scott, 2006, p. 490). In this vein, the question of recipient species is allowed into discussion on the basis that if the animal is closely related to humans, there is less leeway for adding human material before it becomes ‘too human’ for our comfort. An alternative argument could be made, but is not, that a closely related species is more likely to suffer like us from this experimentation.

In this vein, the question of recipient species is allowed into discussion on the basis that if the animal is closely related to humans, there is less leeway for adding human material before it becomes ‘too human’ for our comfort. An alternative argument could be made, but is not, that a closely related species is more likely to suffer like us from this experimentation.

The exclusive agenda-setting power of the emphasis in the bioethical governance discourse solely on problems that accrue for humans is revealed through its sharp contrast with much of the previous debate on the ethics of this kind of research. For example, in debates over the genetic modification of animals, the problem of the possible negative impact on the animal’s wellbeing from the gene introduced has been a significant part of the debate (ECVAM, 1998; Boyd Group, 1999, p. 4.2.1; APC, 2001, p. 24). The ‘Beltsville Pig’, genetically engineered with genes to increase growth rate, suffered a range of disorders including painful bone and joint problems and diminished vision, and was frequently cited as an example of the negative impact on the animal of transgenic technology. The focus on the human also runs counter to existing regulatory frameworks for the use of animals in scientific research. In the majority of countries, these are based on well-established ethical frameworks for animal welfare, with the principle of the ‘3Rs’ (of Replacement of animals where possible, Refinement to scientific procedures and husbandry in order to minimise actual or potential adverse impact on the animal, and Reduction in the number of animals used through, for example, improved experimental design or use of new imaging techniques), first outlined by Russell and Burch (1958), having attained the near hegemonic status in relation to use of animals in bioscience that the principle of autonomy has attained in biomedical ethics.

**Conclusions**

As we have discussed in this paper, the deployment of bioethical expertise helps to establish the principles and operational rules of governance as an anticipatory process in the development of the human-to-animal research field. We have shown how, in this particular field, bioethical experts are moving from a responsive to an anticipatory legitimating role in the governance of science. In so doing, they offer a governance alternative to the frequent reliance of anticipatory governance on wider public involvement; one that takes the operation of governance back into the traditional confines of the expert domain that characterised the scientific advisory system. There are three stages to the anticipatory governance contribution of bioethical experts.

First, there is the definition of the governance agenda: what is not problematic (i.e. current ‘routine practice’) and what is problematic (i.e. criteria for concern). Second, there is a filtering out of potential principles. Through a combination of scientific/technical and philosophical arguments, the candidate principles of
(un)naturalness, species boundaries, and moral status have been rejected. Technically, bioethical experts argue that it is impossible to determine what is ‘natural’, where species boundaries lie, or what qualities are relevant for conferring ‘moral status’. In other words, these categories are social constructs with no firm foundation in biology and therefore should be discarded. Philosophically, bioethical experts reject the elision of ‘is’ and ‘ought’ by which the existence of such systems of classification in the present is used to justify their continued utility in the future. Because such categories are used to make moral sense of the world, the philosophers charge, is no reason that we should rely on them in perpetuity. The social constructs that elicit unease at the thought of mixing between human and animal can (biologically) and perhaps should (ethically) be deconstructed. Third, there is the filtering in of a particular operating principle of governance and the establishment of a discussion on how it may be implemented. In the case of human-to-animal research the emerging dominant principle for the adjudication of chimera production is that of human dignity, an established component in the wider discourse of governance in the biosciences.

Bioethical expertise is deployed in this proactive and anticipatory approach to governance by entwining scientific and philosophical expertise so that judgements against science are also found to be philosophically unfounded, and conversely, those activities that are permissible are deemed acceptable, on both scientific and ethical grounds. Through what is presented as an organic process, the emerging bioethical framework for human-to-animal chimera research becomes a legitimating framework within which ‘good’ science can safely progress. Science gives bioethicists access to new governance territory; bioethicists give science access to political acceptability.
How likely is it that bioethical experts will play a similar anticipatory governance role in other areas of science? If we look at the parallel example of social scientists moving their engagement with science upstream, it has been observed that the institutional characteristics of biotechnology have limited the opportunities for social scientific input to assess and manage the impacts of the technology, whereas nanotechnology is more receptive to early engagement between sociologists and scientists (Macnaghten et al., 2005). However, the case of human/animal chimeras suggests that the involvement of bioethical experts in the anticipatory governance of a new scientific field is likely to be dependent on: (a) whether there is an existing debate in a related field that has already harnessed bioethical expertise; (b) the availability of bioethical principles that can be applied to the task in hand; and (c) the feasibility of producing a form of anticipatory governance that can be translated into policy. Not all areas of science will be able to meet these criteria and the use of bioethical expertise in anticipatory governance is therefore bound to be selective.

Acknowledgements

This research was supported by a Wellcome Trust Biomedical Ethics Strategic Award, ref 086034, to Professor Clare Williams. The authors would like to thank the anonymous reviewers for Science as Culture for constructive comments on the draft manuscript. They would also like to thank the Wellcome Trust for making available the images used in this article under the Creative Commons Licence.

Notes

1Stem cells per se are not considered an issue (Karpowicz et al., 2005); human blood and skin stem cells, for example, have been introduced into animals with little concern ‘perhaps because they are not identified with what is essential to being human’ (2005, p. 108). Rather, the problem comes with pluripotent stem cells—stem cells capable of regenerating into many different tissue types.

2Indeed the scientific concept of ‘species’ is only one way of classifying the natural world (Dupré, 2002). The classificatory systems employed by different cultures may have implications for the public acceptability of different biological mixings carried out by science (Roberts et al., 2004).

3Or, in a refinement of this argument, that if such manipulation did confer full moral status on the animal, it would not be possible to afford the creature the respect due from the ‘moral obligations entailed by that status’ (Streiffer, 2009; see also Streiffer, 2005).

References

Academy of Medical Sciences (AMS) (2007) Inter-Species Embryos (London: Academy of Medical Sciences).
Academy of Medical Sciences (AMS) (2009) Press Release: Academy Launches Study on the Use of Animals Containing Human Material (London: Academy of Medical Sciences).
Ahuja, A. (2006) A human brain trapped inside a mouse’s body—not a good idea, The Times, September 4, p. 19.
Andorno, R. (2009) Human dignity and human rights as a common ground for a global bioethics, Journal of Medicine and Philosophy, 34(3), pp. 223–240.
Animal Procedures Committee (APC) (2001) *Report on Biotechnology* (London: Animal Procedures Committee).

Animal Procedures Committee (APC) (2002) *The Use of Primates under the Animals (Scientific Procedures) Act (1986): Analysis of Current Trends with Particular Reference to Regulatory Toxicology* (London: Animal Procedures Committee).

Barben, D., Fisher, E., Selin, C. and Guston, D. (2008) Anticipatory governance of nanotechnology: Fore-sight, engagement and integration, in: E. Hackett, O. Amstersdamska, M. Lynch and J. Wajcman (Eds) *The Handbook of Science and Technology Studies*, 3rd ed., pp. 979–1000 (Cambridge, MA: MIT Press).

Baylis, F. and Fenton, A. (2007) Chimera research and stem cell therapies for human neurodegenerative disorders, *Cambridge Quarterly of Healthcare Ethics*, 16(2), pp. 195–208.

Behringer, R. R. (2007) Human–animal chimeras in biomedical research, *Cell Stem Cell*, 1, pp. 259–262.

Biotechnology and Biological Sciences Research Council (BBSRC) (2000) *Ethics, Morality and Animal Biotechnology*.

Birke, L. and Michael, M. (1998) The heart of the matter: Animal bodies, ethics, and species boundaries, *Society & Animals*, 6(3), pp. 245–261.

Boyd Group (1999) *Genetic Engineering: Animal Welfare and Ethics*. Available at http://www.boyd-group.demon.co.uk/genmod.htm (accessed 4 May 2010).

Boyd Group (2002) *The Use of Non-Human Primates in Research and Testing* (Leicester: British Psychological Association).

Castle, D. (2003) Hopes against hopeful monsters, *The American Journal of Bioethics*, 3(3), pp. 28–30.

Caulfield, T. and Brownsword, R. (2006) Human dignity: A guide to policy making in the biotechnology era? *Nature Reviews Genetics*, 7(1), pp. 72–76.

Chimbrids project (undated) CHIMBRIDS: Chimeras and Hybrids in Comparative European and International Research: Scientific, Ethical, Philosophical and Legal Aspects. Available at http://www.jura.uni-mannheim.de/imgbchimbrids/index.php?option=com_content&task=view&id=20&Itemid=42 (accessed 23 June 2011).

Council of Europe (1997) *Convention on Human Rights and Biomedicine*. Available at http://conventions.coe.int/Treaty/EN/Treaties/html/164.htm (accessed 4 May 2010).

Danish Council of Ethics (2008) *Man or Mouse? Ethical Aspects of Chimaera Research*. Available at http://www.etiskraad.dk/graphics/03_udgivelser/engelske_publikationer/human-animal-crossbreeds/man-or-mouse/index.htm (accessed 4 May 2010).

deGrazia, D. (2007) Human–animal chimeras: Human dignity, moral status and species prejudice, *Metaphilosophy*, 38(2–3), pp. 309–329.

de Melo-Martin, I. (2008) Chimeras and human dignity, *Kennedy Institute of Ethics Journal*, 18(4), pp. 331–346.

Dupré, J. (2002) *Humans and Other Animals* (Oxford: Oxford University Press).

European Centre for the Validation of Alternative Methods (ECVAM) (1998) The use of transgenic animals in the European Union, *Alternatives to Laboratory Animals*, 26, pp. 21–43.

Fiester, A. and Düwell, M. (2009) The fundamental debates on moral status: What makes entities morally significant? in: J. Taupitz and M. Weschka (Eds) *CHIMBRIDS—Chimeras and Hybrids in Comparative European and International Research: Scientific, Ethical, Philosophical and Legal Aspects*, pp. 61–70 (Dordrecht: Springer).

General Assembly of the United Nations (1948) *The Universal Declaration of Human Rights*. Available at http://www.un.org/en/documents/udhr/ (accessed 4 May 2010).

German Ethics Council (2008) *Topics*. Available at http://www.ethikrat.org/topics/topics?set_language=en (accessed 4 May 2010).

Greely, H. (2003) Defining chimeras . . . and chimeric concerns, *The American Journal of Bioethics*, 3(3), pp. 17–20.
Greely, H., Cho, M., Hogle, L. and Satz, D. (2007) Thinking about the human neuron mouse, The American Journal of Bioethics, 7(5), pp. 27–40.

Greene, M., Schill, K., Takahashi, S., Bateman-House, A., Beauchamp, T., Bok, H., Cheney, D., Coyle, J., Deacon, T., Dennett, D., Donovan, P., Flanagan, O., Goldman, S., Greely, H., Martin, L., Miller, E., Mueller, D., Siegel, A., Solter, D., Gearhart, J., McKhann, G. and Faden, R. (2005) Moral issues of human–non-human primate neural grafting, Science, 309(7373), pp. 385–386.

Guston, D. (2008) Innovation policy: Not just a jumbo shrimp, Nature, 454(7207), pp. 940–941.

Haimes, E. (2002) What can the social sciences contribute to the study of ethics? Theoretical, empirical and substantive considerations, Bioethics, 16(2), pp. 89–113.

Harmon, S. (2009) Of plants and people, EMBO Reports, 10(9), pp. 946–948.

Hoeyer, K. and Tutton, R. (2005) ‘Ethics was here’: Studying the language-games of ethics in the case of UK Biobank, Critical Public Health, 15(4), pp. 385–397.

Hurwitz, B. (2002) What’s a good doctor, and how can you make one? Marrying the applied scientist to the medical humanist, British Medical Journal, 325(7366), pp. 667–668.

Hyun, I., Taylor, P., Testa, G., Dickens, B., Jung, K. W., McNab, A., Robertson, J., Skene, L. and Zoloth, L. (2007) Ethical standards for human-to-animal chimera experiments in stem cell research, Cell Stem Cell, 1(2), pp. 159–163.

Irwin, A. (1995) Citizen Science: A Study of People, Expertise and Sustainable Development (London: Routledge).

Irwin, A. and Michael, M. (2003) Science, Social Theory and Public Knowledge (Maidenhead: Open University Press).

Irwin, A. and Wynne, B. (1996) Misunderstanding Science? (Cambridge: Cambridge University Press).

Jasanoff, S. (2005) Designs on Nature: Science and Democracy in Europe and the United States (Princeton, NJ: Princeton University Press).

Johnston, J. and Eliot, C. (2003) Chimeras and ‘human dignity’, The American Journal of Bioethics, 3(3), pp. 6–8.

Jordan, M. C. (2010) Bioethics and ‘human dignity’, Journal of Medicine and Philosophy, 35(2), pp. 180–196.

Kaebnick, G. (2010) HCR turns forty; what’s next? Hastings Center Report, 40(1), p. 2.

Karpowicz, P., Cohen, C. and van der Kooy, D. (2004) It is ethical to transplant human stem cells into nonhuman embryos, Nature Medicine, 10(4), pp. 331–335.

Karpowicz, P., Cohen, C. and van der Kooy, D. (2005) Developing human–nonhuman chimeras in human stem cell research: Ethical issues and boundaries, Kennedy Institute of Ethics Journal, 15(2), pp. 107–134.

Kearnes, M. and Macnaghten, P. (2006). Introduction: (Re)Imagining Nanotechnology. Science as Culture, 15(4), pp. 279–290.

Kelly, S. E. (2003) Public bioethics and publics: Consensus, boundaries, and participation in biomedical science policy, Science Technology & Human Values, 28(3), pp. 339–364.

Macklin, R. (2003) Dignity is a useless concept, British Medical Journal, 327(7429), pp. 1419–1420.

Melo-Martin, I. de. (2008) Chimeras and human dignity, Kennedy Institute of Ethics Journal, 18(4), pp. 331–346.

Macnaghten, P. (2004) Animals in their nature: A case study on public attitudes to animals, genetic modification and ‘Nature’, Sociology, 38(3), pp. 533–551.

Macnaghten, P., Kearnes, M. and Wynne, B. (2005) Nanotechnology, governance, and public deliberation: What role for the social sciences? Science Communication, 27(2), pp. 268–291.

Munzer, S. R. (2008) Human–nonhuman chimeras in embryonic stem cell research, Harvard Journal of Law and Technology, 21(1), pp. 123–178.

National Research Council (2005) Guidelines for Human Embryonic Stem Cell Research (Washington, DC: National Academies Press).
Nelson, N., Geltzer, A. and Hilgartner, S. (2008) Introduction: The anticipatory state: Making policy-relevant knowledge about the future, *Science and Public Policy*, 35(8), pp. 546–550.

Nuffield Council on Bioethics (NCoB) (1996) *Animal-to-Human Transplants: The Ethics of Xenotransplantation* (London: Nuffield Council on Bioethics).

Nuffield Council on Bioethics (NCoB) (1999) *Genetically Modified Crops: The Ethical and Social Issues* (London: Nuffield Council on Bioethics).

O’Malley, M. A., Calvert, J. and Dupré, J. (2007) The study of socioethical issues in systems biology, *American Journal of Bioethics*, 7(4), pp. 67–78.

O’Malley, M. A. and Dupré, J. (2005) Fundamental issues in systems biology, *Bioessays*, 27(12), pp. 1270–1276.

President’s Council on Bioethics (2002) *Human Cloning and Human Dignity* (Washington, DC: President’s Council on Bioethics).

Robert, J. S. and Baylis, F. (2003) Crossing species boundaries, *The American Journal of Bioethics*, 3(3), pp. 1–13.

Roberts, M., Haami, B., Benton, R., Satterfield, T. and Henare, M. (2004) Whakapapa as a classificatory construct of Maori and its implications for genetic engineering, *The Contemporary Pacific*, 16, pp. 1–28.

Rogers-Hayden, T. and Pidgeon, N. (2007) Moving engagement ‘upstream’? Nanotechnologies and the Royal Society and Royal Academy of Engineering’s inquiry, *Public Understanding of Science*, 16(3), pp. 345–364.

Russell, W. and Burch, R. (1958) *The Principles of Humane Experimental Technique* (London: Methuen & Co).

Salter, B. and Jones, M. (2005) Biobanks and bioethics: The politics of legitimation, *Journal of European Public Policy*, 12(4), pp. 710–732.

Salter, B. and Salter, C. (2007) Bioethics and the global moral economy—the cultural politics of human embryonic stem cell science, *Science Technology & Human Values*, 32, pp. 554–581.

Savulescu, J. (2003) Human–animal transgenesis and chimeras might be an expression of our humanity, *The American Journal of Bioethics*, 3(3), pp. 22–25.

Scott, C. T. (2006) Chimeras in the crosshairs, *Nature Biotechnology*, 24(5), pp. 487–490.

Shaw, A. (2002) ‘It just goes against the grain’. Public understandings of genetically modified (GM) food in the UK, *Public Understanding of Science*, 11(3), pp. 273–291.

Streiffer, R. (2005) At the edge of humanity: Human stem cells, chimeras, and moral status, *Kennedy Institute of Ethics Journal*, 15(4), pp. 347–370.

Streiffer, R. (2009) Human/non-human chimeras, in: E. Zalta (Ed.) *Stanford Encyclopedia of Philosophy*. Available at http://plato.stanford.edu/archives/spr2011/entries/chimeras/ (accessed 27 October 2011).

Swedish National Council on Medical Ethics (2008) *Human/Animal Combinations in Research*. Available at http://www.smer.se/Bazment/339.aspx (accessed 4 May 2010).

Tallacchini, M. (2009) Governing by values. EU ethics: Soft tool, hard effects, *Minerva*, 47(3), pp. 281–306.

The Royal Society (1985) *The Public Understanding of Science* (London: The Royal Society).

United Nations Educational Scientific and Cultural Organization (UNESCO) (2005) *Universal Declaration on Bioethics and Human Rights*. Available at http://portal.unesco.org/en/ev.php-URL_ID=31058&URL_DO=DO_TOPIC&URL_SECTION=201.html (accessed 4 May 2010).

Wetherall, D. (2006) *The Use of Non-Human Primates in Research* (London: Academy of Medical Sciences, Medical Research Council, The Royal Society, The Wellcome Trust).

Wolpe, P. and McGee, G. (2001) ‘Expert bioethics’ as professional discourse: The case of stem cells, in: S. Holland, K. Lebacqz and L. Zoloth (Eds) *The Human Embryonic Stem Cell Debate: Science, Ethics and Public Policy* (Cambridge, MA: MIT Press).