Not "Human" Enough to be Human but not "Animal" Enough to be Animal - the Case of the HFEA, Cybrids and Xenotransplantation in the UK

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Not 'human' enough to be human but not 'animal' enough to be animal – the case of the HFEA, cybrids and xenotransplantation in the UK

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Abstract: Innovations in scientific and medical technologies, such as xenotransplantation and admixed embryos, invariably become the target of regulatory agencies and often demand new regulatory frameworks. In making decisions associated with these innovations, it is sometimes necessary for regulators to adopt certain positions about the status and significance of the human-animal embryo or body. In the UK, the regulatory and advisory bodies involved in the sphere of human/non-human transfer and exchange of material are: (1) The Human Fertilisation and Embryology Authority (HFEA); (2) the (defunct) UK Xenotransplantation Interm Regulatory Authority and (3) the Home Office's Animal Procedures Committee (APC). In this article, we critically examine the reasons for the HFEA's involvement in regulating and advising in research which uses admixed embryos, given that the HFEA's remit is the government's fertility watchdog regulating in the area of *human* embryos. This expansion, we argue, was partly due to pressure from pro-cybrid supporters and the need to fill an institutional void left by the decommissioning of UKXIRA. Ironically, specific institutions such as UKXIRA may have been better placed to deal with animal-human fusions.

Keywords: xenotransplantation; admixed embryos; regulation, and identity.

INTRODUCTION

The fascination with crossing the human/animal species barrier has a long history. For example, in ancient Egyptian, Greek and Roman myth and iconography, sphinxes (human-lion combinations), centaurs (human-horse combinations), fauns (human-goat combinations) and minotaurs (human-bull combinations) featured heavily. Although the stark physical combinations envisioned by our forebears has not been realised, researchers have not baulked at the possibilities offered by the biological similarities between humans and animals in the understanding of disease and the development of therapies. Technologies have been developed

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which can facilitate the transfer of DNA, cells, tissue and organs from humans to animals, and vice versa. Indeed, a multitude of human-animal variations can be created depending on the nature of the entity envisioned, the specific animal used, the nature and amount of biological material inserted, and the stage of existence or development being addressed. In recent years, two procedures in particular have gained scientific and regulatory attention in the UK: (1) 'xenotransplantation', which describes the transplantation of tissue or organs from one species to another (Deschamps, Roux, Sai, & Gouin, 2005); and (2) 'cybridisation', which is implantation of a human cell nucleus into an enucleated animal egg (usually a cow or rabbit). The former exemplifies the introduction of animal material into a human body; the latter human material into an animal cell.

Importantly, both xenotransplantation and cybrid research are controversial examples of emerging and evolving biotechnologies that raise complex issues relating to (1) the status of the human body (i.e. what is human about the human form), and (2) the nature of human identity (i.e. how does such intermingling effect our sense of humanness and our identification and interaction with other entities). Cybrids and xenotransplantation were both created due to shortages in human embryonic or organ material and share a similar purpose of offering therapeutic solutions to human morbidity. These technologies sit on opposite ends of the animal-human admixture spectrum insofar as xenotransplantation is an 'old' technique which focuses primarily on whole organs placed into human bodies, and cybrids is a 'new' procedure at the molecular level. Both of these biotechnologies depend, to some extent, on the *continuity* in biology between human and non-human animals (so that scientifically generated entities might provide new treatments or cures) despite the fact that UK regulation (as we shall see) focuses on the differences between them. Both rely on an ethic of acceptability of using animal bodies to further human interests. And, finally, both xenotransplantation and cybrid research evoke mythological imagery such as the Greek minotaur or social commentary such as HG Wells' *Island of Doctor Moreau*, and therefore sit at the interface of science fact and science fiction, making them particularly vulnerable to hyperbole within scientific, regulatory, media and public domains.

It is perhaps trite to say that interspecies transplantation (regardless of the direction) poses political, social, and moral challenges to our regulatory system, which in the UK has evolved in a manner that treats animals and humans quite separately. Regulatory decisions concerning hybrid forms (i.e.: concerning innovations in the transfer of DNA, cells, tissue and organs between humans and animals) can have profound epistemic and social implications insofar as they challenge our commonly held conceptions about what is human and what is animal. This is amply evidenced by the heated discussions which took place in 2008 around proposed amendments to the *Human Fertilisation and Embryo Act 1990* (HFEA 1990) which was to allow the mixing of human and animal material at the embryonic level. While there have been efforts to examine various aspects of law and governance relating to the research and use of xenotransplantation and, to a lesser extent, admixed embryos (Brown et al. 2006; Brown and Michael 2004), there has been much less thought given to which of the competing regulatory institutions in the UK most appropriately takes the lead in decision-making in the human-animal setting. In this article, we critically examine how regulatory institutions in the UK respond to the challenges to human identity posed by xenotransplantation and cybridisation. First, we briefly discuss theoretical and epistemological writing in the area. Then we consider the scientific possibilities that characterise this field. Third, we highlight the short regulatory history of these two practices reviewing 1) The Human Fertilisation and Embryology Authority (HFEA); (2) the (defunct) UK Xenotransplantation Interm Regulatory Authority and (3) the Home Office's

Animal Procedures Committee (APC). Finally, we suggest that a regulatory void was inadvertently created with the deregulation of UKXIRA (a process singularly interesting purely for its rare occurrence). This void was made visible by the emergence of novel entities such as admixed embryos hence the HFEA's remit as the government's fertility and embryology authority regulating in the area of *human* embryos had to be extended to regulate the area of admixed embryos. How this was accomplished illustrates a tension between the need for regulation and the classification of species in genetic terms.

I. REGULATING THE BODY

Whereas xenotransplantation arguably constitutes a *barrier threat* to human identity in terms of the transplantation of an animal organ into a human; cybrids pose *a creation threat* insofar as a distinction had to be drawn between what is human and what is animal. In the case of the 'old' xenotransplantation technology the scientific object (e.g. the transgenic pig) was defined formally by those charged with governing use, rather than the scientists involved in the mixing of human and animal cells (Brown, Faulkner, Kent, & Michael, 2006). As will be discussed, the case is more complex with cybrids, as regulatory institutions have had to classify these 'newer' admixed phenomena as human or animal before they can determine what kind of regulation can be applied to them. Scientific innovation may not assist, because previously, linguistic licence had been taken on whether cybrids are 'pseudo-hybrids', 'admix' 'interspecies embryo' or, the term eventually settled upon: 'cybrids'. Concern had been expressed about the discrepancy between the understanding of scientists and regulators in this area (House of Commons Science and Technology Committee, 2007). In short, the status of the cybrid is less clear-cut to regulators than the component parts in the xenotransplantation context were perceived to be. Hence, through their decisions in areas such as xenotransplantation and cybrids, regulators and regulatory institutions are generating new classifications that challenge previous understandings of the boundaries between human and animal entities. Indeed debates around the new technologies often focus on ethical and governmental issues surrounding their regulation, but leave unexplored how 'our attitudes towards them are linked to perennial human anxieties about the strange, the new, and the other' (Jackson, 2002). From the limited research available, public reactions of disgust (or 'yuk' factor) is a description of a response to an issue, that could be seen as irrational, or emotional, but which highlights discourses about 'naturalness' (Michael and Brown 2004). The 'yuk' responses found are probably related to the fact that the process of interspecies mixing rarely happens in nature. Natural combinations between biological species are relatively rare (e.g. animal-animal combinations such as mules or hinnys).

One of the central themes of current discourse on research that mixes human and animal is that of classification. In her classic text, 'Purity and Danger' (1966) the anthropologist Douglas suggests that 'pollution behaviour is the reaction which condemns any object or idea likely to confuse or contradict cherished classifications' (Douglas, 1966). Dirt, or rather uncleanness, is 'matter out of place', something that may be out of synch with the supposed natural order therefore causing ambiguity and concern (1966: 36). Applying this analogy to xenotransplantation, although pigs or any other animal may not necessarily be considered unclean, their usage in xenotransplantation challenges known schemata of what it is to be a 'pig' and what it is to be 'human.' In the case of both xeno-practices and admixed embryos, such entities transgress familiar and taken for granted boundaries between animals and humans (Alter, 2007; Chakrabarty, 2003; Robert & Baylis, 2003). In the case of cybrids, the regulators must

classify new phenomena before they can determine what kind of regulation can be applied to them. There is then a tension in the ordering of things (Foucault, 1966) for scientists and regulators as they work to construct these mixed phenomena as scientific objects that can be controlled, manipulated and regulated either as human or as animal. Similarily, Agamben writes that the entry of *zoē,* (the biological life of all common entities; the 'bare life') into the *bios*, the regulatory sphere, signals a decisive moment in the development of modernity. Where bios and *zoē* converge is a blind spot termed a 'zone of intersection' (Agamben, 1998). Clearly, the regulation of admixed embryos takes place in such a zone of intersection. However, in this area the 'contrasting poles of the human and non-human remain precarious and unstable havens into which regulatory policy-making retreats when confronted with the monstrous' (Brown, 2009). Admixed embryos lie in the zone of intersection where bios and zoē collide therein yet, as Brown suggests, the bios represents 'a constitutional refortification of traditional speciesist hierarchies' (Brown 2009: 162). We consider the contested and controversial efforts (and second efforts) that have been undertaken to govern these practices and the strategy used to demarcate the human and non-human in the case of cybrids.

II. THE SCIENTIFIC SETTING: GENE SPLICING AND SPECIES MERGERS

As one might anticipate, there is a wide range of ways in which human and non-human animals might be mixed by human artifice so as to produce a hybrid entity and these are defined in Table 1.

Table 1

Non-Consumptive Use of Animals	**Description**
For physical properties	An example would be pig heart valves used for transplantation to humans. Here the tissue is essentially 'dead' and is used for its physical properties
For extraction of useful products	Therapeutic products for human use can be derived from animals e.g. pregnant mare serum gonadotrophin (PMSG) which is purified from the urine of pregnant mares and used in human medicine. Some of these may be replaceable using recombinant DNA technology e.g. insulin for treating diabetes was previously extracted from pigs but this source has been replaced by production of human insulin in genetically modified bacteria.
For testing	For example, the capacity of human sperm to fertilise an egg can be tested by allowing them to fertilise an animal egg. The law requires that the resulting 'embryo' is destroyed. Cells derived from human embryonic stem cells have also been tested in animals.
For supply of donor eggs	The proposed use of cow or rabbit egg as the 'host' for a human nucleus. The suggested use is for research purposes only
For products derived from 'humanised' (or	Therapeutic proteins may be produced in milk or eggs. The reasons given are that the normal production capacity for

genetically modified) animals	these types of proteins (large-scale cell culture) is currently becoming limiting and production is expensive. The European Agency for the Evaluation of Medicinal Products (EMEA) has recently approved the first such product, a protein produced in goat milk by the company GTC Therapeutics. Protein production in eggs is still at the experimental level.
For organs derived from 'humanised' (or genetically modified) animals	This is xenotransplantation and the most likely GM animal source is the pig. The intention is to produce organs for transplant into humans in order to overcome the current shortage of donor organs.

As indicated above, the present article is concerned with two examples from Table 1, namely 'use of organs from 'humanised' animals' (commonly referred to as xenotransplantation), and 'the supply of donor eggs' (otherwise referred to as cybridisation). Although xenotransplants maintain their animal cell structure, they can be transplanted into humans, thereby exploiting their properties as functioning organs, by being 'disguised' as human organs via genetic modification. Increasingly, the subject pigs are transgenic – bred and modified to make them more 'acceptable' to human (e.g. they are engineered so as not produce the Gal epitope). It is generally accepted that pigs are amenable to xeno-practices because of their fecundity, but also from an ethical standpoint (Brown & Michael, 2001). In 1984, a UK moratorium on human-animal xenotransplant was called for and enforced until 1992.[1] Surges of interest and activity in xenotransplantation occurred following immunological discoveries in the early 1990s, and advances in animal genetic modification in the late 1990s and early 2000s. However, as research has moved increasingly into the intercellular level, 'new' cybrid technologies have, to some extent, displaced 'old' (and unperfected) xeno-practices. Cybrids are permissible and are created through cell nuclear replacement, where the complete nuclear DNA from a human cell is transferred into an animal egg which has had its nuclear DNA removed. The potential use and demand for this technology has been expanded due to difficulties associated with obtaining human eggs and the desire to produce stem cell lines (e.g. Somatic Cell Nuclear Transfer or cloned stem cell lines). The hope is that research using cybrids will lead to a better understanding of, and new treatments for, diseases such as Alzheimer's, Parkinson's, cystic fibrosis, motor neurone disease and Huntington's through the creation of a supply of 'diseased' stem cells.

III. THE REGULATORY MILIEU: THE UKXIRA, HFEA, AND APC

(1) Xenotransplantation: Regulating Animal Materials into Human Being

In 1995, the 'Animal Tissue into Humans' (1997) report concluded that xenotransplantation would be acceptable provided certain criteria were met, including the establishment of a regulatory body. The United Kingdom Xenotransplantation Interim Regulatory Authority (UKIXRA) was set up following the Nuffield Report (Nuffield Council of Bioethics., 1996) and

[1] The Baby Fae case has been criticised as unethical; commentators have questioned how informed consent could have been realised in a xenotransplantation setting generally and in this case more specifically; they have highlighted the difficulty of differentiating between clinical and therapeutic trials; and used the case to push for close monitoring of xenotransplantation (McLean and Williamson 2005).

the Kennedy Report (Department of Health; The Stationery Office, 1997; Kennedy Report., 1997), each of which examined the ethical implications of xenotransplantation. The Kennedy Report recommended that a national body be set up to *regulate* and *monitor* xenotransplantation. UKXIRA was set up in lieu of a permanent standing committee, charged with, broadly, ensuring that 'animal to human transplantation … [was] …developed safely in the United Kingdom' (McLean & Williamson, 2005). However, the terms of reference were *advisory* and not *regulatory* (Department of Health, 2008). UKIXRA remained in operation for 9 years, from 1997 to December 2006, when it was disbanded and other organisations absorbed its functions and new xenotransplantation guidance was developed (DoH, 2008). The agenda and membership of UKXIRA appears to have declined in the years leading up to its disbandment http://www.dh.gov.uk/ab/Archive/UKXIRA/DH_087870. The official reasons given for its disbandment included an alleged lack of interest, and uncertainty around 'zoonosis' – the transfer of potentially harmful diseases such as PERVs (Porcine endogenous retroviruses) to humans from animals. It is suggested that cross-species infection, transmitted *in vivo* through a xenotransplant, is particularly risky, as the procedure is so novel, and risks are currently unknown (Herring, Cunningham, Whittam, Fernandez-Suarez, & Langford, 2001). Though research and funding does appear to have waned somewhat over the past few years, many researchers remain confident that xenotransplantation will one day be a viable alternative (Groth, 2007). Indeed, some commentators argue that the disbanding of UKXIRA is of concern because xenotransplantation still offers a possible solution to the shortage of transplantable and/or graftable organs and tissues, and that the ethical and safety complexity of xenotransplantation warrants a specialist body to ensure that it does not proceed without adequate controls being in place (McLean and Williamson 2007). For example, before it was disbanded, UKIXRA expressed concern that researchers and desperate patients might be tempted to conduct xenotransplantation experiments overseas, in countries with less stringent regulations since 'countries with the most liberal xenotransplantation procedures (even if this position has been arrived at inadvertently) may well attract research teams or surgeons who wish to conduct experimental procedures that remain unacceptable in countries with tighter regulation' (Ibid 2007: 374).

Such a prediction materialised last year when research into creating pigs with 'humanised' organs was moved from the UK to the US after British regulations prevented experiments (Connor, 2007). The decision to reject the procedures in the UK was taken by the Home Secretary but part of the responsibility for examining applications for xenotransplantation trials now rests with the APC. The APC does not licence applications but reviews and then *advises* the Home Secretary on the animal welfare or ethical implications. The APC also works closely with the Home Office Animals Scientific Procedures Division which is responsible for matters relating to the Animals (Scientific Procedures) Act 1986 that requires licensing of all scientific procedures on animals and the use of an inspectorate to ensure compliance. Like UKXIRA, it is an advisory, Non-Departmental Public Body. For UKXIRA the emphasis is on the risk xenotransplantation posed to humans as well as animal welfare (see above); for the APC, who continue to advise the Home Secretary, their focus in on the cost-benefit balance i.e. cost to animal versus benefit to human – as well as ensuring experiments are conducted appropriately with consideration to welfare (Animal Procedures Committee. http://www.apc.gov.uk/). The APC sub-committees have no specific focus on xenotransplantation or indeed their ethical or legal implications (http://apc.homeoffice.gov.uk/members/composition.htm). UKXIRA, on the

other hand commissioned ethical and legal reviews and in its nascent stage was chaired by a professor of law and ethics.

Essentially, the modern history of the relationship between UKXIRA and xenotransplantation (perhaps more broadly of regulation and scientific innovation) points to the unpredictability of scientific progress and the problematic nature of regulating in uncertainty, alongside the deep-set ethical issues that arise from such animal-human fusion procedures (Bruce, 1998). Such complexity, some have argued, requires a specialist body to examine the social, ethical and practical implications focussing particularly on both the animal and human repercussions (McLean & Williamson, 2007). There is a general trend in the UK whereby the regulatory body often 'fits' the biological one (Brown & Michael, 2004). That is, a regulatory body whose responsibilities map on to the existence of the entity being produced (discussed later). The cyclical nature of innovation is a constant feature and could be recognized as such, regardless of the eventual promise of cure or therapy. The lessons that this behoves us to learn when regulating cybrids shall be addressed below.

(2) Cybrid Research: Regulating human material into Animal Entities

A number of admixed embryos can be created through cell nuclear replacement although they were originally banned under the HFEA 1990 Act. Cybrids are one example that are said to be 99.9% human, with the animal element (0.01%) being 'residual' (e.g. mitochondrial DNA) outside the nucleus of the cell; crudely put, a human nucleus is contained within an animal shell. A key player in the case of cybrids is the Human Fertilisation and Embryology Authority (HFEA) – a statutory body, created in 1991 under the Human Fertilisation and Embryology Act (1990). The HFEA is the UK's independent regulator overseeing the use of gametes and embryos in fertility treatment and research and probably one of the first of its type in the world. HFEA Members are appointed by UK Health Ministers in accordance with the guidance from the Commissioner for Public Appointments (the 'Nolan' Guidelines). The HFEA has eight sub-committees including a specialised ethical and legal advisory group. The HFEA licences centres carrying out In Vitro Fertilisation (IVF), other assisted conception procedures and human embryo research, and provides a range of detailed information for patients, professionals, the public and Government. (http://www.hfea.gov.uk/en/default.html Accessed 12.05.08). If it is accepted that an application for research falls within the HFEA's remit, it must go to the HFEA Licence Committee for consideration.

The HFEA has faced difficulties in the regulation of research, and the interpretation of the HFE Act 1990 has been a nexus for controversy and legal challenge (e.g. see Quintavalle v HFEA [2005] UKHL 28 (HL)). According to the courts, the HFEA has jurisdiction over *human* embryos, irrespective of whether such embryos are produced by fertilisation or by a process involving cell nuclear transfer. In November 2006 UK researchers from Newcastle University and King's College London applied to the HFEA for a three-year licence to create cybrids using human DNA with cow eggs. A month later, the government published its proposals for revision of the HFE Act 1990 (Cm 6989), including proposals aimed at clarifying government policy on the creation of human-animal hybrid and chimeric embryos. The White Paper explained that the Government had found that the HFE Act 1990 did not refer to more novel processes of embryo creation that had been developed since the Act was passed. The government proposed to clarify the extent to which the law applies to such entities, but also to *prohibit their creation*, unless there were circumstances in which they may be allowed under licence; a paradoxical objective of

prohibition but with exception. Many media sources reported this and a group of scientists wrote an open letter to 'The Times', expressing their concern with the proposed legislation arguing that the proposed 'ban' was not based on scientific judgement, but on biased public opinion (Harris 2007). Scientists and others began to openly challenge the government's decision and key protagonists of hybrid creations (mainly scientists, representatives of funding bodies, Labour politicians) eventually 'won' the (media) debate about the creation of cybrids (Williams, Gajevic, Lewis, & Kitzinger, 2009). In response, the UK government essentially conducted a U-turn: the subsequent draft bill made it clearer that the creation of some types of animal-human embryos could be allowed, as these were 'necessary' for research (Department of Health, 2007). In May 2008 the House of Commons voted on amendments to the Human Embryology and Fertilisation Bill, and the amendment to ban the creation of cybrids was defeated in a free vote (336 to 176) (Dyer, 2008). The Human Fertilisation and Embryology Bill successfully passed its final parliamentary stage in November 2008 when the House of Lords accepted amendments to the Bill made in the Commons. The Bill received Royal Assent in December 2008 and is set to come into force in October 2009. The amendments to the HFE Act 2008 suggest that:

> (6) For the purposes of this Act a human admixed embryo is—
>
> (a) an embryo created by replacing the nucleus of an animal egg or of an animal cell, or two animal pronuclei, with—
>
> (i) two human pronuclei,
>
> (ii) one nucleus of a human gamete or of any other human cell, or
>
> (iii) one human gamete or other human cell,
>
> (b) any other embryo created by using—
>
> (i) human gametes and animal gametes, or
>
> (ii) one human pronucleus and one animal pronucleus,
>
> (c) a human embryo that has been altered by the introduction of any sequence of nuclear or mitochondrial DNA of an animal into one or more cells of the embryo,
>
> (d) a human embryo that has been altered by the introduction of one or more animal cells, or
>
> (e) any embryo not falling within paragraphs (a) to (d) which contains both nuclear or mitochondrial DNA of a human and nuclear or mitochondrial DNA of an animal ('animal DNA') but in which the animal DNA is not predominant.
>
> (http://www.opsi.gov.uk/acts/acts2008/ukpga_20080022_en_2#pt1-pb1-l1g1)

This is an extremely varied and broad remit that covers 'any embryo….in which the animal DNA is not predominant'. Here we see a danger in using the term 'admixed embryo' as a catch-all for very different human-animal combination of which the moral implications may diverge significantly. The HFE Act 2008 covers all types of admixed embryos and all can be potentially licensed except under the following conditions:

(1) No person shall place in a woman—

(a) a human admixed embryo,

(b) any other embryo that is not a human embryo, or

(c) any gametes other than human gametes.

(2) No person shall—

(a) mix human gametes with animal gametes,

(b) bring about the creation of a human admixed embryo, or

(c) keep or use a human admixed embryo, except in pursuance of a licence.

(3) A licence cannot authorise keeping or using a human admixed embryo after the earliest of the following—

(a) the appearance of the primitive streak, or

(b) the end of the period of 14 days beginning with the day on which the process of creating the human admixed embryo began, but not counting any time during which the human admixed embryo is stored.

(4) A licence cannot authorise placing a human admixed embryo in an animal.

(5) A licence cannot authorise keeping or using a human admixed embryo in any circumstances in which regulations prohibit its keeping or use.

The HFE Act makes it illegal to place admixed embryos in either a human or animal womb. Further, human embryos, including the admixed variety, are not allowed to develop beyond 14 days, although those that are not considered human (e.g. those that are 40% human, 60% animal) may be allowed to develop longer. In sum, there was and continues to be an apparent lack of reflective, explicit and integrated regulatory approaches to admixed entities e.g. a certain level of *ad hoc*-ery is disclosed, that is catalysed by scientific innovation. Moreover, the HFEAs involvement in the regulation of cybrids was, arguably, forced on it in light of a desire to avoid a perceived gap in the regulatory system, a gap that had become obvious by the disbandment of UKXIRA and the creation of admixed embryos. As we shall now argue it was better to classify the cybrid as human so as to regulate it rather than define it as non-human and therefore unregulated.

IV. THE PROBLEM AND THE FUTURE

Not human enough to be human…the status of the embryo

The reasons for the UK government turn-around from prohibitive to permissive and to allow admixed embryos to go ahead are enlightening when discussing issues of human identity. Although the decision partly stemmed from political pressure from scientific and academic circles and within the cabinet itself, it is arguable the u-turn could not have occurred unless the embryos were defined as human. The HFEA regulates and advises on all *human embryo* research *yet this begs the question of whether any type of admixed embryo should fall within its auspices.*

According to the UK courts, the HFEA has jurisdiction over human embryos, irrespective of whether such embryos are produced by fertilisation or by a process involving cell nuclear transfer. However, only four kinds of embryos in the Bill are even 'nearly human' (above a, c, d and e – b refers to a hybrid with 50% human and 50% animal DNA). Such embryos raise the question: what is inherently unique about human life? How should we gauge humanness? In a report entitled *Human Reproductive Technologies and the Law* prepared in 2005 by the UK House of Commons Science and Technology Committee it was argued that 'while there is revulsion in some quarters that [human-nonhuman] creations appear to blur the distinction between animals and humans, it could be argued that they are less human, and therefore pose fewer ethical problems for research than fully human embryos' (UK House of Commons Science and Technology Committee., 2005)

… *But not animal enough to be animal.*

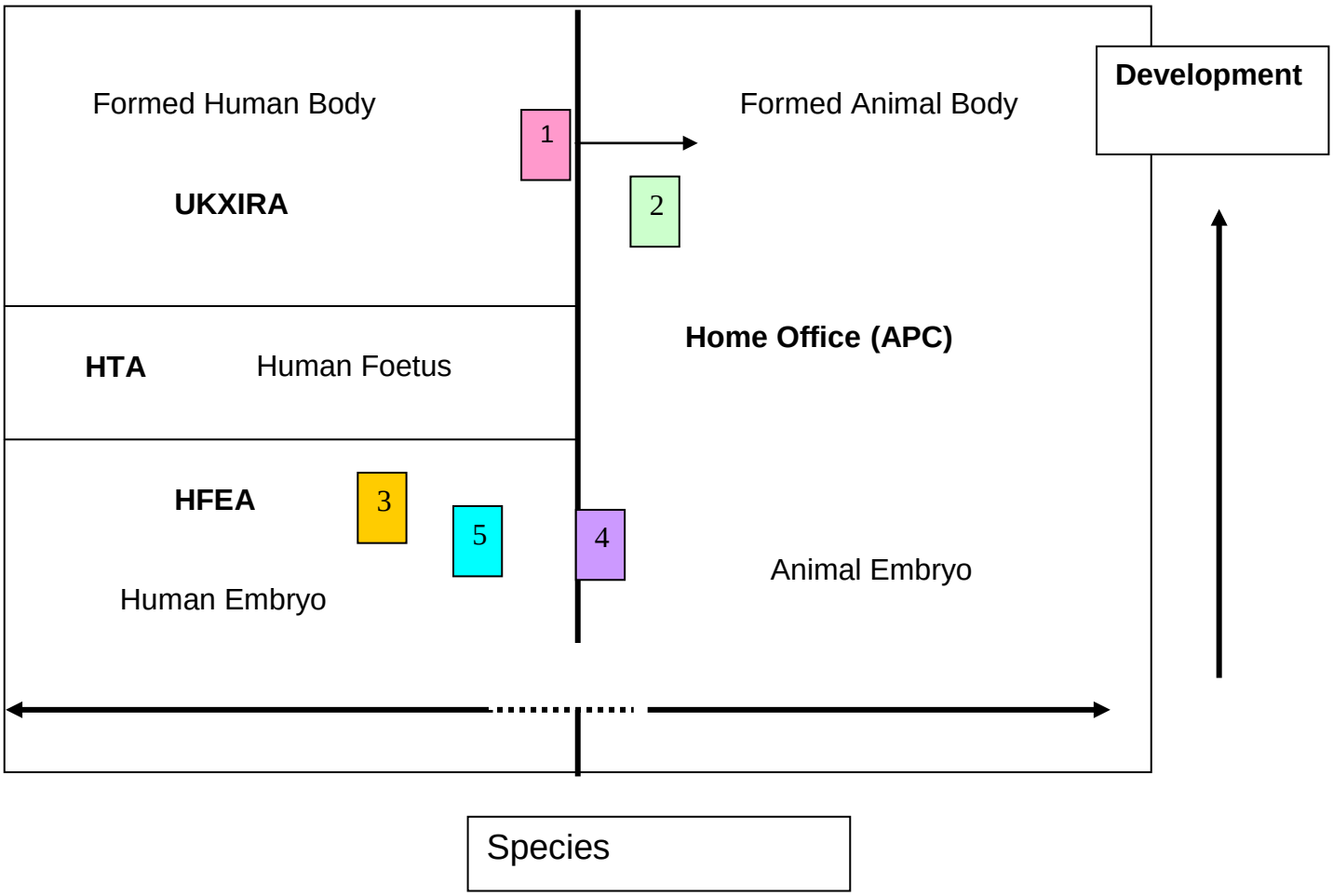
The decision of whether a human-animal chimera or a hybrid embryo would fall within the HFEA remit was based on a paradox – although admixed embryos are a highly differentiated mix of animal-human material, which are considered less human than humans, they are more human than other admixes such as transgenic pigs. Cybrids are said to be 99.9% human and although they are regarded as 'less than human' they can be regulated by the HFEA (O'Dowd, 2007). The amendment to the HFE Act suggests that it can regulate in areas where the animal DNA does not predominate – but this begs the question of where the cut-off point will be i.e., 51% human and 49% animal? It is problematic to make such categorisations of species identity in terms of percentages because DNA does not define species; in fact species are notoriously hard to define in biological terms (e.g. Robert and Baylis 2003). Furthermore, there is contention surrounding the measurement of genetic differences between humans and animals. Although it is often stated that humans are 98% chimpanzee in genetic terms, an exploration of the technical literature behind this figure shows that matching up human and chimpanzee DNA is not a straightforward process (Marks 2003). When comparing human and chimpanzee DNA it is necessary to first identify and define the segment of DNA that is being compared. As Marks (2003) points out, this raises, 'the fundamental problem of homology in biology: What is the precisely corresponding entity in the other species?' (p.137). Such methods of comparison would also lead us to the conclusion that we share 25% of our DNA with all other existing life forms, and approximately 35% of our DNA with daffodils (Marks, 2003). In this context, as Robert and Baylis (2003) argue, the question arises of whether it makes sense to talk of 'human DNA' at all: 'Much of 'our' DNA is shared with a huge variety of apparently distantly related creatures (e.g., yeast, worms, mice, etc). Indeed, given the evidence that all living things share a common ancestor, there is little (if any) uniquely human DNA' (Robert & Baylis, 2003). Points such as these highlight the limitations of trying to reduce the differences between human and animals to percentages of genetic similarity, and problematise the measurements of percentages of human and animal DNA that we see in the regulation of cybrids. Furthermore, the decision to define humanness in terms of DNA percentage is contra to one of the fundamental principles for the HFEA's existence regarding the regulation of embryos, which states that the early embryo has a 'special status' that must be subject to stringent controls and monitoring (Warnock, 1984). This 'special status' reflects the embryos irreducibility to its cellular composition and is a reflection that as humans, we are considerably more than a sum of our parts.

CONCLUSIONS

We have not been concerned with the need for regulation, what that regulation does, nor even whether the HFEA is meeting this need in practical terms. Our concern is to do with the relationship between regulation and the classification and categorisation of human-animal identity. Some might argue that the status of the admixed embryos is largely academic given that, currently, such entities cannot be developed past the primitive streak and no scientist as yet appears to propose this. Further, recent reports suggest that progress has been hampered by the UK funding bodies refusal to fund two of the three licence holders permitted to conduct cybrid research in favour of iPS (induced pluripotent stem cells) (Connor, 2009). However, lessons from xenotransplantation and regulation strongly indicate 1) the cyclical nature of medical progress in this area and 2) that in the UK often the 'regulatory' body fits with the 'biological' one. In agreement with other authors, we suggest that regulation of animal-human entities in the UK was typically mapped onto the species and their development (Brown and Michael (2004) as is shown Figure 1. This can be contrasted with other examples of European legislation where such one-to-one matching has been avoided [2]. Our figure shows the boundary between human and animal can no longer be taken as a given, but is a contested regulatory space. Xenotransplantation [1] is an example of movement between regulatory spaces, but we argue, if in the UK regulation and species development coincide, is not necessarily within the appropriate regulatory institution of the APC. The remit of the APC relates to the welfare of animals and not humans. According to the same criteria, cybrids [4] are in a regulatory space that, in our view, does not neatly fit within the roles and responsibilities of the HFEA.

[2] In 1999, the Council of Europe Working Group did a State of the Art Report and a survey of states which demonstrated that 20% of survey respondents allowed xenotransplant procedures without any legislative authorisation or restriction and that 48% were conducting xenotransplant research, many of them doing so under their animal protection laws (McLean & Williamson, 2005).

Regulatory institutions mapped on to formed and unformed human and animal bodies



1 Xenotransplanted person (whole person with animal organ). 2 GM animal (whole animal with human genes). 3 Human chimera embryo (human embryo with animal cells). 4 True hybrid embryo (50:50 DNA from different animal species). 5 Cybrid (complete human DNA in an enucleated animal egg).

Hence, in the case of admixed embryos, regulators in the UK appear to have implicitly accepted the structural 'fit' between regulatory body and biological body, but chose to (uncritically) redefine the entity rather than the regulatory body. The cybrid has been categorised in reductionist terms based on the percentage of human DNA. Not only does this subvert notions of human and animal dignity (whatever that term means) it contravenes the principles for the existence of the HFEA that rested upon the special status of the embryo. Our solution based on this discussion is to point to the history and experience of previous committees such as UKXIRA, whose primary objective was to ensure that animal to human transplantation was developed both in ethical and safety terms (McLean and Williamson 2005, 98). The transference

of animal-human material at the cellular or embryonic level would have meant an expansion, a change of emphasis but not a change of direction. Hence, UKXIRA (or a similar organisation) could be reconvened and given a permanent standing committee (as was originally intended) with a remit that would include all animal-human fusions. Insomuch as this would bring equilibrium back to the 'regulatory' and 'organic' body balance, as shown in Figure 1, it would also avoid real or perceived, transgressions between what is considered animal and what is considered human given the rapid, and often unpredictable pace of change in this area. To all intents and purposes, experience, independence, public consultation and open governance are required in an area that has the potential to bring back the mythological creatures of the past.

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