The Regulation of Hybrids and Chimeras in the UK

Deryck Beyleveld BSc, MA, PhD,[1] Tom Finnegan LLB, MA,[2] and Shaun D. Pattinson LLB, MA, PhD[3]

Introduction

In this report, we will, for the most part, sidestep discussion of how "chimeras" and "hybrids" are to be defined and distinguished, by simply focusing on the UK's regulation of the activities that CHIMBRIDS has identified as its concern. These are activities that involve "the fusion of human and non-human tissue and cells", and include human/non-human

- **transplantation (i.e. xenotransplantation)**
- **gamete mixing**
- **somatic cell nuclear transfer (into an enucleated ovum)**
- **zygote genetic modification**
- **embryonic cell transfer/fusion.**

We will address each of these possibilities before addressing patent regulation and the wider ethico-cultural background of the UK regulatory position.

Xenotransplantation

Since xenotransplantation, at it broadest, involves the transplantation of non-human animal tissue or cells into human beings (or, at least theoretically, vice versa) and transplantation from one non-human animal species to another, it is open to regulation from both the non-human animal side and the human side.

On the non-human animal side, the Animals (Scientific Procedures) Act 1986 (the "1986 Act") regulates experimental or scientific procedures on the animals it protects *if* the procedures might cause the animal "pain, suffering, distress, or lasting harm" (s2(1)). It is clear that xenotransplantation itself and research into it falls within this regulatory framework to the extent that it involves a protected animal, is likely to have these effects on the animal, and is an experimental or scientific procedure.

Protected animals are "any living vertebrate other than man" (s1(1)) and (as added by an order empowered by s1(3))[4], "any invertebrate of the species *Octopus vulgaris* from the stage of development when it becomes capable of independent feeding". Mammals, birds or reptiles are protected also in the foetal, larval or embryonic form, but only from when "half the gestation or incubation period for the relevant species has elapsed" (s1(2)(a)). The Secretary of State may by order extend protected animals to cover invertebrates of any description or alter the qualifying stage of development specified in section 1(2)(a) (s1(3)).

Immune rejection of alien tissues and cells is a serious problem surrounding

1 Professor of Law and Bioethics, Department of Law, Durham University.
2 Research Assistant, Sheffield Institute of Biotechnological Law and Ethics, University of Sheffield.
3 Reader in Law, Department of Law, Durham University.
4 The Animals (Scientific Procedures) Act (Amendment) Order 1993/2103, Art. 3.

xenotransplantation. The breeding of genetically modified donor animals (usually pigs modified by the introduction of human genes at an early embryonic stage) is often mooted as a way of reducing the effects of this response. These techniques are regulated by the Act, because section 2(3) provides that anything done "for the purpose of, or liable to result in, the birth or hatching of a protected animal is also a regulated procedure" provided it might cause pain, etc. to the animal.

The Act operates by a licensing system and an inspection system. Any person conducting a regulated procedure must hold a personal licence to apply the particular procedure to the animal in question (s3(a)). In addition, the procedure must be carried out in a licenced project (s3(b)) and in a place specified in the personal licence and the project licence (s3(c)). Animals may not be bred for use in a regulated procedure unless a licence to breed for this purpose has been obtained (s7(1)).

Project licences may only be granted for a number of purposes, which include the prevention, "diagnosis or treatment of disease, ill-health or abnormality or their effects, in man, animals or plants" (s5(3)(a)). A licence also requires that the research purposes cannot reasonably practicably be achieved without using protected animals (s5(5)(a)). Regulated procedures used must involve the minimum number of animals, animals with the lowest degree of neurophysiological sensitivity, cause the least pain, etc., and be those most likely to achieve satisfactory results (s5(5)(b)). Licences are not to be granted for the use of cats, dogs, primates or *equidae* unless no other animals are suitable or other suitable animals are not practicably obtainable (s5(6)). Any discomfort or suffering must be kept to a minimum (s10(2)(a), by, e.g., appropriate use of anaesthetics or pain killers.

Section 18 of the 1986 Act enables the Secretary of State to appoint inspectors with adequate medical and veterinary qualifications to advise the Secretary on various applications, and to visit research establishments (s18(2)). Section 19 sets up the Animal Procedures Committee (the "APC") to, *inter alia*, advise the Secretary of State on matters falling under the Act (s20(1)).

The APC has recommended that no licences should be granted "for production of embryo aggregation chimeras . . . nor hybrids which involve a significant degree of hybridisation between animals of very dissimilar kinds".[5] Moreover, since 1999, the Home Office has required all projects to receive local ethical review.[6]

A number of offences are created by the Act and the perpetrator of these is liable to be imprisoned (for various terms depending on the offence), fined, or both (ss22–24). Offences include carrying out regulated procedures without a licence, knowingly permitting someone under one's control to carry out a regulated procedure without a licence, re-subjecting animals to severe pain or distress in a regulated procedure when they have already been so subjected, re-using animals previously anaesthetised in a regulated procedure, and failing to kill animals that will suffer adverse effects of a regulated procedure.

On the human side, until recently, regulation of xenotransplantation in the UK fell under the remit of the Xenotransplantation Interim Regulatory Authority (UKXIRA), set up under

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5 *Animal Procedures Committee Report on Biotechnology* (London: APC, 2001) at p 2

6 See *Guidance on the Operation of the Animals (Scientific Procedures) Act 1986.* (London: TSO, 2000), Appendix J.

Department of Health Guidance following reports published by the Nuffield Council on Bioethics[7] and the Advisory Group on the Ethics of Xenotransplantation[8] (which was set up by the Department of Health). The decisions of UKXIRA were not directly legally binding, and Department of Health Guidance only controls medical activities taking place within the National Health Service (NHS).[9] However, UKXIRA was disbanded on 12 December 2006 and its guidance[10] was replaced by new guidance.[11] This defines xenotransplantation to

> mean any procedure that involves transplantation, implantation, or infusion into a human recipient of either live tissues or organs retrieved from animals, or, human body fluids, cells, tissues or organs that have undergone ex vivo contact with live non-human animal cells, tissues or organs.[12]

Hence, while both porcine and bovine heart valves are currently implanted into humans, because they are treated before they are implanted so as to kill their cells, they do not count as xenotransplants. They are, however, regulated as medical devices by the Medical Devices Regulations 2002/618, implementing Council Directive 93/42/EEC and related Directives.

At the time of publication of the new guidance, no xenotransplantation trials had been undertaken in the UK.[13] The Guidance recommends that "all xenotransplant procedures be carried out with a research protocol approved by a research ethics committee" (REC) and proclaims that it is "extremely important" that such procedures take place "in a controlled research context".[14] The Guidance envisages three situations in which a xenotransplantation procedure may be performed in the UK.[15]

First, xenotransplantation could fall within the Medicines for Human Use (Clinical Trials) Regulations 2004/1031[16] (which implement Directive 2001/20/EC)[17]. If so, the procedure must be approved by the Medicines and Healthcare Products Regulatory Agency (MHRA) and receive the favourable opinion of a recognised REC (Reg. 12(3)). Where the trial involves a genetically modified medicinal product, the relevant REC will be the Gene Therapy Advisory Committee (GTAC) (Regs 2 and 14(5)).[18]

Second, the xenotransplant could constitute research involving NHS patients that falls outside of the Clinical Trials Regulations. This would also require the approval of a Research Ethics Committee (including the GTAC, if appropriate), but not the MHRA.[19]

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7 See Nuffield Council on Bioethics, *Animal-to-human Transplants: The Ethics of Xenotransplantation* (London: Nuffield Council on Bioethics, 1996).

8 See Department of Health, *Animal Tissue to Humans: A Report of the Advisory Group on the Ethics of Xenotransplantation* (London: HMSO, 1997).

9 Such regulation is not insignificant, however, as doctors within the NHS are bound by their employment contracts to follow NHS policy. Furthermore, doctors (whether or not they are in the NHS) are regulated by the General Medical Council (GMC), which has the power to strike doctors off the Medical Register and remove their right to practise if they do not follow its guidance. (See further S. D. Pattinson, *Medical Law and Ethics* (London: Sweet and Maxwell, 2006), ch 2).

10 HSC 1998/126.

11 Department of Health, *Xenotransplantation Guidance* (London: DH, 2006).

12 Ibid, p 1. These words derive from Directive 2003/63/EC (the medicinal products for human use directive).

13 Ibid.

14 Ibid, p 2.

15 Ibid, pp 2–4.

16 As amended by the Medicines for Human Use (Clinical Trials) Amendment Regulations 2006/1928

17 As amended by Directive 2003/63/EC.

18 See also Xenotransplantation Guidance, p 2.

19 Ibid, p 3.

Third, whereas the UKXIRA policy required all xenotransplantation to be treated as research, the new Guidance recommends that it should be so treated but allows the possibility of experimental treatment outside of this context. In this situation, clinicians must obtain the approval of a Clinical Governance Committee as provided for in a Health Service Circular.[20]

It is, therefore, of some regulatory importance to determine whether a proposed xenotransplant falls within the Clinical Trials Regulations. These Regulations apply to any proposed *clinical trial* of a *medicinal product* (including xenogeneic medicinal products). More specifically, an "investigational medicinal product" is defined as "a pharmaceutical form of an active substance or placebo being tested" in a clinical trial (Reg 2). The Regulations provide timeframes for the ethics committee to issue an opinion (Reg 15(10)) and the MHRA to determine whether or not to authorise the trial (Regs 18–20). Special authorisation procedures apply to medicinal products for gene therapy and somatic cell therapy, including xenogenic cell therapy (Reg. 19(1))[21] and to medicinal products with "special characteristics", defined to include products that have an active ingredient that is, contains, or is manufactured using a biological product of human or animal origin (Reg. 20(1)(ii)).[22] It follows that at least some xenotransplantation procedures fall under the Regulations. Xenotransplantation trials will come within the Regulations if they involve the use of a new pharmaceutical product, gene therapy/somatic cell therapy product, or medicinal product with special characteristics.

Contrary to Fovargue[23] we doubt that whole organs transplanted from animals or humans into humans will ordinarily be considered to be medicinal products. For a start, the UK Regulations must be interpreted in line with Directive 2003/63/EC. Part IV of Annex I of the Directive applies to "advanced therapy medicinal products", defined as products that "are based on manufacturing processes focussed on various gene transfer-produced bio-modules, and/or biologically advanced therapeutic modified cells as active substances or part of active substances".[24] Such products include "xeno-transplantation medicinal products" (Annex I, Part IV, para 4). The Directive, therefore, does not treat removed (human or animal) organs, tissues or cells that are not manipulated after removal as medicinal products merely because they are implanted into a human body.[25] Of course, the UK could bring procedures under the remit of the Clinical Trials Regulations even though not required to do so by EC Directives. However, we see no clear grounds for its having done so. The provision in the Clinical Trials

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20 HSC 2003/011. See Xenotransplantation Guidance, p 3–4.

21 Somatic cell therapy medicinal products include
> xenogeneic somatic living cells, the biological characteristics of which have been substantially altered as a result of their manipulation to obtain a therapeutic, diagnostic or preventive effect through metabolic, pharmacological and immunological means. This manipulation includes . . . the use of . . . xenogeneic cells associated with medical devices used ex vivo or in vivo (e.g., microcapsules, intrinsic matrix scaffolds, bio-degradable or not). (Para 2 of Part IV of the Annex to Directive 2003/63/EC)

22 This provision was drawn to our attention by a comment on an early draft of this report: see Sara Fovargue "'Oh Pick Me, Pick Me'—Selecting Participants for Xenotransplant Clinical Trials" (2007) *Medical Law Review* (forthcoming). In this article, Fovargue expands on points made in Sara Fovargue, "Consenting to Bio-risk: Xenotransplantation and the Law" (2005) 25 *Legal Studies* 404 at pp 410–411.

23 Cf. Sara Fovargue "'Oh Pick Me, Pick Me'—Selecting Participants For Xenotransplant Clinical Trials": "Using the definitions provided, whole organ xenotransplants may fall within the ambit of the Regulations".

24 See also Recital 9, which identifies advanced therapy medicinal products as those that are "based on processes focused on various gene-transfer-produce bio-molecules (gene therapy medicinal products) and manipulated or process cells (cell therapy medicinal products) as active substances".

25 The definition in Annex I, Part IV, para 4 (quoted above: n12) is of "xeno-transplantation", not "xeno-transplantation medicinal product".

Regulations on which Fovargue relies (Reg. 20(1)(ii)) does not, in our view, support the conclusion that the Regulations go further than the Directives so as to treat unmodified whole organs transplanted into humans as medicinal products. If Regulation 20(1)(ii) is to apply to whole organs, then they must be medicinal *products* with an *active ingredient* that is of human or animal origin. A pig organ to be transplanted into a human is certainly something of animal origin, but the notion that it is an active ingredient/contains one simply by virtue of being a functioning organ requires an extension of the meaning that "active ingredient" has in pharmaceutical practice, which is the background for this area of regulation. Furthermore, if Fovargue is right then it surely follows that all, at least experimental, human to human transplantation must fall under the Clinical Trials Regulations as well, and this does not seem plausible.

However, pending formulation of an explicit policy on this by the MHRA and possible court cases, all we can say with absolute confidence is that, insofar as xenotransplantation involves or constitutes delivery of advanced therapy xenogeneic medicinal products clinical trials of these products will be required by the UK's Clinical Trials Regulations to obtain authorisation from both an independent ethics committee and the licensing authority (the MHRA) (Reg 12). Failure to meet these requirements is an offence under Regulation 49, punishable by a penalty consisting of a fine, a term of imprisonment, or both (Reg 52). Specifically, Schedule 1, Part 2, paragraph 14 of the Regulations provides that the licensing authority and the ethics committee must agree that any "anticipated therapeutic and public health benefits justify the risks", in order for a trial to proceed.

The prospect of clinical trials involving xenotransplants being granted a licence at this time is small: the risk of xenozoonosis (the transfer of infectious diseases from donor animal to human recipient; also known as "xenosis") is a constant and high risk factor, given the risks of a "lack of information about the infectious potential"[26] (especially in porcine derived xenotransplants: the commonest type, due to the use of primates being considered "unacceptable"[27]) and the possibility of the "emergence of a new human epidemic or pandemic".[28]

It is also worth noting that, to the extent that xenotransplants fall under the Clinical Trials Regulations, it no longer matters whether or not the activity takes place within the NHS, and the requirement to submit to the system set up by the Xenotransplantation Guidance will, in effect, be legally required (because it is inconceivable, at least at present, that the MHRA would not require it to be complied with). However, it is also clear that, to the extent that the Clinical Trials Regulations apply, licences would be unlikely to be granted under them until the risks have been substantially reduced,[29] because, unlike some other EU countries, where issues of human dignity are much to the fore, the main UK reservation about xenotransplants fairly clearly concerns these risks.[30]

Of future relevance is the draft EU Regulation on advanced therapy medicinal products (which will amend Directive 2001/83/EC and EC Regulation 726/2004)).[31] If adopted, this

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26 D. Muir and G. Griffin, *Infection Risks in Xenotransplantation* (London: UKXIRA, 2001) at p 118

27 *ibid*, at p 4.

28 *ibid*, at p 121

29 This, of course, raises the question as to how the risks are to be assessed if no trials are permitted? This, itself raises issues about the proper application of a precautionary approach, which undoubtedly is the guiding principle at the present time.

30 This is emphasized in the Xenotransplantation Guidance, p 2.

31 Xenotransplantation Guidance, p 3.

will add additional regulatory requirements for gene therapy medicinal products, somatic cell (human and animal) therapy medicinal products, and tissue engineered medicinal products.

Summary:

- **Contingent on the level of hybridisation, or the extent of the chimeric properties expressed, a licence may be granted under the 1986 Act for the modification of animals for the purposes of xenotransplantation**
- **To the extent that it applies, licences would be unlikely to be granted under the Clinical Trials Regulations until risks have been reduced**

Human/non-human gamete mixing

Human/non-human gamete mixing is directly regulated by the Human Fertilisation and Embryology Act 1990 (the 1990 Act). This is currently being revised and a draft Bill (the Human Tissues and Embryos (Draft) Bill) has been issued.[32]

We will, however, explain the extant situation before indicating the changes that the Bill proposes.

Section 5 of the 1990 Act establishes the Human Fertilisation and Embryology Authority (the HFEA). The HFEA, under section 9(1), has the power to discharge the "functions relating to the grant, variation, suspension and revocation of licences", provided for within the Act.

Section 4(1)(c) provides that to "mix gametes with the live gametes of any animal, except in pursuance of a licence" is prohibited. The only instance where such a licence will be granted is outlined in Schedule 2, paragraph 1(1)(f), according to which such a process would be permitted if its purpose is to test the "fertility or normality of the sperm". However, the results must be destroyed at no later than the two cell stage.

A recent report of the House of Commons Science and Technology Committee recommended that legislation be passed clarifying the nature of hybrids and chimeras, making their creation legal for research purposes if they are destroyed "in line with the current 14-day rule for human embryo cultures" and prohibiting their implantation in a woman.[33] This would represent a departure from the current rules surrounding this activity, insofar as embryos would be allowed to develop right up until the "primitive streak" stage or 14 days (whichever is the earlier), rather than by the two cell stage.

The attitude towards this procedure in the UK is very sceptical, with current and proposed regulation only permitting it in a research setting, and providing "strong legal safeguards",[34] which reflects "public disquiet about the prospect of creating hybrid embryos".[35]

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[32] www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsLegislation/DH_074718 (1/6/07)

[33] Science and Technology Committee, *Human Reproductive Technologies and the Law: Fifth Session 2004–2005. Volume I: Report, together with formal minutes.* (HC 7-I) (London: The Stationery Office, 2005) at p 32.

[34] HM Government, *Government Response to the Report from the House of Commons Science and Technology Committee: Human Reproductive Technologies and the Law* (Cm 6641). (London: The Stationery Office, 2005) at p 10.

[35] Department of Health, *Review of the Human Fertilisation and Embryology Act: A Public Consultation.* (London: Department of Health, 2005) at p 68.

Summary:

- **No licence would be granted by the HFEA**

Changes Proposed by the Bill

- The Bill proposes to replace the HFEA with a new organisation, the Regulatory Authority for Tissues and Embryos (RATE) (which will also replace the Human Tissue Authority, the responsible Authority for the Human Tissue Act 2004, and which will take over responsibility to regulate blood and blood products from the Medicines and Healthcare Regulatory Authority (MHRA) where this regulation is currently under the remit of the MHRA).
- The mixing of animal and human gametes will still be prohibited except in pursuance of a licence (Clause 17(2), proposed s4A(2)(a)). As before a licence may be granted for testing the fertility or normality of sperm, in which case it cannot be kept beyond the 2-cell stage.[36] It is proposed, however (new Schedule 2, para 3(3)) that regulations may extend the activities for which a licence may be granted for research beyond determination of the fertility or normality of sperm. A licence could be granted by RATE if deemed necessary or desirable for the purposes listed in a new Schedule 2, para 3A(2) or any other purposes specified by regulations (proposed new Schedule 2, para 3A(1).
- It is proposed that a licence cannot authorise hybrid embryos to be kept or stored after the earliest of the following: the appearance of the primitive streak, 14 days from which the process of creating the embryo began, or half the gestation period of any species whose nuclear or mitochondrial DNA is involved (new s4A(3)).

Non-human/human somatic cell nuclear transfer (SCNT)

The regulatory position regarding the transfer of either a non-human somatic nucleus into a human ovum or a human somatic nucleus into a non-human ovum is not entirely clear. That is because there remains some room for debate over the precise impact of the 1990 Act and the Human Reproductive Cloning Act 2001 (the 2001 Act).

There are many possible reasons why someone might wish to create a hybrid embryo using SCNT. One possibility is the creation of a child. Another is the deriving of "human embryonic stem cells, thereby circumventing the shortage of good quality human eggs available for research".[37]

The 2001 Act makes it a criminal offence (carrying a penalty of a fine and/or a term of imprisonment not exceeding ten years) to place in a woman a *human* embryo which has been created otherwise than by fertilisation (s1). Although the Act does not define "human embryo", in our view, this provision would capture placing into a woman an animal egg that has had its nucleus replaced with that of a human cell.[38] In any event, the 1990 Act prohibits

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[36] In addition to the continued availability of a *treatment* licence under Schedule 2, para 1(1)(f), the new Bill seeks to permit a *research* licence to be granted for such an activity (Schedule 2, para 3(2)).

[37] Department of Health, *Review of the Human Fertilisation and Embryology Act: A Public Consultation.* (London: Department of Health, 2005) at p 68.

[38] This was also the view of the House of Commons Select Committee (2002) Report on Stem Cell Research House of Lords Paper 83(i) (London: HMSO, 2002) at para 8.18.

the placing in a woman of any non-human gametes (s3(2)(b)).

The 1990 Act directly addresses the use of ova taken or derived from human embryos or foetuses. Section 3A[39] renders it a criminal offence to use such ova for the purposes of providing treatment services, which would clearly encompass their use in a SCNT procedure.

In the context of an animal nucleus being introduced into a human gamete, a licence would be necessary if the storage of human gametes is involved (s4(1)(a)).

There has been considerable controversy over whether or not the transfer of a human somatic nucleus into an animal egg is covered by the 1990 Act. The 1990 Act requires a licence for, *inter alia*, the creation and use of *human* embryos outside of the body (ss1(2) and 3(1)). The Act says that, except where otherwise stated, "embryo" means "a live human embryo where fertilisation is complete" (s1(1)(a)), including "an egg in the process of fertilisation" (s1(1)(b)). In *R (on the application of Quintavalle) v Secretary of State for Health,*[40] the House of Lords considered whether an entity created by SCNT using a human egg and human somatic cell fell within the 1990 Act. Their Lordships held that the 1990 Act was to be interpreted purposively and the purpose of the Act was to provide for the regulation of live human embryos created outside the body. The wording of section 1(1) was held not to exclude SCNT from the ambit of the Act. Lord Bingham(with whose speech Lords Hoffman and Scott agreed) held that the "essential thrust" of the s1(1)(a) was directed to "live human embryos created outside of the human body", as opposed to "the manner of their creation".[41] Lord Steyn treated the restrictive wording of that section "as merely illustrative of the legislative purpose".[42] Lord Millet held that s1(1) was *not* intended to define "the word "embryo" but rather to limit it to an embryo which is (i) live and (ii) human".[43] In other words, their Lordships ruled that s1(1)(a) was to be read as specifying no more than when a fertilised egg was to be regarded as an embryo.[44] It follows that the creation of any living *human* embryo outside of the body, *using SCNT or any other method*, required a licence from the HFEA. Thus, the essential question for our purposes is: when is the product of trans-species SCNT to be regarded as a *human* embryo?

The Nuffield Council on Bioethics has stated that the 1990 Act "is silent on the combination of animal gametes and human somatic cells. It would be a matter for the courts to decide whether the embryo developing from such a hybrid cell was "human" and thus subject to the Act".[45] In contrast, the Center for Bioethics and Public Policy (CBPP) in its submissions to the House of Commons Science and Technology opined that, firstly, "[c]reating an animal-human hybrid embryo is illegal under the [1990] Act"[46] (while referring to the "fuse[ing] [of] an adult human cell with the enucleated egg of an animal") and, secondly, that "[o]ther developments may, or may not come under current UK legislation, depending on whether or

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39 This provision was introduced by s156 of the Criminal Justice and Public Order Act 1994.

40 [2003] UKHL 13.

41 [2003] UKHL 13, para 14.

42 [2003] UKHL 13, para 26.

43 [2003] UKHL 13, para 45.

44 For a critique of their Lordships' reasoning see D. Beyleveld and S. D. Pattinson, "Globalisation and Human Dignity: Some Effects and Implications for the Creation and Use of Embryos" in Roger Brownsword (ed.) *Global Governance and the Quest for Justice. Volume IV: Human Rights* (Oxford: Hart, 2004) at 185.

45 Nuffield Council on Bioethics, *Stem Cell Therapy: The Ethical Issues* (London: Nuffield Council on Bioethics, 2000) at p 14.

46 *Science and Technology Committee on Human Reproductive Technologies and the Law—Response from the CBPP* (March 2004) at p 1

not the entities created can be properly described as 'human'" [47] such as, for example, the creation of human-animal hybrid embryos by implantation of a human somatic nucleus into an enucleated cow egg.[48]

The confusion surrounding the "human vs. non-human" status of human/non-human hybrid embryos created by SCNT was one of the driving forces behind the House of Commons Science and Technology Committee's suggestion (with which the Government agreed) that the terms "hybrid" and "chimera" be defined in legislation.

This suggested legislation has not yet been enacted, and so the question remains moot. A report chaired by the Chief Medical Officer, generally known as "The Donaldson Committee Report" suggested that the 1990 Act does *not* prohibit the mixing of human cells with animal eggs, but that it *should*,[49] while the House of Lords Stem Cell Research Committee argued that an alternative view is that it is "more acceptable to use [a hybrid embryo] for research"[50] because it does not involve the use of human gametes. The House of Commons Science and Technology Committee enjoins the reader to recall that the 1990 Act "aimed to give protection to the human embryo and not gametes or other forms of embryo". However, while this last point is correct, it shirks discussion of what constitutes a "human" embryo, and thus an embryo subject to the protection of the 1990 Act.

Our personal view is that that the courts should take a wide interpretive approach to this situation and hold that simply because (for example) an embryo contains the mitochondrial DNA of a cow and the nuclear DNA of a human, it is not "non-human" for the purposes of the Act. Similarly, a pig nucleus in a human egg would not give rise to something that was human enough to warrant the classification "non-animal". In our opinion, it is contrary to the purpose of the Act to take the narrow view that a creature that is technically not *wholly* genetically human (regardless of the level of modification), should not be given the protection that a human is granted under the 1990 Act simply because its genetic make-up is not 100% human. What should, instead, be determinative is consideration of the characteristics that the creature that could develop from the resulting embryo would have in relation to the reasons why the Act protects clearly human embryos. In our view, the 1990 Act is based on the idea that (clearly) human embryos have a moral status that makes them worthy of a degree of moral concern and respect that increases with the degree of development of the embryo because embryos have the potential to develop into beings to which the law accords full moral status. Of course, what this property is (the property by virtue of which human beings have dignity, rights, are worthy of moral concern and respect, or simply have moral status or standing) is contested between moral theories (on which see more below). However, it is surely this consideration that should be decisive. Simply put, if the resulting embryo is capable of developing into a being with the characteristics that are deemed to be sufficient for clearly human beings to have full moral standing, then the embryos should be considered to be human.

This, however, does not quite resolve the matter. First, it is not certain what characteristics the courts might hold to be determinate. Secondly, failing actually allowing such a creature to

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47 *Science & Technology Committee Review of Human Reproductive Technologies and The Law: Call for Evidence, Submission from the Center for Bioethics and Public Policy* (May 2004) at p 9

48 The specific example used being reported in: *Details of Hybrid Clone Revealed*, BBC News 1999, http://news.bbc.co.uk/1/hi/sci/tech/371378.stm (1/6/07)

49 Expert Medical Group on Human Cloning, *Stem Cell Research: Medical Progress with Responsibility*, Department of Health June 2000, at Recommendation 6, page 46.

50 *The House of Lords Stem Cell Research Committee Report*, at para 8.18

develop and be born, it will not be possible to ascertain with certainty what characteristics it will have. However, on the latter point, it is arguable that where the human component comes from the somatic nuclear material, the resulting creature is likely not to be relevantly different from clear human beings. If this is so then it is also plausible that, barring making the determinate characteristic being 100% human genetically, whatever the relevant characteristics they will be shared by clear humans and the creatures in question. In any event, in a state of uncertainty, it is arguable that precaution should dictate that the benefit of the doubt be given to the embryos and that they should be protected by the 1990 Act in default of legislation on the matter.

Summary:

Regulation depends on both intent and definition:

- **The 2001 Act prohibits this procedure if the intent is to implant the result into a woman and bring it to term**
- **The 1990 Act prohibits the procedure if the egg used is derived from a human embryo, and is intended for fertility treatment**
- **The HFEA would not grant a licence if the courts determined that the embryo was "human" for the purposes of the 1990 Act. It is at least arguable that the courts would hold (and we believe they should hold) that such a creature was human for the purposes of the Act.**

Changes Proposed by the Bill

- The Bill redefines "embryo" and "gamete". The new proposed s1(1)(a) states that an embryo is a live human embryo and does not include an inter-species embryo (this being defined in proposed s4A(5), which is discussed further in the next sub-section). As in the existing Act, an embryo includes an egg in the process of fertilisation. However, it also includes an egg undergoing any other process capable of resulting in an embryo (proposed s1(1)(b)). The proposal could have been to define fertilisation as any process by which an egg is transformed into an embryo. However, the proposal is instead to follow the House of Lords in the *Quintavalle* case and hold that SCNT is not a process of fertilisation.[51] "Gametes" (except in proposed s4A, where non-human gametes are included) include live human eggs (which include cells of the female germ line at any stage of maturity) and live human sperm, including cells of the male germ line at any stage of maturity (proposed s1(4)). Thus, in line with SCNT not being (for the purposes of the law) a process of fertilisation, enucleated eggs and somatic nuclei are not to be regarded as gametes in the context of SCNT process. (We detect some problems here. To begin with there is some circularity in the definitions. More importantly, perhaps, it could be argued that, according to these definitions, because an enucleated ovum is not an egg (or gamete), SCNT is not a process by which an egg is undergoing a process capable of resulting in an embryo. In our opinion, this can be responded to by viewing SCNT broadly to include the process of enucleation of the egg, in consequence of which SCNT does involve an egg undergoing a process capable of resulting in an embryo. This is, however, somewhat strained and could have been avoided by redefining "fertilisation". In any event, the Bill proposes that the Secretary of State be

[51] [2003] UKHL 13, esp. paras 2, 14, and 15.

given powers to extend the definition of "embryo", "eggs", "sperm" or "gametes" in the light of developments in science or medicine (proposed s1(6)). This does not apply to non-human embryos, etc. (which fall under proposed s4A)).

- Embryos etc. that contain any non-human nuclear or mitochondrial DNA are not to be regarded as human. This is contrary to the recommendations we have made above. However, those recommendations were made, in part, to ensure that hybrid and chimaeric embryos fell under the legislation. The Bill achieves that by having specific provisions relating to these interspecies embryos in the revised Act.
- To improve the flexibility of the new legislation, proposed s4A(7) and (8) define non-human embryos etc. in a fashion that parallels the definitions of human embryos etc., and proposed s1(7) gives the Secretary of State the power to pass regulations to amend these in the light of scientific and medical developments.

Human/non-human zygote gene modification

Genetic modification of zygotes is regulated by the 1990 Act and the 1986 Act.

The modification of a *human* zygote with animal genes would not currently be granted a licence under the 1990 Act. The term "embryo", under the Act, includes the zygote (s1). Schedule 2, paragraph 1(4) does not permit treatment licences authorising altering the genetic structure of any cell while it forms part of the embryo and Schedule 2, paragraph 3(4) prohibits the extension of a licence for the purpose of genetically modifying any cell that forms part of the embryo *unless* this is permitted by regulations.

The 1986 Act regulates the modification of animal zygotes with human genes. As previously stated, a licence would be granted dependent on the nature of the species involved and/or the extent to which such modifications are apparent: for example, a pig hybrid with "some 'human genes'" would be acceptable.[52]

Summary:

- **The HFEA would not grant a licence for this procedure**
- **Possibility of a licence under the 1986 Act is dependent on the animals involved and the level of modification expressed.**

Changes Proposed by the Bill

- Proposed s4A(2)(b) and (c) permit the creation, use and storage of inter-species embryos in pursuance of a licence (up to the appearance of the primitive streak, 14 days, or half the gestation period of a contributing species, whichever is the earliest: proposed s4A(3)). Interspecies embryos are human embryos created by using animal and human gametes; by replacing the nucleus of an animal egg or a cell derived from an animal embryo with a human cell or nucleus; by altering a human embryo by introducing any sequence of nuclear or mitochondrial DNA of an animal; by altering a human embryo by introducing one or more animal cells; or

[52] *Animal Procedures Committee Report on Biotechnology* (London: APC, 2001) at p 20

any embryos with both a haploid set of human chromosomes and a haploid set of animal chromosomes or any other animal nuclear or mitochondrial sequence of DNA (proposed s4A(5)). RATE, therefore, might grant a licence for this procedure.

Human/non-human embryonic cell transfer/fusion

This method of creating chimeras is regulated by the 1990 Act, the 1986 Act and possibly the Clinical Trials Regulations.

There is, once again, controversy over whether or not this procedure is within the remit of the 1990 Act. The House of Lords Science and Technology Committee has suggested that, despite the assertion by the Center for Bioethics and Public Policy (CBPP), that "the creation of new genetic human-animal chimeric embryos and foetuses, do not come under the HFE Act",[53] it is likely that the introduction of a non-human cell into a human embryo would constitute genetic modification of an embryo, which will not be granted a licence for either treatment under Schedule 2, paragraph 1(4) or research under Schedule 2, paragraph 3(4) of the 1990 Act.

However, the Science and Technology Committee uses a narrow interpretation of the term "chimera" (provided by the Canadian Assisted Reproduction Act 2004, s3 of which provides that a chimera is "an embryo into which a cell of any non-human life form has been introduced"), whilst the examples cited by the CBPP in their submission of evidence (the implantation of human cells into mice embryos[54], pig embryos[55] and sheep embryos[56]) refer only to the implantation of *human* cells into *animal* embryos. The 1990 Act is concerned with human embryos, and does not regulate the modification of non-human embryos with human somatic cells.

The 1986 Act, however, does regulate non-human embryos. The APC recommends that no licences should be granted "for production of embryo aggregation chimeras"[57] and goes on to state that "there seems to be no particularly good reason to create [trans-species chimeras]".[58]

That a clinical trial involving, for example, stem cells derived from human/non-human embryo aggregation chimeras in order to treat serious diseases,[59] would be granted a licence under the Clinical Trials Regulations (assuming that they apply) is far from certain. The reason for this it two fold. First, all applications for licences must be passed by an ethics committee (Reg 12(3)). Secondly, under the Regulations (as amended), clinical trials must "be scientifically sound and guided by ethical principles in all their aspects" (Sch. 1, Part 2, para 3), including the principles of the 1996 version of the Declaration of Helsinki (Sch. 1, Part 1, para 2 and Part 2, para 6).

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53 *Science & Technology Committee Review of Human Reproductive Technologies and The Law: Call for Evidence, Submission from the Center for Bioethics and Public Policy* (May 2004) at p 9

54 N. Boyce, *Mixing Species: and Crossing the Line?* At www.usnews.com/usnews/culture/articles/031027/27chimeras.htm (1/6/07)

55 G Vince *Pig-Human Chimeras Contain Cell Surprise*: www.newscientist.com/article.ns?id=dn4558 (1/6/07)

56 S.P. Westphal, "*Humanised" Organs can be Grown in Animals.* At www.newscientist.com/article.ns?id=dn4492 (1/6/07)

57 *Animal Procedures Committee Report on Biotechnology* (London : APC 2001) at p 2

58 Ibid.

59 *Review of the Human Fertilisation and Embryology Act: A Public Consultation* (London: Department of Health 2005) at p.68

Ethics committees might be reluctant to approve chimeric experiments. It has been argued that "intentionally creating compromised human beings or part-human beings might appear to 'all the world' as failing to treat the creature as an end in itself, a use that has been confirmed as morally unacceptable since at least the Declaration of Helsinki".[60] However, the concept of dignity invoked by the idea of "an end in itself"[61] is a contested one, and in the UK tends to be linked more closely to the idea of autonomy than in some other EU countries; and when so linked (as it was in the philosophy of Kant, himself, from whom the idea is derived) instrumentalisation is only forbidden when it involves treating a person as solely a means to the needs of others and not at the same time as an end in itself.[62]

However, much is likely to depend on just what the nature of the hybridisation or production of a chimera would involve. Specifically it will depend on whether or not it would create a being with the moral characteristics of human beings (on which see the last part of this paper). This is a philosophical issue and goes beyond the mere definition of the term "chimera". Thus, although the House of Commons Science and Technology Committee request for clarification of the term "chimera" is understandable, by itself this would do nothing to address the ethical issues that underlie different regulatory stances.

Summary:

- **The HFEA would not grant a licence if the embryo to be modified was human**
- **No licence would be granted under the 1986 Act**
- **It is by no means certain that permission to conduct research creating human/non-human trans-species chimeras would be granted by an Ethics Committee under the Clinical Trials Regulations (if they apply).**

Changes Proposed by the Bill

- Proposed s4A(5)(d) brings such chimeric embryos under the remit of the Act. Therefore, the procedure could be granted a licence by RATE.

Patent Regulation

An important aspect of the regulation of hybrids and chimeras is the ability, or inability, to patent the techniques for creating such creatures, as well as the creature themselves. Given that patent regulation affects each of the above activities in very similar ways, rather than include a discussion of its impact under each of the headings, which would be somewhat cumbersome and repetitive, it is discussed separately.

A patent is not a positive right: it does not grant the owner of a patent the right to create or exploit the invention, merely a right to prevent third parties from doing/creating the thing/process that has been patented. For example, if it is possible under the current regulatory regime to patent chimeric or hybrid creatures (or the techniques used for their creation), this

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60 J. Johnston and C. Eliot, 'Chimeras and "Human Dignity"' [2003] 3 *The American Journal of Bioethics*, 3 at w7.

61 See also Part B, para 10 of the 2000 version of the Helsinki Declaration: "It is the duty of the physician in medical research to protect the life, health, privacy, and *dignity* of the human subject" (our emphasis).

62 Immanuel Kant, *Groundwork of the Metaphysics of Morals* (1785). Translated, with an Introduction by H. J. Paton as *The Moral Law* (London: Hutchinson University Library, 1948), p 91.

would not, by itself, enable the patent holder to exploit such an invention, as use (and, indeed, development) might be regulated or even prohibited by other regulatory rules. Conversely, an inability to patent such creatures/techniques does not mean development or use of the creatures or techniques in question is impermissible. However, this itself does not render the issue of patents irrelevant, as the inability to patent a method/technique has a profound effect on the *practical* regulation of hybrids and chimeras in the UK: if one cannot patent one's technique, then the incentive to proceed with research that could lead to the creation of these creatures is lessened. Thus the question remains: "is it possible to patent hybrids and chimeras in the UK"?

Article 53 of the European Patent Convention 1973 (which was implemented by the UK Patent Act 1977) provides that patents shall not be granted for inventions, the publication or exploitation of which is contrary to "ordre public" or morality. With slight modification, this is mirrored in Directive 98/44/EC on the legal protection of biotechnological inventions, Article 6(1) of which states that "[i]nventions shall be considered unpatentable where their commercial exploitation would be contrary to *ordre public* or morality". With reference to Article 6(1), Article 6(2) of the Directive gives examples of inventions that are "in particular" excluded, viz.,

(a) processes for cloning human beings;
(b) processes for modifying the germ line genetic identity of human beings;
(c) uses of human embryos for industrial or commercial purposes; and
(d) processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial benefit to man or animal, and also animals resulting from such processes.

In addition, Recital 38 states that "processes, the use of which offend against human dignity, such as processes to produce chimeras from germ cells or totipotent cells of humans and animals, are obviously also excluded from patentability".

Furthermore, Article 7 of the Directive states that "[t]he Commission's European Group on Ethics in Science and New Technologies evaluates all ethical aspects of biotechnology". It is, therefore, to be noted that this Group (the EGE) has declared that the "dignity" of the human being should be protected and that chimeras and hybrids are an offence to that dignity and should not be permitted.[63]

Directive 98/44/EC was implemented in the UK by the Patents Regulations 2000/2037, which amended the Patents Act 1977.[64] Regulation 3, implementing Article 6(1) of the Directive, provides that "[a] patent shall not be granted for an invention the commercial exploitation of which would be contrary to public policy or morality". Schedule 2, paragraph 3(b)-(e) duplicates Article 6(2)(a)-(d) of the Directive, but there is no reference in the Regulations to the exclusion of chimeras from germ cells or totipotent cells of human and non-human animals mentioned in Recital 38 of the Directive. There is also no indication that the exclusions of Article 6(2) are examples only, as the words "in particular" are not reproduced in the Regulations.

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63 European Group on Ethics *Citizens Rights and new Technologies: A European Challenge—Report of the European Group on Ethics and Science and New Technologies on the Charter on Fundamental Rights Related to Technological innovation* (Brussels: EGE, 2000).

64 The Patent Act 1977 has been further amended by the Patents Act 2004 in order to take account of amendments to the European Patent Convention. These are not, however, relevant in the present context.

These provisions, combined with the current ethical climate surrounding the creation of hybrids and chimeras discussed above, probably prevent patents being granted for the creation of hybrids or chimeras. However, there is a caveat to this. For, although the doctrine of supremacy of EC law requires domestic law to conform to EC Directives, where they are capable of having direct effect, it is by no means certain that the UK patent office will attend to Recital 38 in applying the Regulations (let alone recommendations of the EGE), as the status of Recitals in EC law is controversial. [65]

Ethical Climate and Background to UK Regulation

The UK is a very multicultural society and there is no consensus or even dominant ethical position amongst the population. However, it is clear that regulation of the use of embryos and foetuses, the UK's abortion law, the 1986 Act, and background documents to the regulation of xenotransplantation, strongly suggest a particular view of the characteristics that confer moral standing or status on those beings that have it. This is at variance with the view taken in many other EU countries, particularly Catholic ones. Catholics are a small minority in the UK, but have been very organised and active in trying to have legislation changed so as to be more in line with their ethico-religious beliefs.[66] Other religious groups have been much less vocal and organised in their attempts to influence legislation.

In this final section, we will discuss this ethical background briefly. This, however, is not the only factor that must be taken into account in understanding the influence of ethics on the UK's regulatory attitude towards chimeras and hybrids. The UK is well-known for it "pragmatic" approach to regulation, which probably owes much to the strong influence of utilitarianism in the UK. The secularisation of the UK and its long-established technology industry must also be taken into account in understanding the influences affecting regulation.

In many EU countries, probably the principal ethical issue identified in relation to the chimeras and hybrids is that of dignity or, more specifically, human dignity. The concept of dignity does not explicitly play much of a role in the UK debate or regulation. However, if human dignity is thought of, as it is proclaimed in the Preamble to the UN's Universal Declaration of Human Rights of 1948, as that property by virtue of which human beings have fundamental rights and freedoms, then a view of human dignity is at least implicit in any view taken about what property or properties make a being worthy of moral concern and respect, and we consider that UK regulation of the area is much influenced by a view of this matter.

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[65] On which see Deryck Beyleveld, "Why Recital 26 of the EC Directive on the Legal Protection of Biotechnological Inventions Should be implemented in National Law" [2000] *Intellectual Property Quarterly* pp 1–26, where it is argued that *prescriptive* recitals are *prima facie* binding in the interpretation they require of Articles. It should be noted that indirect support for this is implied by the Opinion of Advocate-General Jacobs in relation to Case 377-98. In this case the Netherlands challenged the validity of Directive 98/44/EC on, amongst other things, the ground that it did not make patentability of an invention containing, or produced from, human biological material dependent on informed consent of the human source. The Advocate General and the ECJ rejected the claim, not for the reason that Recital 26 of the Directive in fact requires this consent (which one of us had argued to be the case in the publication cited at the beginning of this footnote), but that Recital 26 does not state a requirement of patenting but something that must be implemented outside of patent law. However, the considerable and concerted attention given by the Advocate General in his Opinion to what Recital 26 states is odd if his view is that *if* Recital 26 did prescribe consent for a patent to be granted then it is not at least *prima facie* binding in the interpretation it requires of Article 6(1). See further (and for a critique of the Advocate General's interpretation of Recital 26) Deryck Beyleveld and Roger Brownsword). "Is Patent Law Part of the EC Legal Order? A Critical Commentary on the Interpretation of Article 6(1) of Directive 98/44/EC in Case C-377/98" [2002] *Intellectual Property Quarterly*, pp 97–110.

[66] See S. D. Pattinson, *Medical Law and Ethics* (London: Sweet and Maxwell, 2006), 20–21.

To place the matter in context, it is worth listing some of the different views to be found in moral theories about the basis of moral standing. For example, various theories maintain that the property that is necessary and sufficient for a being to have moral status (to be owed moral concern and respect in its own right) is

(a) being alive;
(b) being sentient (having the capacity to experience pain/pleasure);
(c) being a member of the human species, biologically defined;
(d) being self-conscious (or having personhood);
(e) being a rational agent (in the sense of having the capacity to act for reasons) (or as Kant described it, "a rational being with a will");[67]
(g) having the potential to develop one or other of these properties;
(h) having the potential to develop rational agency, or the past possession of rational agency, as well as the possession of rational agency itself *within* the context of a teleology. One example is the view that all human beings possess moral status as members of the human species, characterised, centrally, by possession of rational agency, because this must be viewed in the context of human beings existing only to fulfil God's purpose.
(i) being a vulnerable rational agent (which is our own position; vulnerability being necessary, because beings that cannot be harmed can hardly require the concern of others). (While this is probably taken for granted in most other views, one of us has argued elsewhere that it is worth taking explicit note of it, because attention to it has important implications for moral theory).[68]

We take the view the best candidate for the position that has exerted the greatest influence on UK regulation is the view that full moral standing derives from being a rational agent coupled with the idea that a degree of moral standing is conferred by being a potential rational agent and the idea that the degree of moral standing is proportional to the degree to which a being approaches being a rational agent. This we maintain is implied if we are to make consistent sense of the following:

- that the UK law permits abortion places greater restrictions on abortion at after the 24th week of development of the foetus than earlier;[69]
- that the 1990 Act permits various procedures to be performed on embryos that are not for its benefit up until a particular stage of its development;[70]
- that the philosophy of the Warnock Committee, which was directly influential in the enactment of the 1990 Act, was that the embryo has a special status as a potential human being that makes it worthy of concern and respect but is less than that of the born human being;[71]
- the special protection given to primates and some other animals[72] by Section 5(6) of

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67 Immanuel Kant, *Groundwork of the Metaphysics of Morals* (1785). Translated, with an Introduction by H. J. Paton as *The Moral Law* (London: Hutchinson University Library, 1948), pp 89–91.

68 See Deryck Beyleveld and Roger Brownsword, *Human Dignity in Bioethics and Biolaw* (Oxford: Oxford University Press, 2001), pp 114–117.

69 Abortion Act 1967 s1, as amended by the 1990 Act.

70 For example, s3(2)(a) subject to s3(4) and Sch 3, para 5.

71 M. Warnock. *Report of the Committee of Inquiry into Human Fertilisation and Embryology* (HMSO: London) Cmnd 9314, para 11.17.

72 Namely, cats, dogs and *equidae.* To be sure, these have a high degree of intelligence, though not on a par with primates. However, so do pigs, which are not protected. This probably reflects the fact that pigs are eaten in the UK, whereas cats, dogs and horses are generally not and have a special position as pets or

the 1986 Act, together with the Act's prescription in Section 5(5)(b) that less sensate beings are to be used in preference to more sensate beings;

- The extension to the meaning of "protected animal " in Section 1(1) of the 1986 Act effected by the Animals (Scientific Procedures) Act (Amendment) Order 1993, which gives special protection to Octopus *vulgaris* (most probably because of recognition of the intelligence displayed by this creature);
- the comments of, e.g., the Kennedy Committee (instrumental in the setting up of UKXIRA, which until recently regulated xenotransplantation) that directly refer to the proportional standing of primates on account of their close approximation to the intellectual capacities of human beings.[73]

This view best accords with preference utilitarianism (as against hedonistic utilitarianism),[74] contractarianism (sometimes called "contractualism"), and Kantian theories, and the former two are very widely accepted in at least academic philosophical circles in the UK.

This position has an effect on the way in which various philosophical arguments are perceived. For example, it affects the force of arguments to the effect that cloning violates dignity by instrumentalising the cloned being.[75] While instrumentalisation (treating a being solely as a means and not as an end in itself) will be prohibited, instrumentalisation will only be seen to occur if a being is treated as a non-autonomous agent. Since the being is only envisaged to have autonomy at the certain stage of development it cannot be instrumentalised before this stage, and so the question of instrumentalisation must be referred to how it will be treated after it reaches this stage.[76]

This position also opens up the possibility of weighing the harms that could be said to be done to various beings in the practices that will produce chimeras and hybrids against the benefits and needs of other beings with moral standing in a way that cannot be regarded as proper by theories that accord full moral status to the beings in question.

In general, this position opens up the way for a pragmatic and consequentialist way of approaching the issues that are not open within certain other positions. In general, cloning, the creation of chimeras, etc., will not be seen to be something to be prohibited at all costs, but something that could, at least in certain circumstances, be justified by overriding benefits to others. Consequently, much of the UK debate in this area has focussed on risks, the idea being that if various practices can be done safely or the risks attending them reduced, then they might become acceptable. And this, in turn, or so we are suggesting, correlates with the fact that much UK regulation is not directly prescriptive but sets up an authority to regulate the activity.

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working animals. The explanation for this is possibly that the intelligence recognised in cats, dogs and *equidae* (and pigs) is not considered to be sufficient to grant special singled out protection to these categories and that those that are singled out are singled out in order to respect public sensitivity to domestic pets and working animals.

73 Advisory Group on the Ethics of Xenotransplantation, *Animal Tissue into Humans* (Department of Health, 1997), p 65, where it is stated that while it is not ethically acceptable to use primates as sources of organs because of their close affinities to humans, it is ethically acceptable to use pigs.

74 Preference Utilitarianism gives standing (at least in the paradigm case) to beings capable of exercising choices, whereas Hedonistic Utilitarianism gives it to those capable of experiencing pain and pleasure.

75 See, e.g., the Explanatory Report to the Protocol to the Convention on Human Rights and Biomedicine on the Prohibition of Cloning Human Beings. For a critical commentary, see Deryck Beyleveld and Roger Brownsword, *Human Dignity in Bioethics and Biolaw*, fn. 43 above, pp 158–164. See also Shaun Pattinson, 'Reproductive Cloning: Can Cloning Harm the Clone?' (2002) 10 *Medical Law Review* 295.

76 See Beyleveld and Brownsword, ibid, p 161.

Finally, this position makes analysis of the influences of economic, scientific, and medical considerations more complex than it might otherwise be. In any country, these considerations create imperatives that can come into conflict with those based on purely ethical principle. However, from the perspective of the UK core ethical position as we have portrayed it, these imperatives can themselves be seen as ethical ones (reflecting the needs of agents), and the permissibility of considering consequences for other beings with status increases the force and permissibility of economic considerations (and reduces the necessity to see them as conflicting considerations in all circumstances). In short, this means that what is sometimes seen as the UK's "pragmatic" rather than ethical approach can be portrayed as, if only in part (because we do not wish to suggest that the UK is not tainted by unethical attention to political imperatives deriving from economic and other imperatives), as, in fact, an ethical approach. It is just that the form and content of the ethical imperatives are, to an important degree and way, different from those in some other EU countries.