Human/Nonhuman Chimeras: Dignity, Organs, Gametes and Pregnancy.

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PRELIMINARIES

PART I: INTRODUCTION

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ABSTRACT

Name of University: The University of Manchester
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The question of whether within chimera research certain human/nonhuman animal chimeras should not be created has received significant attention in the philosophical community. In this thesis I examine, from a philosophical perspective, four questions related to this topic. These are: (i) Can 'human' dignity be invoked as an argument against the creation of human/nonhuman animal chimeras? (ii) Is it morally permissible to kill human/great-ape chimeras in order to solve the human organ shortage crisis? (iii) Is there something inherently wrong with creating human/nonhuman animal chimeras capable of human gamete production and human pregnancy? (iv) Can classic animal ethics issues concerning animal welfare throw light on the issue of killing human/pig chimeras for their human organs. These four questions, in turn, fall within what have been regarded as the three main problematic cases within chimera ethics: (1) the creation of human/nonhuman animal chimeras that could have brains predominantly constituted by human brain cells; (2) the creation of human/nonhuman animal chimeras that could look human-like; (3) the creation of human/nonhuman animal chimeras capable of human gamete production and human pregnancy.

In the introduction I do four things. First, I define what chimeras are and point out some problems with some of the definitions that have been proposed. Secondly, I briefly investigate if there is a sound principled objection against the intentional creation of *all* intraspecific and interspecific chimeras. Thirdly, I present in a detailed fashion the four questions that this thesis poses in response. Finally, I explain how the four papers that are the main body of the thesis form a coherent body of work. In the fifth section of this thesis I present the abstracts of four papers.

In the sixth section I make a comprehensive exploration of the dignity-based arguments that have been advanced against the creation of human/nonhuman animal chimeras that could possess human-like mental capacities, or that could possess certain cognitive capacities that we would not be able to properly classify. In the seventh section I examine the morality of killing human/great ape chimeras for their human organs. This paper is a detailed response to Shaw et al.'s (2014) 'Using Non-Human Primates to Benefit Humans: Research and Organ Transplantation'. The eight section covers two topics. First I discuss the moral problems related to the creation of mainly nonhuman human/nonhuman animal chimeras capable of human gamete production. Secondly, I discuss the moral problems that would be generated by the fact that a sentient nonperson human/nonhuman animal chimera, that is predominantly nonhuman, was pregnant with a human conceptus. In the ninth section I further examine the chimera welfare issues that have emerged from assessing the morality of using human/pig chimeras as human organ sources. In the conclusion of the thesis I present a summary of the main points I have explored, and proceed to present how my dissertation adds to the academic literature on chimera ethics. Finally, I present some areas for further research.

DECLARATION AND COPYRIGHT STATEMENT

DECLARATION

No portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

COPYRIGHT STATEMENT

DEDICATION

On the first day of my B.A. in philosophy, back in August 2004, I sat down next to Adriana Clavel Vázquez. More than ten years afterwards I still sit down next to her every day. Adriana, it is to you that this thesis is dedicated.

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Thesis Related Publications

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- Palacios-González, C. (2015). Human Dignity and the Creation of Human-Nonhuman Chimeras. *Medicine, Health Care and Philosophy*, *18*(4), 487–499. http://doi.org/10.1007/s11019-015-9644-7.
- Palacios-González, C. (2015). The ethics of killing human/great-ape chimeras for their organs: a reply to Shaw et al. *Medicine, Health Care, and Philosophy*. http://doi.org/10.1007/s11019-015-9658-1

Other Publications

- Harris J., Palacios-González, C., & Lawrence D. (2016). The Shylock Syndrome. *Cambridge Quarterly of Healthcare Ethics*. *25*(2), 250-261.
- Giordano, S., Palacios-González, C., & Harris J. (2016). Backstreet Genital Surgery: When Should Doctors Speak Out? In C. Stanton, S. Devaney, A.-M. Farrell, & A. Mullock (Eds.), Pioneering Healthcare Law: Essays in Honour of Margaret Brazier (1 edition, 181–188).
- Palacios-González, C. (2014). The ethics of clinical photography and social media. *Medicine, Health Care and Philosophy*, *18*(1), 63–70. http://doi.org/10.1007/s11019-014-9580-y
- Palacios-González, C., Harris, J., & Testa, G. (2014). Multiplex parenting: IVG and the generations to come. *Journal of Medical Ethics*, *40*(11), 752–758. http://doi.org/10.1136/medethics-2013-101810
- Palacios-González, C., & Lawrence, D. R. (2014). Substance over style: is there something wrong with abandoning the white coat? *Journal of Medical Ethics*, medethics–2013–101900. http://doi.org/10.1136/medethics-2013-101900

Open Peer Commentaries

- Palacios-González, C. (2016). Epilepsy, Decisional Vulnerability and the Nature of Predictive Brain Implants. *AJOB Neuroscience 6*(4), 18-19.
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DESTINATION

From the 1st January 2016 I will be working as a postdoctoral researcher in The Centre for Medical Ethics & Law within The Dickson Poon School of Law at King's College London, on the Wellcome funded project: The Donation and Transfer of Human Reproductive Materials.

PART I.
INTRODUCTION

1. INTRODUCTION

> *"[I]t is revulsion we feel when confronted with the chimaera that bear witness to a violation of the species boundaries that we had naively assumed to be unalterable"* (Jürgen Habermas, 2003).

In laboratories spread across the world there are sheep, mice, pigs, monkeys, and rats that have human cells fully integrated within them. There are mice with human cells in their brains, sheep with human cells in their muscles, and pigtail macaque monkeys with human cells in their hearts (Han et al. 2013; Liechty et al. 2000; Chong et al. 2014). Imagining that somewhere in a university laboratory there is a *live* nonhuman animal with human cells may seem radical, but it is much less so when we realise that scientists are working to create nonhuman animals with *whole* human organs (e.g. livers, kidneys) inside them.

Many people strongly believe that research that engrafts human cells, tissues or organs into nonhuman animals is *deeply immoral*. This position, obviously, comes in different presentations. There are those who are opposed to *any* research where human cells, tissues or organs are engrafted into adult nonhuman animals, and also to *any* research that allows the coming into existence of a nonhuman animal that possesses human cells, tissues or organs.

There are others who welcome research that engrafts human cells, tissues or organs into nonhuman animals, but that oppose, or have strong reservations, about three specific kinds of such research. These are: i) research that could end in the creation of a not-fully human being that possesses human-like cognitive capacities as a result of the engrafted human cells or tissues; ii) research that could produce a not-fully human being which has the external appearance of a human as a result of the engrafted human cells or tissues; and iii) research that could produce a not-fully human being capable of human gamete production and human pregnancy by means of the engrafted human cells or tissues.

This thesis explores two questions. First, whether *the intuition* that holds that the creation of not-fully human beings that possess human-like cognitive capacities resulting from human engrafted cells or tissues is immoral, is cogent. Second, whether *the intuition* that holds that the creation of not-fully human beings capable of human gamete production and human pregnancy by means of human engrafted cells or tissues *is immoral* can be philosophically grounded. Holding such intuitions is *problematic*, I consider, because in general we do not

object to the creation of humans (male and female) that can produce human gametes, to the creation of female humans that can gestate other humans, or to the creation of humans that have 'normal' human-like mental capacities.

- *If we do not object to the creation of these kinds of beings, why do we object to the creation of not-fully human beings that could possess the same characteristics?*

Before I examine the moral issues that arise from the creation of creatures that are a combination of human and nonhuman elements I will do two things. First, I will specify what kind of *part-human beings* this thesis engages with. In order to do this, I will define what chimeras are and how they differentiate from hybrids, cybrids and transgenic beings. Second, I will present an overview of the scientific drive to create them. Specifically, I will show why they are important for human health in terms of organ transplantation, and why are they important for the study of various biological mechanisms and processes.

1.1 CHIMERAS

This thesis discusses some of the moral issues surrounding chimera research. In order to do so we need to know what chimeras are, and how they are different from hybrids, cybrids and transgenic beings. In *everyday* language the term chimera is used to refer to two things: (i) an ancient Greek mythological creature or (ii) an animal composed from parts of different animals. The latter use can refer to any combination of animals. For example, the beings created through taxidermy that compose German artist Thomas Grünfeld's collection 'Misfits' can correctly be called chimeras. Among them we find a creature composed from a bull's head and an ostrich's body, and a creature composed from a swan's head, an otter's body and donkey's legs (Moyes 1997).

The former use only refers to a being that is composed from parts of three specific different nonhuman animals: lion, goat, and snake. Depending on whether we follow Homer's or Hesiod's characterisation, we should imagine it either as only possessing a lion's head, or as possessing the heads of all three animals (Hesiod 1914; Homer 1836). The most famous *three headed* artistic sculpture of a chimera is the 'Chimera of Arezzo'. While there is no iconic sculpture of a one headed chimera, Johann Nepomuk Schaller's work 'Bellerophon Fighting the Chimera' is the closest to being so.

In biological sciences, *contrary to everyday language*, the term chimera is used to refer to organisms that are formed by combining *whole cells* from at least two numerically distinct

sources that are also genetically distinct, into a functional organism. The cells can be in the form of dissociated cells, undissociated cells, tissues or organs. For example, taking some tissue from someone's leg and grafting it in her arm would not make her a chimera.

Chimeras can be intraspecific, interspecific or a mixture of both. Intraspecific chimeras are those created with cells that belong to the same biological species (e.g. if we take some cells from mouse A and graft them in mouse B), interspecific chimeras are those created with cells that belong to different biological species (e.g. if we take some cells from mouse A and graft them in rat C). An example of an intraspecific/interspecific chimera would be if we were to take some cells from mouse A and graft them in mouse B, and then we were to take some cells from rat C and graft them into mouse B. This chimera would be both intraspecific and interspecific. Intraspecific chimeras occur in nature, as when two early embryos fuse inside a womb (Tippett 1983). Even when interspecific chimeras do occur in nature, as with lichen (which is an algae and fungus composite organism (Lepp 2011)), for the most part they are artificially created.[1]

The Academy of Medical Sciences provides the following definition:

> Chimæras are formed by mixing together whole cells originating from different organisms. The new organism that results is made up of a ''patchwork'' of cells from the two different sources. Each cell of a chimæra contains genes from only one of the organisms from which it is made. (…) Primary chimæras are formed by mixing together two early embryos, or an early embryo with isolated embryonic cell types obtained from a different embryo or cultured stem cell line. The resulting chimæra has cells of different origins, in many tissues. Secondary chimæras are formed experimentally by transplanting (or grafting) cells or tissues into animals at later stages of development, including late fetal stages, post-natal or even adult animals. The donor cells are only present in a few tissues. (The Academy of Medical Sciences 2011, 18–19)

Along similar lines Robert Streiffer has defined a chimera[2] as "a single individual composed of cells that have different embryonic origins" (Streiffer 2005, 349), and Insoo Hyun (2013, 108) has defined chimeras as "organisms that are composed of genetically distinct cells originating from two or more zygotes, or the imperfect equivalents thereof, such as parthenotes and SCNT embryolike constructs". A caveat regarding The Academy of Medical Sciences's and Streiffer's definitions is that they do not specify that for an organism to be a chimera the

[1] Throughout this thesis I will concentrate on the moral problems that arise from the creation of chimeras composed only from animal parts: *animal chimeras*. I will not address the moral issues related to the creation of other kind of chimeras, for example, *plant chimeras*. We can create a plant chimera by grafting a branch of a pear tree onto the trunk of an apple tree.

[2] Where in its report 'Animal Containing Human Material' The Academy of Medical Sciences uses the more archaic word "chimæra", throughout this thesis I will use the modern one "chimera".

cells that give it origin must be from *genetically different* sources. This clarification is important in order to rule out as chimeras the following types of real-life cases: consider a human embryo that splits into two separate identical embryos, each becoming a distinct organism. Now imagine that such embryos naturally fuse back together, forming a single organism. Furthermore, imagine that it develops normally and reaches term. While we would not consider such an organism to be a chimera, under The Academy of Medical Sciences's and Streiffer's definitions it is one, given that the cells of which it is composed had their origin in *numerically distinct embryos*. On the other hand, we would hold that when two non-monozygotic embryos completely fuse they *do* give rise to a chimera (Norton and Zehner 2008).

A caveat regarding Hyun's definition is that chimeras can be produced at non-embryonic developmental stages. The Academy of Medical Sciences, as just presented, names these kinds of chimeras 'secondary chimeras'. For example, if I receive an organ transplant from a person that is not my non-identical twin then at an adult age I would have become a chimera. This is so because now I am made up of a ''patchwork'' of cells from two genetically different sources.

It is methodologically important to clarify that within the chimera *philosophical* literature there has not been much discussion of how to define what chimeras are. Most research limits itself either to providing its own operative definition, or to appealing to those offered by professional bodies (such as The Academy of Medical Sciences). Although most definitions of what a chimera is, within the chimera *ethics* literature, aim at distinguishing this type of being from other kinds of organism, there have been cases where this concept, or another umbrella term, has been used to refer not only to chimeras as just defined, but also to hybrids, cytoplasmic hybrids and transgenic animals. Three examples of this broadening of the definition are found in the work of Henry T. Greely, Jason T. Eberl and Rebecca A. Ballard, and John Harris.

In his commentary to 'Crossing Species Boundaries' (Robert and Baylis 2003) Greely defines a chimera as "a single biological entity that is composed of a mixing of materials from two or more different organisms" (Greely 2003, 17). After providing this definition he offers a taxonomy of chimeras (*which includes* hybrids, chimeras understood in a restricted sense, and transgenic beings) and then uses it to identify ethical problems that could arise from certain biological research. He concludes that ethical issues do not arise from the fact of something being a chimera or not. They arise instead as answers to questions concerning the chimera's 'humanity', 'naturalness' and the intended use of the chimera.

Eberl and Ballard, in their 'Metaphysical and Ethical Perspectives on Creating Animal-Human Chimeras', define chimera in a broad sense as "a biological entity composed of genetic material from members of two distinct species" (Eberl and Ballard 2009, 471). Although these authors recognise that their definition would also encompass hybrids they miss two important issues: first, that it would also include transgenic animals and cytoplasmic hybrids; second, that there are intraspecific chimeras. John Harris, in his 'Taking the ''Human'' Out of Human Rights', uses the term *humanimal* to "cover any biological entities, whether individual creatures or cells, that have any mixture of animal and human elements" (Harris 2011, 11). Two issues should be noted about this definition. First, it is as extensive as Greely's definition, including transgenic animals, cytoplasmic hybrids, chimeras, and hybrids. Second, it does not encompass intraspecific mixtures, but only interspecific ones.

It is clear that Greely's, Eberl and Ballard's, and Harris's definitions are broader than that provided by The Academy of Medical Sciences (2011, 18–19) and that offered by Françoise Baylis and Jason Scott Robert:

> Chimeras comprise a mixture of cells from two or more genetically distinct organisms of the same or different species. They are mosaics at the cellular level; individual cells are derived from either the host or the donor but not both. (Baylis and Robert 2006)

This being the case, we need to ponder the effects of such definitional inclusiveness.

I think that adopting a *broad definition* of what a chimera is, when discussing chimera ethics, has at least two negative effects. First, the creation of each of these different kinds of creatures (i.e. hybrids, cybrids, transgenic beings, and chimeras understood in a restricted sense) brings about different ethical dilemmas. It is therefore important to distinguish between these creatures in order to address the ethical dilemmas in a thorough fashion. By defining these distinct types of creatures with *one sole concept* we risk making incorrect generalisations (i.e. the specific problems associated with the creation of each kind of creature fade next to more generally shared issues). For example, the creation of genetically modified crops differs from the process of xenotransplantation. In the case of 'human' xenotransplantation, we need to obtain the patients' informed consent before any transplantation takes place, whereas in the case of genetically modified crops we do not regard that plants should give their consent before we experiment on them. For any ethics discussion to be meaningful it needs to properly encapsulate the discussed subject.

The second negative effect is that using a broad definition can impede cogent legislation from being enacted. Given that certain aspects of the chimera ethics debate aim at being translated

into the biological research policymaking arena it is important that there is no ambiguity about the discussed subject. For example, in 2005 US republican Senator Sam Brownback propounded legislation intended to prohibit the creation of 'human chimeras' because according to him, among other things, "they blur the lines between human and animal" (S. 1373, 2005, Sec.2.(2)). In the proposed legislation eight definitions of chimeras were introduced:

> (1) HUMAN CHIMERA.—The term 'human chimera' means—
>
> (A) a human embryo into which a non-human cell or cells (or the component parts thereof) have been introduced to render its membership in the species Homo sapiens uncertain through germline or other changes;
>
> (B) a hybrid human/animal embryo produced by fertilizing a human egg with non-human sperm;
>
> (C) a hybrid human/animal embryo produced by fertilizing a non-human egg with human sperm;
>
> (D) an embryo produced by introducing a non-human nucleus into a human egg;
>
> (E) an embryo produced by introducing a human nucleus into a non-human egg;
>
> (F) an embryo containing haploid sets of chromosomes from both a human and a non-human life form;
>
> (G) a non-human life form engineered such that human gametes develop within the body of a non-human life form; or
>
> (H) a non-human life form engineered such that it contains a human brain or a brain derived wholly or predominantly from human neural tissues. (S. 1373, § 301(1))

These definitions, as Greely et al. (2007) have noted, not only cover chimeras, in a restricted sense, but also cytoplasmic hybrids and hybrids of various sorts. Now, while the proposed bill aims at prohibiting the creation of *interspecific chimeras* that could haze the 'dividing lines' between humans and nonhuman animals it would fail substantially if passed. Why? Because if the *intention* behind the bill, or at least one of the intentions, is to prevent the creation of chimeras that have something akin to normal adult human-like cognitive capacities, then there are two theoretically possible ways to achieve this while not infringing the terms established by the bill. First by creating human/nonhuman animal 'brain chimeras' that do not possess brains *predominantly* constituted by human cells, but that nonetheless possess enough human brain cells for normal adult human-like cognitive capacities to emerge. For example, imagine that we create a human/chimpanzee chimera with a brain that is 50% human and 50% chimpanzee, and that it possesses human-like cognitive capacities. Given that the chimera's

brain is not *predominantly* constituted by human cells, in a proportional sense of predominantly, the terms imposed by the bill are not infringed.

Secondly, by creating nonhuman animal/nonhuman animal chimeras that have cognitive capacities akin to those of a normal adult human being, but without actually possessing any human brain cells. For example, Monika Piotrowska (2014, 4), while discussing Mark Sagoff's (2007) commentary 'Further Thoughts About the Human Neuron Mouse' to Greely et al.'s (2007) 'Thinking About the Human Neuron Mouse', asks us to consider if there is a moral difference between creating a human-to-nonhuman animal chimera that possesses normal adult human-like cognitive capacities, and creating a nonhuman animal-to-nonhuman animal chimera that also possesses normal adult human-like cognitive capacities. According to the bill's terms we could create the latter creature without violating the bill. While these sample cases are thought experiments and it is open to empirical verification whether or not they are in fact feasible, they show us the importance of clearly defining what constitute chimeras when establishing science policy.

Given these two negative effects of adopting a broad definition of the term 'chimera', a restricted definition should be embraced. Although I do not here present a comprehensive analysis of the definition of the term 'chimera', I propose the following two necessary conditions for something to be a chimera: first, that the cell sources must be from genetically distinct organisms or cell lines; second, that for a chimera to be a chimera there must be organismic continuity among the coexisting cell populations, i.e. that the cells work in a unified way.

1.1.1 CHIMERA TYPES

The definition of chimera that the Academy of Medical Sciences provides makes a distinction between primary chimeras and secondary chimeras. Here I will explain this distinction. The creation of chimeras, as has already been said, involves the grafting of *whole* cells, or the fusion of early embryos. These cells can be present in the form of dissociated cells (i.e. single cells), undissociated cells (i.e. groups of cells), tissues or organs. Obviously, in the case of intentionally created chimeras, the *number* of engrafted cells varies depending on what researchers are trying to achieve, or the way in which the chimera is created. Now, the Academy of Medical Sciences's distinction between primary and secondary chimeras relies upon how are they created and the *timing* of the cell grafting.

Primary chimeras are those created by the fusion of two early embryos, or the engraftment of embryonic stem cells into an early embryo: "Primary chimæras are formed by mixing together two early embryos, or an early embryo with isolated embryonic cell types obtained from a different embryo or cultured stem cell line. The resulting chimæra has cells of different origins, in many tissues" (The Academy of Medical Sciences 2011, 18–19). Primary chimeras have cells of *both origins* in most, if not all, of their bodies when they are generated by embryo fusion. This is because an adult body's cells originate in those of the early embryo. In this case, the early embryo is a *composite* of cells that, in turn, had their origin in numerically distinct entities (i.e. two early embryos) that were also genetically distinct. The fact that these chimeras possess cells of both origins in many tissues and organs means that they have, throughout their bodies, some of the biological species characteristics of both the donor's and the recipient's respective species. For example, a goat-sheep chimera (sometimes called a geep) was produced by fusing a goat and a sheep embryo. This chimera possessed patches of both sheep's woolly hair and goats' 'hairy' hair. (Fehilly, Willadsen, and Tucker 1984).

Secondary chimeras, on the other hand, are created when we graft cells (in the form of dissociated cells, undissociated cells, tissues or organs) into animals that are not at an early embryonic stage of development: "Secondary chimæras are formed experimentally by transplanting (or grafting) cells or tissues into animals at later stages of development, including late fetal stages, post-natal or even adult animals. The donor cells are only present in a few tissues" (The Academy of Medical Sciences 2011, 18–19). For example, if we engraft, *postnatally,* a rat's muscular tissue into the leg of a mouse this would produce a chimera that only possesses a small number, in absolute terms, of rat cells. In the case of secondary chimeras, we do not find cells from the donor in many tissues because the recipient's body is fully developed (even if not completely grown), and thus the donor's cells are not integrated into the body's developmental process.

As well as the timing of the cell engraftment (or embryo fusion), we have to take into account the number and type of transplanted cells and the recipient's and donor's species in order to predict how this will affect the chimera's development. The biological species to which the donor and recipient belong is particularly relevant because the evolutionary distance between them partially determines whether the cells will be able to integrate and how effectively they are able to function (The Academy of Medical Sciences 2011).

The type of transplanted cell is important because a pluripotent stem cell transplanted into a foetus will contribute to its development more extensively than the engraftment of a specialised stem cell. Why is this the case? Because pluripotent stem cells, in contrast with specialised stem cells, have the potential to differentiate into many types of specialised body cells. Specialised stem cells, on the other hand, can only produce more specialised cells of the same kind; this will become relevant when I discuss the phenomenon of behavioural transfer and capacities enhancement. At this point, and mainly for the purposes of clarity, I present a schematic list of possible interspecific and intraspecific chimeras (with examples):[3]

(i) Human-to-nonhuman animal embryonic, foetal or adult chimeras.
- Han et al. engrafted human glial progenitor cells into the brains of neonatal immunodeficient mice (Han et al. 2013).

(ii) Human-to-human embryonic, foetal, or adult chimeras.
- Human-to-human organ transplantation. For example, uterus transplantation (Brännström et al. 2015).

(iii) Nonhuman animal-to-human embryonic, foetal, or adult chimeras.
- Nonhuman animal-to-human organ transplantation. For example, Stephanie Fae Beauclair received a baboon's heart in order to treat a fatal heart defect (Bailey LL, Nehlsen-Cannarella SL, Concepcion W, & Jolley WB, 1985).

(iv) Nonhuman animal-to-nonhuman animal embryonic, foetal, or adult chimeras.
- A wood mouse/house mouse chimera was created by injecting wood mouse embryonic stem cells into a house mouse early embryo (Xiang et al. 2008).

Having explained what chimeras are and how are they created, I will now discuss how hybrids, cybrids and transgenic animals are created, and how they differ from chimeras.

1.2 HYBRIDS

Hybrids are the offspring of organisms that belong, at the very least, to different biological species. While their viability depends on biological factors, they are for the most part sterile and only on rare occasions are they capable of successful pregnancies. One example of a hybrid

[3] A conceptual issue that so far has not been explicitly addressed arises here. What is the difference between a human-to-nonhuman animal chimera and a nonhuman animal-to-human chimera (i.e. human/nonhuman animal chimera and a nonhuman animal/human chimera)? Here I am assuming that cells, tissues or organs from the first part of the binomial are grafted into an embryo, foetus or adult of the second part of the binomial. This rationale also guides my use of the term 'human/nonhuman chimeras' (HNH-chimeras) throughout the four articles that are the main body of this thesis. However, this characterisation creates at least one challenge that I will highlight but I will not address here: how are we to classify embryo fusion cases? For example, how are we to classify an entity that is created by the fusion of a human embryo with a chimpanzee embryo?

is a 'liger', which is the offspring of a male lion and a female tiger. In this case, the liger's progenitors belong to different species within the same genus.

Hybrids can be (i) intraspecific when the progenitors belong to different *subspecies*, for example a grizzly/kodiak bear hybrid; (ii) interspecific when the progenitors belong to *different species* but to the same *genus*, for example a liger; (iii) intergeneric when the progenitors belong to different *genera*, for example a goat/sheep hybrid; and finally (iv) interfamilial when the progenitors belong to different *families*, for example a guineafowl.

Hybrids can occur naturally or by intentional intervention. For example, a naturally occurring hybrid is the grizzly/polar bear. For long time it was thought that these two types of bear were capable of generating offspring, but only recently has DNA analysis proved that these hybrids occur in nature (Höflinger 2012). While we know of many animals that interbreed in *captivity*, factors such as geographical distance or geological barriers limit interbreeding amongst wild nonhuman animals.

Humans, on the other hand, can and do intervene in the creation of nonhuman animal/nonhuman animal hybrids. An intentionally occurring hybrid, for example, is a hinny: a hinny is a hybrid produced by a male horse and a female donkey. Humans can intentionally produce hybrids in two ways: they can use assisted reproductive techniques, as in the case of the generation of New World/Old World hybrid camels (Skidmore et al. 2001); or they can enclose the animals in the same space in order to mate, just as in the case of the ligers.

When we discuss the topic of hybrids, the cases that spring to mind are those of nonhuman animals (i.e. nonhuman animals of different species producing offspring). While this is the norm, part-human hybrids do not belong to the realm of science fiction: when Neanderthals and modern humans coexisted there were cases of hybridization (Vernot and Akey 2014; Sankararaman et al. 2014). We are certain of this thanks to genome sequencing, and furthermore the presence of 'Neanderthal genes' within us has been linked to predisposition to certain mental illnesses and allergies (Dannemann, Andrés, and Kelso 2016; Simonti et al. 2016).

In addition to this *historically known hybridization*, in the twentieth century Russian scientist Il'ya Ivanov tried to create a human/great ape hybrid, with the patronage of the Soviet Union, in a series of ethically appalling experiments. In the first half of the 1920s the Soviet government sponsored Ivanov to travel to Africa, to 'French Guinea' (nowadays Guinea), in order to create a human/great-ape hybrid. Ivanov's plan was to artificially inseminate female

chimpanzees with human sperm and so create a hybrid of the two species (Rossiianov, 2002). Ivanov believed his expedition to be a scientific one with scientific goals, but it was seen by some members of the Soviet government as an important political mission. For example, and as cited by Kirill Rossiianov:

> Sergey Novikov, the Berlin representative of the Commissariat of Enlightenment, referred to the hybridization project as an "exclusively important problem for Materialism," while Lev Fridrichson, the representative of the Commissariat of Agriculture, thought that "the topic proposed by Professor Ivanov, . . . should become a decisive blow to the religious teachings, and may be aptly used in our propaganda and in our struggle for the liberation of working people from the power of the Church." (Rossiianov 2002, 286)

Ivanov's plan failed and no such hybrid was created while he was in Africa. Back once more in the Soviet Union, now Georgia, after what was a troublesome expedition to Africa he decided to seek human women volunteers who would allow him to inseminate them with sperm obtained from Tarzan, a 26-year-old male orang-utan. This plan also did not come to fruition.

The difference between hybrids and chimeras is that hybrids are created through reproductive processes and their cells' nuclear DNA material is a *mixture* of the nuclear DNA material of individuals that belong to different species. Animal chimeras, in contrast, are not created though reproductive processes and their cells' nuclear DNA is derived in its entirety from either donor or recipient but not from a mixture of both.

1.3 CYBRIDS

A nuclear-cytoplasmic hybrid (known as a 'cybrid') is created when the nucleus of an egg is removed and replaced with the nucleus from a cell from a different species. The procedure for creating a cybrid is the same as that which created Dolly (Somatic Cell Nuclear Transfer), the difference being that in Dolly's case all the cellular elements belonged to the same biological species (Wilmut et al. 1997). A cybrid's cellular elements can belong to the same *subspecies* and form an intersubspecies cybrid, or they can belong to different species and form an interspecies cybrid.

The most publicised examples of cybrids involving human components so far are a human/cow cybrid and a human/rabbit cybrid. While the authenticity of the research that produced the first human/cow cybrid is still in doubt, the human/rabbit cybrid is a genuine development. There is no doubt in this case that Chinese scientists successfully transferred human somatic nuclei into enucleated rabbit oocytes, and that from those reconstructed cells they generated stem cell lines (Abbott and Cyranoski 2001; Chen et al. 2003; Wade 1998).

Researchers have created cybrids for two reasons. First, as a vehicle for generating 'humanesque' embryonic stem cells for medical research: there is a scarcity of human oocytes for human stem cell research, so the possibility of using nonhuman animals' eggs has been embraced (Holden 2005). Additionally, using nonhuman animal eggs seems to sidestep many of the ethical dilemmas present in human egg donation (John and Lovell-Badge 2007).[4]

The second reason for creating cybrids is to help in the fight for the preservation of endangered species (Pasqualino, Galli, and Ptak 2007). The creation of cybrids that possess the nuclear material of an endangered species and other cellular elements from a closely related species can be used by scientists to boost numbers in endangered populations. The cybrid is transferred into the womb of a member of the species that provided the egg. Ideally, a pregnancy ensues and afterwards the live birth of healthy offspring.

In the most publicised case of cybrid research related to endangered nonhuman animals, the somatic cell nuclei of giant pandas were transferred to rabbit enucleated eggs and then transferred into domestic cats (Chen et al. 2002). Although this did not result in a successful pregnancy, the procedure showed that panda/rabbit cybrids can implant in the uterus of a third species, the domestic cat. In a less widely known, but successful, case, researchers were able to obtain a live offspring from an Ovis orientalis musimon/Ovis aries cybrid pregnancy (Loi et al. 2001). The scientists obtained cells from two female Ovis orientalis musimon specimens and transferred the nuclei of those cells into oocytes obtained form the species Ovis aries. They then transferred the embryos into the womb of a member of this same species. Of the two pregnancies that ensued, one produced an apparently healthy mouflon.

Cybrids are created by inserting the nuclear DNA of a cell that belongs to one biological species into an enucleated egg that belongs to another different biological species. The resulting entity will possess the nuclear DNA of one biological species and the cellular structure and mitochondrial DNA (which is only inherited via the maternal line) of a different biological species. This differs importantly from animal chimeras where, as previously outlined, the entirety of their cells come from either the donor or the recipient, but not from a mixture of the cellular material of these two (for example, their nuclear DNA may come from one organism and their mitochondrial DNA from another).

[4] For a discussion on the ethical aspects of human/nonhuman animal cybrid research see: Human Fertilisation and Embryology Authority (2007a; 2007b; 2007c), Baylis (2009), Baylis (2008) and Jones (2010).

1.4 TRANSGENIC BEINGS

A transgenic animal can be defined as an animal whose genome has been intentionally altered by the insertion of one or more exogenous gene(s). Here a gene from *another* species is inserted with the aim of causing or suppressing a specific trait. The genetic modifications can be carried out at the somatic level or they can be carried out at the germline level. Somatic modifications are genetic modifications which *are not* inherited by further generations. For example, we could harvest T-cells from an adult mouse and then insert a rat's exogenous gene into them before finally transplanting them back to the mouse.

Germline modifications, on the other hand, are genetic modification which *are* inherited by further generations. For a genetic modification to be a germline modification it has to occur very early on in the creature's development, as in order to affect the system that produces reproductive cells, the modification must affect whole body. In this scenario, the reproductive cells will be created with a copy of the exogenous gene, which will then be inherited by the next generation. For example, GloFish are transgenic zebrafish that have been altered by the insertion of a green fluorescent protein. When GloFish are exposed to light in the ultraviolet range they exhibit green fluorescence (or other coloured fluorescence depending on the type of protein inserted) (Pray 2008). When two GloFish breed this protein will be inherited by their offspring, because the original genetic modification that created GloFish was carried out at an early developmental stage.

There are multiple ways to produce transgenic beings. One method is pronuclear injection (Engelhard et al. 2010). For this technique, we first obtain the gene or genes that we want to transfer, and then the sperm and oocytes from the animal that we want to modify. Using IVF we 'produce' a zygote. In the first hours after fertilization, the oocytes' and sperm's chromosomes are housed in different membranes called the 'pronuclei'. Using a micropipette, we can inject the exogenous DNA into either the male pronucleus or the female one. A downside of this method is that the insertion of the transgene is not targeted, which means that it occurs randomly within the recipient's chromosomes. Given this fact, researchers usually develop more than one line of animal in order to detect similar modifications on the animals' phenotype that cannot be attributed to other factors (Piotrowska 2011, 51–53).

Humans have created transgenic animals for a variety of reasons, but most are created to be disease models. In these cases, a 'human' gene that is known for its causal relationship with a disease is transferred into a nonhuman animal to enable it to manifest this human disease. The

most famous instance of a genetically modified nonhuman animal is the OncoMouse (Hanahan, Wagner, and Palmiter 2007), a genetically modified mouse which carries a dominant human 'oncogene' (a gene that is known for its capacity to cause cancer). Other transgenic animals are created with the intention of obtaining enhanced naturally-occurring products. For example, transgenic cows have been developed to produce milk that contains more protein, and in one instance casein (Brophy et al. 2003). Transgenic animals can also be created to produce pharmaceutical proteins (Houdebine 2009). For example, transgenic cows are used to produce human antihrombin III, a type of protein molecule that inhibits certain enzymes that cause blood clotting.

In transgenesis, we introduce an exogenous gene into an organism's cells, and in so doing we create a transgenic being. We do not create chimeras by inserting exogenous genes but by grafting *whole* cells (in their various presentations) or fusing embryos that are numerically distinct and that belong to genetically diverse organisms. Transgenic beings and chimeras are therefore significantly different. It is true that chimeras can be produced with cells where one or more exogenous gene(s) have been introduced, but this does not alter the fact that what creates a chimera is the grafting or fusion of *whole* cells.

1.5 PART-HUMAN CREATURES

Chimeras, hybrids, cybrids and transgenic beings can all be created with human elements. For example:

- Human/nonhuman animal chimera: Human brain cells engrafted into a mouse brain (Han et al. 2013).
- Human/nonhuman animal cybrid: Human nuclear DNA inserted into a rabbit's enucleated egg (Chen et al. 2003).
- Human/nonhuman animal hybrid: Human/Neanderthal hybrid (Dannemann, Andrés, and Kelso 2016).
- Human/nonhuman animal transgenic beings: Transgenic goat capable of producing human lactoferrin (Zhang et al. 2008).

With the exception of human/nonhuman hybrids, which do not exist at the present moment, all other part-humans have been created and are used in medical research. As I have made clear, while all of these creatures are part-human, all of them are created in different ways. Chimeras, specifically, differ from all other part-humans examined because the parts which are 'mixed'

are *whole* non-reproductive cells. This means that each cell's DNA (whether or not it is genetically modified), from both 'donor' and 'recipient', does not intermingle. At this point we can move forward and discuss in more depth the drive to research human/nonhuman animal chimeras in the scientific community, in order to lay the grounds for discussion of some of the ethical issues with this research.

1.6 ORGAN TRANSPLANTATION

One of the reasons researchers are dedicating a great deal of time and resources, both academic and monetary, to human/nonhuman animal chimera research is to 'develop' human organs inside nonhuman animals. If this research proves to be successful, the benefits for humans would be enormous, as I will explain. One researcher working on this issue is Juan Carlos Izpisua Belmonte of the Salk Institute in the United States of America. He actively researches how to create human solid organs (for example, hearts or kidneys) within pigs (Izpisua Belmonte 2016).

There are two main reasons scientists like Izpisua Belmonte are trying to create human organs inside nonhuman animals: to study human organ organogenesis, and to obtain transplantable human organs. I will focus on the latter issue.

Organ transplantation has radically advanced since, in 1954, Richard Herrick received a kidney from his twin monozygotic brother Ronald Lee Herrick and became the first truly successful kidney transplant patient (Murray, Merrill, and Harrison 1958). Thanks to powerful immunosuppressant drugs that prevent the body from attacking the transplanted organ, successful organ transplantation nowadays is *not* reliant on monozygotic siblings (i.e. it is not necessary that both donor and recipient possess the same genetic code). People that receive allogeneic heart transplants (i.e. they receive an organ that is genetically dissimilar but that belongs to the same biological species) can now expect their lifespan to be extended by a matter of years, and in some cases even decades. In addition to extending life, most organ transplantations now widely improve patients' wellbeing. For example, after a kidney transplant a patient that was previously subject to constant dialysis will experience less dietary restrictions, fewer fluid restrictions, an increase in their energy levels, and the elimination of the need to be attached to a machine sometimes several times a week. Some people even may return to work full-time.

While it is widely accepted in developed countries that the benefits of organ transplantation are enormous, there is still a *chronic* lack of organs. In October 2015, for example, there were

5,400 patients on the waiting list for kidney transplantation in the UK, and more than 400 had already waited *half a decade* for the much needed organ (NHS Blood and Transplant 2015). Efforts made by governmental and nongovernmental organisations to substantively increase the numbers of organ donors have been less than successful. On occasion, an individual's need for an organ is so great that they make a public appeal for donation. A recent high profile instance of this concerned Eugene Melnyk, owner of the Canadian Ottawa Senators hockey team. In 2015 he publicly pleaded for someone to donate part of their liver. In just *a few days* he received the organ; a very rare, very short waiting period (Humphreys and Payne 2015). It is not surprising that people make such appeals, as the failure to obtain transplantable organs contributes to patients' suffering and early death. In the United States, for example, 20 people die each day waiting for an organ (U.S. Department of Health & Human Services 2011).

This chronic lack of organs for transplantation, experienced both by patients and medical teams, is the reason some scientists have started exploring 'non-traditional' approaches to obtaining human organs. Traditionally, organs are obtained by live human organ donation and human cadaveric organ donation. The list of non-traditional organ sources includes: mechanical organs, 3D printed organs, xenotransplantation, and the creation of nonhuman animals with human organs. In the next sections, I will focus on these two last possibilities: xenotransplantation, and the creation of nonhuman animals with human organs.

1.6.1 XENOTRANSPLANTATION

Xenotransplantation is the procedure by which organs, cells or tissues are transferred between individuals of biologically distinct species (it would also count as xenotransplantation if the organs were transferred between members of distinct *subspecies*). In the past, this kind of organ transplantation between human and nonhuman animals took place between genetically *unmodified* individuals. Nowadays, however, genetic engineering is being considered in order to increase the probability of success by reducing the factors that cause organ rejection. Some people think that looking to nonhuman animals to satisfy the human organ need is morally permissible since, in their view, nonhuman animals *have less* moral worth than humans. This course of action is therefore morally less problematic than imposing a post-mortem mandatory organ donation scheme. Even if this were the case, which is open to debate, xenotransplantation has had, to date, a history of failure.

Doctors first attempted to replace human organs with nonhuman-animal organs in the early 1900s. On 26th January 1906, French surgeon Mathieu Jaboulay carried out the first heterotopic

xenotransplantation. He transplanted the kidney of a recently dead pig to the bend of the elbow of a 48 year old woman. On that day and the following day, he was able to collect urine, which was interpreted as a sign that the kidney was working. On the third day, he had to remove the organ due to thrombosis (Deschamps et al. 2005, 96). The twentieth century is plagued by cases of xenotransplantation failure, but maybe the most famous example is that of Baby Fae. Stephanie Fae Beauclair was born in 1984 with what at the time was a fatal heart condition: hypoplastic left heart syndrome. Hypoplastic heart syndrome is a congenital heart defect in which a patient's heart is severely underdeveloped. In an effort to save her life doctors decided to use a nonhuman animal as a heart source, and on 26th October 1984, Leonard Bailey transplanted a baboon's heart into the child. Baby Fae became the first neonate to receive a cardiac xenotransplant at just 12 days old (Bailey et al. 1985). She thrived for two weeks, but died just 20 days after the procedure, when her body finally rejected the foreign organ.

Nonhuman animal-to-human xenotransplantations have been, for the most part, unsuccessful because of the recipient's immune system response to the foreign organ: the human body detects and attacks the nonhuman organ because it 'considers' it to be a harmful foreign object. While failure has been the result so far of transplanting nonhuman organs into humans, recent advances in biotechnology could change this. The advent of a new generation of immunosuppressant drugs and of genetic engineering, particularly the advances gained by using the genome-editing technology CRISPR/Cas9, has restored hope in the field of xenotransplantation. Two examples of advances in this area are worth mentioning. First, in 2015 the company eGenesis announced that they had edited the pig genome in 62 places at once. The objective behind these edits was to modify those genes that could cause either organ rejection or infection once the organ was transplanted into a human (Reardon 2015). Second, scientists were able to keep a transgenic pig's heart alive in a baboon for 945 days. Although the heart was heterotopic and ultimately non-life sustaining, this was a major feat for the field (Regalado 2015). Finally, it should be noted that all xenotransplantation procedures create a chimera; in this case the chimera is the end-result of the procedure – the baboon with a pig's heart.

1.6.2 CHIMERA ORGANS

Another possible non-traditional source of human organs is to 'grow' them inside nonhuman animals. Whereas in xenotransplantation the organ that is transplanted is sourced from an intact or genetically modified nonhuman animal, and therefore genetically belongs to a different

species than that of the recipient, the idea here is radically different. Instead of transplanting organs from genetically distinct creatures, the nonhuman animals would possess functional *human* organs that could then be used for transplantation. The aim is to transplant *a human organ* into a human.

In a series of breakthrough experiments, Kobayashi et al. (2010) and Usui et al. (2012) employed embryonic stem cells and induced pluripotent stem cells to generate organs within animals that had been genetically modified so that organ agenesis would occur. Kobayashi et al. (2010) used mouse embryonic stem cells and induced pluripotent stem cells to generate *mouse* pancreases in mice with pancreatic agenesis. This showed that blastocyst complementation of organogenesis could be achieved intraspecifically (i.e. using cells that belong to the same biological species as the recipient). Kobayashi's team were also able to generate *rat* pancreases in mice with induced pancreatic agenesis. This showed that blastocyst complementation of organogenesis could also be achieved interspecifically (i.e. using cells that belong to a different biological species than that of the recipient). The mice from the *intraspecific* experiment "survived to adulthood without abnormalities, indicating that the PSC-derived [pluripotent stem cell derived] pancreas was functional" (Rashid, Kobayashi, & Nakauchi, 2014, 407). These experiments show that in practice it is possible to 'generate' an organ belonging genetically to one species within the body of another species.

That blastocyst complementation of organogenesis has been shown to work interspecifically in nonhuman animals suggests that we could use this technique to generate human organs within nonhuman animals. We could, for example, developmentally compensate for an organ niche at the embryo stage of a nonhuman animal with human embryonic stem cells, or with human induced pluripotent stem cells. This would work by first obtaining a pig blastocyst, for example, from a mutant strain in which the gene(s) that are necessary for the formation of the pancreas are deficient, thus creating an 'organ niche'. We would then inject human embryonic stem cells, or human induced pluripotent stem cells, into the blastocyst. These cells developmentally compensate for the 'lacking' organ, which means that the pig would have 'grown' a pancreas, in this case, from cells that originated in a human. Theoretically, the human organ could then be used for transplantation purposes.

Even more excitingly, we could use this technique to create 'tailor made' organs: organs whose DNA is identical to the patient's DNA. Suppose that someone needs a kidney. If this technology were available, scientists could take the patient's somatic cells and turn them into

induced pluripotent stem cells, which they could then use to grow the kidney within a modified pig. This kidney could then be harvested and transplanted into the patient: the patient would receive an organ that is composed of cells that possess her own DNA, and so her body would not attack the organ as a foreign object. In a sense, it is as if the patient had received an organ transplant from her monozygotic twin. This technique would enable us to generate many different types of organs on demand, and we would not have to wait for them to become available through the traditional channels.

Presently, researchers are trying to interspecifically generate organs in larger nonhuman animals, with the ultimate goal of generating human organs within nonhuman animals (Rashid et al. 2014). For example, Juan Carlos Izpisua Belmonte, as previously mentioned, is researching the creation of human solid organs within pigs. Pigs are an obvious choice for generating human organs, given that "developmental/genetic engineering techniques like somatic cell nuclear transfer (SCNT) are readily available" (Rashid et al. 2014, 407).

1.7 BASIC BIOLOGICAL RESEARCH

Chimeras are being created all around the world to assist in studies into various biological mechanism and processes. Human/nonhuman animal chimeras have been used in the investigation of the following areas: human haematopoiesis; the development and function of the human immune system; the nature of infectious diseases; the nature of autoimmune diseases; cancer etiology; human cell development, maturation and migration; and the development of human organs for regenerative medicine purposes (Lapidot 2001; Tam and Rossant 2003; Shultz, Ishikawa, and Greiner 2007; Sun et al. 2007; Rashid, Kobayashi, and Nakauchi 2014). It is important to note that while the use of nonhuman animals to study human diseases and basic biological processes has yielded important results, these animals, given that they are not human, cannot fully replicate human physiology and thus their usefulness is limited (Behringer 2007).

Despite these limits, intraspecific and interspecific primary chimeras can be used to understand the development of vertebrates (Douarin and McLaren 1984):

> Embryonic cells (…) that are identifiably marked, are isolated from specific regions or at different embryonic stages, combined with normal embryos, and traced throughout subsequent development, revealing the origins of the different types of cells, organs and tissues in the developing animal. (The Academy of Medical Sciences 2011, 27).

The use of human/nonhuman animal chimeras in stem cell and developmental research is so important that it has been labelled by scientists as *indispensable* (Hyun et al. 2007). They offer

us a window into human biological processes that other forms of study (e.g. in vitro, human research, computer modelling) simply cannot for ethical and practical reasons.

Disease pathology can be studied using chimeras, just as normal development can. For this, we can use both primary and secondary chimeras. When scientists decide to use secondary chimeras to study diseases they usually use immunodeficient animals as cell recipients; the immune system of immunocompromised animals will be not strong enough to attack the engrafted exogenous cells, which can belong to the same or different biological species.

'Neurological chimeras' form the basis of a remarkable area of research that encompasses both disease pathology and normal development. In this case, exogenous cells or tissues are grafted directly into the brains of developing animals (or early embryos in the hope that the exogenous cells will populate, further down the line, the brain), usually mice. While normal stem cells can be engrafted to study neurological development, cell fate and other biological processes, genetically modified stem cells or cells obtained from stem cell lines that possess genes that will cause a neurological disease (e.g. Parkinson's disease) can also be grafted. For example, we could graft human stem cells that possess the genes associated with Parkinson's disease into the brains of an immunodeficient strain of mice. This would allow us to study the biological basis of the disease in a brain that is composed of both mouse and human cells.

Researchers at the Salk Institute have injected human embryonic stem cells into the brain ventricles of foetal mice in order to investigate whether such cells could differentiate effectively into human neurons capable of functioning, and whether they could integrate themselves into the mice's brains. This experiment was successful, and the development of functional human embryonic stem cell-derived neurons was achieved in a mouse's brain. The human embryonic stem cells not only successfully implanted in the brain of the embryonic mouse, but they differentiated into functional neural lineages and generated mature active neurons that integrated into the adult mouse's forebrain (Muotri et al. 2005; Hyun 2013).

In another experiment, researchers grafted human neural stem cells into the brains of Old World monkeys. While the monkeys were in a foetal stage, cells were engrafted into the lateral brain ventricles. The goal was to use traceable human stem cells, in this case neural stem cells, to investigate whether the populations of human stem cells would distribute through various regions of the central nervous system. They found that the human stem cells distributed into two subpopulations: one contributed to corticogenesis while the other remained

undifferentiated and contributed to a secondary germinal zone (Ourednik et al. 2001; Hyun 2013).

Research such as the examples just discussed into neurological chimeras has raised fears that scientists might create human/nonhuman chimeras that are 'mainly' nonhuman but that possess human-like mental capacities. I will discuss this in more detail later.

One of the findings from research on human/nonhuman neurological chimeras, and chimeras in general, is that the biological context in which the cells are grafted has a strong influence on how the cells will behave and how they will integrate. This, importantly, helps to dispel fears that the cells possess deterministic agency that stems from an immutable essence. As Hyun phrases it, "[w]hen transplanted into animals, human stem cells do not carry with them an Aristotelian-like deterministic agency or a biological 'human essence'" (Hyun 2013, 119). This is not to say that a donor's cells cannot modify function or alter certain species-typical capacities in the recipient. However, it does tell us that the introduction of a cell, or set of cells, will not *necessarily* produce a chimera with the *properties* that are species-typical in the donor.

Broadly speaking, there are two categories of chimera research: research that occurs in vitro, before the development of the primitive streak (i.e. research that is performed on creatures unable to experience pain or pleasure); and research that occurs in vivo, on a sentient being (i.e. research on creatures that are capable of experiencing pain and pleasure). From both kinds of research, in vivo and in vitro, a multitude of ethical questions arise, as I will discuss later.

1.7.1 VACCINE RESEARCH

An area of research that merits special attention is the use of human/nonhuman animal chimeras as tools for developing vaccines against diseases, some of them deadly, that attack humans. For example, human/nonhuman chimeras have been used in research on malaria, dengue, Hepatitis B, HIV, and Hepatitis C (Bhan, Singer, and Daar 2010; Davis and Stanley 2003; Legrand et al. 2009; Sacci Jr. et al. 2006).

Chimeras can be used to fight disease in two ways. First, we can use them as biological models that can contract a disease that may or may not occur naturally in the nonhuman animal, and then study how it affects the human cells. For example, scientists have created human/mouse chimeras with humanised livers in order to study the exoerythrocytic stage of the protozoan parasite plasmodium falciparum, which is one of the parasites that causes malaria in humans. In simpler terms, they were able to study the developmental stage of the parasite in the liver

parenchyma cells of the vertebrate host before the red blood cells were invaded (Sacci Jr. et al. 2006). Until researchers were able to make use of chimeras, it had been difficult to research this phase of the parasite's life-cycle, as alternative methods necessitated live study in humans or non-human primates. Both of these options would require the experimental infection of either humans or non-human primates, which presents higher ethical and economic hurdles.

So far, the most important human/nonhuman chimera created to study human disease is the SCID-hu mouse. The SCID-hu mouse is a mouse strain with severe combined immunodeficiency that possesses components from the human immune system. Because the mouse's immune system is deficient, the human immune system cells are not attacked and thus they can function in a similar way as they do in humans, for example defending the body from pathogens. Davis and Stanley (2003, 850) provide a list of diseases that have been studied with the help of the SCID-hu mouse. This shows how important these human/nonhuman chimeras are for human disease research:

- Viral: HIV, measles, molluscum contagiosum, human papillomavirus, respiratory syncytial virus, hepatitis B, hepatitis C, varicella zoster virus, vesicular stomatitis virus, cytomegalovirus, herpes simplex virus, dengue flavivirus, human herpesvirus-6, human herpesvirus-8 (Kaposi's sarcoma), Epstein-Barr virus, enteroviral endocarditis.
- Bacterial: Helicobacter pylori, Shigella, pseudomonas (cystic fibrosis), group A streptococcus (impetigo), salmonella, chlamydia trachomatis, neisseria meningitides.
- Parasitic: Entamoeba histolytica, cryptosporidium parvum, plasmodium falciparum, schistosoma spp., rrichuris spp, toxoplasma gondii.

The second use for human/nonhuman animal chimeras in vaccine research is as models for testing vaccine candidates. For example, as reported in Bahn et al.:

> The Bill and Melinda Gates Foundation has funded a project at Peking University, China, through its Grand Challenges in Global Health Initiative, to develop a "humanized" chimeric mouse model with an immune system and liver similar to humans for testing and development of potential HIV and HCV vaccine candidates. (Bhan, Singer, and Daar 2010, 4)

It could be argued that the best setting to test a new vaccine candidate is in humans but, as Bhan et al. point out, "translating laboratory findings [such as vaccines] directly into humans without adequate testing in animal models is risky, is frowned upon by regulatory agencies, and is not acceptable under current ethics guidelines" (Bhan, Singer, and Daar 2010, 1). Therefore generating biological models, in this case chimeras, in which to test vaccine

candidates without imposing great economic costs, and which are shown to be morally permissible for testing, is an important goal of biological research.

In the past, nonhuman animals were used to meet this goal (Hendriksen 1996). The introduction of human/nonhuman chimeras appears to reduce problems with the translational gap between nonhuman-animal research and human research (the failure to translate research carried out on nonhuman animals into clinical trials in humans). This is because chimeras possess human cells and thus the effectiveness of vaccines can be examined by investigating how they affect human cells directly.

Jason Scott Robert (2006), on the other hand, has argued that using human/nonhuman animal chimeras in research in fact generates *two inferential gaps*. In 'standard' nonhuman animal research, aimed at improving human health, an inferential gap exists between the nonhuman animal and the human: what might work in one might not work in other (Greek and Menache 2013). In chimera research there are two inferential gaps, one between the nonhuman animal and the chimera, and another between the human and the chimera. Instead of bridging the gap, which is one of the aims of creating chimeras, we in fact generate two. It could be advanced against Robert that in investigating the effectiveness of a new vaccine candidate we only need to do research in human/nonhuman animal chimeras and then research on humans. This would bring us back to just one inferential gap, just as with standard nonhuman-animal research. It could then be claimed that the inferential gap between the chimera and the human is shorter than that between the nonhuman animal and the human. In spite of these arguments, Robert is right to say that we cannot claim with absolute confidence that what will work in the chimera setting will work in the human setting, and that "we may end up learning more about the part-human animal itself than about either source or host" (Robert 2006, 842).

1.8 HUMAN/NONHUMAN CHIMERA RESEARCH, BEHAVIOURAL TRANSFER AND CAPACITIES ENHANCEMENT

The most discussed topic within the academic literature on chimera ethics is the creation of human-to-nonhuman animal chimeras that could possess human-like attributes, such as human-

like mental capacities.[5] This worry stems from research which has revealed two phenomena: behavioural transfer and capacities enhancement.[6]

Behavioural transfer occurs when the recipient exhibits, *de novo* for the kind of being it is, some of the donor's species typical behaviours, due to the engrafted cells. For example, Balaban et al. (1988) transplanted embryonic tissues from Japanese quails into domestic chicken embryos. The resultant quail/chicken chimeras exhibited quail-like behaviour. Specifically, they were capable of making *quail-specific* crowing sounds rather than chicken-specific crowing sounds. Using this case as a precedent, some have posited that it might be possible to produce human/nonhuman animal-brain chimeras that possess human-like cognitive capacities.

Capacities enhancement occurs when some of the recipient's species-specific capacities are heightened due to the presence of engrafted cells, tissues or organs. For example, and as described above, Han et al. (2013) produced human/mouse chimeras by grafting human glial progenitor cells into the brains of neonatal immunodeficient mice. These chimeric mice, when compared with wild controls, showed enhanced learning and memory "as assessed by Barnes maze navigation, object-location memory, and both contextual and tone fear conditioning" (Han et al. 2013, 342). The possibility of capacity enhancement raises concerns that scientists might eventually create chimeras with enhanced sensory capacities. For example, how are we to handle a human-to-nonhuman animal chimera that has an enhanced capacity for feeling pain? The existence of these theoretical possibilities has moved professional bodies and academics towards recommending we pay special attention to the nature of the donor and recipient, the number and type of transplanted cells or tissues, and the timing of the engraftment or transplantation (Greene et al. 2005). In the specific case of human-to-nonhuman animal chimeras, the 'transfer' of the following characteristics has also warranted special consideration: human-like appearance, human-like intelligence, or human reproductive capacity (The Academy of Medical Sciences, 2011; Greely, 2013).

[5] Monika Piotrowska (2014) has successfully shown that if the creation of chimeras with human-like mental capacities is a concern, then we should be equally worried about the creation of certain nonhuman animal/nonhuman animal chimeras.

[6] These changes can be framed as both qualitative changes and quantitative changes.

2. PHILOSOPHICAL BACKGROUND

Despite the fact that methods for the intentional creation of animal interspecific and intraspecific chimeras have existed since at least the last quarter of the twentieth century (Fehilly, Willadsen, and Tucker 1984b; Balaban, Teillet, and Le Douarin 1988), *the ethics literature* on chimera research, as a sole subject, only sprang into existence after the publication of 'Crossing Species Boundaries' by Jason Scott Robert and Françoise Baylis (2003). This paper caused such an impact that the *American Journal of Bioethics* published, in the same issue, twenty-four responses to it: an uncommonly high number of peer commentaries for a paper that did not address a 'traditional' medical ethics topic.

I venture to say that the contemporary ethics debate on chimera research started with the publication of that paper. We could, perhaps, try to trace the ethical discussion of this topic to the ethics of xenotransplantation. However, even in instances when, in a proper sense, xenotransplantation is a form of chimerisation, the themes that have primarily been discussed when considering transplanting nonhuman-animal organs to humans are not about the creation of chimeras *per se*. The topics that have largely been debated include: justice, harms to *human* recipients of nonhuman animal organs, and public health risks due to the possibility of xenozoonosis (Clark 1999; Melo et al. 2001; Hughes 2007; Greely et al. 2007; Sparrow 2009).

In the time since the publication of Robert and Baylis's paper, the literature on chimera ethics has grown substantially. Not only have several journal articles, books, and book chapters been written on this topic, but professional bodies have examined it and proposed ethical guidelines on carrying out intraspecific and interspecific chimera research. In this section I present in a succinct way the main arguments within chimera ethics, in order to properly situate my research. The reconstruction of arguments from the chimera ethics academic literature will further serve to show the foundations on which my work is built, and what future research on chimera ethics could be done. Two things bear mentioning before I begin. First, this summary should by no means be understood as an exploration of *all* ethical topics that are, or that could be, directly or tangentially related to chimera ethics. Second, in no way am I implying that the topics that have been identified in the current literature are the only ones that exist, or even the most important ones.

2.1 SAME ARGUMENTS DIFFERENT NAMES

The arguments that have so far been examined in the chimera ethics academic literature are:

(i) The species identity argument.
(ii) The 'playing god' argument.
(iii) The moral confusion argument.
(iv) The moral taboo argument.
(v) The species integrity argument.
(vi) The unnaturalness argument.
(vii) The human dignity argument.
(viii) The conferring of personhood argument.
(ix) The human brain argument.
(x) The human gametes argument.
(xi) The human appearance argument.
(xii) The eating chimeras argument.
(xiii) The chimeras as organ sources argument.

Some of these arguments, although presented with different names, concern the same point. I will mention which ones do so, in order not to unnecessarily multiply arguments. The species identity argument and the species integrity argument (i and v) discuss the moral relevance of crossing species boundaries (Robert and Baylis 2003; Karpowicz, Cohen, and van der Kooy 2004; Karpowicz, Cohen, and van der Kooy 2005). The conferring of personhood argument and the human brain argument (viii and ix) discuss whether we should not create certain chimeras because they could possess human-like intelligence (Streiffer 2005; Greely et al. 2007; Greely 2013).

I will thoroughly examine (vii) the human dignity argument, (xiii) the chimeras as organ sources argument, and (x) the human gametes argument in the main section of this thesis. Given that the strongest version of the human dignity argument also touches upon the topic of creating chimeras that could possess human-like intelligence I will jointly discuss (vii), (viii), and (ix). It is also worth mentioning that I will comment on the human appearance argument (xi) in the conclusion.

2.2 THE SPECIES IDENTITY ARGUMENT (I AND V)

Robert and Baylis (2003) addressed, in a thorough way, two topics in 'Crossing Species Boundaries': the concept of biological species identity and the ethics of crossing species boundaries. In fact, they used the findings on the former to defend the position that from a moral standpoint it seems to be irrelevant to cross species boundaries. Their argument proceeded in the following way. First, they pointed out that any post-Darwinian biological framework should renounce, and vehemently deny, an immutabilist account of biological species. Secondly, they noted that although this should be the case, it is common among biologists, and other commentators, to regard biological species: (i) as possessing particular identities and (ii) to hold that the boundaries between them are fixed rather than fluid (Robert and Baylis 2003, 2). Thirdly, after highlighting this common inconsistency of thought, they examined some contemporary biological species definitions, in order to challenge what I will call the 'respect of species identity argument'. A version of the respect of species identity argument goes something like this:

1. It is immoral not to respect objects or subjects that possess intrinsic value.
2. Biological species possess intrinsic value.
3. The identity of biological species is determined by the state in which we find them in nature.
4. Human actions that tamper with the identity of biological species fail to respect their intrinsic value.
5. Intentional animal chimerisation is achieved through human action and tampers with the identity of biological species.

   ∴
6. The intentional creation of animal chimeras is immoral because it fails to respect the intrinsic value of biological species.

An initial point to make is that the first premise of this argument must be understood in absolute terms. By this I mean that we should understand (1) as not allowing for counterbalancing arguments. This is necessary for the argument to work, otherwise we could easily present counterbalancing arguments which allow us to morally violate something or someone's intrinsic value. For example, suppose that temple "X" possesses intrinsic value. If we were to accept that it is morally unproblematic to violate the intrinsic value of certain objects under certain circumstances then it is easy to image a case where we could violate "X's" intrinsic

value without this being viewed as morally problematic. Imagine that we need to build a road to connect a remote village with a hospital, and that the only way of doing so is by destroying the temple. Under an absolutist interpretation of (1) we should assert that no matter the benefits of connecting the village to the hospital, the act of destroying "X" is immoral. If, on the other hand, we were to accept that we can offer counterbalancing arguments to show that an act is not immoral, then we could posit that the benefits conferred to the villagers by being able to access healthcare outweigh the duties we have towards the temple.

Returning to the respect of species identity argument, there are several ways in which we could try to show that it is flawed. For example, we could challenge (3) or (4). We could challenge (3) by showing that in fact human interventions in nature have occurred since humanity appeared, and that it is not possible to know the 'true' identity of biological species that have come into contact with humans; we might call this the intractability defence. We could also challenge (3) by arguing that the identity of biological species should be defined in relation to how humans affect them. Another option is to challenge (4). We could do this by presenting a case where biotechnology is used to save a biological species from extinction, and thus argue that biotechnologies do not necessarily disrespect biological species' intrinsic value, given that saving a species is an act of respect for its intrinsic value. The current effort to save the American chestnut tree from a fungal infection by inserting a gene from wheat is a good example (Fessenden 2015).

While challenging (3) and (4) is a viable approach, the Robert and Baylis's strategy is more elegant, I think. They show that upholding (2) is deeply problematic by proving that there is no such thing as a *biological species*. Their strategy is twofold. First, they show that there are no biological essences. Second, they show that current biological species definitions are problematic to the point that it would be epistemically unwise to endorse any of them as a reliable foundation for a moral claim about crossing species lines. If their arguments are true, then it makes no sense to state that chimerisation tampers with the identity, or nature, of biological species; it makes no sense because there are no such things as biological species to be tampered with.

The authors advance their first point by presenting well known hybridization cases as proof that there are no *fixed boundaries* among biological species, and thus that there are no immutable essences:

> The idea of fixed species identities and boundaries is an odd one, though, inasmuch as the creation of plant-to-plant and animal-to-animal hybrids, either artificially or in nature, does not foster such a vehement response as the prospective creation of interspecies combinations involving human beings. (Robert and Baylis 2003, 2)

According to Robert and Baylis, any biological theory that endorses biological species essentialism needs to hold that there are clear dividing lines between one biological species and another, and that these lines are unbreachable. Given that this is false, because species lines can be crossed, then biological species essentialism must be false.

To prove their second point, they bring to our attention the fact that there is currently no single authoritative biological species definition, and then show that the most promising definitions are problematic to the point that they cannot be used to ground a moral argument against crossing species boundaries. A fact that attests to the lack of an authoritative definition is that depending on the research context in which biological scientists work, they employ different definitions of biological species. Three of the most promising definitions are: (i) a reproductive isolation definition, (ii) an evolutionary definition, and (iii) a homeostatic property cluster definition.

Even these definitions are problematic to the point that they cannot ground an argument against crossing species boundaries. For example, (i), a definition in terms of reproductive isolation and lack of genetic exchange, only applies to species that reproduce sexually. It would also follow that if there were morphologically identical populations that, by mere chance, did not breed we should, paradoxically, count them as different species. Definition (ii), a definition in terms of population persistence over geological time, is complicated to operationalise and has a higher degree of indeterminacy than (i). Finally, the main problem with (iii), a definition that utilises clusters of properties to distinguish between species, is how to properly determine the list of relevant properties that differentiates one species from another (Robert and Baylis 2003, 3).

Robert and Baylis therefore conclude that any argument against crossing species boundaries that relies on one of these three definitions has a weak foundation: how are we to defend the identity of something that we cannot even properly define? Even with this being the case, "notions of 'species essences' and 'universal properties of species' persist, always in spirit if not always in name, in discussions about breaching species boundaries" (Robert and Baylis 2003, 4).

Robert Streiffer has presented two rebuttals to Robert and Baylis's strategy. His first is that:

> Definitional difficulties, though, do not in and of themselves provide reasons for thinking that a concept is morally irrelevant. There are, after all, intractable disagreements about how to delineate many key concepts relevant to ethics, including: killing and letting die, life and death, consciousness, rationality, equality, justice, respect, rights, and goodness. (Streiffer 2014)

However, Robert and Baylis are not dismissing biological species as a moral concept because of these definitional difficulties. They are pointing out that any attempt to build a moral argument on the basis of a biological species definition is problematic because of the issues with the definitions: it would be like building on sand.

Streiffer's second point is that someone who holds that species identity is morally relevant does not need to claim that the boundaries between species are unbreachable, or even clearly defined:

> For example, the groups constituting one's family and one's fellow citizens change over time, and yet we owe special duties to our compatriots and to our kin in virtue of our special relationships to them. So, fixed boundaries are not necessary for moral relevance. And the mere fact that bacteria naturally transfer genes across species boundaries does not mean that the activity is natural when it is performed by humans. (Streiffer 2014)

While Streiffer's second point, that fixed boundaries are not necessary for moral relevance, is correct, in the cases that Robert and Baylis are discussing, we do not even know who our family is, and thus towards whom we have special moral obligations.

I think that Robert and Baylis establish a satisfactory case against (2) by showing that species essences do not exist, and that the definitions that we currently possess are problematic to the point that we would not want to construct our moral arguments upon them. However, even if we did agree on one of the three definitions, either consensually or by presenting sound arguments, there are still ways to challenge the respect for species identity argument, as my previous analysis suggests.

2.3 THE 'PLAYING GOD' ARGUMENT (II)

The 'playing god' argument is commonly evoked when discussing the ethics of new biotechnologies, and thus could be applied to the creation of chimeras. It can be understood in at least two ways: as a religious argument or as a secular argument. The religious version, in turn, has two varieties: a positive variety and a negative variety. The positive variety states that there is nothing morally wrong with humans altering god-created nature because god wants us to do this, and has given us the tools to do so. On this account, the creation of chimeras is not, *in principle*, morally problematic. As Gary L. Comstock has asserted:

> If humans are made in the divine image, and if God desires that we exercise the spark of divinity within us, then it should be no surprise that inquisitiveness in science is part of our nature. Creative impulses are found not only in literary, musical, and plastic arts. It is unclear why the desire to investigate and manipulate the chemical bases of life should not be considered as much a manifestation of our God-like nature as the writing of poetry and the playing of sonatas should be. (Comstock 2012, 185)

The negative version of the argument posits that it is morally problematic to 'play god', because we are assuming a role that god has claimed a monopoly on. We know that god has claimed this creational monopoly because she has let us know in a direct or indirect (by interpreting how she acted on other occasions) way. Thus the creation of something that god did not create goes against god's will, and this is morally wrong (this argument assumes that going against god's will is morally condemnable). The spirit of the comments made by Catholic bishop Domenico Mogavero regarding Craig Venter's 'synthetic cell', as reported by Alessandra Rizzo, provides an example of this position: "Pretending to be God and parroting his power of creation is an enormous risk that can plunge men into a barbarity (…) [scientists] should never forget that there is only one creator: God" (Rizzo 2010). The intentional creation of chimeras, judged on these grounds, is morally condemnable.

Robert and Baylis present an alternative interpretation of this negative variant: the creation of chimeras does not constitute taking a role that god has a monopoly on, but shows that god does not exist. The argument goes as follows: some religious traditions hold that all of god's creations are perfect and also that the world is complete. Thus the world is complete and perfect. For the world to be perfect it should contain all possible creatures. The creation of chimeras would show that there are creatures that were not created by god. Thus the world is neither complete nor perfect, in that it is not inhabited by all possible creatures. If the world is neither perfect nor complete then god is either imperfect or does not exist. God cannot be imperfect therefore god does not exist (Robert and Baylis 2003, 7). The authors do not address the question of why, if god does not exist, 'playing god' should be a moral problem.

Two things should now be clear about the religious interpretations of the 'playing god' argument. First, as Streiffer has clearly outlined, "(t)he content of God's will with regard to the manipulation of nature (…) is subject to speculation on both sides" (Streiffer 2014). Second, the religious interpretation of the 'playing god' argument is only binding for those that hold certain religious views. People that do not hold this religious perspective will not be compelled by it.

The secular version of the 'playing god' argument does not necessitate the existence of any god. It is not in reality an argument about god, but about the 'proper' limits of human agency in relation to the consequences of its actions. This variant asserts that humans are neither omnipotent nor omniscient, and so there are certain actions that they should refrain from, given the possible negative consequences that could occur. According to this argument, 'proper' human agency is restricted by our inability to foresee bad consequences. One of the actions humans should refrain from is creating entities that are not present in nature (e.g. chimeras), given that we cannot predict the negative consequences of such creation acts. However, this argument cannot be posited as a *principled objection* against the creation of *all* chimeras for two reasons: first, certain intraspecific chimeras occur in nature, thus the intentional creation of these chimeras is morally unproblematic; second, because this argument depends on the overall badness of the consequences of creating such creatures, there are clear counterexamples. For example, the development of the OncoMouse has not resulted in ecological havoc. This being so, the morality of chimera creation must be determined in a case by case fashion.

2.4 THE MORAL CONFUSION ARGUMENT (III)

After examining the problems caused by the inadequate definitions of biological species and by the 'playing god' argument, Robert and Baylis propose, in a tentative way and without endorsing it, an argument to explain why it is morally objectionable to create human/nonhuman chimeras: the inexorable moral confusion argument:

> All things considered, the engineering of creatures that are part human and part nonhuman animal is objectionable because the existence of such beings would introduce inexorable moral confusion in our existing relationships with nonhuman animals and in our future relationships with parthuman hybrids and chimeras. (Robert and Baylis 2003, 9)

They argue that moral confusion of an inexorable kind would emerge because, at least in regard to "folk" species essentialism (the popular belief that biological species are fixed and possesses essences), there is a clear demarcation between the type of being that possesses inherent full moral status (humans), and those that do not (nonhuman animals). For these authors, human beings' moral status "is categorical insofar as humanness is generally considered a necessary condition for moral standing" while nonhuman animals do not inherently possess moral status (Robert and Baylis 2003, 9). Nonhuman animals' moral status "depends in part on features other than species membership, such as the intention with which the animal came into being [and] is contingent on the will of regnant human beings" (Robert and Baylis 2003, 9). If we

take this foregranted, then creating human/nonhuman chimeras would produce entities that are neither fully human nor fully nonhuman, and thus their moral status would be uncertain.

It is not only the *uncertainty* regarding the moral status of these creatures that is troublesome. According to these authors, we do not possess the epistemically necessary powers to rightly determine human/nonhuman chimeras' moral status, and thus to establish our moral obligations towards them. Inexorable moral confusion would reign in our interactions with human/nonhuman chimeras.

In addition, Robert and Baylis think that the overall social consequences of the creation of human/nonhuman chimeras would be negative because they would threaten entrenched beliefs about humans' standing in nature:

> Indeed, asking—let alone answering—a question about the moral status of part-human interspecies hybrids and chimeras *threatens the social fabric in untold ways* [emphasis added]; countless social institutions, structures, and practices depend upon the moral distinction drawn between human and nonhuman animals. Therefore, to protect the privileged place of human animals in the hierarchy of being, it is of value to embrace [folk] essentialism about species identities and thus effectively trump scientific quibbles over species and over the species status of novel beings. The notion that species identity can be a fluid construct is rejected, and instead a belief in fixed species boundaries that ought not to be transgressed is advocated. (Robert and Baylis 2003, 10)

The inexorable moral confusion argument is deeply flawed, at least as presented in 'Crossing Species Boundaries'. An initial, minor problem is one of ambiguity, as Louis C. Charland has argued: from Robert and Baylis' work, we cannot clearly distinguish whether their assertion about the introduction of inexorable moral confusion "is intended as a purely descriptive claim about what is objected to, or whether what is objected to is normatively endorsed" (Charland 2003, W2). In a further publication Robert and Baylis have clarified that they did not normatively endorse the inexorable moral confusion objection. They merely think that it is a good way to explain some people's intuitive feeling that creating human/nonhuman chimeras is morally wrong:

> We do not claim (and are at pains to indicate this) that chimeras are morally confusing, and that moral confusion is a bad thing. We take no position whatsoever on whether chimeras should be created. Instead, given the bad arguments to date about what is wrong with chimera research (in terms of crossing species boundaries), we say that those who object to chimera research may be able to better defend their objection in terms of moral confusion based on crossing moral (if not biological) boundaries between species (…). (Baylis and Robert 2007, 44)

A second, and far more serious, problem with this argument is that it neglects the animal ethics debate on nonhuman animals' moral status (this debate has been going on in contemporary

philosophy since the 1970s), and more importantly it fails to take into consideration the specific debate about the moral status of great apes. As David DeGrazia has said:

> Anyone familiar with that literature knows that nearly all of the most respected scholars in animal ethics attribute at least some moral status (some moral, noninstrumental value) to sentient animals and would never dream of saying that 'humanness is generally considered a necessary condition of moral standing' without further comment. (DeGrazia 2007, 311)

Because Robert and Baylis do not take into consideration animal ethics, they fail to realise that there are moral status theories that accommodate, without the peril of inexorable moral confusion, the existence of human/nonhuman chimeras. For example, a cognitive capacities account of moral status.

The third problem is a methodological one. Robert and Baylis claim that asking questions about human/nonhuman chimeras' moral status is sufficient to threaten the social fabric. They appear to mention this in order to reinforce the reason some people might think that we should not create human/nonhuman chimeras. The difficulty with this claim, as Savulescu has rightly noted, is that Robert and Baylis's assertion could be used by old-fashioned racists to, for example, defend anti-miscegenation laws (Savulescu 2003) – they could claim that asking about the morality of interracial marriages threatens the social fabric in untold ways, and therefore it should not be done. The fundamental flaw in Robert and Baylis' point is that asking questions that could affect social institutions, structures and practices is foundational to philosophy, as anyone who has read Plato will know. Did questions about the wrongness of slavery, the wrongness of discrimination against women and the wrongness of racism affect the social fabric in significant ways? Surely they did, but it is contrary to the spirit of philosophy, moral advancement, and the development of the sciences to defend that we should not ask 'radical' questions only for the sake of the *status quo*. As Savulescu says, "The social costs of acceding to irrational confusion are, at least historically, much greater than the costs of clearing it up and reforming society" (Savulescu 2003, 25).

A fourth problem with the inexorable moral confusion argument is the way in which these authors understand what it is to be confused. Where Robert and Baylis think that the kind of confusion that we would fall into is inexorable, John Harris has argued that the confusion objection is triply problematic:

> (…) it suggests that confusion is to be avoided, that once confused it is impossible (or impossibly difficult) to become unconfused, and the paternalist suggestion that whereas those who appeal to the objection from confusion are not themselves confused and see

> clearly the way out of the fly bottle, ordinary people require to be protected from the necessity of thinking their way through the relevant issues. (Harris 2010, 266)

Furthermore, a simple thought experiment shows us that the creation of human/nonhuman chimeras would not *necessarily* produce a state of *inexorable* moral confusion. Imagine that we create a human/chimpanzee chimera that *undoubtedly* had normal adult human cognitive capacities, and that such chimera was educated so as to develop its full cognitive potential. If this were ever to be the case, and the signs of those cognitive capacities were undeniable, then it would be obvious, or at least ought to be, that we should treat such chimeras just as we treat other normal adult human beings. If what I am saying here is true, and I think it is, then Robert and Baylis' argument is weaker than they think.

The supposed inexorable moral confusion resulting from the creation of human/nonhuman chimeras cannot therefore be an argument against their creation, because it is derived from a patently incorrect moral framework, which in turn may rely on an incorrect understanding of biology. As Hilary Bok has asserted, "chimeras do not introduce confusion into our moral views. They reveal ways in which those views are inadequate and make us think about how we might improve them" (Bok 2003, 26).

2.5 THE MORAL TABOO ARGUMENT (IV)

Robert and Baylis define a taboo, following Douglas (2002), as the crossing of a profoundly held conceptual boundary. An example, still present in the Western world, of a deeply held conceptual boundary is that between humans and nonhuman animals. For many people, humans and nonhuman animals belong in qualitatively different places in the 'great chain of being'. This being the case, the creation of human/nonhuman chimeras, who do not fit properly into such a classificatory scheme, is regarded as taboo because their creation is a "threat to valuable and valued conceptual, social, and moral boundaries that set human beings apart from all other creatures" (Robert and Baylis 2003, 8). One thing that is unclear from Robert and Baylis's characterisation is whether a taboo is breached if someone that does not hold a conceptual boundary crosses one that is deeply held by someone else.

The taboo argument, defined in such terms, has a similar problem, if categorised as a *principled* objection against the creation of human/nonhuman chimeras, to the biological species identity argument. This is that "we have no biological account of unambiguous humanness, whether in terms of necessary and sufficient conditions or of homeostatic property clusters" (Robert and Baylis 2003, 8). This means that an argument based on a taboo such as the divide between

humans and nonhuman animals cannot be grounded in an empirical definition of what humans are, and thus needs to rely on a social and moral construct of humanness. This being the case, we have to accept that the boundaries between humans and nonhuman animals can in fact be socially and morally renegotiated. In turn, this justifies why the creation of human/nonhuman chimeras is not immoral for certain groups or individuals: they do not accept, *in principle*, the existence of a profound conceptual boundary between humans and nonhumans. This version of the argument leaves the matter unresolved, given that no answer to guide universal action is provided to the question about the morality of creating chimeras.

A defence of the taboo argument is presented, and then dismissed, by Phillip Karpowicz, Cynthia B. Cohen, and Derek van der Kooy, who follow Jeffrey Stout's (2001) work on taboos. These authors advance the argument that taboos "are said to be legitimized by moral intuitions, held in common by all people, about which ends are desirable. Intuition that becomes social convention is thus taken to be a meaningful phenomenon" (Karpowicz, Cohen, and van der Kooy 2004, 333). There are two problems with using this account of taboos to assert that the creation of chimeras is immoral. First, moral intuitions are not cross-culturally universal. For example not all societies hold a taboo against cannibalism, as evidenced by the ancient Aztecs. Second, even within a community people have diverse moral intuitions. Which intuition should we follow? The fact that moral intuitions can vary between societies and between individuals within societies leaves us with two unsatisfactory options. The first is the tyranny of the majority, and the second is to embrace moral relativism. Finally, the case for holding a taboo argument is even flimsier when we realise that taboos have supported immoral practices such as anti-miscegenation laws, sexism, and homophobia.

2.6 THE UNNATURALNESS ARGUMENT (VI)

Another argument that has been levelled against biotechnologies, and thus would apply to the generation of chimeras, is the unnaturalness argument. There are two ways in which to understand it: as a teleological argument or as a class-of-action argument. Those that understand it as a class-of-action argument defend, in its simpler form, that natural things are intrinsically good while unnatural things are intrinsically bad. The core of this argument, in Robert Streiffer's words, is that there is a link between unnaturalness and wrongfulness (Streiffer 2014). If true, this argument would clearly show that the intentional creation of certain chimeras is immoral. I say 'certain chimeras' because in nature some forms of intraspecific chimerism occur, for example, an organism that has its origin when two

genetically nonidentical embryos fuse inside the womb. Putting aside the metaphysical problems of defining what it is for something to be 'natural', a fatal problem with this version of the argument is that it would entail that having cancer is a good thing, because it is natural, while having an operation to remove the cancer would be morally problematic given that it is unnatural. This is clearly absurd.

A more sophisticated account of this argument is the teleological one, which Karpowicz et al. (2004, 2005) have explored on two occasions. This version of the argument maintains three things: that natural objects possess a telos, that it is good for these objects to possess this telos, and that it is morally objectionable to interfere with the telos of natural objects. This being the case, the intentional creation of chimeras is morally objectionable because it disrupts the telos of one or more natural objects (for example, if we create a chimera by fusing two embryos that belong to two different species, the telos of both embryos would be tampered with). This argument is an intrinsic objection, in that it focuses on the intrinsic properties of the object. The main problem with this argument is that it "leaves us to speculate endlessly about the 'natural' purposes of virtually all living things, and offers few clues as to what decisions are right" (Karpowicz, Cohen, and van der Kooy 2004, 332). For example, would a teleological view consider nonhuman-animal vaccination as interfering with the natural telos of animals and thus morally wrong? This being the case, we cannot categorically assert that a teleological argument would, *in principle*, prohibit the creation of chimeras.

2.7 PRINCIPLED ARGUMENTS AGAINST THE CREATION OF CHIMERAS

So far, I have shown that the species identity argument, the 'playing god' argument, the moral taboo argument, and the unnaturalness argument are arguments that are commonly presented against biotechnologies. These arguments, in addition to the moral confusion argument, can also be levelled against the general, intentional creation of intraspecific and interspecific chimeras. Even when, intuitively, it appears that these arguments possess some merit, this overview shows that all are found wanting when considered as *principled objections* against the intentional creation of chimeras.

The research that forms the body of this thesis therefore focuses on arguments against the creation of *particular* human/nonhuman chimeras. In the first paper I will examine arguments designed to show that the creation of human/nonhuman chimeras that are persons or borderline persons is morally problematic. In the second paper I will examine what moral duties we have towards human/great-ape chimeras in the context of human organ transplantation. In the third

paper I consider whether it is morally problematic to create human/nonhuman chimeras capable of human gamete production and human pregnancy. In the fourth paper I examine if classic animal ethics issues concerning animal welfare can throw light on the issue of killing human/pig chimeras for their human organs.

I have shown in this section that these 'general' arguments fail to prove that it is inherently wrong to create, in all instances, human/nonhuman chimeras. Given that these are the main arguments explored to date within the academic literature, it is clear to me that the moral quandaries relating to particular instances of chimera research are underexplored. If the generalised objections against chimera research have failed, maybe objections against particular cases of chimera research would be more successful? By researching the four particular instances of chimera research just mentioned, I make a contribution to the existing research in this area and open new paths to explore.

At this point it is important to outline in more detail the overarching narrative of the four cases that I will explore. Specifically, how are the discussions about human/great-ape chimeras, human/nonhuman chimeras and 'human' dignity, human/nonhuman chimeras capable of human gamete production and human pregnancy, and classic animal ethics and the killing of human/pig chimeras for their human organs interconnected? The papers that I present in this thesis form a coherent body of work, together addressing two of three cases that have been regarded as particularly worrisome within chimera ethics, (i) and (iii). These are: (i) the creation of human/nonhuman chimeras with human-like cognitive capacities; (ii) the creation of human/nonhuman chimeras that could look human-like; (iii) the creation of human/nonhuman chimeras capable of human gamete production and human pregnancy. These cases are so prevalent within the academic literature that they appear in all major reports that aim to provide ethical guidance on chimera research: 'Animals Containing Human Material' (The Academy of Medical Sciences 2011, 110–111); 'Human–Animal Mixtures in Research' (Deutscher Ethikrat 2011, 113); and 'Guidelines for Human Embryonic Stem Cell Research' (National Academies of Science 2005, 50).

According to these reports the generation of human/nonhuman chimeras that could look human-like merits special ethical attention, and should only be carried out if the benefits that could be obtained are great enough. These three groups have also recommended that human/nonhuman chimeras with human-like mental capacities should not be created. On the topic of human/nonhuman chimeras capable of human gamete production and human

pregnancy the groups have each offered different guidance. The German Ethics Council recommends not creating human/nonhuman chimeras that are capable of human gamete production and also recommends against human/nonhuman chimera human pregnancies. The UK Academy of Medical Sciences and the US National Academies of Science, on the other hand, only recommend against allowing breeding, or intentionally breeding, nonhuman animals where human stem cells have been grafted.

What is it that sets these three cases apart? According to Greely, it is that we care about them:

> I think the policies actually adopted with respect to human/nonhuman chimeras point us to an important reality, usually overlooked and never stressed in the debates about human/nonhuman chimeras (…). We *care about* [emphasis added] three kinds of chimeras: those with "humanized" brains (and hence, potentially, human behavior), those with human egg or sperm, and those with certain forms of human outward appearance. (Greely 2013, 681).

But why do we care about them? I think that the reason most people particularly care about these three chimera cases, contrary, for example, to the possibility of creating nonhuman/nonhuman chimeras with human-like mental capacities (Piotrowska 2014), is because they entail the 'transfer' of aspects that are widely regarded as uniquely human.

These three cases forcefully invite us to re-examine what it means to be a human and, conversely, to be a nonhuman animal. It is a new concept for us to consider: until the second half of the twentieth century there were no nonhuman animals engrafted with human cells, tissues or organs living among us. This being the case, we are left to ponder two things. First, what are, if any, the necessary and sufficient conditions that a being must satisfy in order to be regarded as a human, or a nonhuman animal? Second, is being regarded as a human in any sense morally relevant? Furthermore, the possibility of chimera research involving the transplantation of human material to nonhuman animals that could cause behavioural transfer or capacities enhancement also serves to illuminate the debate about speciesism, without relying on the argument from species overlap (also called 'the argument from marginal cases').

3. RESEARCH QUESTIONS

In this section I will present an outline of the main research questions on which my investigation of chimera ethics is based. I aim to clearly present what I am trying to answer in each of the four papers that compose the main section of this thesis.

3.1 CAN 'HUMAN' DIGNITY BE INVOKED AS AN ARGUMENT AGAINST THE CREATION OF HUMAN/NONHUMAN CHIMERAS? (ARTICLE 1)

The concept of 'human' dignity is a pervasive one in medical ethics. It is therefore not surprising that it has appeared in the discussion around the ethics of creating human/nonhuman chimeras. In fact, several arguments that have at their base the concept of 'human' dignity have been advanced against the creation of human/nonhuman chimeras.[7]

There are at least three types of objection to human/nonhuman chimera research based on the concept of 'human' dignity. There are those that defend a *principled* ban on the creation of *all* human/nonhuman chimeras, those that suggest prohibiting the creation of *person* human/nonhuman chimeras, and those that further the prohibition to the creation of *person* and *borderline person* human/nonhuman chimeras.

There are two main questions to which this section of the thesis aims to respond. The first is if in fact the concept of 'human' dignity can be put forward in a cogent way to construct an argument against the creation of human/nonhuman chimeras. The second question that I address is whether the arguments that have been advanced against the creation of human/nonhuman chimeras that have at their base the concept of 'human' dignity are successful in proving their case.

3.2 IS IT MORALLY PERMISSIBLE TO KILL HUMAN/GREAT-APE CHIMERAS TO SOLVE THE HUMAN ORGAN-SHORTAGE PROBLEM? (ARTICLE 2)

There is an organ-shortage crisis for transplantation purposes. Several strategies have been adopted by governments around the world to increase the number of available organs. Overall, these strategies have had little success. In the near future it might be possible to create human/nonhuman chimeras to solve the human organ-shortage problem. It has been proposed that human/pig chimeras and human/great-ape chimeras might be suitable.

It is obvious that killing and harming nonhuman animals for medical research requires us to present sound arguments in favour of doing so; sentient nonhuman animals have an interest in not suffering and it would be morally wrong to inflict suffering upon them without good reason. As this is the case for medical research that employs nonhuman animals, it seems logical that

[7] It bears mentioning that throughout this paper I only use the concepts of dignity that the authors that I am critiquing use. This means that my discussion is methodologically limited to such concepts of dignity. For an in depth discussion of the concept of dignity see Beyleveld and Brownsword (2002) and Ashcroft (2005).

we also need to present strong arguments to kill human/nonhuman chimeras for their human organs.

With this in mind, in this chapter I try to answer the question of whether it could be morally permissible to kill human/pig chimeras and human/great-ape chimeras for the sake of saving human lives. I address both cases by examining the arguments that have been advanced by Shaw, Dondorp, and de Wert (2014) and Shaw, Dondorp, Geijsen, and de Wert (2015). These authors argue that killing human/pig chimeras and human/great-ape chimeras for their human organs is morally permissible. While I examine both cases, in this paper I pay more attention to human/great-ape chimeras because of the higher ethical thresholds that need to be surpassed to carry out medical experiments with great-apes.

3.3 IS THERE SOMETHING INHERENTLY WRONG WITH CREATING HUMAN/NONHUMAN CHIMERAS CAPABLE OF HUMAN GAMETE PRODUCTION AND HUMAN PREGNANCY? (ARTICLE 3)

In stem cell research, reproductive research and regenerative research there is a lack of human oocytes for experimentation. The lack of human oocytes has been so acute that scientists have turned to human/nonhuman animal cybrids while waiting for more human oocytes to become available. The advent of human/nonhuman chimera research may change this because there is a theoretical possibility that human/nonhuman chimeras could be capable of human gamete production and human pregnancy. Research into the creation of human organs within human/nonhuman chimeras has suggested that it might be possible to create human reproductive systems within nonhuman animals. In this chapter I seek to answer two questions which arise from this. First, is it morally problematic to create human/nonhuman chimeras capable of human gamete production? In order to answer this question I examine what value human gametes possess and what reasons we have for producing such type of chimeras.

The second question I try to answer is whether there would be a moral obligation to terminate the conceptus if ever a nonperson human/nonhuman chimera become pregnant with a human conceptus. To answer this question I examine the different scenarios that could occur when a nonperson human/nonhuman chimera becomes pregnant with a human conceptus, and also under what circumstances we would be morally required to terminate such pregnancies.

3.4 KILLING HUMAN/PIG CHIMERAS FOR THEIR HUMAN ORGANS: EXPLORING THE WELFARE ISSUES (ARTICLE 4)

In Article 2 I try to answer the question of whether it is morally permissible to kill human/pig chimeras and human/great-ape chimeras for their human organs. In that paper, I concentrate a lot of effort on examining if it is morally permissible to kill borderline persons for their human organs. In Article 4, I examine the question of whether the classic animal ethics issues concerning animal welfare can throw light on the issue of killing human/pig chimeras for their human organs. Contrary to my discussion of human/great-ape chimeras, here I only focus on the ethics of killing nonperson sentient beings for such purposes. In reality, I think, researchers will aim to develop human organs within human/pig chimeras because of the constraints on great-ape research, and because producing human/pig chimeras will evoke less societal resistance to this type of technology.

In order to answer this question I establish bridges between the meat-eating debate and chimera research, nonhuman-animal-fairness issues and medical research, and nonhuman-animal-wellbeing issues and the conditions in which chimeras would need to be kept for transplantation to be safe. This chapter shows that any comprehensive account of chimera ethics needs to address both general ethics topics and animal ethics topics.

4. PHILOSOPHICAL APPROACH

Before I move forward I need to briefly present the pertinent ethical issues that the articles that compose this thesis touch upon. The papers that comprise this thesis were written to fit the characteristics of specific academic journals. This means that the length and composition of the papers was restricted in accordance with individual journal requirements. As a consequence, in the papers I did not have enough space to explore all the ethical issues that I mention. Using this space to examine the pertinent ethical issues that appear in the papers will help me to present a richer philosophical picture, and it will help to paint a clearer picture of this burgeoning field to a reader that has not specialised in the topic of chimera ethics.

Two questions, ‘what is moral status?’ and ‘what is harm?’, are particularly relevant to the four papers that I present in this thesis. In the body of the thesis I point towards a counterfactual account of harm, and I present the definition of moral status advanced by Frances Kamm (2007, 229). However, I have not had the space to explore these issues and so in the following two sections I present an overview.

4.1 MORAL STATUS

The question of how we should morally treat a certain being depends, partly, on what kind of value does that being possesses. Given that this thesis aims at responding how we should treat human/nonhuman animal chimeras then we need to establish what kind of moral value does these creatures possess, and in order to do so we need to look into the topic of moral status.

To state that something possesses moral status is to affirm that it possesses an intrinsic moral worth. This means that it possesses a worth that is not based on its capacity to be used to perform a certain activity (i.e. it does not possess instrumental worth). It also means that our consideration of such an object should not be comprehended in terms of duties towards other moral agents (i.e. 'X' is valuable because 'Y' regards it as valuable, and I have a duty to regard as valuable that which 'Y' regards as valuable) or indirect duties (i.e. the duties that I have towards 'X' are in fact duties owed to myself).[8]

The question that we must ask now is what *grounds* such intrinsic worth. There are various possible answers. Some hold that the only thing that grounds such worth is belonging to human kind (i.e. belonging to certain biological species). Under this account being human is a *necessary* and *sufficient* condition for possessing intrinsic moral worth. While some find this stance appealing, it is easy to come up with real cases and thought experiments that question its veracity. For example, imagine a lizard-like alien that had the same mental capacities as us (i.e. was capable of thinking as normal human adults think). Furthermore, imagine that you have to decide if we should treat the alien as humans regularly treat cows, for example, or if we should treat it as humans should be treated. As Harris puts it: "We will be deciding whether an appropriate response to them would be to have them for dinner in one sense or in the other" (Harris 2006, 9-10). Presented with this case it seems obvious that if you had to decide how to

[8] The most famous proponent of an indirect-duties stance with respect to animal ethics is Immanuel Kant. He claims: "But so far as animals are concerned, we have no direct duties. Animals are not self-conscious and are there merely as a means to an end. That end is man. (…) Our duties towards animals are merely indirect duties towards humanity. Animal nature has analogies to human nature, and by doing our duties to animals in respect of manifestations which correspond to manifestations of human nature, we indirectly do our duty towards humanity" (Kant 1963, 239). Although Kant's position regarding nonhuman animals seems to be antithetical to their consideration as beings with intrinsic worth, in a recent work Christine Korsgaard (2012) has shown that an interpretation of Kant's corpus allows us to construct a case for both the moral claims and legal rights of nonhuman animals.

treat this alien you should decide to treat it as we should treat humans. This shows that it is false that being human is a necessary condition for possessing intrinsic moral worth.

It could be argued that this imagined case proves nothing, as it seems such lizard-like aliens do not exist. However, we have archaeological evidence that there were other hominids that had a high level of intelligence (enough intelligence to perform intentional burials, for example (Rendu et al. 2014)), and that in the past coexisted and mated (now they are extinct) with modern man (Simonti et al. 2016). This means that in our past there were other *non-Homo sapiens* beings, for example the Neanderthals, that, if they existed today, we would recognise as possessing moral status. This case also shows, with a historical example, that being human is not a necessary condition for possessing intrinsic moral worth.

These imaginary and historical cases deal a fatal blow to the claim that being human is a necessary condition for possessing intrinsic moral worth, and makes us wonder if belonging to *Homo sapiens* (which is usually regarded as the condition for humanness) is sufficient for possessing intrinsic moral worth. It seems that we cannot posit that being human is sufficient to possess intrinsic moral worth, as being human is just a matter of biology. As David DeGrazia[9] notes: "[S]trictly speaking, what it is to be *Homo sapiens is simply* [emphasis added] a matter of biology: It is to be an organism that has descended from a particular branch of the tree of terrestrial life, an organism whose genome lies somewhere within a particular range, or the like" (DeGrazia 2007, 312).

The lizard-like case and the Neanderthal suggest that maybe intrinsic moral worth is dependent on the possession of rational capacities. The similarity between the two cases is that the creatures in them possessed a high level of intelligence. In fact, we would consider all these beings to be *persons*. Traditionally we regard as persons beings that possess human-like rationality. John Locke, in his seminal *An Essay Concerning Human Understanding*, provides the following definition of who a person is:

> [W]e must consider what person stands for; which, I think, is a thinking intelligent being, that has reason and reflection, and can consider itself, the same thinking thing, in different times and places; which it does only by that consciousness which is inseparable from thinking and seems to me essential to it; it being impossible for any one to perceive without perceiving that he does perceive. (Locke 1964, bk. II, chap. 27, sec. 9)

[9] In the article 'Human Dignity and the Creation of Human–Nonhuman Chimeras' I again discuss this quote.

That rationality plays a role in the possession of intrinsic moral worth becomes even more promising when we realise that it can account for and explain cases that a species based account (that holds that being member of a particular biological species is a *necessary* and *sufficient* condition for possessing intrinsic moral worth) cannot. However, it is important to note that a cognitive capacities account is problematic if we want to defend that *all humans* possess intrinsic moral worth. There are humans that are not rational, and there are humans that not only are not rational but that do not have the potential to be rational. Genetically-caused anencephalic humans are an example of the latter case; foetuses, those in a persistent vegetative state, and newborns are all examples of the former.

That there are humans that are not rational, and that do not possess the potential to be rational, requires either that we accept that they do not possess intrinsic worth, or that there are other things that grant intrinsic moral worth. The fact that there are humans that do not have the potential to be rational forms the basis of 'the argument from species overlap'. The argument from species overlap[10] "points out that the criteria that are commonly used to deprive nonhuman animals of moral consideration fail to draw a line between human beings and other sentient animals, since there are also humans who fail to satisfy them''(Horta 2014, 142). In the ethics literature, this argument has been used to defend two different conclusions. First, that without very strong moral reasons it is morally impermissible to harm nonhuman animals and humans that lack the potential for rationality. For example, Alastair Norcross (2004) has argued against eating factory-farmed meat in this way: if it is morally impermissible to rear in factory-farming settings and then eat humans that lack the potential for rational thought, then it is morally impermissible to rear in factory-farming settings and then eat nonhuman animals that lack the potential for rational thought. The second conclusion is that it *is* morally permissible to harm either nonhuman animals or humans that lack the potential for rationality when there are good enough reasons for doing so. For example, Peter Singer has advanced that if medical experimentation is morally permissible on nonhuman animals then it should also be in non-rational humans:

> Note, however, that this same argument gives us a reason for preferring to use human infants - orphans perhaps - or severely intellectually disabled humans for experiments, rather than adults, because infants and severely intellectually disabled humans would also have no idea of what was going to happen to them. So far as this argument is concerned nonhuman animals and infants and severely intellectually disabled humans are in the same category; and if we use this argument to justify experiments on

[10] This argument is also known as the 'argument from marginal cases'.

> nonhuman animals we have to ask ourselves whether we are also prepared to allow experiments on human infants and severely intellectually disabled adults. If we make a distinction between animals and these humans, how can we do it, other than on the basis of a morally indefensible preference for members of our own species? (Singer 2011, 52)

One way to defeat the species overlap argument is by defending that the *material basis for moral agency* (in the case of human beings these are *genetic bases*) is what grounds moral status, as Mathew Liao (2010) has done. Liao's account does not rely on species membership to grant moral intrinsic worth, nor on the possession of rational capacities. For him, so long as an entity possesses the *material basis for moral agency* it would possess moral intrinsic worth. While Liao's account, if successful, explains why human embryos and foetuses, and those humans in persistent vegetative states, possess intrinsic moral worth, it cannot claim that *all humans* possess intrinsic moral worth. There are humans that lack the genetic basis for moral agency (for example, humans with genetically-caused anencephalia). Finally, if Liao is correct then this further shows that belonging to human-kind cannot be regarded as a *sufficient* condition for possessing intrinsic moral worth, as there are humans that lack the grounds for intrinsic moral worth.[11]

While the material basis for moral-agency criteria and personhood criteria accounts for many of our intuitions (namely that humans, intelligent lizard-like beings, and Neanderthals have moral status), neither accounts for other strong moral intuitions that we possess. For example, why do we consider that kicking a rock is morally irrelevant whereas kicking a puppy is morally problematic? If we, in fact, maintain that only those that possess the aforementioned criteria have moral status then we should accept that kicking a rock and kicking a puppy must be equally morally irrelevant, but we refuse to do so. Furthermore, kicking a puppy seems to be morally wrong not because the puppy belongs to someone else, as kicking an un-owned puppy is equally wrong. Kicking the puppy is also not wrong because I have violated an indirect duty to myself (e.g. not being cruel).

The reason kicking a puppy is not regarded as morally irrelevant is because puppies can *feel pain.* Sentience (the capacity to subjectively experience pain and pleasure) appears to be a *sufficient condition* for possessing moral worth. As Jeremy Bentham wrote:

[11] Christopher Grau (2010) has criticised Liao's account. According to Grau, Liao's position grants moral status to those that may not possess it, and does not provide grounds offering such status to those that might well deserve it. For a response to such critiques see Mathew Liao (2012).

> The day may come, when the rest of the animal creation may acquire those rights which never could have been withholden from them but by the hand of tyranny. (...) It may come one day to be recognized, that the number of the legs, the villosity of the skin, or the termination of the os sacrum, are reasons equally insufficient for abandoning a sensitive being to the same fate. What else is it that should trace the insuperable line? Is it the faculty of reason, or, perhaps, the faculty of discourse? But a full-grown horse or dog is beyond comparison a more rational, as well as a more conversable animal, than an infant of a day, or a week, or even a month, old. But suppose the case were otherwise, what would it avail? the question is not, Can they reason? nor, Can they talk? but, Can they suffer? (Bentham 2007, Chapter 17, section IV, note 122)

At this point, Kamm's moral status definition becomes clear: an entity possesses moral status when ''*in its own right and for its own sake, it can give us reason to do things such as not destroy it or help it* [emphasis in the original]'' (Kamm 2007, 229). The reasons given to not destroy or to help a being could be that it is capable of subjectively experiencing pain and pleasure, or that it can provide us with rational reasons for helping it or not harming it (for example, an artificial intelligence that was unable to feel pain and pleasure, but that possessed truly human-like rationality).

Now we need to explore whether the moral status that a puppy possesses *is the same* as that a normal adult human possesses. More generally, we need to ask if there are degrees of moral status (for example, higher and lower moral status) or if moral status is the same for all that possess it. In order to answer this question we cannot appeal to moral status, as DeGrazia explains: "Working out whether we have weaker obligations to some beings (e.g., cats) than to other beings (e.g., persons) must be determined on the basis of normative and theoretical considerations that make no prior assumptions about moral status" (DeGrazia 2008, 185).

There are two models that can explain whether there are differences in moral status, as identified and developed by DeGrazia (2008): (a) the unequal consideration model of degrees of moral status, and (b) the unequal interests model of degrees of moral status. According to the unequal consideration model, it is worse to kill or harm a normal adult human being (a person) than a sentient non-person because the person is due full moral consideration whereas sentient non-persons are due less consideration: "To grant *equal consideration* to two beings A and B is to hold that we should grant roughly equal moral weight or importance to *A's and B's (prudentially) comparable interests."* (DeGrazia 2008, 187) For example, when normal adult human beings and non-person sentient animals have comparable interests, those of the person possess more moral weight because of the more complex psychological relationship which the normal adult human has, which affirms that persons possess greater moral status than

sentient non-persons.

The unequal interests model holds that it is worse to kill or harm a person than a sentient non-person because the *equal considerations* to which persons and sentient non-person are entitled grants them equal moral weight *only in cases* of comparable interests (DeGrazia 2008, 188). When the interests of these beings are not comparable, then the party with the strongest interest can be said to have the greatest moral status. For example, the interest in remaining alive seems to be non-comparable between persons and non-persons since persons lose much more by their death (for example, their family life) than sentient non-persons. It is worth mentioning that under the unequal interests model equal consideration is due to all sentient beings' interests, but only when they are comparable.[12]

Before moving forward I will, lastly, make explicit that throughout this work I am taking for granted that the destruction of human embryos for biomedical research is morally acceptable, and also that the derivation of human embryonic stem cells from them is morally acceptable.[13] I am assuming this because human embryos do not possess the morally salient features that would grant them moral status: they do not possess an *actual capacity* for sentience nor that for rationality, even if they have the potential to possess both. Detailed arguments as to why this is so can be found in Harris (2006) and Mary Ann Warren (2000).

One could argue that Liao's account shows that they do possess such morally salient features because they possess the *material basis for moral agency*. My response to this rejoinder is that Liao's account is a version of the potentiality argument, and this argument is found wanting. The most popular version of the potentiality argument asserts that human embryos are as morally worthy as normal human adults because they have the potential to be rational and sentient (Manninen 2007). Another version of the potentiality argument maintains that *possessing* such potential is what makes them morally worthy, for example possessing the material basis for moral agency. The main problem with this second version of the potentiality argument is that somatic cells possess the potential to become human embryos, as cloning has shown. Thus it follows, on Liao's account and this potentiality account, that all of our somatic cells are as morally valuable as normal human adults are, which is evidently absurd. Even if it

[12] At this point I will not discuss the differences between a sliding scale moral status theory and a two tier moral status theory. I will not do so since in the paper 'The Ethics of Killing Human/Great-Ape Chimeras for their Organs: A Reply to Shaw Et Al.' I explain what these theories entail, and some of their theoretical shortcomings.
[13] This is particularly relevant in the paper 'Ethical Aspects of Creating Human/Nonhuman Chimeras Capable of Human Gamete Production and Human Pregnancy'.

was shown that I am fundamentally wrong, and that the intentional destruction of human embryos and human embryonic stem cell research is morally impermissible this would not close the door to the cases that I am discussing in the main body of this work. Why not? Because, in principle, induced pluripotent stem cells would allow for the creation of the chimeras that I discuss.[14]

Having presented a panorama of the moral status question, I can now move on to examine what is to be harmed and how human/nonhuman chimeras can be harmed.[15]

4.2 HARM

Any piece of work that examines the creation and use of part-human entities in medical research necessarily needs to explore the notion of harm and what is to be harmed. The first thing to note is that when we talk about harm we assume that only sentient beings can be harmed, by which we mean that only beings that have the subjective capacity for experiencing pain and pleasure can be harmed. I cannot harm a body of water by hitting it with a stick, and neither can I harm a soap bubble by popping it. On the other hand, a person can harm a toddler if she hits her with a stick. A second thing to note is that to be harmed means to be in a certain kind of *state*: to undergo harm is either to be put into or to be in a state where one is in a bad condition (Hanser 2008, 421). Broadly speaking there are two accounts of harm: comparative accounts of harm and non-comparative accounts of harm.

Non-comparative accounts of harm maintain that:

> [T]o suffer harm is to come to be in—or perhaps better, is simply to be in—a certain sort of non-comparatively bad state. It is to come to be in (or is simply to be in) a state in which one fares, not worse than one fared, or would have fared, in some alternative state of affairs, but simply badly. The seriousness of a given harm, according to this

[14] For a recent, comprehensive work on the morality of stem cell research see Cohen (2007), Hyun (2013) and Devolder (2015).

[15] The grounds for moral status that I have presented here are not the only ones that exist. While most of them gravitate around mental capacities, there are at least two theories of moral status that radically depart from an *only mental capacities approach*. These are: relational theories of moral status and intentional theories of moral status. According to relational accounts, a being's moral status is not only dependent on the inherent capacities that it possesses but it can be either enhanced (Steinbock 2011), or completely modified (Kittay 2005, 2009) in respect of the relations in which it stands with other beings that possess higher moral status. Intentional accounts of moral status, on the other hand, hold that in beings with higher moral status intentional actions can modify the moral status of beings with lower moral status. For example, according to this theory entering into a 'rearing-relationship' can change the moral status of the being with a lower moral status (Jaworska and Tannenbaum 2014; 2015). For a critique of this position see DeGrazia (2014). For a comprehensive overview of the grounds of moral status see Jaworska and Tannenbaum (2013).

> way of thinking, is proportionate to the (non-comparative) badness of this state. (Hanser 2008, 422)

John Harris is among those that defend a non-comparative account of harm. He suggests that to be harmed is to be in a 'harmed condition', which he defines in the following way: "a harmed condition is defined relative both to *one's rational preferences* [emphasis added] and to conditions which might be described as harmful, not relative to normal species functioning but relative to possible alternatives" (Harris 2001, 384). For example, if I have a *rational preference* not to have achondroplasia then I can affirm that I am in a harmed condition by virtue of the fact that I have achondroplasia. Most comparative accounts of harm, as I will explain next, maintain that it *is not possible* to harm someone by 'bringing' her into existence, meaning that my parents did not harm me even if I have congenital achondroplasia. However, Harris believes that we *can* harm someone by 'bringing' her into existence: "Where B is in a condition that is harmed and A and/or C is responsible for B's being in that condition then A and/or C have harmed B" (Harris 1998, 110). This means, for Harris, that the parents of the person with achondroplasia *harmed her* if she has a strong rational preference not to have this condition.

One of the problems with Harris's account is that it is *too expansive*, as identified by Glover (2006, 13) and Purshouse (2015, 4), given that we can have many rational preferences that are unfulfilled by our bodily conditions but that nonetheless seem to be non-harmful. For example, I can have a rational preference for being two meters tall, having brown eyes, and being left handed. If I have those rational preferences then I can affirm that my parents harmed me because they are responsible for me being in a state that is not the one I have a rational preference to be in. Furthermore, it seems that I can affirm that I have been harmed by my parents if I have a rational preference to have wings and I do not possess them. This account stretches the notion of harm too far, to the point that all people have been harmed by their birth in some sense or other.

Another non-comparative account of harm is defended by Guy Kahane and Julian Savulescu (2012). According to them deviating from what is *species-statistically normal* provides the best explanation for what it is to be in a harmed state. It is important to realise that they are not talking about biological normalcy but about statistical normalcy. For example, when (A) causes (B) to be in a condition that is below the statistical norm we can assert that (A) has harmed (B). Kahane and Savulescu's account explains why becoming blind at a young age is a harm (because it deviates from what is statistically normal), whereas not possessing a IQ of 160 is

not a harm (this latter case cannot be explained by Harris's account). A problem with this is that if the majority of the population went blind at the same time then being blind would no longer be considered as being in a harmed state, as it is now the statistical norm. This seems absurd, as sudden blindness would impede many people's lives and would set their interests back in a substantial way. Glover provides us with an alternative example. He asks us to image a world where HIV/AIDS has spread among the majority the population. Under the statistical account proposed, those that contract HIV/AIDS could not be said to be harmed by the disease, which is clearly false (Glover 2006, 12). A further problem is that if someone had a condition that placed her outside the statistical norm but which made her flourish, and she is then 'cured' and so loses her abilities then we cannot say that she has been harmed by the loss, which is clearly wrong (Gardner 2015).

In addition to the four aforementioned problems with non-comparative accounts of harm there is the issue that it is seems impossible to accurately establish what makes a state of affairs non-comparatively bad, without falling into the same problems as the statistical normalcy and the rational preferences accounts.

Comparative accounts of harm, on the other hand, maintain that "to suffer harm is to be put into a certain sort of *comparatively bad state* [emphasis added]—a state that is worse for one than some relevant alternative state." (Hanser 2008, 421) In a broad sense, comparative accounts of harm compare X against X*. Maybe the most famous comparative account of harm is that developed by Joel Feinberg (1984). For Feinberg, an action, or inaction, performed at time T1 harms someone (A) if it causes (A) to be worse off at a subsequent time T2 than she would have been at T2 had the agent not interacted with, or acted with respect to, (A). Feinberg's account is a *subjunctive historical account of harm*. In his words: "A harms B only if his wrongful act leaves B worse off than he would be otherwise in the normal course of events insofar as they were reasonably foreseeable in the circumstances" (Feinberg 1986, 153). It may seem that we can only be worse off in relation to how things were previously, in the past, but this is not the case. Imagine that someone will become an astronaut on Friday but that on Thursday she is illegally detained. While she is no worse off than before, given that on Thursday she was also not an astronaut, she is still harmed by being detained because she is worse off than she would otherwise be had there been no detention.[16]

[16] This is a modified version of Feinberg's 'Miss America contestant' example (Feinberg 1986, 149).

In addition to this kind of comparative harm account (where we compare 'counter-facts'), there are also *temporal accounts of harm*. According to a temporal account, an action, or inaction, realised at time T1 is harmful to (A) if and only if it causes (A) to be worse off at some later time T2 that she was at T1. For example, if my dog was hit by a bike and one of its legs was broken, we could assert that my dog was harmed because it is obvious that it was better off before it was hit by the bike. An obvious problem with temporal accounts of harm is that *worsening* is held both as a necessary and sufficient condition for determining if someone has been harmed, but this seems not to be the case (Williams 2014, 57). For example, if I could not walk due to a bad hip, and had an operation to fix this but the surgeons did a mediocre job and left me with a limp I could not state, under the temporal account of harm, that I was harmed since I am *no worse off* than before. In the past I could not walk, now I can walk with a limp. On the other hand, a subjunctive historical account of harm easily explains why I have had been harmed in the case of the mediocre operation. Given this problem with the temporal account of harm, a subjunctive historical account should be preferred.

Under comparative accounts of harm reproductive scenarios cannot be regarded as *causing harm*, because there is no prior state against which we could compare the creature's situation; this is the *non-identity argument* (Boonin 2008). For example, (A) cannot claim that her parents harmed her by virtue of the fact that she is congenitally blind since there is no scenario in which she could have been sighted. If her parents chose to have a sighted child then (A) would not exist because the conditions of the conception would change and thus the gametes that gave raise to (A) would not have fused.[17] While this is the case, there is one procreative act that merits special attention. An act which 'brings' a child into existence with, for example, such a poor quality of life that it would have been better for the child to never have been born. These cases are known as *wrongful life cases.* Even if we cannot claim that 'bringing' such beings into existence harms them, we have to accept that their existence is inherently burdensome for them and that we have strong moral reasons to stop their suffering.

At this point I need to make clear what it is to be harmed in the morally relevant sense of the term. I can be struck by a rock-fall while walking at the bottom of a cliff and this would cause me harm, but it would not cause me harm *in the morally relevant sense* of the term. For a harm

[17] There are some that hold that *it is counterintuitive* to hold that reproductive choices cannot harm the people that they 'bring' into existence. Those who hold that there is something puzzling about certain reproductive choices, for example choosing for disability, have to explain how is it that they can harm those that they create. This is known as the non-identity problem (Parfit 1984; Roberts 2015). See also Boonin (2008), who successfully explains why there is no such thing as a non-identity problem.

to occur in the morally relevant sense, it needs to be linked to the act or omission of a free rational agent (i.e. a moral agent). Such actions or omissions, performed by a moral agent, can constitute a *wrong*, but they are wrongs only in the absence of a satisfactory justificatory reason. There are actions that cause harms but that are not wrongs (being washed away by a wave), there are actions that cause bodily-harmless harms and are wrongs (the astronaut case, if the detention was unwarranted), and there are actions that cause harms and are wrongs (a person cutting my leg with an axe without proper justification for doing so). For a further discussion on harm see Hanser (2008) and Williams (2014).

In addition to comparative and non-comparative accounts of harm, we can distinguish between person-affecting harms and impersonal harms (or non-person-affecting harms). Person-affecting accounts of harm maintain that for a harm to be a harm it must harm *someone.* This means that it is a *necessary* condition for harm that a particular individual is affected. Impersonal accounts of harm, on the other hand, maintain that an action can be harmful without harming anyone in particular. For example, imagine a society where children are born in a condition that decreases their overall amount of wellbeing. We cannot claim that the children have been harmed, under a comparative account of harm, but someone can posit that harms have ensued in an impersonal way. They would maintain that this society is overall worse off than one where the same amount of non-disabled children were born. Impersonal harm, in fact, is a free-floating harm that does not attach to any particular individual. Because there are well document problems with the notion of impersonal harm, I favour a *person affecting notion* of harm. In what follows I briefly examine some of the problems of an impersonal account of harm.

A first issue with an impersonal account of harm, is that this notion is intuitively difficult to grasp. How can harm ensue if no one is made worse off? A second issue with an impersonal account is that it is committed to the view that certain values (for example, welfare or happiness) should be sought for their own sake (Williams 2014, 46). A third issue with an impersonal account is that, in order to avoid harm, we would have to selectively reproduce with the aim of increasing the amount of that which makes life worth living (e.g. pleasure, desire satisfaction). For example, if a society highly regarded cheerfulness, and this trait was associated with the presence of certain genes, then avoiding harm would mean coupling reproduction with prenatal genetic diagnosis to choose for those embryos that possessed these genetic characteristics. In the end we would be morally compelled to create a large amount of children with the genes that predispose for cheerfulness, if this was possible, to avoid

impersonal harm.

One final issue, which I regard as the most severe problem for an impersonal account of harm, is what Parfit calls the 'repugnant conclusion'. The 'repugnant conclusion' is best presented with an example:

> For any possible population of at least ten billion people, all with a very high quality of life, there must be some much larger imaginable population whose existence, if other things are equal, would be better, even though its members have lives that are barely worth living. (Parfit 1984, 342)

If what is important is the cumulative amount of what makes life worth living then we must accept that both population sets could fare equally well when considered from an overall perspective. Even more so, for example, a "huge population of low-quality but worthwhile lives would be considered morally preferable to a smaller population with a higher quality of life" and this seems deeply problematic (Bennett 2014a, 35).

Even when the problems associated with impersonal harm might appear to be merely academic this is not true. The issue of harm is of paramount *practical importance* for when discussing the morality of selecting for or against disability, for example (Hayry 2004; Bennett 2009, 2014a, 2014b). Most mainstream medical ethicists regard disability not as *mere-difference* but as *bad-difference*, among them Harris (2001). For someone to have a disability is for them to be worse off. If we should abide by an impersonal account of harm, in the sense of choosing the course(s) of action that would generate a world with more of what makes it better, then it would follow that we should *select against* disability. This would follow given that under this account disabled people would possess less of what makes the world better.

Throughout this thesis I endorse a person-affecting subjunctive historical account of harm, given that it is the most satisfactory account of harm that presently exists. Now that I have explained what I understand by 'moral status' and which account of harm I endorse, I can move on to present a summary of the articles that compose this thesis.

5. ARTICLE SUMMARIES

5.1. ARTICLE I: HUMAN DIGNITY AND THE CREATION OF HUMAN/NONHUMAN CHIMERAS

5.1.1. ABSTRACT

In this work I present a detailed critique of the dignity-related arguments that have been advanced against the creation of human/nonhuman chimeras that could possess human-like

mental capacities. My main claim is that the arguments so far advanced are incapable of grounding a principled objection against the creation of such creatures. I conclude that these arguments have one, or more, of the following problems: (a) they confuse the ethical assessment of the creation of chimeras with the ethical assessment of how such creatures would be treated in specific contexts (e.g. in the laboratory), (b) they misrepresent how a being could be treated solely as means towards others' ends, (c) they fall short of demonstrating how humanity's dignity would be violated by the creation of such entities, and (d) they fail to properly characterise the moral responsibilities that moral agents have towards other moral agents and sentient beings.

5.1.2 DETAILED SUMMARY

Within this paper I critically examine the dignity-based arguments that have been advanced against the creation of human-to-nonhuman animal chimeras that could possess human-like mental capacities. I focus on the arguments that have been advanced by Karpowicz et al. (2004, 2005), Johnston and Eliot (2003), de Melo-Martín (2008), and MacKellar and Jones (2012). I start by investigating the most prominent definitions of what 'human' dignity is, those that have been advanced within the chimera ethics literature, and by pointing out some of the problems of using these definitions to ground arguments against the creation of human-to-nonhuman animal chimeras.

Afterwards, in the main section of the article, I examine eleven objections against the creation of human-to-nonhuman animal chimeras that have at their base the concept of 'human' dignity; I do so from a species neutral position. I conclude that all the arguments that so far have been advanced against the creation of such chimeras are found wanting, for at least one of the following reasons: (a) they fail to properly distinguish between the moral problems that arise from creation acts from the moral problems that arise from their treatment once they exist, (b) they misconstrue what it is to be treated solely as a means towards others' ends, (c) they fail to properly show how humanity's dignity would be debased by the creation of human-to-nonhuman animal chimeras, and finally (d) they do not consider the moral duties that moral agents would have towards human-to-nonhuman animal chimeras with human-like mental capacities, regardless of the intention for which they were created.

5.2 ARTICLE II: THE ETHICS OF KILLING HUMAN/GREAT-APE CHIMERAS FOR THEIR ORGANS: A REPLY TO SHAW ET AL.

5.2.1. ABSTRACT

The aim of this paper is to critically examine David Shaw, Wybo Dondorp, and Guido de Wert's arguments in favour of the procurement of human organs from human/nonhuman-primate chimeras, specifically from great-ape/human chimeras. My main claim is that their arguments fail and are in need of substantial revision. To prove this I first introduce the topic, and then reconstruct Shaw et al.'s position and arguments. Next, I show that Shaw et al. (1) failed to properly apply the subsidiarity and proportionality principles; (2) neglected species-overlapping cases in their ethical assessment; (3) ignored the ethics literature on borderline persons; and (4) misunderstood McMahan's two-tiered moral theory. These mistakes render an important part of their conclusions either false or problematic to the point that they would no longer endorse them. Finally I will briefly mention a possible multipolar solution to the human organ shortage problem that would reduce the need for chimeras' organs.

5.2.2 DETAILED SUMMARY

In this paper I critically examine the morality of killing human/great ape chimeras for their human organs. In order to do so I present a detailed response to Shaw et al.'s (2014) 'Using Non-Human Primates to Benefit Humans: Research and Organ Transplantation'. In the first part of the paper I introduce the human organ shortage crisis topic and I reconstruct Shaw et al.'s position on nonhuman animal research and moral status.

Afterwards I explain why they think that neither a cognitive capacities account of moral status nor McMahan's Time-Relative Interest Account are capable of answering whether it is morally permissible to kill human/primate chimeras for their human organs. I also present why they believe that the proportionality and subsidiarity principles can provide us with a clear-cut answer to the question of in what circumstances it would be morally permissible to kill human/primate chimeras for their human organs. While discussing this I note how their position would apply to the case of killing human/great-ape chimeras.

Having reconstructed their position I revisit the discussion on moral status, in order to show that Shaw et al. mischaracterise how a two-tier moral theory would deal with the killing of human/primate chimeras. At the same time, I address the question of what moral status great apes do possess and defend the position that great apes should be considered borderline persons. With this as a background I investigate how great apes should be treated according to

a two-tier moral theory, and I advocate for a level-up solution to the problem of borderline persons. Thus I defend that in principle it is immoral to kill human/great ape chimeras for their organs.

5.3 ARTICLE III: ETHICAL ASPECTS OF CREATING HUMAN/NONHUMAN CHIMERAS CAPABLE OF HUMAN GAMETE PRODUCTION AND HUMAN PREGNANCY

5.3.1. ABSTRACT

In this paper I explore some of the moral issues that could emerge from the creation of human/nonhuman chimeras capable of human gamete production and human pregnancy. First I explore whether there is a cogent argument against the creation of human/nonhuman chimeras that could produce human gametes. I conclude that so far there is none, and that in fact there is at least one good moral reason for producing such types of creatures. Afterwards I explore some of the moral problems that could emerge from the fact that a human/nonhuman chimeras could become pregnant with a human conceptus. I focus on two sets of problems: problems that would arise by virtue of the fact that a human is gestated by a nonhuman creature, and problems that would emerge from the fact that such pregnancies could affect the health of the human/nonhuman chimeras.

5.3.2 DETAILED SUMMARY

This paper covers two issues: what are the moral problems related to the creation of human-to-nonhuman animal chimeras capable of human gamete production, and what moral problems would be generated by a human pregnancy within a human-to-nonhuman animal chimera.

I start by examining three arguments against the creation of human-to-nonhuman animal chimeras capable of human gamete production: a general argument against the creation of chimeras, an intrinsic value argument, and an instrumental value argument. I show that none of these arguments mount a successful case against creating chimeras capable of human gamete production. Afterwards I examine three arguments for creating chimeras capable of producing human gametes: a saving persons argument, an unburdening women argument, and a restoration of fertility argument. I show that of these three arguments the strongest is the saving persons argument.

In the second part of the paper I examine some of the ethical problems that could emerge from the reproduction of human-to-nonhuman animal chimeras that produce human gametes. I present a taxonomy of possible problematic issues regarding the human pregnancy of a

chimera. I concentrate on the question of whether we are morally required to terminate such human pregnancies. I defend the position that we are not morally obliged to terminate them, with the exception of wrongful life cases. I also show that the moral problems that could emerge from a chimera pregnancy in some sense mirror those that emerge from pregnancies of fully incompetent familyless women. At the end of the paper I address how the interests of the human-to-nonhuman animal chimeras could be affected by the human pregnancy.

5.4 ARTICLE IV: KILLING HUMAN/PIG CHIMERAS FOR THEIR HUMAN ORGANS: EXPLORING THE WELFARE ISSUES

5.4.1. ABSTRACT

In this paper I further examine the chimera welfare issues that have emerged from assessing the morality of using human/pig chimeras as human organ sources. First, I briefly introduce the topic of chimera-generated human organs. Secondly, I point out the gaps in recent academic work on the ethics of harvesting human organs from human/pig chimeras. Thirdly, I examine how obtaining human organs from human/pig chimeras relates to the meat-eating debate, and how the latter illuminates the moral permissibility of the former. Fourthly, I examine whether it is unfair to kill human/pig chimeras for their human organs. Fifthly, I examine whether the way in which the overall wellbeing of the chimeras would be impacted would morally prevent us from using them for their human organs. Finally, I examine if it is immoral to carry out chimera research in order to produce transplantable human organs in light of the amount of nonhuman animals and chimeras that would have to be experimented upon and killed.

5.4.2 DETAILED SUMMARY

In this paper I first highlight the research shortcomings of Shaw et al.'s (2015) work "Creating Human Organs in Chimaera Pigs: An Ethical Source of Immunocompatible Organs?" I prove that these authors failed to properly acknowledge and take into consideration the relevant academic literature that exists on chimera ethics, and that specifically deals with the objections that they present and address in their work.

In the second section of the paper I investigate and expand on the responses that Shaw et al. provide to four chimera welfare objections: the meat-eating objection, the unfairness objection, the overall wellbeing objection, and the numbers objection.

While examining the meat-eating objection, I note that an analogy between killing nonhuman animals for their meat and killing human/pig chimeras for their human organs can be made

when the person in question would die because they needed the meat or the organ for survival. I show that the meat-eating debate in fact throws light on when killing human/pig chimeras for their organs is morally permissible. In order to examine the unfairness objection, I point out that we need to obtain empirical data in order to assess whether it is true that if all humans donated their organs, after death for example, there would still not be enough to solve the human organ scarcity problem, and thus that it is fair to kill human/pig chimeras for their human organs. I also examine whether it is morally permissible to kill human/pig chimeras to obtain patient-derived iPS cell organs. In order to do this I compare the interests at stake: those of the person and the human/pig chimera. I also investigate if the fact that the human/pig chimera's life-span would be reduced morally precludes us from killing them for their human organs.

The overall wellbeing objection, at least as Shaw et al. present it, supposes that we would be morally required to kill the human/pig chimeras after they are used for their organs. I put this assumption into question. I maintain that if the harvesting of the organs would not necessarily kill the human/pig chimera, and they could afterwards have worthwhile lives, then they should not be killed. I defend that to do otherwise would be immoral. Finally, I examine whether the total number of nonhuman and part-human creatures that would be killed and harmed in the process of creating technology that would make human-transplantable organs available within human/pig chimeras makes this research avenue immoral. To do this, I first unpack what the subsidiarity principle would require from us in terms of the morally permissible conditions that would allow for such research to be carried out. I also examine if it is morally permissible to kill human/pig chimeras for the sake of non-person sentient human beings or non-sentient non-person human beings.

PART II.
THE ARTICLES

6. ARTICLE I: HUMAN DIGNITY AND THE CREATION OF HUMAN–NONHUMAN CHIMERAS

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6.1 INTRODUCTION

In this paper I present and critically examine the dignity-related arguments that have been advanced against the creation of human–nonhuman chimeras that could possess human-like mental capacities. The paper is divided into three main sections. In this first section I present a brief account of what chimeras are and what role they play in biological sciences research. In the second section I examine, and show the pitfalls of, the human dignity definitions that for the most part have been used when arguing against the creation of such chimeras. In the third section I investigate the dignity-related arguments advanced by Karpowicz et al. (2004, 2005), Johnston and Eliot (2003), de Melo-Martín (2008), and MacKellar and Jones (2012) and show why they are found wanting.

While Karpowicz et al.'s arguments have been examined before,[18] this paper adds to the current discussion on the ethics of creating human–nonhuman chimeras in several new ways. First, I present new counterarguments against Karpowicz et al.'s position. Second, I explore, for the first time, the arguments advanced by Johnston and Eliot, de Melo-Martín, and MacKellar and Jones. Finally, I show that from a species neutral perspective the dignity-related arguments that have been advanced against the creation of chimeras with human-like mental capacities do not only apply to the creation of human–nonhuman chimeras that are *preponderantly nonhuman*, but also apply to human–human chimeras, and to human–nonhuman chimeras that are predominantly human.

6.1.1 THE MYTHOLOGICAL CHIMERA

We owe the canonical characterisation of the mythological Chimera to the Ancient Greek epic poet Homer. In the sixth book of the Iliad (179–181) Homer narrates how Glaucus, captain in the Lycian army, is going to face the Greek hero Diomed in single combat. Prior to their fight, Diomed asks who is he to face for fear that his opponent might be a god. Glaucus responds by telling the story of his lineage, and reveals that he is the grandson of Bellerophon, who by

[18] For previous critiques of Karpowicz et al.'s arguments see: Streiffer (2005), Robert (2006), Ravelingien et al. (2006), Baylis and Fenton (2007), DeGrazia (2007), de Melo-Martín (2008) and Cooley (2008).

command of King Iobates killed Chimera. It is in these lines of the Iliad that Homer depicts this mythological creature:

> First, dire Chimaera's conquest was enjoin'd;
> A mingled monster of no mortal kind!
> Behind, a dragon's fiery tail was spread;
> A goat's rough body bore a lion's head;
> Her pitchy nostrils flaky flames expire;
> Her gaping throat emits infernal fire. (Homer 1836)

Homer's characterisation is not the only one to be found in Ancient Greek mythology. In the Theogony (319–325), Hesiod describes Chimera not as a one-headed being with the body parts of three different animals, but as a creature composed of the heads and body parts of three different animals:

> She [Echidna] was the mother of Chimaera who
> breathed raging fire, a creature fearful, great, swift
> footed and strong, who had three heads, one of a
> grim-eyed lion, another of a goat, and another of a
> snake, a fierce dragon; in her forepart she was a lion;
> in her hinder part, a dragon; and in her middle, a goat,
> breathing forth a fearful blast of blazing fire. (Hesiod
> 1914)

In the broader mythological context the term chimera has come to mean any entity that is constituted of different parts of different kinds of animals. For example, sirens, harpies, centaurs and the Minotaur are considered to be chimeric entities (Brem and Anijar 2003). Chimeras, in this wider sense, are depicted in Ancient Greek mythology both as dangerous creatures—like the sirens, who succeeded at shipwrecking sailors, and the Minotaur, who devoured those sent into his labyrinth—and as noble creatures—like the centaur Chiron, who trained Heracles.

6.1.2 NON-MYTHOLOGICAL CHIMERAS

In the second half of the twentieth century, interspecific chimeras 'escaped' the bounds of mythology and literary studies to be intentionally created and studied in life sciences faculties around the world.[19] Chimeras, contrary to transgenic animals, are not created by the insertion of one, or multiple, exogenous genes. They are beings formed by combining whole cells of

[19] It is worth mentioning that although contemporary chimeras are tamer than those depicted by the Ancient Greeks we cannot discard the possibility that someone could find a way to weaponise a chimeric being. (Scott 2006; Savulescu 2013).

genetically different organisms into a single organism.[20] The UK Academy of Medical Sciences provides this definition, which I will endorse throughout the paper:

> Chimæras are formed by mixing together whole cells originating from different organisms. The new organism that results is made up of a ‘‘patchwork’’ of cells from the two different sources. Each cell of a chimæra contains genes from only one of the organisms from which it is made. (…) Primary chimæras are formed by mixing together two early embryos, or an early embryo with isolated embryonic cell types obtained from a different embryo or cultured stem cell line. The resulting chimæra has cells of different origins, in many tissues. Secondary chimæras are formed experimentally by transplanting (or grafting) cells or tissues into animals at later stages of development, including late fetal stages, post-natal or even adult animals. The donor cells are only present in a few tissues. (The Academy of Medical Sciences 2011, 18–19)

Two of the first chimeras to be intentionally created were a goat-sheep chimera and a quail-chick chimera (Fehilly et al. 1984; Le Douarin et al. 1974; Balaban et al. 1988). Contrary to these *intentionally* created chimeras they can also occur naturally, for example when two non-monozygotic early human embryos fuse inside the womb (Tippett 1983; Norton and Zehner 2008).

Intentionally created chimeras can be intraspecific—when the cells that create such creatures originate within organisms (or cultured cell lines) that belong to the same biological species—or they can be interspecific—when the cells that create such beings originate within organisms (or cultured cell lines) that belong to different biological species (Xiang et al. 2008). It is worth noting, as the definition of the Academy of Medical Sciences points out, that the production of chimeras is affected by the number of engrafted cells, the origin of those cells, and by the time of the mixing. This means that alterations in these variables would produce different outcomes in respect to the kinds of beings produced. Having this in mind should guard us against what John Harris calls the ‘mermaid myth’: the idea that if we create a chimeric entity the resulting creature would necessarily possess easily recognizable phenotypic features from all ‘progenitors’ (Harris 2011).

Along with chimeras and transgenic animals there is another type of being that can be created both naturally and through biotechnology: hybrids. Hybrids are the offspring of organisms that belong to different biological species. For example, a mule is a hybrid produced by a female horse and a male donkey. Humans can ‘produce’ hybrids in two ways: through artificial reproductive techniques (artificial insemination or in vitro fertilization) or by setting the

[20] For a discussion about the possible chimeric entities that could exist see Greely’s (2003) *Defining Chimeras… and Chimeric Concerns*.

conditions so a fertile male and female of different biological species mate. The viability of the hybrids, in both cases, will depend on biological factors.

6.1.3 HUMAN–NONHUMAN CHIMERAS

Chimeras, primary and secondary, can be produced with human components. In biological sciences human–nonhuman chimeras (henceforth HNH-chimeras) have been used in research into human haematopoiesis, the development and function of the immune system, infectious diseases, autoimmunity, cancer, and regenerative medicine (Shultz et al. 2007). They have also been used as research tools for the creation of vaccines against deadly diseases such as malaria, dengue, Hepatitis B, HIV and Hepatitis C (Davis and Stanley 2003; Sacci Jr et al. 2006; Yauch and Shresta 2008; Legrand et al. 2009; Bhan et al. 2010); and have been employed for the study of human cell development, maturation and migration (Sun et al. 2007; Tam and Rossant 2003; Lapidot 2001).

The creation and use of most contemporary human-developed HNH-chimeras has not been seen to present new ethical concerns, other than those related to the destruction of human embryos, animal ethics and research ethics. In part, this has been the case because such entities have been predominantly constituted by nonhuman components. Nonetheless, the possibility of creating HNH-chimeras with brains composed largely of human brain cells has raised ethical concerns about the morality of such experiments (Greely et al. 2007). The main question is if it is morally permissible to create HNH-chimeras that would possess the capacities that are generally associated with 'human' dignity or personhood.4[21] For example, is it morally permissible to engraft sufficient human stem cells, or neural stem cells, into a great ape embryo so it develops normal human-like cognitive capacities?

In response to the possibility of creating HNH-chimeras with dignity, or personhood, related capacities, several authors have advanced dignity-related arguments in order to prove that doing so *would be immoral and should not be done*. Now, before examining such arguments (see Sect. 3.2.2 'Dignity and HNH-chimeras with human-like mental capacities

I will commence by emphasising a well-known problem with dignity-related stances: that there is no consensus about what dignity means (the term has even been regarded as a useless concept; Schroeder (2010); Macklin (2003)). Having this in mind, in the next section I will not

[21] Throughout the paper I will use the term 'person' to refer to beings that possess dignity conferring psychological capacities.

try to provide a final account of dignity, but I will critically examine the definitions that Karpowicz et al. (2004, 2005) have proposed.

6.2 'HUMAN' DIGNITY

Karpowicz et al. have argued that even when the creation of certain types of HNH-chimera is morally *unproblematic*, human dignity would be denied, undermined or denigrated by the creation of HNH-chimeras that possess human-like functional and emergent psychological capacities[22,23] (Karpowicz et al. 2004, 2005). Let's examine what they understand by human dignity.

In their 2004 paper Karpowicz et al. defined human dignity as a ''widely shared concept that refers to being worthy or respected because one is human'' (Karpowicz et al. 2004, 333). According to this definition, humans' moral value is grounded on their belonging to the *Homo sapiens* species (according to the common understanding of what 'human' means). Thus, any being that belongs to this biological species would possess human dignity, and any being that does not belong to it would not possess human dignity.

Karpowicz et al. go on to clarify that ''Human dignity is based on the recognition that human beings possess, will possess, or have possessed functional and emergent psychological capacities that indicate they are worthy of respect'' (Karpowicz et al. 2004, 333). We can assert that Karpowicz et al.'s definition of human dignity entails the following elements:

> (1) Human dignity refers to being worthy or respected because one is human.
>
> (2) Human dignity is based on the recognition that humans possess, will possess or have possessed functional and emergent psychological capacities that indicate they are worthy of respect.

There are two things that must be noted about this definition. First, that it does not explicitly state the sort of moral status beings with dignity possess. Let's remember that to state that an

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[22] Unless specified otherwise when I talk about functional and emergent psychological capacities I am talking about statistically normal human-like functional and emergent psychological capacities.

[23] Eberl and Ballard (2008, 45) have correctly asserted that it is largely unknown if the engraftment of undifferentiated pluripotent human stem cells into a nonhuman animal embryo could lead to the development of a functioning cerebrum supportive of self-conscious rational thought. Although, as Alter (2007) states, to imagine an ape-human viable hybrid or any other chimera that contains the best features of each may be to imagine science fiction I will proceed in this paper assuming that this might be possible. One case that partially supports this idea is the creation of human-mouse chimeras where their long-term potentiation ''was sharply enhanced (…), as was their learning, as assessed by Barnes maze navigation, object-location memory, and both contextual and tone fear conditioning.'' (Han et al. 2013, 342).

entity possesses moral status is to realise that ‘‘*in its own right and for its own sake, it can give us reason to do things such as not destroy it or help it’’* (Kamm 2007, 229). Even so, the authors implicitly assume, as it will become clear, that to possess dignity is to have a unique moral value.

Second, there is a tension between their two clauses. The source of this tension is that 1 is far more extensive than 2. For 1, being human is a necessary and sufficient condition for possessing human dignity, while for 2 being human is a necessary but not a sufficient condition for possessing human dignity. While it is embedded in both clauses that being human is a necessary condition for possessing dignity, the sufficiency requirements are different in each case.

Why is this important? It is so because on the one hand, on 1, every human being—from the moment of conception to the moment of death—possesses human dignity. For example, an anencephalic child possesses human dignity. While, on the other hand, on 2, there are some human beings that do not fulfil the conditions for possessing human dignity. Human beings that do not possess, will not possess and have never possessed functional and emergent psychological capacities cannot be recognized as possessing human dignity. For example, a child with genetically caused anencephalia. The question that Karpowicz et al. have to answer is how anencephalic child type cases fit into their account of human dignity without being inconsistent with a definition that includes both 1 and 2.

Baylis and Fenton think that the only way Karpowicz et al. can make their human dignity definition work is by endorsing the idea that belonging to a class that contains members that possess certain cognitive or emotional capacities (thus effectively renouncing to 2) is what grants such moral worth:

> At the same time, both of these points in tension [what I have called 1 and 2] rely on an implicit appeal to a principle conferring intrinsic moral value on *x* if *x* belongs to a class *A* that contains members who manifest certain cognitive or emotional capacities, even if *x* herself does not. *X* is thus valued, or possesses moral significance, because *x* is a member of class *A*. In this case, the class is all humans. (Baylis and Fenton 2007, 201)

If this is the case then a better way of expressing Karpowicz et al.’s human dignity definition would be:

> (1) Human dignity refers to being worthy or respected because one is human.
>
> (2’) Human dignity is based on the recognition of being worthy or respected because one belongs to the *Homo sapiens* species, which is characterised by the fact that

normally humans possess, will possess or have possessed functional and emergent psychological capacities.

There are at least two problems with this 'new' approach to human dignity. The first is that even when it clearly explains who possesses human dignity it does not explain why belonging to such a class (i.e. the *Homo sapiens* species) confers such moral worth—this objection has been long noted in animal ethics literature. It is simply stated, but not explained, that any member of the class *humans* has dignity. Now, if they maintain that species belonging *is what* confers such unique value then this definition is speciesist. Speciesism, in this case anthropocentrism, asserts that our human biological commonality confers us superior moral worth than those who are not members of our species (Singer 2009). Just as with racism and sexism, speciesism extracts a normative conclusion (humans have more moral worth than all other creatures) from an arbitrarily chosen morally insignificant fact. To be a member of the *Homo sapiens* species ''is simply a matter of biology: It is to be an organism that has descended from a particular branch of the tree of terrestrial life, an organism whose genome lies somewhere within a particular range, or the like'' (DeGrazia 2007, 312). Finally, species belonging appears not to be what confers dignity. For example, if we were to find extraterrestrial life forms with mental capacities like ours we would most certainly accept that they possess dignity. For example, if in real life we found a Vulcan alien—Spock—we would accept that killing him is tantamount to killing a human person.

The second problem that arises from this account is that if we concede that being human (i.e. belonging to the *Homo sapiens* species) is a *necessary* condition for possessing *human* dignity, then using such a definition to construct a *general argument* against the creation of HNH-chimeras with human-like mental capacities becomes deeply problematic. Why? Because certain HNH-chimeras with human-like mental capacities cannot be categorised as being human, and therefore they would not fulfil a necessary condition for possessing dignity: *belonging to the Homo sapiens species*. For example, a human-chimp chimera that is completely chimpanzee except for its human brain would certainly not classify as belonging to the *Homo sapiens* species. If we accept this, then we also have to accept that human dignity arguments cannot be raised against the creation of HNH-chimeras with human-like mental capacities in *all cases*. Therefore, even if Karpowicz et al.'s arguments were correct, the creation of certain HNH-chimeras with human-like mental capacities would not violate human dignity. Resnik (2003, 35) has made a similar point when commenting on the possibility of

patenting a human embryo with chimpanzee genes: ‘‘I argued that it would threaten but not violate human dignity because the humanzee would not be a human being’’.

One could challenge the previous point by arguing that HNH-chimeras belong to the *Homo sapiens* species by virtue of the engrafted cells, and thus have human dignity. A problem with this strategy is that those defending it would have to provide a reasonable explanation for how this happens and where the limits lie (i.e. how and under what circumstances the engraftment of X number cells ‘makes’ a nonhuman animal belong to the *Homo sapiens* species).[24] They would also have to explain whether ‘species transition’ is bidirectional, or not, in cases concerning human beings (i.e. if we engraft X amount of nonhuman-animal cells into a human would such a human ‘become’ part of that nonhuman animal species). As Streiffer (2005, 357) asks, ‘‘when faced with an organism that has some human cells and some nonhuman cells, how is one to decide whether the organism is human, and hence, whether it is a human being?’’.

The tension between clauses 1 and 2 can be solved by appealing to an anthropocentric principle (i.e. reformulating 2 into 2’). However, the cost of maintaining such a definition of human dignity is that we are stuck with a speciesist account that cannot support a general dignity-based argument against the creation of HNH-chimeras with human-like mental capacities. This being the case, we need to look for an alternative human dignity account if we want to advance a general argument against the creation of such creatures.

6.2.1 A PSYCHOLOGICAL CAPACITIES ACCOUNT OF ‘HUMAN’ DIGNITY

There is another way in which to interpret Karpowicz et al.’s human dignity definition, so that it could support a general critique of the creation of HNH-chimeras with human-like mental capacities. This interpretation holds that what grants dignity is the possession of certain psychological capacities. In this instance, we need to reformulate 1:

> (1’) Human dignity refers to being worthy or respected because one is a human that possesses, will possess, or has possessed functional and emergent psychological capacities.
>
> (2) Human dignity is based on the recognition that humans possess, will possess or have possessed functional and emergent psychological capacities that indicate they are worthy of respect.

[24] The creation of intraspecific chimeras does not present this indeterminacy problem.

When we reformulate 1 we admit that there are some humans that do not, and cannot, possess human dignity—all those human beings that do not possess, will not possess and have never possessed functional and emergent psychological capacities. It becomes clear that Karpowicz et al. are embracing a potentiality account of moral worth,[25] and thus the number of humans that do not possess dignity are reduced to those that by means of their congenital constitution lack the potentiality to develop such psychological capacities. At this point, let's specify the mental capacities that they regard as conferring moral worth.

According to Karpowicz et al., human beings' moral worth does *not only* depend on the capacities for reasoning, choosing freely, and acting for moral reasons [as Kant (1998) proposes], or entertaining and acting on the basis of self-chosen purposes [as Gewirth (1982) asserts]. Karpowicz et al. (2005, 120) instead assert that what grants certain humans their unique worth are the previous capacities plus ''those for engaging in sophisticated forms of communication and language, participating in interweaving social relations, developing a secular or religious world-view, and displaying sympathy and empathy in emotionally complex ways''. For them, dignity is a cluster concept where none of the former capacities by itself is sufficient for possessing dignity, but when they appear together they paradigmatically point towards what it is to have dignity.

Now, if we accept that species belonging is a morally insignificant fact, then we have to accept that species membership in 1' and 2 should also be regarded as morally irrelevant. This being the case, we can actually remove this condition (namely, belonging to the *Homo sapiens* species) without any loss. In fact, the definition of human dignity that these authors provide in their 2005 paper could be interpreted as pointing in that direction: ''Human dignity is a widely shared notion that signifies that humans typically display certain sorts of functional and emergent capacities that render them uniquely valuable and worthy of respect'' (Karpowicz et al. 2005, 120).

It is important to note that this definition is not a direct quote from their 2004 paper, but a new definition that abandons 1, modifies 2 and specifies the value that human beings have. In fact, being human is eliminated as *a necessary condition* for possessing dignity, and thus leaves open the possibility for other beings to possess dignity. If a capacities-based interpretation of dignity is warranted then their assertion that ''The family of capacities associated with human

[25] There are different versions of the potentiality account. One of them is that human beings possess moral worth from the moment of conception because they have the potential to develop certain capacities that are not present during the first period of their development, that are morally worthy.

dignity seems to belong uniquely to human beings'' (Karpowicz et al. 2005, 122) could in fact be construed as claiming that *so far* there is no other being (biological or non-biological) known to humans that possesses such capacities.[26] Their second definition could be stated, in a species neutral fashion, as follows:

> (3) Dignity is a widely shared notion that signifies that some beings typically display certain sorts of functional and emergent capacities that render them uniquely valuable and worthy of respect.

Karpowicz et al. realise that if they adopt a capacities account of dignity then there are humans that could not be viewed as possessing it. Confronted with this scenario they embrace Alan Gewirth's position when dealing with so called 'marginal cases'.[27] For Gewirth (1982, 27–28) dignity is ''a characteristic that belongs permanently and inherently to every human as such''. A problem with this strategy is that Gewirth's stance is *inconsistent* with a logical implication of Karpowicz et al.'s capacities based approach—namely, that there are humans that do not possess dignity. The authors try to solve this inconsistency in the following way:

> We tend to ascribe it [dignity] to all humans, no matter how seriously impaired or ill they may be, because there is no clear agreement about just how many dignity-associated capacities a person must possess to be said to have human dignity. To avoid the possibility of mistakenly failing to treat those with severe disabilities as ends in themselves, human dignity proponents ascribe dignity to all humans. (Karpowicz et al. 2005, 121–122)

This solution can be formulated as:

> (4) We ascribe dignity to *all humans* because there is no agreed amount of dignity-related capacities one must possess in order to have dignity, and also to avoid the mistake of treating seriously impaired or ill humans as mere means rather than as ends in themselves.

Robert Streiffer has argued that such a solution is not warranted because there are clear cut cases where a human being does not possess such morally worthy capacities:

> [A]n appeal to uncertainty and disagreement seems implausible given that there is no real uncertainty or disagreement that a newborn fails to have the capacities they cite

[26] Karpowicz et al.'s qualifications for possessing dignity are so stringent (e.g. developing a secular or religious world-view) that no nonhuman animal appears to have them.

[27] The argument from marginal cases, or argument from species overlap, points out that ''the criteria that are commonly used to deprive nonhuman animals of moral consideration fail to draw a line between human beings and other sentient animals, since there are also humans who fail to satisfy them.''(Horta 2014, 142) For further discussion see: (Singer 2001; Horta 2014; Pluhar 2006; Dombrowski 2006; Kaufman 1998).

> and so would, on their view, clearly lack the special moral status that accompanies individuals with human dignity. (Streiffer 2005, 357)

While I agree with Streiffer that there are clear cut cases that do warrant such a solution, it must be said that Karpowicz et al. could claim that there is a problem with his counterexample: because they assume a potentiality account, Streiffer's new born counterexample does not work in all cases. It does not work because a new born possesses dignity in so far as she possesses the dignity-related capacities in a potential state.[28]

Karpowicz et al. are correct that there are cases where a 'prudential' solution is warranted (e.g. where the amount of capacities possessed by a being situates her in a grey area), but there are other cases where it is clearly not warranted (e.g. when humans, due to a congenital condition, do not possess the potential to develop such capacities). Given that there are cases where this solution is unwarranted (e.g. anencephalic cases), Karpowicz et al. should abandon it in its present form. If they do not then they will have to accept that they are proposing an *ad hoc* speciesist solution.

Karpowicz et al.'s dignity account can be interpreted in two ways. The first way has an explanatory gap, and cannot ground a general argument against the creation of HNH-chimeras with human-like mental capacities. We should therefore abandon it. The second interpretation, because it focuses on capacities and is species neutral, can be used to construct a general argument against the creation of such chimeras. Throughout the rest of the paper I will adhere to the second interpretation, although I will leave out Karpowicz et al.'s Gewirth-like solution to the species-overlapping cases given that it is not warranted. Now I will assess the dignity-related arguments that have been presented against the creation of HNH-chimeras with human-like mental capacities.

6.2.2 DIGNITY AND HNH-CHIMERAS WITH HUMAN-LIKE MENTAL CAPACITIES

(I) The first argument that Karpowicz et al. (2004, 333) propose against the creation of HNH-chimeras is that ''Chimeras, by combining the appearance and functional capacities of humans and animals, seem to risk denying human dignity''. The authors assert that the first part of this argument should be dismissed, because dignity has nothing to do with the outward appearance

[28] While I will not expand on the subject of potentiality, I must say that potentiality accounts generally have been found wanting. For a recent discussion see Stier and Schoene-Seifert (2013).

of HNH-chimeras or with the intuitions that such appearances might elicit from us. The argument, after removing its redundant section, could be expressed like this:

> (5) HNH-chimeras risk denying human dignity by combining the functional capacities of humans and nonhuman-animals.

However, we should also eliminate 'human', from 'human dignity', so to favour a species neutral dignity argument:

> (5') Chimeras risk denying dignity by combining the functional capacities of humans and nonhuman animals.

According to this argument—which is similar to that advanced by the US National Academy of Science (National Academies of Science 2005, 55)—the creation of HNH-chimeras whose psychological capacities are a 'combination' of human and nonhuman ones risks denying dignity. The first problem with this argument is that it is not clear *which HNH-chimeras* risk denying dignity. If it indicates that *all HNH-chimeras*—whose psychological capacities are a combination of human and nonhuman mental capacities—risk denying dignity (as it seems to imply), then it is easy to provide a thought experiment that calls this argument into question. Suppose that a human person gives her informed consent for her brain to be grafted with modified elephant neural stem cells, in order to treat a memory disorder. This action creates a HNH-chimera that 'combines' the functional capacities of humans and nonhuman-animals. Even so it does not appear to risk denying dignity, and if it does it is not clear why.

If the authors are instead suggesting that the creation of 'predominantly' nonhuman HNH-chimeras—where the nonhuman animal component belongs to a species that does not possess human-like psychological capacities—is what risks denying dignity then they face another problem: when we create a HNH-chimera that effectively combines human and nonhuman functional capacities we do not deny dignity but rather *a being with dignity is created*. For example, if we could engraft enough human neural stem cells into a pig embryo that it develops human-like mental capacities, then we would have created a HNH-chimera with dignity. The creation of this HNH-chimera does not deny dignity, as before chimerisation the pig embryo does not possess dignity to be denied.[29]

[29] It must be clear that even if nobody's dignity is denied in this case there can be other welfare considerations that should be taken into account when making a full ethical assessment of the creation of HNH-chimeras. For example, a chimerisation process, that is not identity affecting, could 'confer' dignity to a certain creature while at the same time it could impose serious bodily harms.

(II) The second argument that Karpowicz et al. advance states that 'human' dignity would be undermined by the transfer of emergent psychological human functions into *research subjects*. They claim:

> If such a chimera exhibited signs of emergent human mental capacities, conducting biomedical experiments upon it might be essentially equivalent to conducting the same experiments on a human person. Human dignity would be undermined by the transfer of emergent and supercellular psychological human functions into research subjects that by consequence would possess the same capacities themselves. (Karpowicz et al. 2004, 333–334)

The argument encompasses two elements and can be expressed as follows:

> (6) If a chimera exhibited signs of emergent human mental capacities, conducting biomedical experiments upon her might be essentially equivalent to conducting the same experiments on a human that possessed dignity.
>
> (7) Dignity would be undermined by the transfer of emergent and supercellular psychological human functions into research subjects that by consequence would possess the same capacities themselves.

It is true that if a HNH-chimera possessed the same mental capacities as a human person, then we should assess the morality of the procedures carried out upon her as if they were carried out upon a human person. But it is false that dignity would be undermined if the recipient of such capacities was a research subject that by virtue of the procedure had gained these capacities. If Karpowicz et al.'s argument is correct then the following case would also undermine dignity: suppose that scientists engraft normal human stem cells into a pre-term congenitally anencephalic child. Imagine that by virtue of this intraspecific chimerisation process this research subject is able to develop, otherwise unattainable for her, normal human mental capacities. Now, it is evident that this procedure does not undermine dignity by means of transferring emergent and supercellular psychological human functions *into a research subject* (in this case a human research subject).

Karpowicz et al.'s argument could also be interpreted as stating that dignity is undermined when dignity-possessing research subjects are not treated as possessors of dignity, a claim which is endorsed by de Melo-Martín (2008, 338) and Streiffer (2005, 362–366). It should be noted that if this is the true sentiment of the argument, then it cannot be advanced as a principled objection against the creation of HNH-chimeras with human-like mental capacities. Why not? Because such interpretation *disaggregates* the ethics of creating HNH-chimeras with human-

like mental capacities from the ethical evaluation of how research subjects are treated. At best such an argument would reveal something that everybody accepts, namely that moral agents should treat other beings according to their moral status. Greene et al. (2005, 386) have advanced a similar point in asserting that one option is to not create HNH-chimeras, and the other option is ‘‘to understand the mental capacities of engrafted animals and to treat them in a manner appropriate to their moral status’’. At this point we can reformulate 7 into 7’:

> (7’) Dignity cannot be undermined by the transfer of emergent and supercellular psychological human functions into research subjects that by consequence would possess the same capacities as human persons, but it can be undermined by the mistreatment that such subjects might receive from other moral agents.

(III) Karpowicz et al.’s third argument focuses on the impact that creating HNH-chimeras with human-like mental capacities would have on the possibility that humans could exercise their own dignity-related capacities:

> [A]n argument from human dignity would maintain that to create a human-nonhuman chimera would either diminish or wholly eliminate the possibility that humans could exercise the cluster of capacities and characteristics that are associated with human dignity, treating them solely as a means to others’ ends. (Karpowicz et al. 2005, 121)

To state that the mere creation of a being with dignity diminishes or eliminates the possibility that other humans (or other beings with dignity) could exercise their dignity-related capacities is mistaken. If this assertion was true then it would also be true that every time an extraterrestrial alien person is born, supposing that there are human-like intelligent aliens in the universe, her birth would somehow diminish or eliminate the possibility that humans could exercise their dignity-related capacities. To assume that every alien person’s birth leaves all human persons worse off in this sense is clearly false. The fact that another being with dignity is created does not affect humans’ ability to exercise their dignity-related capacities. DeGrazia (2007, 236), along these same lines, has rightly pointed out that if we coexisted with other hominid non *Homo sapiens* borderline, or paradigmatic, persons, their existence would not diminish or eliminate the possibility that we could exercise our dignity-related capacities. He provides the following example: if we were to find a living member of the *Homo floresiensis* species this would not diminish or eliminate the possibility that we, humans, could exercise our dignity-related capacities.

A more charitable interpretation of this argument could be offered: we could assume that Karpowicz et al. are not talking about *humans* (in ‘‘humans could exercise’’) but about *HNH-*

chimeras. Even so, the argument remains problematic. First let's see a reconstructed version of it:

> (8) An argument from dignity would maintain that to create a human–nonhuman chimera would either diminish or wholly eliminate the possibility that human–nonhuman chimeras could exercise the cluster of capacities and characteristics that are associated with dignity, treating them solely as a means to others' ends.

This revised version of the argument is problematic in two ways. The first problem mirrors that of the 'uncharitable' interpretation of it. How could the creation of HNH-chimeras with dignity-related capacities by itself cause that other HNH-chimeras could not exercise their dignity-related capacities? This seems plainly false. Second, even if the argument is to be understood as stating that to create a HNH-chimera would either diminish or wholly eliminate the possibility that she could exercise her dignity-related capacities, given that she will be treated solely as a means to others' ends, it remains problematic. First, it does not *necessarily* follow from the fact that HNH-chimeras with dignity-associated capacities are created that they would be treated merely as means towards others' ends. Here it is implied, incorrectly, that researchers would be oblivious to, or negligent of, the HNH-chimeras' moral status. Secondly, it is possible, as observed by most commentators, that researchers could overlook the chimera's moral status but it does not follow from this possibility that creating HNH-chimeras with human-like mental capacities would violate dignity. If this was true then it would also be true that slaves violate dignity when they intentionally have children that in turn will be slaves, given that such children are going to be treated solely as means to others' ends, and this is clearly false.

(IV) The fourth argument that Karpowicz et al. advance is grounded on the degree of functionality of the dignity-related capacities that HNH-chimeras would possess:

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

There are three problems with this line of argumentation. First, from a species neutral version of it, the implausible conclusion that we should not 'give' these necessary physical components (e.g. neural tissues) to certain humans that are congenitally severely cognitively impaired would follow. According to the argument, we should not give such physical components to

those congenitally severely cognitively impaired humans that have bodies where the components would either not be able to function at all or function only to a highly diminished degree. This strikes us as evidently false.

Secondly, given that Karpowicz et al. endorse a functionality threshold for what counts as a denigration of dignity it would also follow—if we rejected their potentiality account—that we denigrate human dignity when we restore someone's dignity-related capacities to a highly diminished degree. This is an implausible conclusion: we can easily imagine a case where at time T^1 someone possesses all dignity-related capacities, then at T^2 she loses them all due to an accident or illness, and then at T^3 some of the physical components necessary for the development of the dignity-related capacities are restored by a doctor through an intraspecific or interspecific chimerisation process. The only caveat is that at T^3 the physical components necessary for the development of such dignity-related capacities are encased in a body where they would not be able to function at all or they would only function to a highly diminished degree. Karpowicz et al. would have to accept that these 'restorative' procedures would denigrate dignity. This, again, strikes us as false.

The third, and final, problem with this argument is that it incorrectly assumes that such procedures *would diminish or eliminate the capacities associated with dignity*, when encasing the physical components necessary for their development in a body where they would either not be able to function at all or function only to a highly diminished degree. ''The creator of the human–nonhuman chimera would do even worse [than a torturer or enslaver]—he or she knowingly would diminish or eliminate the very capacities associated with human dignity'' (Karpowicz et al. 2005, 121). Now, this is incorrect because prior to the procedure there are no dignity-related capacities, at least not those that Karpowicz et al. specify, that could be *diminished or eliminated*. As de Melo-Martín (2008, 342) points out, ''such capacities cannot be destroyed or diminished unless there already is a creature with those capacities full present''. Contrary to what Karpowicz et al. state, a certain degree of dignity-related capacities would emerge, but such emergence is dependent on other biological factors (e.g. the body where the human neural stem cells are transplanted).

(V) The fifth, and final, argument that Karpowicz et al. advance is a variation of the 'treatment-argument' presented in their 2004 paper. In this new version, they state that to create a HNH-chimera with dignity-related capacities would denigrate dignity because the HNH-chimera would not be able to exercise such capacities due to its role as a research subject:

> To create such a chimera would violate human dignity because the resulting being could not fully exercise the dignity-related capacities associated with the human brain, due to its role as a research subject specifically produced to serve as a human proxy in experiments that it would be unethical to undertake on human beings themselves. (Karpowicz et al. 2005, 123)

This argument is problematic because, as explained previously, such treatment of a HNH-chimera is not a *necessary* feature of its creation. It does not necessarily follow from the fact that someone is an experimental subject that she will not be able to exercise their dignity-related capacities. Secondly, irrespective of the intentions for which the HNH-chimeras were created, moral agents have a *moral obligation* to treat them in accordance with their moral status. Just as it would be immoral for a researcher to carry out harmful or destructive experiments on a child created for the purpose of those experiments, it would be immoral to fail to respect the moral value that HNH-chimeras possess by means of their capacities.

So far I have tried to show that Karpowicz et al.'s dignity-related arguments against the creation of specific HNH-chimeras—those with functional and emergent psychological capacities—fail to prove that *in principle* their creation would violate, deny or denigrate dignity. Now I will turn to examine three arguments that Johnston and Eliot have advanced against the creation of HNH-chimeras with human-like mental capacities. Before examining these authors' arguments, it must be said that for them the only HNH-chimeras that risk offending dignity are those that are compromised (i.e. those that are harmed by virtue of being a mix of human and nonhuman).

(VI) Johnston and Eliot argue that dignity would be offended in so far as ''[i]ntentionally creating compromised human beings or part-human beings is cruel to the creature created (…)''[30] (Johnston and Eliot 2003, W7). Along the same lines, MacKellar and Jones have argued that ''Indeed, it seems that the attempt to create a part human, part nonhuman being would be wrong to that being'' (MacKellar and Jones 2012, 176).

I should note that this argument cannot be levelled as a *general argument* against the creation of HNH-chimeras with human-like mental capacities. Why? Because in *creation contexts* it is important to take into consideration the non-identity problem as identified by Parfit (1984). The non-identity problem may be interpreted to show that reproductive choices, or in this case the creation of some HNH-chimeras, cannot harm the created individual unless her life is a life

[30] Even when presented in Johnston and Eliot's paper as a ''post-creation wrongful treatment argument'', this argument can also be interpreted as a ''wrongful creation argument''.

not worth living.[31] This is so under a comparative account of harm, and because her only other 'option' was never to have been. Cooley (2008, 2) has made a similar point: ''As long as [HNH-chimeras] have lives worth living or good lives, one cannot say legitimately neither that their creation and existence injured them in some way nor that their existence are inherently bad''. This being the case, we must reject this argument as a general argument against the creation of HNH-chimeras with human-like mental capacities.

(VII) The second argument that Johnston and Eliot advance maintains that the creation of such chimeras reflects badly on those creating them and those allowing their creation:

> Intentionally creating compromised human beings or part-human beings reflects badly [and can be said to offend dignity] both on those who create the chimera and on those societies or governments allowing its creation. What kind of an institutional intention do we exhibit when we create compromised human beings or part-human beings for our laboratory use?'' (Johnston and Eliot 2003, W7)

This argument cannot be weighed as a principled objection against the creation of compromised human beings or part-human beings (with our without human-like mental capacities). It cannot be so because the institutional intentions behind their creation are not *necessarily bad or evil*. Even more so, those intentions can be benevolent and on a par with treating such beings in accordance with their moral status. For example, the intention behind creating a 'compromised' human being, through a chimerisation procedure, could be to enhance the capacities of a congenitally severely cognitively disabled human. It is hard to see how this could offend dignity. Secondly, this argument, from a species neutral perspective, also entails that those who intentionally reproduce knowing that they may create a 'compromised' human (a severely ill or impaired human) would offend dignity and this (except in wrongful life cases) appears not to be the case.

(VIII) The third, and final, argument that Johnston and Eliot advance questions society's role in determining the moral acceptability of the creation of HNH-chimeras with human-like mental capacities:

> Finally, intentionally creating compromised human beings or part-human beings might appear to ''all the world'' to be using another human, or a part-human, as a means to an end rather than as an end in itself [and thus to offend dignity], a use that has been

[31] In order for this counterargument to work we need to differentiate between two types of creation acts: 'true' creation acts (e.g. the fusion of two non-monozygotic early embryos) and creation as modification acts (e.g. grafting liver human cells into a post-natal mouse). 'True' creation acts are characterised by the fact that without their occurrence the created entities would not have existed (i.e. the numerical identity of the creature depends on chimerisation act).

> confirmed as morally unacceptable since at least the Declaration of Helsinki. (Johnston and Eliot 2003, W7)

This final argument is also unsound: the fact that something might appear to 'all the world' as X does not mean that it is morally on par with X and should not be done. Even when it might appear to 'all the world' that I am trying to drown a child when in fact I am trying to save her, it does not follow that I should stop trying to save her. Likewise, the fact that 'all the world' thinks that a HNH-chimera will be used solely as a means towards others' ends does not mean that this is going to be the case. If we create HNH-chimeras with human-like mental capacities then we should treat them in accordance with their moral status. At this point it is safe to claim that Johnston and Eliot's arguments are found wanting.

As well as advancing these arguments, Johnston and Eliot have pointed out that there are two ways of understanding human dignity arguments. The first one focuses on the dignity of individuals (i.e. the dignity of a human) while the second one focuses on the dignity of a class of individuals (i.e. humanity's dignity). According to the authors the second approach may lay the ground for new criticisms of the creation of HNH-chimeras that possess human-like psychological capacities (Johnston and Eliot 2003). Alongside this idea, de Melo-Martín (2008) has advanced that previous critics of the dignity-related arguments— namely Françoise Baylis and Andrew Fenton, and David DeGrazia—have failed to properly identity if Karpowicz et al.'s arguments were directed at individuals or at a class of individuals. According to her, the class-based counterarguments advanced by Baylis and Fenton, and DeGrazia are skewed because Karpowicz et al.'s arguments concerned individuals:

> [C]ritics and proponents of the human dignity argument do not have a similar understanding of how chimera research poses a threat to human dignity. Thus, although the critics' arguments might be right, given that these arguments do not address the particular way in which proponents believe that human dignity would be threatened, they cannot conclude that this threat does not exist. (de Melo-Martín 2008, 343)

de Melo-Martín then advances two new arguments, from humanity's stance, against the creation of HNH-chimeras with human-like mental capacities.

(IX) de Melo- Martín's (2008) first argument states that a threat to humanity's dignity would occur if scientists created HNH-chimeras with human-like mental capacities such that the chimeras were not able to flourish according to their nature. Even when this appears to be an individual dignity argument the author considers it otherwise. In order to show us why this is a humanity's dignity argument she asks us to image a scenario where we replaced the HNH-chimeras for normal human beings:

> It is clear, however, that were researchers to use human beings for experimental purposes, it would be reasonable to argue that such action would constitute a threat not just to the dignity of the particular humans involved, but also to the dignity of human beings as a whole. This would be the case, because all humans would be diminished by engaging in or condoning such activities. (de Melo-Martín 2008, 339)

This argument is problematic because it assumes that if all society knew about such practices, and it was clear that the experimental subject possessed dignity, all of society would engage in or condone such activities. Contrary to this assumption, I think that there would be substantial societal objection and that we would witness a large call to ban such research. While this is an empirical claim, I think that similar cases, for example people's negative reactions to torture, the experimentation with great apes, and the hunting of dolphins, show that not all humans would engage in or condone such activities. Therefore, *not all humans* can be diminished by engaging in or condoning such activities because not all humans would engage in or condone such activities.

(X) The second argument that de Melo-Martín advances is that it is quite unlikely that HNH-chimeras will live in a context where society will allocate enough resources for them to flourish and function in accordance with their higher capacities:

> [I]t is highly improbable that society would use resources to ensure that such creatures develop to the fullest extent of their capacities. Here again, the human dignity at stake would not be that of the creatures in particular, although their dignity might also be violated, but that of all human beings. (de Melo-Martín 2008, 339)

If this argument is correct then even without creating HNH-chimeras humanity's dignity has be violated. Why? Because most human societies do not use their resources to ensure that all individuals within that society (abled and disabled) develop *to the fullest extent* their dignity-related capacities. On many occasions societies are not able to allocate such resources for reasons such as bad administration, because the resources available are scarce, or because they allocate resources to achieve other ends. For example, think of a hypothetical well-off society that decided to allocate most of its resources to fight climate change, and thus prevent an existential catastrophe. Because of this public schools' funding is reduced and students are not able to develop their capacities to their *fullest extent*. If de Melo-Martín is correct then humanity's dignity has been violated in this case, and this appears not to be the case.

A more charitable interpretation of this argument could be offered. It could be asserted that society should provide means for HNH-chimeras to be able to develop their dignity-related capacities to an *adequate extent*, otherwise humanity's dignity would be violated. It is true that if we create HNH-chimeras with human-like mental capacities then we have a moral obligation

to allocate the adequate resources so they develop to an adequate extent. It is also true that the amount of resources dedicated to this task would most probably depend on local or federal regulations. If this was the case then, just as in the previous argument, it seems more accurate to state that only the dignity of those that participated in or condoned the allocation of insufficient resources for the chimera to develop to an adequate extent would be diminished. In this case, we must assert that the dignity at stake is not that of all human beings.

(XI) The final argument that I will examine has been advanced by Calum MacKellar and David Jones. In their book 'Chimera's Children', these authors posit that the intentional creation of 'intermediate' beings—those that undermine the biological distinctions between humans and nonhuman animals (e.g. chimeras or hybrids)—with an unclear moral status would be the first step in a slippery slope towards putting into question the dignity of all those that possess it:

> [N]ew beings would begin to exist to whom/which it would be very difficult to ascertain, with any amount of certainty, whether or not universal, absolute, inalienable, and inherent dignity should be conferred. In addition, if a being were denied the inherent dignity to which he or she was entitled, then the dignity of every individual in the whole global network, including every human being, would be put into question. This is because the whole network of persons (whether or not they are 100 per cent human) would no longer be consistent, coherent or dependable. (MacKellar and Jones 2012, 196)

There is one fatal problem with this argument: it does not follow from the fact that someone's dignity is denied (intentionally or accidentally) that the dignity of all dignity- possessing creatures would be put into question. For example, not even under the most abominable political regimes has the dignity of *all humans been* put into question. It is always the dignity of the slave, and not of the enslaver, that has been questioned. Throughout history enslavers have managed to construct consistent, coherent and dependable networks of exclusion without putting themselves into danger. It is true that some HNH-chimeras' moral status could be uncertain but in such cases we should err on the side of caution when dealing with them, not for humanity's sake but for their sake.

6.3 FINAL REMARKS

In this paper I have tried to show that the dignity-based arguments that have been advanced so far fail to make a principled case against the creation of HNH-chimeras with human-like mental capacities. I engaged with arguments by Karpowicz et al. (2004, 2005), Johnston and Eliot (2003), de Melo-Martín (2008), and MacKellar and Jones (2012), and found all of them to be problematic. These arguments are problematic because: (1) they confuse the wrongness of

creating HNH-chimera with the wrongs and harms that would be imposed upon such HNH-chimeras in certain contexts; (2) they misrepresent how a being could be treated solely as means towards others' ends; (3) they do not provide a satisfactory account of how the creation of HNH-chimeras would violate humanity's dignity; and (4) they disregard the fact that if such HNH-chimeras had dignity then moral agents would have the same moral obligations towards those chimeras as they do towards other beings with dignity (no matter that the HNH-chimeras were created with the intention of being research subjects).

7. ARTICLE II: THE ETHICS OF KILLING HUMAN/GREAT-APE CHIMERAS FOR THEIR ORGANS: A REPLY TO SHAW ET AL.

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7.1 INTRODUCTION

A chimera, in biological sciences, is an organism which at cellular level is composed from at least two different sets of cells, which originated in genetically diverse organisms. Chimeras can be divided in two broad groups: primary chimeras and secondary chimeras. ‘‘Primary chimæras are formed by mixing together two early embryos, or an early embryo with isolated embryonic cell types obtained from a different embryo or cultured stem cell line. The resulting chimæra has cells of different origins, in many tissues. Secondary chimæras are formed experimentally by transplanting (or grafting) cells or tissues into animals at later stages of development, including late fetal stages, post-natal or even adult animals. The donor cells are only present in a few tissues’’ (The Academy of Medical Sciences 2011, 18–19). It should be emphasised that the number, origin of the cells, and the timing of the mixing could produce very different outcomes in respect to the kinds of capacities a chimera could possess.

There are interspecific chimeras and intraspecific chimeras. Intraspecific chimeras are those where the sets of cells that make up the organism belong to *the same* biological species. For example, a human chimera can be created when two non-monozygotic early embryos fuse completely and grow into one body. The resulting entity is an organism that at cellular level is a ‘patchwork’ of both sets of human cells (Tippett 1983). Interspecific chimeras are those where the sets of cells that make up the organism belong to *different* biological species. For example, a goat/sheep chimera can be created by combining blastomeres from four-cell goat embryos with blastomeres from four-cell sheep embryos, the resulting entity is an organism that at cellular level is a ‘patchwork’ of goat cells and sheep cells (Fehilly et al. 1984).

Intraspecific nonhuman/nonhuman chimeras and interspecific human/nonhuman chimeras (henceforth, HNH-chimeras) are used both in biological research that aims at improving, or maintaining, human health and in research that aims at advancing our understanding of various biological mechanisms and processes. For example, human-mouse chimeras have been used in the research of human haematopoiesis; development and function of the immune system; infectious diseases; autoimmunity; cancer; human cell development, maturation and migration; and regenerative medicine (Shultz et al. 2007; Rashid et al. 2014; Sun et al. 2007; Tam and

Rossant 2003; Lapidot 2001). HNH-chimeras have also been proposed as possible tools for creating vaccines against deadly diseases such as malaria, dengue, Hepatitis B, HIV and Hepatitis C (Davis and Stanley 2003; Sacci Jr. et al. 2006; Legrand et al. 2009; Bhan et al. 2010).

In recent work David Shaw, Wybo Dondorp, Niels Geijsen, and Guido de Wert have examined, from an ethical and legal position, the procurement, for human transplantation purposes, of human organs created within HNH-chimeras. In one paper Shaw examined the legal status of creating HNH-chimeras for obtaining human organs under Swiss legislation; in another, Shaw, Dondorp, Geijsen, and de Wert assessed the ethical issues surrounding the procurement of human organs from human/pig chimeras; and in a final paper Shaw, Dondorp, and de Wert assessed the ethical issues surrounding the procurement of human organs obtained from human/nonhuman-primate chimeras (Shaw 2014; Shaw et al. 2014; Shaw et al. 2015). This philosophical research stems, in part, from recent advances in induced pluripotent stem cell (iPSC) research, and the *ad hoc* creation of solid organs within intraspecific and interspecific chimeras (Kobayashi et al. 2010; Isotani et al. 2011; Usui et al. 2012; Matsunari et al. 2013; Kobayashi et al. 2014; Rashid et al. 2014).

The aim of this paper is to critically examine the arguments that have been advanced by David Shaw, Wybo Dondorp, and Guido de Wert in favour of the procurement of human organs obtained from human/nonhuman-primate chimeras, specifically from *human/great-ape chimera*s. There are two important reasons for examining such arguments. First, for those that hold that there are degrees of moral status, based upon cognitive capacities,[32] the ethics of using great apes for medical research that aims at benefiting humans is a topic that merits special attention. Second, the ethics of using chimeras for their human organs is a topic that warrants notice in the medical ethics literature at this point given recent developments in biological sciences. For example, in a recent paper Madhusudana Girija Sanal has sketched a road map for how to create a transplantable human liver within a human/chimpanzee chimera (Sanal 2011).

My claim is that the arguments that these authors have advanced fail to support their conclusions, and thus they are in need of substantial revision. In order to prove this first I present a detailed reconstruction of Shaw et al.'s arguments. Secondly, and relying on a cognitive capacities account of moral status, I show that Shaw et al. committed major errors:

[32] In this work I use ''cognitive capacities'', ''mental capacities'' and ''psychological capacities'' interchangeably.

(1) not properly applying the subsidiarity and proportionality principles; (2) not including species overlapping cases in their ethical assessment; (3) ignoring the ethics literature on borderline persons; and (4) misunderstanding McMahan's two-tiered moral theory. Finally I will mention a possible multipolar solution to the human organ shortage problem that would reduce the need for HNH-chimeras' organs.

7.1.1 HUMAN ORGANS, NONHUMAN ANIMAL RESEARCH, AND MORAL STATUS

Shaw et al. start their inquiry, in 'Using Non-Human Primates to Benefit Humans: Research and Organ Transplantation', by bringing forward a well-known fact about the current status of human organ transplantation: there is a scarcity of human organs. This in turn means two things: (1) that many people that are currently affected by fatal illnesses that can only be treated by organ transplantation—to a full or less extent—will die waiting for an organ, and (2) that many people in need of an organ will experience pain and suffering while waiting for it. For example, in the UK three people die every day due to the shortage of transplantable organs; and in United States thirty people die every day, or are removed from the waiting list due to being too ill to receive a transplant (Humphreys 2014; NHS 2014).

There are several courses of action that can be taken in order to increase the number of human organs available for transplantation: (1) changing from an opt-in donation system to a default opt-out donation system, (2) creating incentives for people to donate their organs after their death, (3) creating incentives for people to make live organ donations, (4) making after-death organ donation obligatory, and (5) creating educational campaigns to increase the number of organ donations. In addition to these proposals there are five alternative strategies, which do not require 'human' donation as such: (6) the creation of in vitro organs using scaffolds, (7) 3-D printing of human organs, (8) xenotransplantation, (9) the creation of mechanical organs and (10) *chimera based organ transplantation*.

As I have previously stated, Shaw et al. decided to explore the last possibility in part because of recent scientific breakthroughs in chimera research. Of all the possible kinds of HNH-chimeras that could be created for obtaining human organs they focus on two: human/pig chimeras and human/nonhuman-primate chimeras.[33] Their selection is not arbitrary: those

[33] Even when it is possible that human organs could be created within other HNH-chimeras, for example human/elephant chimeras or human/mouse chimeras, it is important to notice that the anatomical structure of the human body restricts the 'type' of organs that could be used for transplantation.

chimeras are considered to be the best possible biological candidates for the creation of transplantable human organs.

Before moving forwards two things should be made clear about the current state of this research. First, the creation of *human* solid organs within HNH-chimeras has not been accomplished.[34] Second, there are still substantial technical hurdles that must be overcome in order for the creation of transplantable solid human organs to be feasible. Given these facts Shaw et al.'s discussion assumes, *ex hypothesis*, that this research will be successful and thus that the technical hurdles will be overcome. Assuming the former evades issues of risk and harm, due to imperfect research, but it allows them to focus on the morality of *killing* HNH-chimeras for their human organs. Throughout the rest of the paper I will also assume that this research will be successful.

After acknowledging that human organs for transplantation are a scarce resource, and assuming that human organs from chimeras will be available, Shaw et al. turn their attention to animal research. They point out that nonhuman animal research, for human health purposes, is carried out all around the world; and that the present day moral justification for doing so is that its aims (i.e. the improvement and maintenance of people's health) are so important that, in principle, they trump over all nonhuman animals' interests (e.g. avoiding pain, being comfortable, staying alive). Two caveats should be mentioned. First, and I will return to this point in the section 4.2 ''The Case Against Killing Human/Great-Ape Chimeras for Their Organs'', there are morally relevant distinctions between killing certain animals and killing others. Second, this is not to say that all medical research that employs nonhuman animals can be morally justified.

When questioned about *how* nonhuman animal research should be carried out Shaw et al. appeal to the well-established principle of '3 Rs' (replacement, reduction and refinement) which, according to them, in turn is grounded in two other principles. ''The 3 Rs are in turn based on two key principles: proportionality and subsidiarity. These state, respectively, that any use of animals for research must be proportional to the prospective benefit, and that animals should only be used when no reasonable alternative is available'' (Shaw et al. 2014, 573).

The normative force of the proportionality and subsidiarity principles, when applied to nonhuman animal research, in turn relies, at least in part, on a theory of moral status. Such theory should be able to explain why it is morally distinct to use, for research purposes, certain

[34] Here 'HNH-chimera' should be understood as a chimera predominantly constituted by nonhuman components and with only 'a few' human cells.

nonhuman animals rather than normal adult human beings. In their paper Shaw et al. do not *explicitly* endorse a particular theory of moral status, but it can be inferred that they are adopting a *non-speciesist cognitive capacities account*. This is supported by the fact that they reject an anthropocentric account of moral status (being a member of the *Homo sapiens* species is a necessary or sufficient condition for possessing moral status), that they accept that certain nonhuman animals possess moral status (sentience being a sufficient condition for possessing it, given that it is a sufficient condition for possessing experiential welfare), and also that they appear to align themselves (Shaw et al. 2014, 574) with Singer's definition of personhood [a person is a ''rational and self-conscious being'' (Singer 1993, 87)]. If this is correct then it is safe to assume that they would accept that the creatures with most moral worth are persons, after them sentient beings and lastly (and if possible) non-sentient creatures.

7.1.2 BORDER-LINE CASES AND ANIMAL EXPERIMENTATION

Shaw et al. maintain that even when a cognitive capacities account of moral status can be used to determine the moral permissibility of most nonhuman animal research there are 'border-line cases' where it *cannot* provide a 'clear-cut' answer. For example, is it morally permissible to carry on painful and destructive research in a nonhuman primate that has the relevant psychological capacities to a slightly lower degree than a human person? Confronted with such 'border-line cases' Shaw et al. quote McMahan's 'Time-Relative Interest Account' as a *possible alternative explanation* of why harming nonhuman animals with *slightly less* psychological capacities than human persons is less objectionable than harming human persons. They cite the following paragraph:

> The Time-Relative Interest Account offers an explanation of why the killing of animals is less seriously objectionable than the killing of persons. Because the psychological capacities of animals are significantly less well developed than those of persons, the range of goods accessible to them is narrower and the degree of psychological unity within their lives is less. They therefore have a weaker time-relative interest in continuing to live than a person normally does. (McMahan 2003, 204)

After citing this paragraph, Shaw et al. assert that the *sliding scale* nature of McMahan's Time-Relative Interest Account also *cannot* tell us if the use, for research purposes, of nonhuman animals with *slightly less psychological capacities* than human persons is morally justified. Therefore, for them, a cognitive capacities account of moral status and McMahan's Time-Relative Interest Account are unable to show where the 'cut-off' between morally permissible and impermissible research should be (Shaw et al. 2014, 574). This 'cut-off' is of paramount prominence for Shaw et al.'s discussion about killing human/nonhuman-primate chimeras for

their organs, because, as they accept, some nonhuman primates in fact possess *only* slightly fewer psychological capacities than human persons (the most prominent example being great apes) and thus belong to the 'grey area' between persons and non-persons. Finally, it is important to emphasise, for reasons that will become clear afterwards, that Shaw et al. only cite McMahan's previous paragraph.

Once they have pointed out the supposed *sliding scale* problem of both accounts they move on and claim that the consensus on the use of nonhuman primates—which, depending on the species, may or may not be in a personhood 'grey area'—for research that benefits human health is that their use is *necessary and justified* (Shaw et al. 2014, 575). The *scientific rationale* behind this is that nonhuman primates are biologically the most similar to humans and they offer the most accurate nonhuman animal model.

Even when a scientific rationale is provided, Shaw et al. need to further morally justify the use, for research purposes, of nonhuman primates with slightly fewer psychological capacities than human persons (taking for granted that, in principle, it is morally permissible to sacrifice sentient beings for the sake of persons). They need to do so because according to them neither a cognitive capacities account of moral status nor the Time-Relative Interest Account were able to tell us if using such nonhuman animals for research is morally permissible. The way in which Shaw et al. provide the needed moral justification is by invoking the subsidiarity and proportionality principles. They assert: ''Given that the only alternative would be to use humans, the subsidiarity criterion [for using nonhuman primates for research] is met, and given the substantial potential benefits of some of the treatments that may result, the proportionality test is also met'' (Shaw et al. 2014, 574).

It is important to point out that the authors realise that if they accept a cognitive capacities account of moral status then the claim that *all* nonhuman primates have less moral value than *all* human beings is in fact incorrect. This is why they emphasise that ''to the extent that primates actually meet the criteria for personhood they should be treated as persons rather than animals, making the proportionality and subsidiarity principles irrelevant'' (Shaw et al. 2014, 574). Shaw et al. then stress that they ''assume that the current consensus position is correct, and primates (*with the possible exception of great apes*) [emphasis added] are not persons [and thus can be used for certain research purposes]'' (Shaw et al. 2014, 574).

A problem arises here: Shaw et al. do not take into account, for their ethical assessment, the fact that *there are humans that are not persons*, and thus they do not distinguish throughout

their text between human persons and human nonpersons. In the section 'The Case Against Killing Human/Great-Ape Chimeras for Their Organs' I will show why this important omission has serious repercussions for their arguments.

7.1.3 THE CASE FOR KILLING HUMAN/PIG CHIMERAS FOR THEIR ORGANS

Once they have examined whether it is morally permissible to use nonhuman primates for research that benefits human health and found that with the *possible* exception of great apes it is justified according to the proportionality and subsidiarity principles, Shaw et al. query if it would be morally justified to kill human/pig chimeras for their human organs. For them the question is easy to answer: yes. If we accept, they claim, that the use of certain nonhuman animals for destructive research is morally justified when the aims are those of saving human lives or improving human health, then, by a matter of consistency, we would also have to accept that, in principle, the use of human/pig chimeras as organ suppliers is morally justified. This justification works as long as human lives are saved or improved by such organs to the same extent that nonhuman animal research improves and saves human lives (and taking for granted that such chimeras are not persons).

Shaw et al. also argue that contrary to nonhuman animal research, that can lead to dead-ends, produce only indirect benefits, or produce results that are useless for human health improvement (due to the translational gap between nonhuman animal research and human research), the use of human organs that had their origin in human/pig chimeras would in most cases save at least one human life. This point is made to reinforce the position that killing human/pig chimeras for their organs is morally less problematic than most destructive nonhuman animal research.

While for these authors sacrificing a human/pig chimera in order to *save* a human life seems morally unproblematic, it appears that cases where its killing would *only* bring an improvement to someone's well-being (e.g. reducing the suffering of dialysis) needs further justification, which Shaw et al. do not provide. This justification is required because the fundamental interests of the human/pig chimera must be weighed against the human's interest in not suffering gravely. In this respect McMahan's Time-Relative Interest Account may provide the needed justification. According to it, the 'badness' of death is a function of the lost opportunities of worthwhile life (however this is defined: preference satisfaction, pleasure, etc.), considered from a whole-lifetime perspective but proportionally adjusted to the strength of one's psychological unity over time—the more psychological unity over time one has the

more death harms one. If this is the case, we can say that a human person's interest in not greatly suffering would trump over the human/pig chimera's interest in staying alive if the human person's time-relative interest in not suffering is weightier than the chimera's time-relative interest in remaining alive. While is difficult to precisely calculate the amount of pain a person should be experiencing for it to be morally permissible to kill such chimera, I think that a *human person's great suffering* would justify the painless killing of a human/pig chimera.

While the sacrifice of human/pig chimeras for the procuration of human organs for saving or lessening great suffering of human persons seems morally justifiable, the morality of procuring human organs from human/nonhuman-primates needs further elaboration.

7.1.4 THE CASE FOR KILLING HUMAN/NONHUMAN-PRIMATES CHIMERAS FOR THEIR ORGANS

In order to investigate the morality of killing human/nonhuman-primate chimeras for their organs, Shaw et al. test whether such cases meet the proportionality and subsidiarity principles. They take this course of action because, as stated previously, they consider that a cognitive capacities account of moral status and McMahan's Time-Relative Interest Account cannot provided a 'clear-cut' answer to the question of whether it is morally permissible to kill beings that possesses *slightly less* mental capacities than humans.

For them, killing human/nonhuman-primate chimeras for their organs is proportional given the potential direct benefits that would be conferred to humans.[35]4 Such benefits are not only measured in the number of saved lives, but also in the reduction of suffering due to the shortening of waiting time that elapses between someone needing an organ, and her receiving it. Once they have accepted this they wonder if the distinction between greater and lesser apes is morally relevant:

> The fact that *great apes* [emphasis added] might be necessary due for organ creation also raises the question of whether the distinction between lesser and great apes is relevant in this context. Most primates used in research, and all used in the UK, are smaller primates. While these could be used for organ production (especially for children), *bigger primates are more likely to be appropriate donors* [emphasis added]. (…) While the creation of human organs inside primates appears to meet the proportionality criterion (*with the possible exception of great apes*) [emphasis added], the subsidiarity principle raises further questions. (Shaw et al. 2014, 576)

[35] It is important, again, to stress that Shaw et al. do not distinguish between human persons and human nonpersons and thus they only talk about benefits conferred to humans.

Justifying the killing of human/nonhuman-primate chimeras for their human organs, in terms of the subsidiarity principle, is more challenging because it must be shown that there are no reasonable alternatives for obtaining the much needed organs. To do this Shaw et al. first identify two possible readings of the subsidiarity principle, a strict reading and a permissive reading, and then they investigate their normative force. The strict reading asserts that if there is a reasonable alternative to the use of chimeras then we should not use them. The permissive reading affirms that using chimeras is permissible if non-problematic alternatives have not been established.

Once they have identified these two readings, Shaw et al. argue that even when the strict reading is accurate, in the description of the states of the world, it lacks normative force for the people who will die without an organ transplantation. It lacks such force because it does not follow from the fact that there are other reasonable possible courses of action that they can in fact be followed: ‘‘for the specific people who will die soon without an organ there really is no alternative, suggesting that the restrictive reading of the subsidiarity principle is too strict’’ (Shaw et al. 2014, 576). Given this Shaw et al. conclude that the *permissive reading* of the subsidiarity principle should be embraced. Therefore killing human/nonhuman-primate chimeras for their organs is morally justifiable, because there is *no real* reasonable non-problematic alternative available.

At this point Shaw et al. make a clarification in respect to what they think are justifiable aims for using human/nonhuman-primate chimeras’ human organs: ‘‘it could also be argued that primates should only be sacrificed to create organs when it’s necessary to *save life* [emphasis added] rather than to improve quality of life. While lessening the suffering of dialysis for kidney patients, for example, is a good goal, it is not clear that it is worth sacrificing a great ape for; in contrast, *such a sacrifice seems more appropriate if a human will die without it* [emphasis added]’’ (Shaw et al. 2014, 577).

There are two ideas here that merit unpacking. The first is that human/nonhuman-primate chimeras should only be killed when otherwise a human would die. In such an assertion it is implied that human/nonhuman-primate chimeras’ time-relative interest in staying alive trumps over the human’s time-interest in not suffering. Two things should be further noted here. First, these authors do not address whether a specific degree of suffering (e.g. unbearable suffering) would merit killing human/nonhuman-primate chimeras. Second, they also do not address the question of whether human/nonhuman-primate chimeras should be killed for the sake of the

health of human nonpersons, or humans with the same mental capacities as those of the chimeras providing the organs.

The second idea is that for Shaw et al. *it would be morally justifiable* to sacrifice a human/great-ape chimera for procuring human organs when a human would die without them. It is important to highlight that even when Shaw et al. had previously accepted that it is possible that great apes, and in this case human/great-ape chimeras, are in fact persons they have now asserted that *they are sacrificable* when doing so would save *any* human live. The idea that great apes' lives are sacrificable when the life of a human is at stake is a common one, as McMahan has pointed out: ''Most people believe that it would be permissible, and perhaps morally required, to kill an adult chimpanzee if the transplantation of its organs could save the life of an adult human being'' (McMahan 2009, 584).

To sum up, Shaw et al. defended that killing human/nonhuman-primate chimeras for their organs would only be morally justified when such actions in fact would save a human's life. They defended this by employing the proportionality and subsidiarity principles, while noting that neither a cognitive capacities account of moral status nor McMahan's Time-Relative Interest Account could provide a 'clear-cut' answer to the morality of killing human/nonhuman-primate chimeras for their organs. This conclusion also applies, *in terms of the subsidiarity principle*, to cases of killing human/great-ape chimeras for their human organs.

7.2 THE CASE AGAINST KILLING HUMAN/GREAT-APE CHIMERAS FOR THEIR ORGANS

Shaw et al. have argued that the subsidiarity principle would *allow* killing human/great-ape chimeras for their organs when doing so would save a human's life, and they have left open to further investigation (with the phrase 'with the *possible* exception of great apes') whether the proportionality principle would also allow for such killing. In this section I will show two things: (1) contrary to what Shaw et al. assert the subsidiarity and proportionality principles in fact *would not allow* killing human/great-ape chimeras for their organs, and (2) defending the killing of human/nonhuman-primate chimeras for their organs is more complicated than they appreciate.

It could be argued at this point that the interpretation I am offering of Shaw et al.'s position is uncharitable, given that they *do not explicitly endorse* the killing of human/great-ape chimeras for their organs. To this possible rejoinder I offer two rebuttals. The first is that Shaw et al.'s paper discusses the killing of creatures with slightly less psychological capacities than human

persons, which is how we would define great apes. The second is that Shaw et al. accept that there are proper motives for killing a great ape (e.g. saving a human life) and that there are other inappropriate motives for doing so (e.g. increasing someone's quality of life).

7.2.1 REVISITING MORAL STATUS

To understand where the problem lies with Shaw et al.'s conclusion we need to remember that they appealed to the subsidiarity and proportionality principles after they 'found' that a cognitive capacities account of moral status and McMahan's Time-Relative Interest Account could not tell us, in a 'clear-cut' fashion, if it would be morally permissible to kill human/nonhuman-primate chimeras (including human/great-ape chimeras) for their human organs. In order to clear things up we need to go back to the discussion about moral status.

To state that an entity possesses moral status is to realise that ''*in its own right and for its own sake, it can give us reason to do things such as not destroy it or help it* [emphasis in the original]'' (Kamm 2007, 229). Such action guiding reasons are based, at least partly, on the entities' interests, or time-relative interests. This in turn means that our consideration of an entity that possesses moral status should not be primarily conceived in terms of indirect duties towards ourselves, or duties towards other moral agents.

Among the beings with moral status there is a subset that we call persons. Persons are considered to be a distinct set of beings based on the specific cluster of capacities that they possess. The capacities that are commonly associated with personhood are: autonomy, rationality, self-awareness, linguistic competence, sociability, moral agency, and the capacity for intentional action. Providing a comprehensive list of necessary and sufficient capacities for personhood is unfeasible, because of the way in which they relate with each other. As DeGrazia has pointed out, someone is a person when she possesses the aforementioned capacities in a clustered way, not analysable in terms of one specific subset, to the point that suffices for a complex form of consciousness to be. To be a person one needs to possess enough of these capacities ''where 'enough' takes account both of how many of these properties are instantiated and of the degree to which each is instantiated'' (DeGrazia 2007, 320). Someone that is capable of normative self-governance (i.e. that is capable of reflecting upon her beliefs and actions and changing them accordingly) is taken to be a *paradigmatic person* under a cognitive capacities account of personhood.

The distinction between persons and nonpersons becomes relevant when they have conflicting interests. For example, in the transplantation cases that we have been discussing (i.e. the

human/pig chimera cases), the interest that a person possesses in remaining alive is in direct conflict with the interest that a nonperson chimera has in remaining alive. One way of dealing with such conflict of interests is to weigh them according to the Time-Relative Interest Account and to resolve in favour of that that possesses stronger interests. If we did so we would have to resolve the conflict in favour of the person, because death deprives her of a broader range of goods than those that the nonperson would be deprived of.[36]

It is important to bear in mind that having moral status or being a person is species neutral. This means that from a normative stand point it should be regarded as irrelevant to which biological species an entity belongs when assessing if it possesses, or not, moral status, and if it is, or is not, a person. It is true that there are biological species whose members regularly possess some cluster of these capacities, but this does not mean that there cannot be members of this species that lack enough of the capacities to have moral status or to be persons (e.g. human foetuses or the congenitally severely cognitively impaired). This clarification about moral status and personhood is important because until recent times it was considered that all humans had more moral worth than *all* nonhuman animals and that *only* humans had the requisite capacities for personhood.

7.2.2 THE MORAL STATUS OF GREAT APES

The question that we need to answer now is if great apes are persons, and thus if the strength of their interests is the same as those of human persons. Before advancing any further let's remember that when we talk about great apes we are talking specifically about chimpanzees, bonobos, gorillas, and orang-utans. There are really strong indications that great apes in fact possess many of the characteristics that we associate with personhood.

Among the empirical evidence that we possess for asserting that great apes possess many personhood-relevant properties[37] is the following: chimpanzees use tools such as stones to crack nuts, sticks to reach for insects, and moss for sponges. All great apes perform intentional actions and participate in social manipulation. All of them are bodily self-aware, and this self-awareness is revealed prominently in their imitation of bodily gestures and use of televised images of their out-of-view arms to reach concealed objects. They are capable of using mirrors

[36] In the following section I discuss how conflict of interests between persons and borderline persons should be resolved.

[37] The empirical evidence supporting this claim is cited at length by DeGrazia (1997, 2005, 2007) and Ravelingien et al. (2006).

to inspect otherwise imperceptible markings. Great apes also have social structures and they establish long-term relationships, dominance hierarchies, and allegiances. They shift allegiances, have knowledge of their position within a group, and expectations of others' behaviours in accordance with their position in the group. All great apes have a rudimentary culture, they transmit, from one generation to another, novel behaviours such as knowledge of which leaves can be used for certain medicinal purposes, how to create certain types of tools and how to construct nests. Furthermore, there is evidence of proto-moral agency among certain great apes, the strongest of which is altruistic actions that do not appear either to be conditioned or instinctive. Finally there is at least one bonobo, one gorilla and one orang-utan that after intensive human language training were able to acquire and understand, to some extent, human spoken and sign language.

Now, even when great apes possess all these capacities they are not as linguistically competent as normal adult humans are, and they are not as capable of normative self-governance as normal adult humans are. This being the case, and under a strict interpretation of what personhood is, we should agree that great apes *are not* paradigmatic persons.[38] Even when this is so we should acknowledge that great apes are *borderline persons*, just as David DeGrazia has forcefully and satisfactorily defended (DeGrazia 1997, 2005, 2007). What does it mean to say that great apes are borderline persons? It means, in the first place, that great apes inhabit the grey area between paradigmatic persons and nonpersons. They are beings with *slightly fewer psychological capacities than normal humans*. It is important, at this point, to remember that for Shaw et al. it is *only if* primates meet the criteria for personhood that the proportionality and subsidiarity principles should be regarded as irrelevant (Shaw et al. 2014, 574). This further affirms that for them the proportionality principle in fact would allow for the killing of human/great-ape chimeras for their human organs, just as the subsidiarity principle does.

Before moving on we need to address the more general question of how moral respect relates to possessed cognitive capacities. If we accept, just as Shaw et al. seem to do, that moral status follows from certain cognitive capacities and that in the natural world beings exist within a continuum of cognitive capacities (that go from none at all to personhood related capacities) then we have to accept either: (1) that moral consideration should be proportional to the capacities a being possesses, or (2) that there is a threshold above which all beings must be

[38] DeGrazia defends that the three great apes that are linguistically competent in fact are fully-fledged persons. In what follows I will not discuss the possibility of linguistically competent great apes or human/great-ape chimeras.

treated alike. One obvious difficulty with a proportional respect approach (in contrast with a threshold one) is that it accepts differences in moral worth between persons. For example, because on this approach moral worth follows from the possession of more sophisticated capacities, seven year old normal human children, who have less sophisticated cognitive capacities than other persons such as eighteen year old normal humans, could be considered as having less moral worth. This being the case a two-tiered morality account, one for persons and the other one for nonpersons, seems more appropriate (Harris 1985).

In point of fact McMahan, in 'The Ethics of Killing', develops and endorses a two-tier account of morality! According to it a morality of *identical respect* must hold among persons, making their killing *equally prima facie wrong*, while for nonpersons the Time-Relative Interest Account should prevail. As he says, when discussing the morality of late term abortion:

> It is important to remember that the Time-Relative Interest Account is not a complete account of the morality of killing, but is instead just one component of the more comprehensive Two-Tiered Account. According to the Two-Tiered Account, the wrongness of killing beings who are above the threshold of respect is governed by a requirement of respect. Thus even if a person has a very weak time-relative interest in continuing to live because the amount of good in prospect for him is quite small, it would nevertheless be just as wrong to kill him as it would be to kill any other person, if other things are equal. For his worth as a person is a function of his intrinsic nature and is unaffected by the amount of good the future holds in prospect. It is only in the case of beings that fall below the threshold of respect that the morality of killing is governed by the Time-Relative Interest Account. (McMahan 2003, 276)

The former quote highlights one of the fundamental problems with Shaw et al.'s paper: by only citing one paragraph of McMahan's position, and not contextualizing it, they present a *deeply incorrect* version of McMahan's moral theory. In actuality McMahan's two-tiered account is completely capable of accommodating cases of animals with slightly less psychological capacities than normal human adults, as will become clear in the next section.

7.2.3 THE MORALITY OF KILLING BORDERLINE PERSONS

So far I have only stated that great apes and human/great-ape chimeras are borderline persons. I now need to present a convincing case for the following claim: great apes and human/great-ape chimeras should be treated as paradigmatic persons. The justification for treating such creatures as paradigmatic persons is that the gap between the strength of the interests of persons and the strength of the interests of borderline persons is so small, and blurred, that they should be treated alike. This is a level-up solution to the 'problem' of borderline persons. As DeGrazia has stated:

> [O]n any reasonable model of moral status [Unequal Considerations Model or Unequal Interests Model] borderline persons – whether human or nonhuman –have full moral status, or (though this may come to the same) ought to be regarded as having it. To treat borderline persons accordingly is to regard them much as we regard human children: not as substantially autonomous or as having full-fledged moral agency but as deserving moral protections of full strength. (DeGrazia 2007, 323)

The conclusion, if we adopt a level-up stance, is that it, *in principle*, is morally impermissible to kill human or nonhuman borderline persons for their organs. Thus: *it is morally impermissible to kill great apes and great-ape/ human chimeras for their organs.*

A possible rejoinder which Shaw et al. could advance, is that in fact borderline persons should be treated according to McMahan's Time-Relative Interest Account. They could try to justify this point by stressing that borderline persons' interests should in fact be treated with slightly less consideration than those of persons, but that that slight difference allows for their killing. This slight difference explains why it would be less seriously objectionable to kill borderlines persons (e.g. human/great-ape chimeras) than to kill human persons. If Shaw et al. decided to embrace this position they would be opting for a level-down solution to the 'problem' of borderline persons. While this position might appear sensible, it has some logical implications that Shaw et al. should address in order for their case to be regarded as plausible.

The first implication, from a species neutral perspective on moral status and personhood, of such a level-down stance is that this would also mean that *all creatures* with the same, or less, psychological capacities than great apes could be sacrificed for their organs and this would be morally justifiable. Thus *all humans* that have the same, or less, psychological capacities than great apes can be morally sacrificed for their organs. Among the humans that could therefore be morally sacrificed are infants, toddlers, and adults that have less or the same mental capacities than great apes. Even if Shaw et al. claimed, and we agreed, that infants and toddlers should not be sacrificed for their organs because they have the *potential* to become paradigmatic persons, they would have to accept that there are two sets of cases where humans could be morally sacrificed for their organs. Cases where a human did not have the potential to become a paradigmatic or borderline person, and cases where they only had the potential to develop to a stage analogous to that of a great ape. For example, those so congenitally severely cognitively impaired as to fall within or below the borderline personhood threshold.

The second implication is that it would be morally unjustifiable to sacrifice human/great-ape chimeras for the sake of human borderline persons, contrary to what Shaw et al. endorsed. This is because human/great-ape chimeras and human borderline persons would have time-relative

interests of the same strength. While it would be morally permissible to kill a human/great-ape chimera for saving the life of a human person, according to the level-down position; it would be morally impermissible to kill the chimera for saving the life of a human borderline person and even less for saving the life of a human nonperson.

The third implication is that Shaw et al. would have to accept that instead of waiting a decade, or more, while scientists develop human/great-ape chimeras whose organs we could use for transplantation, we should start using human borderline persons' organs *today*! By killing and using the organs of human borderline persons and nonpersons right away we could avoid the deaths of large numbers of human persons. Even more so, some of the resources that we would need for the creation and maintenance of the human/great-ape chimeras could be saved, and repurposed for other morally worthy ends, given that human borderline persons and nonpersons occur naturally.

At this point Shaw et al. could try to avoid the level-down problems by relying on a relational account of moral status. They could claim that the relations that such human borderline persons, and nonpersons, have with their relatives and those that care for them (i.e. human persons) in fact either enhance their moral status (Steinbock 2011), or grant them the moral status of a paradigmatic person (Kittay 2005, 2009). Thus while it would be morally permissible to kill human/great-ape chimeras for their organs it would not be morally permissible to kill human borderline persons and nonpersons for their organs. One difficulty with this approach is that it does not automatically entail that we would not be able to harvest organs from *all* humans that are borderline persons or nonpersons. It instead implies that it would only be immoral to harvest organs from humans that are borderline persons or nonpersons and that *have a special relation* with some other person. Thus, all human borderline persons and nonpersons that are *not* in such relationships could in fact be killed for their organs. The second difficulty is that this same conclusion, regarding special relations, would apply to great apes and human/great-ape chimeras.

For example, if a person raised, or took care of, a great ape and established with her a significant relation then the moral status of this great ape would be modified to the same degree as that of a borderline human that enters the same type of relationship with another person. This shows that even an appeal to a relational account of moral status entails neither a total prohibition of the killing of human borderline persons and nonpersons for their organs, nor the complete moral acceptability of the killing of human/great-ape chimeras for their human organs.

Shaw et al. could claim that even if human borderline persons were not in relationships that enhanced their moral worth it would be inconceivable to take them out of their homes to be killed for their organs. Even if we accept this, we can still imagine possible scenarios where we could morally obtain and kill such human borderline persons, and nonpersons, for their organs (if the levelling-down approach were correct). For example, we could raise abandoned human borderline persons and nonpersons for such purposes, just as we would raise human/great-ape chimeras, in a special location. It is easy to imagine a location where those that 'take care' of such humans do so remotely and without knowing who they are taking care of, and thus do not generate any significant relation with them. If these conditions were met then it would be morally unproblematic to kill such human borderline persons, and nonpersons, for their organs.

The fact that personhood and moral status are species neutral entails that the conclusions that Shaw et al. happily apply to great apes and human/great-ape chimeras would also apply, in principle, to humans that are borderline persons. Confronted with this problem Shaw et al. have either to accept that it is morally acceptable to kill great apes, human/great-ape chimeras and some *human borderline persons* for their organs, or they would have to reject this proposition. I think that the authors would endorse the latter stance.

In this section I have tried to show that a hybrid account of morality can explain why killing borderline persons for their organs is morally inadmissible. If this is correct then it follows that Shaw et al.'s appeal to the subsidiarity and proportionality principles to solve the issue is unwarranted. I have also shown that Shaw et al. failed to realise an important implication of adopting a species neutral stance. This implication is that their conclusions equally apply to human borderline persons and nonpersons (or some human borderline persons and nonpersons, if we endorse a relational account of moral status).

7.3 FINAL REMARKS

Is it morally permissible to kill human/nonhuman-primates chimeras' for their organs? The answer depends on the cognitive capacities that such chimeras possess. On the one hand, if such nonhuman primates have great enough cognitive capacities to classify them as persons, or borderline persons, then the answer is that, in principle, *it is morally impermissible to kill them for their organs*. On the other hand, if they are not persons, or borderline persons, then the answer is that it could be permissible to kill them for their organs. Now, according to a species neutral account this second statement also entails that certain human beings, those that

are nonpersons, could be morally sacrificed for their organs (e.g. those unloved humans that are congenitally severely cognitively impaired). Is this correct?

It is what logically follows from the argument. Even if we accepted a relational account of moral status there would most probably be certain human nonpersons that could be morally sacrificed for their organs. It is true that many will find this option appalling. Is there a way to be consistent and at the same time reject the use of unloved human nonpersons as organ sources? I doubt there is to a full extent: even when this might be the case there is still a well-known multipolar option that would widely reduce the need to kill nonpersons (human or otherwise). The multipolar option would entail, among other things, adopting health programmes that promoted healthy lifestyles, a default opt-out donation system, creating incentives for people to autonomously make live organ donations, and substantively investing in research that aimed at the creation of mechanical organs, 3-D printed human organs and in vitro organs using scaffolds. In addition to this multipolar solution we should also further discuss the ethics of making after death organ donation mandatory (Harris 2002). All these efforts would bring down the number of people that would need to rely on killing nonpersons (human or nonhuman) in order to acquire healthy organs.

8. ARTICLE III: ETHICAL ASPECTS OF CREATING HUMAN–NONHUMAN CHIMERAS CAPABLE OF HUMAN GAMETE PRODUCTION AND HUMAN PREGNANCY

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8.1 INTRODUCTION

In the second half of the twentieth century, interspecific chimeras went from the realm of mythology and literary studies to being created and studied by the faculties of life sciences around the world. Today, most human–nonhuman chimeras (henceforth HNH-chimeras) are used to investigate and model human biological functions and diseases that would be difficult to study in other settings (e.g. cell cultures or computer simulations).

Chimeras are formed by combining whole cells of genetically different organisms into a single functional organism. The UK Academy of Medical Sciences provides this definition:

> Chimæras are formed by mixing together whole cells originating from different organisms. The new organism that results is made up of a "patchwork" of cells from the two different sources. Each cell of a chimæra contains genes from only one of the organisms from which it is made. (…) Primary chimæras are formed by mixing together two early embryos, or an early embryo with isolated embryonic cell types obtained from a different embryo or cultured stem cell line. The resulting chimæra has cells of different origins, in many tissues. Secondary chimæras are formed experimentally by transplanting (or grafting) cells or tissues into animals at later stages of development, including late fetal stages, postnatal or even adult animals. The donor cells are only present in a few tissues (The Academy of Medical Sciences 2011, 18–19).

HNH-chimeras (in particular humanized mice) have been used in research into human autoimmunity, hematopoiesis, and cancer biology (Shultz et al. 2007). They may further serve in the development of vaccines against deadly diseases (Bhan et al. 2010 ; Davis and Stanley 2003 ; Sacci Jr. et al. 2006), and the development of human organs for transplantation (Rashid et al. 2014). It should be emphasised that the number and origin of the cells, and the timing of the mixing could produce very different outcomes in respect to the kinds of characteristics a chimera could possess (Greely et al. 2007 ; Karpowicz et al. 2005 ; The Academy of Medical Sciences 2011).

In most respects, the creation and use of HNH-chimeras for research purposes is not regarded as presenting additional ethical concerns alongside those related to the destruction of human embryos, animal ethics, and research ethics. In part, this has been the case because such entities

have been predominantly constituted by nonhuman components, with only a few human cells. Nonetheless, there are three specific types of HNH-chimeras that have raised red flags among policymakers, researchers, and ethicists:

> (1) HNH-chimeras that could have brains predominantly constituted by human brain cells;
>
> (2) HNH-chimeras that could look humanlike;
>
> (3) HNH-chimeras capable of human gamete production and human pregnancy.

Of these three cases, the one that has generated the most academic debate is the possible creation of HNH-chimeras with brains predominantly constituted by human brain cells (e.g. the neuron mouse, Greely et al. 2007). The other two cases have not been comprehensively explored; I presume that this is in part due to the fact that the ethics debate around the creation of HNH-chimeras is fairly recent. In fact, only Greely (2013) has explored some of the ethical issues regarding the creation of these three types of 'sensitive' cases. The aim of this paper is to further discuss the moral issues surrounding the creation of HNH-chimeras capable of human gamete production and human pregnancy.

At this point, someone could state that the ethics of creating HNH-chimeras capable of human gamete production and human pregnancy has been dealt with by three major advisory groups (the UK Academy of Medical Sciences, the German Ethics Council, and the US Committee on Guidelines for Human Embryonic Stem Cell Research), and that all of them have recommended either not creating HNH-chimeras that could produce human gametes or not letting HNH-chimeras breed. To such a claim I would reply that these three groups have *only* stated that such courses of action should not be taken; they have not elaborated on the ethical reasons that ground such prescriptive measures.

Next I present the recommendations of these groups. The Academy of Medical Sciences has stated that:

> A very narrow range of experiments should not, for now, be licensed because they either lack compelling scientific justification or raise very strong ethical concerns. The list of such experiments should be kept under regular review by the proposed national expert body, but should at present include: (…) Breeding of animals that have, or may develop, human derived germ cells in their gonads, where this could lead to the production of human embryos or true hybrid embryos within an animal (The Academy of Medical Sciences 2011, 111).

The Committee on Guidelines for Human Embryonic Stem Cell Research has recommended that:

> Embryonic Stem Cell Research Oversight (ESCRO) committees or their equivalents should divide research proposals into three categories [a, b and c] in setting limits on research and determining the requisite level of oversight: (…)
> (c) Research that should not be permitted at this time. (…)
> (iii) No animal into which hES cells have been introduced at any stage of development should be allowed to breed (National Academies of Science 2005, 58).

While the US and UK groups focused on the reproduction of HNH-chimeras, the German group focused on the creation of HNH-chimeras that could produce human gametes:

> In addition to these limits [those of the German Embryo Protection Act, Sect. 7], the following additional prohibitions should be incorporated in the Act:
> – prohibition of the transfer of animal embryos to humans;
> – prohibition of the insertion of animal material into the human germline;
> – prohibition of procedures potentially resulting in the formation of human egg or sperm cells in an animal (Deutscher Ethikrat 2011, 113).

With these recommendations in mind, I will first explore whether there is a cogent moral argument for not creating HNH-chimeras that could produce human gametes, and then what moral problems could emerge from the fact that a HNH-chimera could become pregnant with a human conceptus.

8.2 ARGUMENTS AGAINST CREATING HNH-CHIMERAS CAPABLE OF HUMAN GAMETE PRODUCTION

In this section I explore whether there is a cogent argument that could ground the claim that the creation of HNH-chimeras capable of producing human gametes is morally problematic, as the German Ethics Council appears to think (Deutscher Ethikrat 2011).

Given that the German Ethics Council has not advanced a specific argument against the creation of HNH-chimeras that could produce human gametes, I will depart from a hypothetical strong normative claim, and I will then investigate whether there is an argument that could justify it. In doing so, I will try to build a strong case against the creation of this specific type of HNH-chimera that does not rely on an appeal to religious beliefs.

> (A) It is morally wrong to create HNH-chimeras that could produce human gametes.

At first glance, there are two possible ways in which we could try to justify (A). The first points to the general immorality of creating any type of HNH-chimera, and the second to the specific value of human gametes. Let us examine the first one.

8.2.1 THE GENERAL WRONGNESS OF CREATING HNH-CHIMERAS

An argument regarding the general wrongness of creating HNH-chimeras would claim something like this: creating *any* type of HNH-chimera is morally wrong. HNH-chimeras that could produce human gametes are a subset of the set HNH-chimeras. Therefore it is morally wrong to create HNH-chimeras that could produce human gametes.

While this argument might appear compelling, it fails because it rests on the soundness of the first premise, and this premise is false. There are several arguments that have been advanced in order to try to demonstrate its truth, and all of them have been found wanting: Robert and Baylis (2003) have examined and refuted the claim that crossing species boundaries is morally wrong; Robert and Baylis (2003) examined whether the creation of HNH-chimeras would produce a state of inexorable moral confusion that rendered their creation morally problematic (they did not take any stance on this issue), and later on Harris (2010), and Haber and Benham (2012) examined and refuted such a proposition; Karpowicz et al. (2004, 2005) and Cohen (2007) have examined and refuted the assertion that creating HNH-chimeras is morally wrong because they are unnatural or they transgress a moral taboo; Savulescu (2013) has examined and refuted the claim that HNH-chimeras would inherently threaten our humanity; and finally, DeGrazia (2007) and Palacios-González (2015) have refuted the charge that the creation of HNH-chimeras is morally problematic because it violates 'human' dignity.

At this point, one could argue that what has actually been concluded in most of the previous papers is that, *in principle*, the creation of nonperson-HNH-chimeras (that are predominantly nonhuman) is morally permissible, but that *the morality of creating HNH-chimeric-persons is still an unresolved moral issue*. It is worth noting that most discussions use a Lockean, or Lockean-like, account of personhood, where a person is "a thinking intelligent being, that has reason and reflection, and can consider itself as itself, the same thinking thing in different times and places" (Locke 1964, bk. II, Chap. 27, Sect. 9).

Let us grant for the sake of argument that creating HNH-chimeric-persons is morally problematic and should not be attempted. Now, even if we accept this claim, this does not entail a *principled point* against the creation of HNH-chimeras that could produce human gametes. Why not? Because human gametes can be produced by nonperson-HNH-chimeras. For example, we could create a human-mouse chimera that had mouse-proper mental capacities but that could produce human gametes.

8.2.2 THE VALUE OF HUMAN GAMETES

Given that a principled argument against creating *any* HNH-chimera has not been found so far, those who hold (A) could still try to defend it by advancing the argument that human gametes have certain worth that would be debased if they were to be generated within nonperson-HNH-chimeras. Commenting on the possibility of human gametes having certain worth, Greely has claimed that:

> Unless one sacralizes human gametes, there is no reason to be any more concerned about their mere presence in a human/nonhuman chimera than there is to be concerned about the presence of liver cells, kidney cells, or tumor cells—and far less than for human neurons. (…) In the normal course of events, sperm and eggs are not cherished, protected, and treated with respect. In all humans' lives, their gametes live and die, in the billions for men and in the hundreds for women, almost always futilely and never mourned or subject to "proper" or "respectful" disposal (Greely 2013, 684).

While most people would agree with Greely's remark, it is important to highlight that the reasons he presents to show that human gametes do not have worth are problematic.[39] In acknowledging the fact that people do not cherish, protect, and treat human gametes with respect, it does not necessarily follow that they possess no worth. People's beliefs can match, or not, the type of worth an entity possesses. For example, people used to believe that normal cows had no moral worth. The fact that some believed such a thing did not make it true. Given this problem with Greely's remark, it is better to present a different argument.

There are two types of worth human gametes could have: they could have intrinsic worth or they could have instrumental worth. Defending the claim that human gametes have intrinsic worth—understanding intrinsic worth as possessing moral status—is a nonstarter. A being possesses moral status when "*in its own right and for its own sake, it can give us reason to do things such as not destroy it or help it* [emphasis in the original]" (Kamm 2007, 229). Human gametes, in their own right and *for their own sake*, cannot give us reasons not to destroy them or to help them, since they do not have interests. Even those who contend that the human embryo is a person (or potential person)[40] admit this (Gómez-Lobo 2004). Now, even if we were to accept the *outlandish* claim that human gametes have intrinsic worth, it is difficult to

[39] I would like to thank an anonymous reviewer for bringing this point to my attention.

[40] A way of attacking one version of the potentiality argument (a human embryo has the moral worth of a normal adult human being because it has the potentiality to become one) is to point out that the unfertilized egg might also possess the potential to become a person. The unfertilized egg would possess the same moral worth as a normal adult human being by virtue of the possibility of technology-aided parthenogenesis (Devolder 2015; Devolder and Harris 2007). A possible defence against this attack is to further distinguish between the potentiality of a human embryo and that of a parthenote (Austriaco 2011).

see why it would be debased by virtue of being created within a nonperson-HNH-chimera. In principle, an entity that possesses intrinsic worth possesses it independently of external circumstances, such as the place where it was created.

The second option is for human gametes to have instrumental value. Given that instrumental value is dependent on the making or completion of a task, we can indeed assert that human gametes can possess instrumental value. For example, when someone resorts to IVF, eggs and sperm become valuable as means to achieve reproduction.

Now, even if human gametes have only instrumental value, someone could press the argument by claiming that their instrumental value would *always* be debased by being generated within a nonperson-HNH-chimera, and therefore that we should not create chimeras that could produce them. The problem with this claim is twofold. First, we could try to achieve certain specific goals with chimeric-generated human gametes that we would not want to achieve with human-generated human gametes, and thus it is in relation to their usefulness for achieving such goals that their instrumental value should be measured.

Second, even if the instrumental value of chimeric-generated human gametes were measured against the goals that human-generated human gametes can achieve, this does not *necessarily* entail that chimeric-generated human gametes would have less instrumental value. Why not? Because if the value of chimeric-generated human gametes is related to achieving certain goals, within certain standards, then as long as they achieve these goals, it is simply not true that their instrumental value would be debased. This means that if the final result (reproduction or research) is not affected by the circumstances of their generation (inside a nonperson-HNH-chimera), then both sets of human gametes (human-generated and chimeric-generated) could have the same instrumental value.

8.2.3 INTUITIVE MORAL RESPONSES TO HNH-CHIMERAS CAPABLE OF HUMAN GAMETE PRODUCTION

A further option is available to those who hold that we should not create chimeric entities that could generate human gametes: to appeal to our intuitive moral responses. Within the literature on the ethics of creating HNH-chimeras, we find an example of this in Streiffer's commentary to the Robert and Baylis (2003) paper 'Crossing Species Boundaries'. There he states that "[e]ven opponents of the yuck factor [an intuitive negative moral response] must concede that, sometimes, we know that an action is wrong merely on the basis of our reaction to it, even if we cannot satisfactorily justify that reaction" (Streiffer 2003, 38).

The first problem with this strategy when using it to ground a normative claim is that different people have different intuitive moral responses regarding the same subject. This means that we tend to end up with many contradictory intuitions that try to establish different normative claims. For example, some might intuit that creating nonperson-HNH-chimeras that could produce human gametes is morally unproblematic, while others might intuit the opposite.

It is true that our intuitive moral reactions to certain states of affairs are strong, but it is important to qualify what role those intuitions should play in our moral life. In recent work, Jonathan Glover has advanced the idea that such intuitive moral responses can have at least two functions: as excluders or as early warning systems. He goes on to assert that we must have a great deal of confidence in our intuitive moral responses for them to be used as excluders [i.e. "a sign that a morally impassible barrier has been reached" (Glover 2015, 38)]. This is so because the intuitive moral response is taken as a final evaluation regarding the subject that is being examined. For example, think of someone whose intuitive moral response to interracial marriage was deeply negative, and that she used such a response as an excluder that settled the matter. It is true that later on such a person can assess, from an ethical theory, whether the situation that prompted the intuitive negative moral response is, in fact, immoral. The problem here is that if the person strongly believes that her intuitive moral responses are *always* right, she has no reason to doubt them or to thoroughly examine them.

Even if this person does not believe that her intuitions are morally infallible, she can still use them as excluders by acknowledging that, at certain times, we cannot satisfactorily justify our reactions, just as Streiffer asserts. For example, the abovementioned woman could do exactly this if she were to find no good argument to support her intuitive moral response to interracial marriage. Settling for our moral intuitions, when no rational justification can be provided, seems morally risky, given the long history of human intuitions in support of deeply immoral practises (e.g. slavery).

An alternative approach to using our intuitive moral responses as excluders is to use them as an early warning system. When we use them in this fashion, we assume that they are first responses and are open to rational criticism and discussion. Glover divides our intuitive moral responses into three types: 'trained moral nose', 'strange smell', and 'human responses'. The 'trained moral nose' responds to situations in accordance with a set of relevant moral beliefs. For example, when someone tries to disguise a religious argument as a secular argument, those with a trained moral nose will notice a 'religious smell'. The trained moral nose relies little on

intuition, given that arguments can promptly be provided, and thus we are no longer in need of the intuitive moral nose. The second source of intuitive moral responses are 'strange smells'. These strange smells appear in unfamiliar situations that might threaten previously engrained category divisions. For example, when IVF first appeared, many felt that it had a 'strange smell'—a smell that originated from the disruption of entrenched reproductive categories. The last moral nose is the 'human response'. This nose is activated when we feel sympathy for others (people or certain nonhuman animals) that suffer or are denied respect. An important caveat regarding this one is that we can override it if there are sufficiently strong motives for doing so (Glover 2015, 33–43).

If we regard our intuitive moral responses to the creation of nonperson-HNH-chimeras that could produce human gametes as an early warning system, we can then examine which of the three alarms it sets off. In the first part of Sect. 5.2.1 'The general wrongness of creating HNH-chimeras', I have shown that those with a 'trained moral nose' have so far failed to show that the creation of nonperson-HNH-chimeras capable of producing human gametes is immoral. Those who hold that creating such chimeras produces a 'strange smell' could justify this by asserting that the creation of human gametes within chimeras is an unfamiliar situation that modifies a previously engrained category division (i.e. only humans produce human gametes). It is important to realise that people who detect this 'strange smell' do not necessarily need to hold that the creation of such chimeras is immoral. I am inclined to think that the 'strange smell' hypothesis is behind most intuitive moral responses to the creation of chimeras that could produce human gametes. Finally, some people can have a 'human response' when confronted with the creation of such chimeras. They would claim that using them for biomedical research or reproductive purposes is immoral, given that they are not properly respected. It is true that chimeras' moral status would require from us certain things, but it is also true that if strong reasons are presented, these can trump the chimeras' interests. What should we make of this discussion of our intuitive moral responses? That it is better to understand them as an early warning system, and that in the case of creating HNH-chimeras capable of human gamete production, they appear to be of either the 'strange smell' or the 'human response' kind.

At this point we can conclude that, so far, it has not been possible to construe a *principled* argument that grounds the hypothetical strong normative claim (A). At best, we could present particular arguments against using chimeric-generated human gametes for certain specific ends (if they were not good enough for attaining those ends).

8.3 ARGUMENTS IN FAVOUR OF CREATING HNH-CHIMERAS CAPABLE OF HUMAN GAMETE PRODUCTION

Three arguments can be advanced in favour of creating nonperson-HNH-chimeras capable of human gamete production: the saving persons argument, the unburdening women argument, and the restoration of fertility argument. Of these three, only the first seems strong enough to justify the creation and posterior destruction of such chimeras. The second and third arguments could justify the extraction of such gametes (which would imply a certain degree of harm), but it is not clear that they could justify the destruction of the chimeras.

8.3.1 THE SAVING PERSONS ARGUMENT

Let us examine the saving persons argument. By producing chimeras capable of producing human gametes, we could reduce the shortage of human eggs. This shortage is relevant because it slows, and in certain cases stops, valuable medical research that could save lives (Maher 2008). For example, two areas that would benefit from a surplus of human eggs are regenerative medicine and embryonic stem cell research. Now, with regard to obtaining the gametes, there are two options: the chimeras could be terminated after the extraction, or they could not. In either of these two scenarios, the extraction of eggs is morally permissible if killing sentient nonpersons in order to save persons' lives is morally permissible.

It should be noted that the strength of this argument also depends on two further facts. The first is that iPS cells cannot replace hESCs, and that in vitro gametogenesis (from which human embryos would be produced and then embryonic stem cells derived) cannot replace hESCs. If the contrary were the case, then harming or killing such chimeras would be immoral. The second requisite is that the harms that a chimera would endure are proportionally less than those that a human person would have to endure by donating her eggs. If the harms to the chimeras were equal to or larger than those experienced by a human person, justifying the morality of such practices would be more difficult.

8.3.2 THE UNBURDENING WOMEN ARGUMENT

The second argument that we could put forward for favouring the production of these chimeras is that of unburdening women. By means of creating nonperson-HNH-chimeras capable of producing human gametes, we would reduce the number of women subject to the risks that donating eggs for research purposes entails. This second reason would extend to egg extraction, or donation, for reproductive purposes if chimeric-generated gametes could, and would, be used for such purposes. Among the medical risks of egg donation are mild, moderate or severe

ovarian hyperstimulation syndrome, ovarian torsion, infection, rupture of ovarian cyst, and intraabdominal bleeding. Some of these risks are moderate, while others can be life threatening (Maxwell et al. 2008).

Three things should be noted about this second argument. First, it can be regarded not as an independent argument but as a positive externality of the first argument. Second, if it is construed as an independent argument, we must further show when such acts are, in fact, morally permissible. Why? Because while it seems permissible to harm the chimera in order to unburden women, it is not obvious that the possible harms to the human person are reason enough for killing the nonperson-HNH-chimera.[41] I will not expand on this point, because here I am taking this second argument not as an argument *per se* but as a positive externality of the first argument.

The third thing to note is that this second argument could in certain scenarios be used as a counterargument to the creation of such human gamete-producing chimeras.[42] If the quality and usefulness of such chimeric-generated human eggs were inferior to those produced by women, but not to the point of being useless, they could simply be used as an intermediate step in experiments that in the end would require women's eggs anyway. Suppose that scientists are trying to achieve X and that they employ chimeric-generated gametes as a way to do so. They realise that such gametes are only partially appropriate for the research. If this were the case, they could use chimeric gametes to get closer to X, and then at some point they would switch to using women's eggs. The creation of nonperson-HNH-chimeras that could produce human gametes would, in these circumstances, end up promoting egg donation, with all the dangers that it implies.

Three things should be noted regarding this possible counterargument. The first is that it is dependent on the attainment of certain empirical facts. The only way we have of knowing whether chimeric-generated human gametes could be equivalent (in terms of research or reproductive potential) to human-generated human gametes is to actually develop and test them (while constantly trying to refine the ways in which they are generated). The second point is that chimeric-generated human gametes could be used as an alternative to human-donated eggs

[41] An important caveat must be mentioned: this objection would not necessarily apply in all cases, because we could create HNH-chimeras that could produce human gametes and at the same time lack moral status. For example, we could try to create anencephalic pig-human chimeras that could produce human gametes.

[42] Here I follow the argument advanced by Baylis (2008) when critiquing the creation of cytoplasmic hybrid embryos (such embryos are produced when human nuclear DNA is inserted into the enucleated egg of a nonhuman animal).

while other methods for generating human gametes are perfected—for example, the mass production of in vitro-generated gametes from induced pluripotent stem cells (Palacios-González et al. 2014). The third point is that even if researchers eventually need additional quantities of human-generated human eggs, this is not necessarily bad overall, despite the possible dangers. The harms of egg donation in such circumstances should be weighed against the good that could be done—supposing, of course, that such donations are made with proper informed consent, and not under duress or undue influence.

8.3.3 THE RESTORATION OF FERTILITY ARGUMENT

The third argument, the restoration of fertility, claims that restoring human fertility is of such importance that we should create and use nonperson-HNH-chimeras that could produce human gametes for this end. This might be an option, for example, when patients become infertile due to medical treatments (such as cancer treatment) or trauma. In fact, research into this area has already started. Scientists have *xenografted* human reproductive tissues into young Swiss nude and SCIDNOD [non-obese diabetic/severe combined immunodeficient] mice in order to study how to preserve the fertility of patients enduring gonadotoxic cancer treatments (Arregui and Dobrinski 2014 ; Geens et al. 2006 ; Kim et al. 2005 ; Weissman et al. 1999 ; Wyns et al. 2008). Now, the merit of this third argument depends on whether the strength of the reproductive interests of such humans would trump over the interests of the nonperson-HNH-chimeras. While the case where a chimera would be harmed, but not killed, by the retrieval of the gametes seems morally permissible, it is not clear to me that the cases where the chimera would be killed are equally so.

To sum up, three different arguments can be advanced for creating and using nonperson-HNH-chimeras capable of producing human gametes. Of these three arguments, the first (the saving persons argument) is the strongest, given that it morally permits harming and killing such chimeras. The other two arguments (the unburdening women argument and the restoration of fertility argument) seem to permit harming the chimeras, but it is not clear that they would allow for their killing (although this is open to further investigation).

At this point we could offer a different explanation of the German Ethics Council's stance. Instead of assuming that their recommendation is grounded on a moral claim about the general wrongness of creating HNH-chimeras that could produce human gametes (or the debasement of the value of human gametes), we could posit that their claim is a practical recommendation in order to avoid human or hybrid pregnancies within HNH-chimeras. As Greely has noted:

> The worry [about creating HNH-chimeras that could produce human gametes] *must* be not about the gametes in themselves, but about the possibility that the gametes will be effectively used—that human sperm or eggs in chimeras will fertilize or be fertilized (Greely 2013, 684).

Now I will turn to some of the ethical problems that could emerge from the reproduction of nonperson-HNH-chimeras that produce human gametes.

8.4 HUMAN PREGNANCIES WITHIN NONPERSON-HNH-CHIMERAS

Depending on the biological makeup of the nonperson-HNH-chimeras, the following pregnancies are *theoretically* possible: (i) nonhuman animal pregnancy, (ii) hybrid pregnancy (e.g. a human egg is fertilized by a nonhuman sperm), or (iii) human pregnancy. In this section I will explore the third possibility, and by this I mean the moral quandaries that could arise from the fact that nonperson-HNH-chimeras could get pregnant with human conceptus.[43]

There are three possible ways in which human chimeric pregnancies might occur: (i) sexual reproduction, (ii) artificial insemination, or (iii) IVF and embryo transfer. It is important to bear in mind that only sexual reproduction (if the biological conditions are met) can be achieved without human intervention. This means that nonperson-HNH-chimeras' human pregnancies could be either intentionally sought or could happen accidentally.

In order to *avoid* accidental human pregnancies, Greely has proposed (i) creating HNH-chimeras of only one sex, (ii) using HNH-chimeras that are reproductively immature, and euthanizing them before they reach reproductive maturity, (iii) sterilizing them, (iv) euthanizing them if they get pregnant, or (v) physically segregating them by sex (Greely 2013, 686).

A human pregnancy within a nonperson-HNH-chimera could raise moral concerns for two sets of reasons:

> (B) It could be morally problematic because of what could happen to the human conceptus.
>
> (C) It could be morally problematic because of what could happen to the nonperson-HNH-chimeras during pregnancy and labour.

[43] While I will not discuss the issues surrounding the reproduction of HNH-chimeric-persons here, it is worth pointing out what Cobbe has clearly stated: "[I]f a chimera with apparently human mental faculties should be either kept in isolation or unable to reproduce with similar creatures because of enforced prohibitions against breeding, this entails automatic denial of what many would otherwise see as fundamental rights in humans" (Cobbe 2011, 142).

Although here reasons (B) and (C) can be neatly divided, in actual pregnancies they could overlap, adding complexity to the moral evaluation of such cases. Let us start by examining (B). There are three things that could happen to any embryo produced within a nonperson-HNH-chimera that could be regarded as morally problematic.

(B.1) It could die in utero due to intrinsic biological circumstances.

(B.2) It could be terminated by human action.

(B.3) It could develop well and long enough to be able to survive in the extrauterine environment.

Let us examine each of these scenarios.

8.4.1 IT COULD DIE IN UTERO DUE TO INTRINSIC BIOLOGICAL CIRCUMSTANCES (B.1)

Before discussing (B.1) it is important to realise that almost all reproductive scenarios involving HNH-chimeras will probably fall under this heading. Why? Because HNH-chimeras that are currently used for research are biologically incapable of carrying to term any human pregnancy (e.g. human-mouse or human-pig chimeras). As Greely rightly says, "[d]epending on the nonhuman component of the chimera, a 'human' pregnancy could be disastrous; no human fetus could develop successfully inside a mouse or a rat" (Greely 2013, 685).

There are three scenarios that fall under (B.1) that could be regarded as morally problematic: (B.1.1) the human embryo could fail to implant in the body of the nonperson-HNH-chimera and therefore die; (B.1.2) it could implant, start to develop, and die without any detrimental effect to the health of the nonperson-HNH-chimera; or (B.1.3) it could die after implantation, and such event could have a detrimental effect on the health of the nonperson-HNH-chimera.[44]

One of the reasons why *natural* human embryo loss (i.e. that which depends on the intrinsic characteristics of the embryo or the intrinsic biological traits of the woman) is not regarded as a morally problematic event in itself is because the loss is not intentionally sought, and therefore no one is blameworthy. If this is the case for human-occurring human pregnancies, all else being equal, the same reasoning should then apply to cases of *natural* embryo loss in chimeric pregnancies. Why? Because if moral blameworthiness rests on the fact that the loss

[44] Even when case (B.1.3) is part of the broader category of how human pregnancies could affect the interests of nonperson-HNH-chimeras, I will restrict my discussion to how the chimera's health could be affected and the moral implications of this.

is intentionally sought, then as long as it is not, there appears to be no moral problem in this regard.

One could argue that naturally occurring human embryo loss is morally problematic in cases of nonperson-HNH-chimera pregnancies. Why? Because scientists are in fact intentionally *creating*, or facilitating the creation of, human embryos for research purposes that would be 'destroyed' by means of 'placing' them in an environment where they cannot survive. Thus, even when the destruction of the embryo is not *intentional* per se, it is in fact foreseeable, and it is morally wrong not to stop a foreseeable bad outcome that can indeed be stopped.[45]

There are two problems for those who hold this position. The first is that they would necessarily be committed to the claim that women who knew that they cannot carry a pregnancy to term because of certain medical conditions would be doing something morally wrong when placing themselves in a position where they could get pregnant. This strike us as evidently false.

The second problem is that this counterargument depends on the human embryo possessing moral worth—worth that is far from proven. Why is this the case? Because if there is something morally wrong with scientists participating in, or causing, a human pregnancy within a nonperson-HNH-chimera that will not come to term, then it must be, in part, because something valuable would be lost. In this case, the thing considered to be of value is the embryo's life. However, human embryos lack the morally relevant properties that would make their intentional, or foreseeable, destruction morally wrong. Even more so, the fact that they possess such properties in a potential state does not, in actuality, confer them moral worth. What this means in practical terms is that their destruction, intentional or accidental, is of no moral consequence[46] (Devolder 2005; Devolder and Harris 2007; Harris 1985).

Following a similar line MacKellar and Jones have advanced a 'confusion' argument against causing or allowing *any* nonperson-HNH-chimera human pregnancies. For them "[t]here is indeed a risk that human embryos and human foetuses could be considered in the same manner as those of animals (with no special protection being granted) if they were to be found in an animal. As a result, this may further undermine the conferring of any respect and dignity on human embryos and foetuses" (MacKellar and Jones 2012, 81).

[45] This objection does not apply to those cases where the process by which the embryo is formed makes it unviable.

[46] For a discussion about how the legal permissibility of abortion would support a liberal policy on human embryonic stem cell research that involved the creation of HNH-chimeras, see Streiffer (2010).

The force of this argument is not as strong as these authors believe: this concern applies neither to those who think that the human embryo possesses an intrinsic worth comparable to that of a normal adult human being, nor to those who think that the human embryo does not possess intrinsic moral worth. It does not apply to the former group because they, *in principle*, accept the assertion that regardless of where such embryos are located, they possess intrinsic moral worth.[47] It does not apply to the latter group because they, also *in principle*, reject the intrinsic moral worth of the embryo, regardless of where the embryo is. Thus the risk of considering the human embryo as a thing that it is not (i.e. a nonhuman animal embryo) should be understood as a risk of *biological* confusion and not as a risk of *moral* confusion. Additionally, if the human embryo does not possess intrinsic moral value, then the distinction between embryos with 'dignity' and embryos without 'dignity' does not hold, given that all of them are dignity-less embryos. At this point we can conclude that cases (B.1.1), (B.1.2), and (B.1.3) are morally unproblematic from *a human embryo loss perspective*.

Now, causing or allowing pregnancies of the type (B.1.1) and (B.1.2) could be regarded as morally unproblematic, because on the one hand, human embryos do not have intrinsic moral worth, and on the other hand, the health of the nonperson-HNH-chimeras would not be jeopardized by the pregnancy. While this might be the case, we should not overlook the fact that all of the chimera's interests, not only its health, should be taken into account when assessing the different courses of action. Case (B.1.3) is, in an important respect, different from (B.1.1) and (B.1.2). The difference is grounded on the fact that from the start, we know that such pregnancies will have a negative toll on the chimera's health. This being the case, scientists should present strong moral reasons either for causing such human pregnancies or for not promptly terminating them.

The practical implications of this section are: there would be nothing morally wrong with allowing or causing human pregnancies to occur if they are of type (B.1.1) or (B.1.2), and if the human pregnancy would have a detrimental health effect on the nonperson-HNH-chimera, as in case (B.1.3), we must then provide strong reasons for causing or letting such pregnancies continue.

[47] I would like to thank an anonymous reviewer for bringing this point to my attention.

8.4.2 IT COULD BE TERMINATED BY HUMAN ACTION (B.2)

Now I will explore (B.2). Here, I do not address whether it is permissible to terminate a human pregnancy, but what moral reasons there could be to terminate a human pregnancy that occurs within a nonperson-HNH-chimera.[48] There are at least six reasons that could be advanced to show that we are morally required to terminate a nonperson-HNH-chimera human pregnancy: (B.2.1) because of the ill effects such pregnancies would have on the health of the nonperson-HNH-chimeras; (B.2.2) because the human will nonetheless eventually die in utero; (B.2.3) because the child born would have a wrongful life; (B.2.4) because, if carried to term, such a human is likely to have major health problems; (B.2.5) because such pregnancies would be morally repugnant; and (B.2.6) because any child born this way would be severally discriminated against. Before examining these cases, it is important to bear in mind that cases (B.2.3), (B.2.4), (B.2.5), and (B.2.6) would necessarily require that the human conceptus is viable, so for the sake of argument, I will treat these four scenarios as feasible.

In a research context, case (B.2.1), along with (B.1.3), would morally require the termination of such humans if (i) the scientific gains from such pregnancies do not outweigh the harms that the nonperson-HNH-chimeras would suffer from it, or (ii) there are no scientific gains from such pregnancies. This is grounded on the fact that, whereas human embryos do not possess intrinsic value (as previously stated), nonperson-HNH-chimeras would be sentient[49] (which confers upon them moral worth), and their interests should be weighed against possible scientific gains.

On the other hand, if there were an instance (B.2.1) where there would be detrimental health effects for the nonperson-HNH-chimera but the human would be viable, and (i) the group in charge decided not to terminate the pregnancy, regardless of the law and the health consequence to the nonperson-HNH-chimera, or (ii) the pregnancy somehow remained undetected until the conceptus was able to survive in an extrauterine environment, then those in charge of the chimera would have to tackle the *really substantial* practicalities that a human being born from such entity would entail. By this I do not mean the certain media frenzy, but what should be done with a child born in these circumstances. I think that even in this farfetched scenario, two things should be obvious: (i) in terms of child protection, such cases should be

[48] I take for granted that there is no further need to develop the arguments in favour of the legal and ethical permissibility of some abortions.

[49] It could be the case that through further genetic engineering, nonperson-HNH-chimeras could be created to be non-sentient, see note 5.

treated *on a par* with cases of fully incompetent familyless women who are pregnant, and (ii) regardless of her *gestational origins*, such child would be entitled to the same treatment as any child born to a woman, given that her moral status would be the same as that of any other human child. It should be noted that while most conservatives would much rather reject the idea of a nonperson-HNH-chimera getting pregnant with a human conceptus, as soon as it got pregnant, they would necessarily be committed to the defence of such life, since for them, a human embryo has the same moral status as that of a normal adult human.

If the human conceptus will eventually die in utero, case (B.2.2), either by legal requirement or by natural causes, we would be morally required to abort it as soon as possible when there were no scientific gains to expect from its development, and when its existence negatively affects the health (or other interests) of the nonperson-HNH-chimera (just as in cases (B.2.1) and (B.1.3)). The abortion should take place early on, given that late-term abortion could have a deeper negative impact on the chimera's health.[50] Finally, as stated above, if there are scientific reasons for letting the pregnancy carry on, then such reasons should be weighed against the interests of the nonperson-HNH-chimera.

Of all the cases, I think that (B.2.3) might be the easiest to deal with, because morality requires that either wrongful lives (i.e. lives of such overall poor quality that they would have been better to never have been) should not be brought to birth (when endorsing an impersonal account of morality) or, if so, they should be terminated as soon as they start to suffer (when endorsing a person-affecting account of morality).[51] In practical terms this means that if we knew that the developing human would have a wrongful life, we would then be morally compelled to terminate her. And, just as stated above, if there were possible scientific gains that could be obtained from such pregnancies, that override the health interests of the nonperson-HNH-chimera, then the developing human should be left to develop only for as long as her life is non-wrongful.

Now let us suppose that a nonperson-HNH-chimera is pregnant with a human, and that all the scientific data gathered pointed to the conclusion that even when the developing human has major health problems, she is viable and would have a life worth living. What should we do in such cases? Although, as Hank Greely rightly recognises, "[m]any countries, including the

[50] I would like to thank an anonymous reviewer for bringing this point to my attention.

[51] For a recent discussion on the moral permissibility of creating wrongful lives, see Smajdor (2014) and Williams and Harris (2014).

United States, allow abortion of fully human fetuses for broad reasons, and others allow abortion for reasons of fetal health" (Greely 2013, 685), I think that (B.2.4) cases do not straightforwardly require the termination of such conceptus. As the non-identity problem shows us, as long as such human life is worth living, we would not make her worse off by not aborting her (Parfit 1984, Chap. 4), because the only other option for her would be to never have been.[52] In point of fact (and as stated previously), we should treat (B.2.4) in the same way as we would treat pregnancy cases of family-less fully incompetent women (that had the same capacities as the nonperson-HNH-chimera) who are pregnant with a developing human that has severe health problems. I think moral consistency requires this action and nothing less. I also maintain that if someone recommended treating those cases in different ways, because in one instance the *pregnant creature* is fully human and in the other the creature is a chimera, such call for action would clearly be speciesist. Now, if we are not morally required to terminate those humans that have severe health problems and are gestated by familyless fully incompetent women (even if doing so is not morally problematic), we are then also not morally required to terminate the pregnancy of a nonperson-HNH-chimera that gestates a human with severe health problems (it should be added that we are required to take into consideration the interests of the pregnant creature when deciding the course of action, and that this might yield different results). If this ever happened, just as was discussed in (B.2.1), those in charge of the chimera would be required to take appropriate measures for the child to be properly taken care of.

Case (B.2.5) should be classified as no more than a 'yuck factor' instance, as explained in (2.3). The fact that these pregnancies might prompt strong intuitive moral responses is not reason enough for terminating them. Suppose that a child with a life worth living could be born from a human-chimpanzee chimera. If this were the case, then what could be regarded as repugnant? Someone might claim that such pregnancies are repugnant because they are unnatural or because they cross the species barrier. This objector to nonperson-HNH-chimera human pregnancies has the burden of proof to show that such arguments are different from those that have already been levelled against the creation of any type of HNH-chimera, and that have been found wanting. I think that in order to be significant for debate, any claim stating that such pregnancies are morally repugnant must be backed up by explicit rational arguments.

[52] The fact that this human is not made worse off does not imply that under a non-comparative account of harm she could not be regarded as being harmed, nor that there could not be impersonal reasons for not carrying to term such pregnancies.

Finally, someone could claim that the main moral reason we have for terminating such pregnancies is that any child born of them would be harshly discriminated against, case (B.2.6). Many might think that this is the most compelling argument against nonperson-HNH-chimeras giving birth to a human child, but I consider this point to be terribly misleading. As I have previously said, a human child born of a nonperson-HNH-chimera would have the same moral status as any other human child born to a woman. This means that society (scientists included) should treat her accordingly to her moral status, and this entails that she is not discriminated against on the basis of who bore her. The fact that such a child would be born of a *different* type of entity should in no way be detrimental to the child's flourishing and opportunities. If we think that discrimination against a child because of her origins is wrong (regardless of what these origins are), then (B.2.6) should not be taken seriously as an argument for terminating such pregnancies. Think of the reaction if a racially mixed couple were told that they should not have a child because the child would be the object of discrimination due to her 'strange' origins. Such advice is morally ill informed, and in such situations the proposed prescriptive measure is immoral and thus does not warrant enactment.

From this section we can conclude that unless the life of the developing human would be a wrongful one, we are *not morally required* to terminate nonperson-HNH-chimera human pregnancies in *all* cases.

8.4.3 IT COULD DEVELOP WELL AND LONG ENOUGH TO BE ABLE TO SURVIVE IN THE EXTRAUTERINE ENVIRONMENT (B.3)

What moral problems could there be if a human is successfully born from a nonperson-HNH-chimera? Although I think that this could be perceived by some as the most outrageous scenario, it is actually not especially problematic. This is because, as I stated earlier, a child born from a nonperson-HNH-chimera would have the same moral status as any other human child. At this point, someone could claim that it is unreal to think that such a child would be treated adequately, given that she would be born either as part of an experimental project or as an accident. Such person could also claim that being born under these circumstances would mean that this child would never be accorded moral status, and that this is reason enough for not letting nonperson-HNH-chimera human pregnancies happen.

My response to this claim is twofold. First, it does not follow from the fact that a future child could be mistreated (either intentionally or accidentally) that the only adequate response is to prevent her existence (once again, think of the case of the racially mixed couple). It is true that

in the history of science, there are cases where scientists have failed to respect the moral status of their research subjects (for example, the Tuskegee syphilis experiment), so in order to tackle this possibility of mistreatment, scientific governing organisations should enact clear guidelines addressing how to proceed if these types of cases ever were to occur, on top of relying on the morality of researchers.

Second, it is important to realise that it would be very difficult to claim that a child that is generated by human gametes, produced by HNH-chimeras, and then brought to term by a HNH-chimera, has been made worse off[53]: it is highly likely that if these generative specific acts had not happened she would not have existed. We need to remember that a particular child's existence is necessarily tied to the fusion of the specific gametes that produced her. This means that if she was not created at the specific time, and in the specific way in which she was created, then the most probable alternative is that either no child would have been created or a nonidentical child would have been created. This means that as long as the child's life is worth living, the type of generative action that brings her into existence does not make her worse off.[54]

Given that a child born from a nonperson-HNH-chimera would have the same moral status as any other child, the supposed moral problems generated are, in fact, not specific to chimera gestation, but are general problems about population ethics and child protection that we confront on a regular basis.

8.4.4 SUCH PREGNANCIES COULD BE MORALLY PROBLEMATIC BECAUSE OF WHAT COULD HAPPEN TO THE NONPERSON-HNH-CHIMERAS DURING THE PREGNANCY OR LABOUR (C)

Another line of argument against allowing nonperson-HNH-chimeras to become pregnant with humans is that (i) we do not know what the consequences for the health of the nonperson-HNH-chimeras could be, and (ii) given that nonperson-HNH-chimeras do not lose anything by not becoming pregnant, we should not allow pregnancy to occur.

[53] As discussed in (B.2.3) the only case in which a child could be made worse off by her existence is if she had a wrongful life.

[54] Two questions are left open. The first is whether the numerical identity of an individual would be affected if she were either gestated by a HNH-chimera or a woman. The second is whether prenatal harm would ensue depending on whether one or the other gestates. For a discussion about possible persons and the problem of prenatal harm see Williams (2013).

I will start with point (ii). It is true that the nonperson-HNH-chimera would not lose anything by not becoming pregnant with a human, and this is indeed an argument in favour of not allowing them to become so (just as we do not usually encourage fully incompetent women to get pregnant).[55] On the one hand, if there is nothing that we could scientifically gain from such human pregnancies, then in order to not affect the chimera's health (or other interests), we should prevent such cases from happening by following one of Greely's recommendations. On the other hand, if there are scientific gains that could be obtained from allowing a human pregnancy (noting that the duration of the pregnancy would depend on current legislation), we might be losing something important if such pregnancies did not occur. This means that, depending on the scientific scenario, there might be moral reasons to either let such human pregnancies happen or not to let such pregnancies happen. For example, there is at least one theoretical possibility, whose morality is open to further elucidation, for why scientists might want to do this: if nonperson-HNH-chimeras could be used to create human organs for transplantation, then at a certain point they might try to create human female reproductive organs within a nonperson-HNH-chimera. If this were ever to be the case, scientists could be tempted to explore the functionality of such uteri by transplanting a human embryo into it and observing what happens.

The argument against letting nonperson-HNH-chimeras become pregnant with a human conceptus, which hinges upon the fact that we do not know what the health consequences for the chimeric entities could be, is similar to that explored in cases (B.2.1) and (B.1.3). Just as in those cases, the answer here is that we could be morally compelled to carry out such pregnancies, even against the health interests of the chimeric entity, when the scientific gains that would be obtained from the pregnancy outweigh the ill health effects on the nonperson-HNH-chimera. It is true that this threshold is high, but this does not imply that there are no circumstances in which it could be met.

8.5 FINAL REMARKS

This work is divided into two broad parts. In the first part, I have tried to show that, so far, there is no good argument against the production of nonperson-HNH-chimeras that could produce human gametes. I have also advanced that there is at least one good moral reason for creating nonperson chimeras capable of producing human gametes: there is a shortage of human eggs for research. In the second part, I explored some of the ethical aspects that could

[55] I would like to thank an anonymous reviewer for bringing this point to my attention.

be encountered if a nonperson-HNH-chimera were pregnant with a human. The moral problems that arise from such pregnancies fall into two categories. First, there are the moral problems that we would encounter if we fixed our sight on the product of such pregnancies. Second, there are the moral problems that would emerge from the fact that there is no previously gathered safety data from these pregnancies, and therefore no data on how the interests of the nonperson-HNH-chimeras could be affected. For both sets of problems, I have tried to provide some answers that hinge upon the moral status of the embryo and how moral consistency would require us to act in cases where a nonperson-HNH-chimera became pregnant with a human. Even when I have not given definitive answers, or provided a complete road map of the moral problems that could be present in such pregnancy cases, I think that this first mapping of the moral landscape is important insofar as it is a topic that has been neglected in the bioethical literature, but that could be technologically possible in the not-far-distant future.

9. ARTICLE IV: KILLING HUMAN/PIG CHIMERAS FOR THEIR HUMAN ORGANS: EXPLORING THE WELFARE ISSUES

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9.1 INTRODUCTION

This paper uses David Shaw et al.'s article "Creating Human Organs in Chimaera Pigs: An Ethical Source of Immunocompatible Organs?" as a springboard for discussing the chimera welfare issues that emerge from research into developing human organs within human/nonhuman chimeras, specifically into human/pig chimeras. As such I will follow the path that Shaw et al. laid down in their paper, and expand on the subjects that they explore. This work advances 'chimera ethics' by exploring and taking seriously the welfare issues that relate to research carried out upon human/pig chimeras that *are sentient beings*, but that nonetheless are not persons (i.e. that are not rational and self-conscious beings). This topic has, for the most part, not been sufficiently explored in the academic literature.

Shaw et al. have theorised that in the not-distant future it might be possible to tackle the human organ scarcity problem by employing *human/pig chimeras* (Shaw et al. 2015), following recent breakthrough research in the creation of interspecific and intraspecific chimeras (Kobayashi et al. 2010; Usui et al. 2012; Isotani et al. 2011; & Matsunari et al. 2013). In the biological sciences the term chimera is used to refer to organisms that are formed by combining whole cells from at least two numerically distinct sources that are also genetically distinct into a functional organism. The cells can belong to the same biological species, originating an intraspecific chimera, or they can belong to different biological species, originating an interspecific chimera.

One way in which we could 'grow' human organs within 'pigs' is by interspecies blastocyst complementation for the developmental compensation of an organ niche. In this scenario, we would first develop genetically modified pig embryos that lacked the adequate genetic information to develop certain organ(s), for example the liver. Next, and while the embryos are in a very early developmental stage, we would complement them with human induced pluripotent stem cells (hiPS cells), or human embryonic stem cells (hESC). These human cells would *compensate* for the lacking organ and would produce it. If everything proceeds as planned, we will have a transplantable *human* liver composed in its majority of human cells (or completely if we found a way for the organ's vascular system to also be developed by human

cells) within a 'pig' (Rashid et al. 2014). Technically speaking this procedure would create a human/nonhuman interspecific chimera that would be mostly constituted by nonhuman components and only by 'a few' human cells.

In their paper "Creating Human Organs in Chimaera Pigs: An Ethical Source of Immunocompatible Organs?" Shaw et al. highlight two possible advantages of this type of research, and examine four possible ethical objections to it. The possible advantages are: i) an *almost unlimited* source of human organs, and ii) the creation of *personalised chimera organs* by means of using the patient's induced pluripotent stem (iPS) cells. Contrary to the situation in most Western countries at this point, where organ donation is dependent on the number of people willing to make live donations or donate their organs after death, we would be able to create an almost unlimited source of human organs by creating *on demand or in advance* human/pig chimeras with transplantable human organs. Just as we have created an enormous pig-farming industry for the consumption of their meat, we could create a human/pig chimera human-organ-harvesting industry. Just imagine the difference between needing an organ and knowing that you could ask (or pay) for it to be developed in a matter of months, and needing an organ and joining a waiting list and waiting for it to be available, with the knowledge that you may never receive it.

The second possible advantage of creating human organs within human/pig chimeras is that, by using the patient's iPS cells, we would avoid many of the current problems with allogeneic transplants (i.e. organs that do not come from a genetically identical source). Let's remember that if we create human organs with the patient's iPS cells within human/pig chimeras then, when transplantation occurs, the patient's immune system will not regard the transplanted organ as a foreign object, and thus will not attack it. This is incredibly important because organ rejection is the most common reason for allogeneic organ transplantation failure. In the case discussed, the immune system does not regard the chimera's organ as a foreign object because, *in a certain sense*, it is an autologous organ transplantation (i.e. a transplantation that employs the patient's 'own' organ): the chimera-sourced organ and the human patient possess *the same* genetic code. It should be obvious, at this point, that these ideas are predicated on the fact that such research would prove to be successful, and that the creation of such chimeras at an industrial, or large, scale would be possible.

The four ethical objections that Shaw et al. examine are: i) the risk of zoonosis objection, ii) the human features objection, iii) the animal welfare objection[56], and iv) the human dignity objection. In this work, as I say at the outset, I will further Shaw et al.'s chimera welfare discussion while setting aside the other three objections. Specifically, I will engage with the four answers that these authors provide, in turn, to the four animal welfare objections that they advance against using human/pig chimeras for their human organs. Finally, I will establish the circumstances under which it is morally permissible to use human/pig chimeras for their human organs.

9.2 CHIMERA ETHICS LITERATURE

Before I examine Shaw et al.'s discussion on animal welfare I want to draw attention to a troublesome element of their research: they omit to cite and discuss, or even acknowledge the existence of, the literature on chimera ethics that deals with the four objections that they examine. Academic practice requires that researchers cite the relevant work as appropriate; while Shaw et al.'s paper is not a literature review they *should* have cited prior work of relevance to their topic. I will briefly map the chimera ethics field, and in so doing I will show some of the important work that has been omitted.

The most widely debated topic in the literature of chimera ethics is that of human dignity, which has been discussed for over a decade. The literature on human dignity objections against the creation of human/nonhuman chimeras, and the response to such objections, encompasses papers, book chapters and encyclopaedia entries. In spite of this breadth of interest, Shaw et al. only discuss The Academy of Medical Sciences' (2011) report "Animals Containing Human Material" and MacKellar's (2007) "Chimeras, Hybrids and 'Cybrids'". Additionally, they fail to acknowledge that the quote they cite from MacKellar's text is in turn referencing the discussion on human dignity by the US Committee on Guidelines for Human Embryonic Stem Cell Research. This is the section that Shaw et al. (2015, 973) quote from MacKellar's text:

> Some people worry that to produce creatures that blur the boundaries between humans and animals could threaten to undermine the concept of human dignity since it is a dignity specifically reserved to humankind. (MacKellar 2007, 2)

This is the text that MacKellar is making reference to:

> Research in which hES cells are introduced into nonhuman primate blastocysts, or in which animal or human ES cells are introduced into human blastocysts, should also not

[56] In this work I will follow Shaw et al. in using the term 'animal welfare' when discussing 'human/nonhuman chimera welfare' issues.

> be conducted at this time. These kinds of studies could produce creatures in which the lines between human and nonhuman primates are blurred, a development that could threaten to undermine human dignity. (National Academies of Science 2005, 55)

Furthermore, the following important research into human dignity and human/nonhuman chimeras was also omitted: Resnik (2003), Johnston & Eliot (2003), Karpowicz Cohen & van der Kooy (2004), Karpowicz, Cohen & van der Kooy (2005), Streiffer (2005), Ravelingien, Braeckman & Legge (2006), DeGrazia (2007), Baylis & Fenton (2007), Cohen (2007), de Melo-Martín (2008), Cooley (2008), MacKellar & Jones (2012), and Streiffer (2014). If Shaw et al. had acknowledged and built on this existing work, they would have discovered far stronger dignity-based objections against the creation of human/nonhuman chimeras than those that they address. The objections that they *do* tackle not only are they already present in the existing literature, but are for the most part the weakest ones.

Let's move on to examine the discussion around the zoonosis objection to the creation of human/nonhuman chimeras. This topic is explored in the literature on at least two related fields. Firstly, the debate on xenotransplantation and xenozoonosis contains commentary on the zoonosis objection (Barker & Polcrack 2001; Melo et al. 2001, Hughes 2007; Sparrow 2009). It could be argued that the debate on xenotransplantation is distinct from that on chimera ethics, and thus that it is not warranted to address the ethics literature of the former when discussing the latter. After all, in xenotransplantation cases we *do not create* human organs for transplantation, we only harvest nonhuman organs from nonhuman animals (that could have been previously genetically modified or not) and then transplant them into a human. However, consider that all xenotransplantations *produce* interspecific human/nonhuman chimeras because a nonhuman organ is placed into a human: the field of chimera ethics becomes relevant once more. Furthermore, we can find a discussion of the xenozoonosis objection within chimera ethics *per se.* The following authors, for example, have addressed this issue when discussing human/nonhuman chimera based organ transplantation: National Academies of Science (2005), Scottish Council on Human Bioethics (2006), Huther (2009), The Academy of Medical Sciences (2011), and Streiffer (2014).

It is true that animal welfare issues have not been as extensively discussed as those of human dignity, for example. But even so, we find that academic work on chimera ethics in relation to the moral status of human/nonhuman chimeras does address some animal welfare issues by establishing the moral responsibilities we would have towards different types of

human/nonhuman chimeras in medical research settings, and by investigating when a human/nonhuman chimera should be regarded as a person. Important work in this area includes: Streiffer (2005), DeGrazia (2007), Greely, Cho, Hogle & Satz (2007), Hyun et al. (2007), Streiffer (2010), Savulescu (2013), Piotrowska (2014), and Streiffer (2014).

Finally, the possibility of creating human/nonhuman chimeras that possess human features is central to the human/nonhuman chimera ethics debate. This scenario is viewed as one of three *particularly problematic* cases within human/nonhuman chimera research, alongside the creation of human/nonhuman chimeras with human-like cognitive capacities, and the creation of human/nonhuman chimeras capable of human gamete production and human pregnancy. These three cases are perceived as important enough to have been discussed in the three major reports that exist on the creation of human/nonhuman chimeras: the "Guidelines for Human Embryonic Stem Cell Research" of the US National Academies of Science (2005), "Animals Containing Human Material" by The Academy of Medical Sciences (2011), and "Human–Animal Mixtures in Research" by the German Ethics Council (2011). Additionally, Henry T. Greely's (2013) "Human/Nonhuman Chimeras: Assessing the Issues" dealt with this issue. Having noted this flaw in Shaw et al.'s research we can advance and revisit their animal welfare discussion.

9.3 REVISITING THE ANIMAL WELFARE OBJECTIONS

I assume here that the human/pig chimeras discussed would possess pig-proper mental capacities. This is important, as if these chimeras were to possess normal human-like mental capacities then killing them for their organs would be tantamount to killing human persons for their organs. Explicitly presenting this assumption makes it clear that animal ethics is best suited to dealing with the ethical quandaries that could arise from the killing of such chimeras.[57]

[57] It must be noted that if we follow a mental capacities approach for establishing who is a person (i.e. a rational and self-conscious being) then we have to accept that there are certain humans that are not persons. This means that there are certain humans whose mental capacities are such that they are neither rational nor self-conscious beings. Realising this is important since the morality of killing such humans is in important respects similar to that of killing nonhuman animals that are not persons. In fact, in ethics these human cases are used to show some of the moral problems with killing nonhuman animals. Usually they are discussed under the argument from marginal cases, or the argument from species overlap, which points out that ''the criteria that are commonly used to deprive nonhuman animals of moral consideration fail to draw a line between human beings and other sentient animals, since there are also humans who fail to satisfy them'' (Horta 2014, 142).

9.3.1 MEAT-EATING DEBATE

The first objection that Shaw et al. examine is that "(at least) one animal will be sacrificed for every human saved" (Shaw et al. 2015, 973). After presenting this objection they assess a *possible* response to it: that it would be odd to object to the killing of human/pig chimeras in order to save human lives when it is generally regarded as morally acceptable to rear pigs in order to eventually kill and eat them. The authors recognise that this response is problematic because it is predicated on the assumption that in regular circumstances it is morally unproblematic to eat pigs; this issue has long been contested within animal ethics (Singer 2001, Regan 2004, McMahan 2008). It has been contested on various grounds, for example because of the high environmental impact of a meat based diet, and because for most people eating meat is not necessary for maintaining health.

Shaw et al. decided to *remain neutral* on the question of whether eating meat is morally problematic, but they did assert that "creating chimaera organs seems no worse than killing animals in order to eat them" (Shaw et al. 2015, 973). Despite Shaw et al.'s neutrality on this question, it is helpful to look into the ethics of meat-eating, as there are links between this debate and the discussion around killing human/pig chimeras for their organs. Exploring these links will help us demonstrate that it would in fact be morally permissible to kill human/pig chimeras for their human organs.

To find the similarities between these two issues, we must pay attention to those cases where eating meat is necessary for a person's *survival*. By this I mean cases where killing sentient animals for their meat is the only nutritional option for us, and *our remaining alive* depends on it. The described scenario has been discussed in the context of different animal ethics theories, for example rights based approaches and utilitarian approaches. Peter Singer, while discussing speciesism, has maintained that:

> On a purely practical level, one can say this: killing animals for food (except when necessary for sheer survival) makes us think of them as objects we can use casually for our own nonessential purposes. Given what we know about human nature, as long as we continue to think of animals in this way we will not succeed in changing the attitudes that, when put into practice by ordinary human beings, lead to disrespect-and hence mistreatment-for the animals. So it might be best to make it a simple general principle to avoid killing animals for food except when *it is necessary for survival* [emphasis added]. (Singer 2001, 229)

Tom Regan, while discussing the now famous lifeboat scenario (where five survivors, four human persons and one dog, find themselves in a lifeboat that only has room for four), has maintained that:

> Death for the dog, in short, though a harm, is not comparable to the harm that death would be for any of the humans. To throw any one of the humans overboard, to face certain death, would be to make that individual worse-off (i.e. would cause *that* individual a greater harm) than the harm that would be done to the dog if the animal was thrown overboard. (Regan 2004, 324–5)

Both a rights based and a utilitarian approach accept, on different grounds, that killing a sentient animal for food is morally permissible when *our survival* depends on doing so. Both approaches agree on this, broadly speaking, because death harms human persons in a more substantive way than it harms sentient animals. Now, if killing and eating sentient animals in such instances is morally permissible then, other things being equal, it should also be morally permissible to kill human/pig chimeras for their human organs *if our survival depends* on it, and there are no other *morally acceptable means* available to us to obtain the much needed organ(s). This clearly shows that the ethics of meat-eating can shed light onto the ethics of killing chimeras for their human organs, and, in fact, it can provide us with a simple argument for the moral permissibility of killing human/pig chimeras for their human organs.

9.3.2 UNFAIRNESS

The second objection that Shaw et al. examine is that "it is unfair to kill animals for their organs when many humans refuse to donate their organs after death" (Shaw 2015, 973). In order to respond to this objection they make two claims. First, they claim that although the objection is valid we would still need human/pig chimera human organs, because even if everybody donated their organs there would still be a shortage. Second, they claim that chimera based organ 'donation' could be a better solution than human organ donation in terms of efficacy, because, as stated previously, the incidence of organ rejection would decline as the organs would be developed with the patient's own iPS cells.

There are two issues with Shaw et al.'s first point. First, it is an *empirical claim*, and they do not present any data to support it. Intuitively it appears that there would not be enough organs for transplantation but this is, in fact, an unresolved question whose answer would determine, in part, if killing human/pig chimeras is morally permissible or not. Second, if they are correct, which might be the case, it *would not* follow that we have *carte blanche* to kill human/pig chimeras in order to transplant *allogeneic chimera human-organs*. What would follow is that

killing these chimeras for their organs is morally permissible when *all other* morally acceptable courses of action have been exhausted. This means that people would have to resort first to receiving human organs from a human source, either through cadaveric donation or live donation, and only if this failed would they be able to receive organs from a human/pig chimera. The argument behind this is that this course of action should reduce, overall, harm. A different assessment is needed to elucidate whether it is morally permissible to kill human/pig chimeras in order to obtain human organs derived from the patient's iPS cells when there are enough human allogeneic donated organs available (more on this later).

Additionally, there are two reasons why maximizing human organ donation is preferable to obtaining human organs from human/nonhuman animal chimeras. First, we would *reduce even further* the risk of xenozoonosis caused by chimera human-organ transplantation which, even if the risk is small, is always a good thing to do: it is worthwhile to remember that a disease could be transmitted from the nonhuman animal to the human by means of the transplanted human organ. Second, the amount of resources needed for creating chimeras and taking care of them would diminish. This is particularly important if costs were to be covered by governmental medical budgets, which are always scarce.

Regarding Shaw et al.'s second point, on efficacy of treatment and organ rejection, it is true that chimera organs produced with the patient's iPS cells could reduce, or even eliminate, the incidence of organ rejection, but this descriptive claim is only interesting in that it raises the following question: is it morally permissible to kill human/pig chimeras in order to obtain patient-derived iPS cell organs, when we could obtain enough allogeneic organs for all of our transplantation needs via human live donation or human cadaveric donation? An answer to this question is that using human organs obtained from nonperson sentient chimeras in cases where we could have used human organs obtained from a human is morally permissible if the health benefits to the patient are great enough that they trump over the chimera's interest in continued existence.

9.3.4 OVERALL WELLBEING

The third objection that Shaw et al. examine is that while pigs can be ethically farmed (having contented lives before being killed) human/pig chimeras will most probably have shorter lives and reduced wellbeing. They would have to be kept in sterile conditions, and the fact that they are chimeras, in this case that they have a human organ instead of a pig organ, could produce pain or discomfort. To this objection Shaw et al. reply that "[n]onetheless, given that society

generally accords humans greater importance than animals, it appears that creating organs in this way would not threaten animal welfare in a new or unique way" (Shaw et al. 2015, 973).

Shaw et al.'s response to this objection is problematic in an important respect: it does not tell us anything *relevant* about the morality of killing human/pig chimeras for their organs. It is true that society, in general, might accord greater importance to humans than to nonhuman animals. It is also true that when compared with current nonhuman animal research creating organs in this way might not threaten animal welfare in a *unique or novel way*. Even if both of these points are true, the authors *are only* presenting how society, in general, behaves at this point towards nonhuman animals. What is lacking is *a discussion* of whether such behaviours are morally problematic or not, and how this relates to the killing of chimeras for their human organs. An analogy might help illustrate this point: imagine that a society where women are generally disenfranchised is discussing a new practice that maintains such disenfranchisement. Now imagine that someone advances, as a defence of this new practice, that given that their society generally disenfranchises women it appears that this new practice would not threaten women's societal stance in a new or unique way. It is clear that the question which should be asked is *not* whether women's present position in that society would be threatened in a *new or unique way* by the new practice. The question to be asked is whether the present position of women in that society is morally acceptable or not.

In order to properly reply to this objection we need to consider whether the fact that chimeras would possess shorter life-spans and reduced wellbeing amounts to an impassable moral barrier for the harvesting of their organs. Even when we take into account both of these harms, killing human/pig chimeras for their human organs *can be* morally justifiable. First, the moral permissibility of killing a sentient being, when our survival depends on it, is not altered by the fact that it lived a short life before being killed. In the lifeboat scenario it is morally irrelevant whether the dog we throw overboard is two months old or seven years old. What makes it morally permissible to throw the dog overboard is that a human person would lose much more in dying than the dog does.

Second, in cases where non-vital organs are harvested, enabling chimeras to survive and have worthwhile lives, they should not be killed: the aim of the procedure, the organ transplantation, does not necessitate the death of the chimera. To kill chimeras in these cases would inflict *unnecessary harm* to sentient beings, and this is immoral (DeGrazia & Sebo 2015). Furthermore, there could be instrumental reasons not to kill the chimera. For example, if only

one of two kidneys is harvested then, depending on the patient's condition, we might want to keep the human/pig chimera alive in order to use the other kidney if this becomes necessary.

Third, it must be noted that it is down to *empirical* research to determine what level, if any, of isolation human/pig chimeras should endure when they are used as organ sources. How their wellbeing would be affected is therefore also open to investigation. It is possible that they could live in small groups, thus increasing their overall wellbeing, without that affecting their suitability for organ transplantation. Chimeras' wellbeing should suffer *only* when it is necessary for the transplantation purpose. Unnecessary harm should not be inflicted upon them just for the sake of cutting expenses, for example.

Finally, if we assume, for sake of argument, that chimeras *would* have to be completely isolated and that they *would* feel pain and discomfort, it still seems that the benefits to human persons of surviving are great enough that maintaining the chimeras under those circumstances is morally permissible. Two things must be stated: that chimeras should only endure these conditions while they are necessary for the transplantation to take place, and that their other basic needs must be met both while waiting for the organ to be harvested and after the procedure has taken place where possible (DeGrazia & Sebo 2015, 427).

9.3.5 NUMBERS OBJECTION

The final objection that Shaw et al. explore is what we could call a 'numbers objection'. They maintain that many nonhuman animals, hundreds or maybe thousands, will have to be sacrificed to research into chimeras and the development of human organs, and that many more will be so if this research proves successful. They therefore importantly ask "whether it is legitimate to use animals for this type of research" (Shaw et al. 2015, 973)?

An obvious answer to this objection, they claim, is that this technology could save many human lives. Two rejoinders can be advanced: first, there are many uncertainties regarding whether such research will be successful; second, "it is not in animals' interests to contribute to the perfection of chimaera organ biotechnology, and that it is actually against the interests of future animals" (Shaw et al. 2015, 973).

Shaw et al. respond to these rejoinders by appealing to the proportionality and subsidiarity principles: "this type of research meets the requirements of proportionality and subsidiarity much more easily than most animal research, though other potential sources of organs (…) should also be pursued" (Shaw et al. 2015, 973). While they do not provide us with a definition

of the proportionality and subsidiarity principles in "Creating Human Organs in Chimaera Pigs: An Ethical Source of Immunocompatible Organs?", in their paper "Using Non-Human Primates to Benefit Humans: Research and Organ Transplantation" they do tell us what they understand by this:

> The 3 Rs [replacing, reducing and refining the use of nonhuman animals in research] are in turn based on two key principles: proportionality and subsidiarity. These state, respectively, that any use of animals for research must be proportional to the prospective benefit, and that animals should only be used when no reasonable alternative is available. (Shaw et al 2014, 573)

Shaw et al. realise that if we adopt a strict definition of subsidiarity then we should conclude that until all other reasonable options have been exhausted, chimera research should not continue. But given that those other options *might fail* they consider that it would be irresponsible to discontinue current chimera research at this point. In fact, they adopt a more lenient version of the subsidiary principle; one "that favours simultaneous pursuit of different organ sources" (Shaw et al 2014, 573).

While I think their point is moving in the right direction, it needs further unpacking in order to properly establish under what conditions chimera research which aims to obtain human organs is morally permissible. It is true that chimera research should continue alongside other *research* into developing human organs. For example, it should continue alongside research aiming to create biomechanical organs, 3-D printed human organs, and in vitro organs using scaffolds. It should continue alongside this other research because we do not know which ones will be successful and which ones will not.

Furthermore, we *should not* be oblivious to the fact that the moral permissibility of research avenues that harm sentient beings in order to obtain human organs is constrained, at least in part, by the greater number of human organs made available under a opt-out donation system, as recently adopted in Wales (Brennan 2015). An opt-out donation system is a *reasonable* and feasible donation system that should be adopted everywhere. Additionally, if enough human organs were available in an opt-out system then we could not use *the scarcity argument* to justify any of these research avenues when discussing allogeneic transplantations. This does not negate the possibility of forwarding *an efficacy argument* to show that research avenues that harm sentient animals are morally permissible, just as in the case of organs created with the patient's own iPS cells.

Finally, any ethical assessment that properly takes into account animal ethics needs to recognise that we cannot just accept that killing human/pig chimeras to benefit humans is *always* morally permissible. For example, would it be morally permissible to kill a human/pig chimera for the sake of a patient that is persistent vegetative state? What about killing a chimera for the sake of a human that congenitally has the same metal capacities as the chimera? Given that sentient beings have moral status (a being possess moral status when "*in its own right and for its own sake, it can give us reason to do things such as not destroy it or help it* [emphasis in the original]'' (Kamm 2007, 229)), then we have to accept that it *would be immoral* to kill human/pig chimeras to benefit adult humans that *are not* sentient beings or that are *only* sentient beings. This follows *only* when comparatively assessing these two entities.

9.4 CONCLUSION

In this paper, I have argued two points. First, I highlighted the research shortcomings of Shaw et al.'s "Creating Human Organs in Chimaera Pigs: An Ethical Source of Immunocompatible Organs?" I showed that these authors failed to acknowledge or even take into account the relevant academic literature dealing with the objections they present in their work. Second, I discussed and expanded on the responses that Shaw et al. provide to the four chimera welfare objections that they themselves advance.

While examining the 'meat-eating debate' I noted that an analogy between these two topics could be made (the survival case analogy), and that this throws light on when killing human/pig chimeras for their organs is morally permissible. Regarding the 'unfairness' objection, I pointed out that we need to obtain empirical data in order to assert that even if all humans donated their organs there would not be enough to solve the human organ scarcity problem, and thus that it is *fair* to kill human/pig chimeras for their human organs when aiming at allogeneic organ transplantations. Secondly I noted that it is morally permissible to kill chimeras to obtain patient-derived iPS cell organs when the benefits to the patient are so great that they trump over the chimera's interests. I also concluded that, in principle, the fact that the chimera's life-span would be shortened does not morally preclude us from killing them for their human organs.

I also found, while discussing the 'overall wellbeing' objection, that when the harvesting of the organ would not necessarily kill the chimera, and they could afterwards have worthwhile lives, they should not be terminated. To terminate them would be to inflict unnecessary harm and this is patently immoral. While discussing the 'numbers objection' I unpacked what the

subsidiarity principle would require from us, in order to establish that it is morally permissible to carry out research to develop allogeneic human organs within chimeras. Finally, I also concluded that if we seriously consider the moral status of the chimeras we have to accept that, under certain circumstances, we cannot kill them when the human that would benefit from doing so is a non-person sentient human being or if they are a non-sentient human beings.

PART III.
CONCLUSION

10. CONCLUSION

10.1 INTRODUCTION

Before I present the concluding remarks of the thesis and the findings of each individual paper I will present the messages of the common thread of the thesis.

This thesis was composed of two levels. On the first level I have done three things. First, I have explained what chimeras are, and how they differ from other biotechnologically created creatures, for example hybrids or cybrids. I have also explicitly mentioned my philosophical assumptions. Secondly, I have addressed specific arguments *against* the creation of particular human/nonhuman animal chimeras and have showed why they are found wanting. For example, I have showed why those arguments that have at their base the concept of 'human' dignity fail to make a *principled* case against the creation of human/nonhuman animal chimeras that could have human-like mental capacities. Thirdly, I have advanced arguments *in favour* of the creation and use of specific human/nonhuman animal chimeras. For example, I have presented arguments in favour of the creation and use of chimeras capable of producing human eggs. The first level, thus, is one where I have engaged with *particular* arguments that deal with the ethical aspects of the creation and use of human/nonhuman animal chimeras.

On the second level, on the other hand, I have presented what I think should be the methodological foundations for an inquiry on chimera ethics to be successful. That is, I have presented what I believe are the relevant starting points for further research to be pertinent and relevant to the academic discussion. While the first level of discussion is easily identifiable throughout the papers, given that the points and arguments explored are discreet in nature, the second level of discussion has not been explicitly presented. The methodological issue is scattered and intertwined throughout the particular arguments examined in each one of the papers and, partly, in the introduction. Whereas in a traditional thesis this methodological issue would appear as a stand alone chapter(s), in a thesis composed of individual papers it can be identified as the common thread that provides structural support for the particular arguments.

In what follows I present the three messages that can be found throughout the thesis: the compartmentalization issue, the harm issue, and the particularly morally problematic issue.

The first message found in the thesis as a whole is that up to this point there has been, for the most part, a compartmentalization trend within chimera ethics. By this I mean two things. Firstly, that the ethical issues surrounding particular areas of chimera research have been, for

the most part, treated in complete isolation from the ethical issues concerning other areas of chimera research. For example, the 'human' dignity issue, related to the creation of human/nonhuman animal chimeras with human-like mental capacities, has been addressed without taking into consideration the ethical aspects of species overlapping cases, related both to the creation of human/pig chimeras and human/great ape chimeras. Secondly, the compartmentalization trend means that the ethical issues related to the creation and use of chimeras have only been addressed by resorting to individual ethics subfields. For example, Shaw et al. (2015) mostly resort to medical ethics to examine the ethical aspects of killing human/pig chimeras for their human organs.

The thesis has shown that the compartmentalization trend has had a negative effect in chimera ethics as a whole, since the normative prescriptions that follow from it are short-sighted in regard to the ethical complexities of the issues treated at hand. I have showed that we are given, at best, highly partial answers, and, at worse, incorrect ones. The papers have showed that ethical issues related to the creation and use of a particular chimera interconnect with the ethical issues of chimera research in general and with the ethical issues related to the creation of other particular chimeras. Moreover, I have showed that these ethical issues do not sit comfortably within the boundaries of medical ethics, for example, but 'overflow' to animal ethics and ethics in general. 'Human' dignity issues require that we discuss moral status issues, personhood issues, and that we address species overlapping cases, for example. This means, among other things, that the present trend in chimera ethics, namely an only-medical-ethics account of the ethics of chimera research, falls short of providing adequate and informed answers to the moral quandaries that the creation and use of chimeras raise.

In the thesis I have shown, while going against this compartmentalization trend, that once we flesh out the connections between the different topics that have been addressed in the academic literature on chimera ethics we can present a more sophisticated account of the moral problems that relate to the creation and use of human/nonhuman animal chimeras. In addition to this, we are also better suited to present appropriate solutions to the moral quandaries that arise from chimera research. In fact, we could assert that going against the compartmentalization trend forces us to present solutions of a 'holistic' kind, since we need to be able to present answers that do not only apply to the presented problem, but that also could be successfully applied across the board. When we are unable to present 'holistic' solutions, on the other hand, we are at least required to present answers that solve specific problems but that do not to generate more moral problems in other areas of chimera ethics than those that they solve.

Thus, one of the messages of the thesis is that in regard to chimera ethics a multifocal approach is better suited to deal with the complexities of chimera research. Even more so, I have also contended that at the present moment it is not even necessary to pay attention to the *newest developments* in certain ethics subfields, like animal ethics, to flesh out inconsistencies and problems with the arguments that have been advanced against the creation of human/nonhuman animal chimeras, and against certain uses of particular kinds of human/nonhuman animal chimeras, for example human/great ape chimeras. If further research on chimera ethics embraces this anti-compartmentalization stance then the whole debate would be able to appropriately move forward more easily. If researchers continue to follow the regnant compartmentalization trend, on the other hand, the chimera ethics debate will continue to be biased and will only be able to provide highly partial answers, or incorrect ones, to the ethical dilemmas that chimera research brings about.

The second message found throughout the thesis is that any ethical discussion of chimera research needs to both abandon biological essentialism and embrace particularism in regard to when harm can occur. By this I mean that in order to know if a chimera has been harmed we cannot appeal to an account of harm that is grounded in both biological essentialism and normal species functioning. We cannot do so given that most interspecific chimeras cannot be characterised as belonging to a specific biological species. I explored this point, for instance, when showing why an account of 'human' dignity that held that being human, i.e. belonging to the *Homo sapiens* species, is a necessary requirement for a creature to possess 'human' dignity cannot even begin to explain how human/nonhuman animal chimeras with human-like mental capacities but that are majorly non-human can violate 'human' dignity.

Once we have renounced to biological essentialism and a normal species functioning account of harm, and embraced a person-affecting subjunctive historical account of harm, we can properly deal with the moral issues that arise from experimenting upon chimeras, interspecific chimeras included. We can do so because such an account of harm looks at *individuals* and their interests in order to establish whether morally relevant harm has occurred or not. This point is of paramount relevance for the overall discussion of chimera ethics given that without a proper account of what counts as morally relevant harm we cannot start to establish what moral responsibilities scientists have towards different kinds of chimeras in various chimera research contexts.

Finally, the third message found intertwined throughout the three papers is that two of the three cases that have been regarded as particularly morally problematic (chimeras capable of human gamete production and human pregnancies, and chimeras with human-like mental capacities) are not particularly so. We should remember that most academic literature on chimera ethics, and the reports on the ethics of chimera research, have branded these two cases as issues of special concern. In the thesis I have shown that in fact these two cases are not particularly problematic, in the sense that they do not present *absolutely novel* situations that we are unable to deal with with the philosophical tools that we already possess. It is important to recognise that these two cases do not require us to develop 'new' philosophical methods so that research can move forward to examine the ethics of creating and using such chimeras. In fact, I have also contended that the third case that has been regarded as particularly morally problematic (chimeras that could look human-like) is not so. Bears to say that I have not advanced any argument for proving this last claim, and that I have left the exploration of this topic for further research.

This point is relevant because branding areas of research as particularly morally problematic at the outset of an ethical investigation, without any deep exploration of the ethical issues that arise from them, has prejudicial effects on science policy making, and can curtail experiments that could save people's lives and reduce great suffering. Remember, for example, that the German Ethics Council report '*Human-animal mixtures in research*' recommended not creating chimeras capable of producing human gametes (Deutscher Ethikrat 2011). Now, even when cultural factors can explain why people think that these research areas are particularly worrisome, we should refrain from 'jumping the gun' into policy and legislative action. For example, in a western context it is clear that most of the negative intuitive responses to certain areas of chimera research have at its base Judaeo-Christian prescriptions regarding the types of morally appropriate interactions that humans and nonhuman animals can have. Once we have shown that having negative intuitive responses is not good enough for grounding moral prescriptions regarding chimera research, and even less so for recommending specific science policy, we can move forward to present proper arguments either in favour or against particular areas of research that involve the creation and use of human/nonhuman animal chimeras.

It is true that there might be other methodological points that we could examine and endorse in order to facilitate the investigation of the ethical aspects of creating and using human/nonhuman animal chimeras. However, even when this is the case, I believe these three common threads serve as a solid methodological foundation for this thesis. Even more so, I

believe that without these three messages in place, we would not be able to explain how interspecific chimeras can suffer morally relevant harm (and harm in general); we would end up spending unnecessary time trying to find 'new' methods for dealing with the moral issues that arise from chimera research, when the ones that already exist work and work well; and our examination of the issues would be short-sighted in their finds by means of overlooking what other ethics' subfield have to contribute to the discussion.

After offering these three common threads I can now move forward to present the concluding remarks of the thesis, and the findings of each individual paper.

The work that I have presented in this thesis revolves around the topic of human/nonhuman animal chimeras. Specifically, I ask what moral quandaries we face when we create and experiment upon human/nonhuman animal chimeras. I could have investigated the moral problems that arise from creating and experimenting upon chimeras, in general, or nonhuman animal/nonhuman animal chimeras, but I decided to focus on the topic of human/nonhuman animal chimeras because of the wide implications for human medicine. As, I hope, is now obvious, this subject matter sits between animal ethics and medical ethics, and it has been, up to this point, understudied.

The detailed questions that this thesis aimed to respond to were:

- Can the concept of 'human' dignity be put forward in a cogent way to construct an argument against the creation of human/nonhuman animal chimeras?
- Are the arguments that have been advanced against the creation of human/nonhuman animal chimeras that have at their base the concept of 'human' dignity successful in proving their case?
- Could it be morally permissible to kill human/great-ape chimeras for the sake of saving human lives?
- Is it morally problematic to create human/nonhuman animal chimeras capable of human gamete production?
- If a nonperson human/nonhuman animal chimera became pregnant with a human conceptus would there be a moral obligation to terminate such conceptus?
- Can classic animal ethics issues concerning animal welfare throw light on the issue of killing human/pig chimeras for their human organs?

The work I presented is structured in the following way. First I offered a historical précis of the ancient Greek chimera. Afterwards I provided the different definitions of 'chimera' that have been used within the medical ethics academic literature, and examined their shortcomings. I discovered that the main problem with the definitions that have been used in the chimera ethics debate, so far, is that they are either under-inclusive or over-inclusive (i.e. they do not include certain kinds of chimeras, or they include transgenic animals, cybrids and hybrids). I proposed the following definition in order to surmount the problems identified in those I examined: *a chimera is an organism that is formed by combining whole cells from at least two numerically distinct sources that are also genetically distinct.* The cells that make the individual may originate either from the host or from the donor, but genetically they are not a mixture of both. This methodological work on the definition the chimera is important because within the chimera ethics debate there has been a cacophony of voices regarding this point. My analysis and definition have set a straight course for any further work on this topic. Having established this, I explained what types of chimera can be created and how they can be created. I distinguished these chimeras from other types of being: hybrids, cybrids and transgenic animals.

With this background in place, I was able to explain why scientists intentionally create human/nonhuman animal chimeras and what goals they are trying to achieve in this research area. At the present moment, scientists use human/nonhuman animal chimeras to study biological processes, such as cell differentiation and oncogenesis, that would be very difficult or immoral to study in other settings, for example in vitro or in humans. They also use human/nonhuman animal chimeras to study deadly diseases in order to create new vaccines, including malaria, dengue, Hepatitis B, HIV, and Hepatitis C. Finally, one of the main goals of this research is to create human-transplantable solid organs within human/nonhuman animal chimeras, for example, human/pig chimeras that would possess solid organs that are fully, or mostly, composed of human cells.

While discussing these research avenues I noticed that chimera research has shown that both behavioural transfer and capacities enhancement are possible when we engraft cells, in the host, at an early developmental stage. I presented two examples, one for behavioural transfer and one for capacities enhancement. The behavioural transfer example was that of quail/chicken chimeras that exhibited quail-like behaviour, instead of the host's expected chicken-like behaviour. The chimeras made *quail-specific* crowing sounds instead of chicken-specific crowing sounds. The capacities enhancement example was that of mice with human glial cells

engrafted in their brains. These engrafted cells caused the enhancement of their memory and learning capacities when compared with wild populations.

After this 'scene setting' was complete, I started my ethical inquiry by pondering whether there is a sound *principled* objection against the creation of *all intraspecific* and *interspecific* chimeras. This question led to an examination of the existing literature: I not only assessed the main arguments that have been explored within the literature on chimera ethics, but also those that are present within the literature concerning the ethics of biotechnological research. I considered the following arguments: the species identity argument, the 'playing god' argument, the moral confusion argument, the moral taboo argument, and the unnaturalness argument. I found that *so far nobody has been able to make a successful case to show that it is, in principle, morally problematic to create intraspecific and interspecific chimeras*. This finding is important within the context of chimera ethics because it allows us to explore *particular instances* of chimera research with the knowledge that there is no principled case against the creation of human/nonhuman animal chimeras overall. Most of the past discussion on chimera ethics was occupied with rejecting arguments that tried to show that in principle it is morally impermissible to create human/nonhuman animal chimeras. We have now moved to examining the morality of specific instances of human/nonhuman animal chimera research.

The questions, outlined above, that I set out to answer are deeply intertwined. They all fall within the scope of what are regarded as the three most morally problematic cases within chimera ethics: (1) the creation of human/nonhuman animal chimeras that could have brains predominantly constituted by human brain cells; (2) the creation of human/nonhuman animal chimeras that could look human-like; (3) the creation of human/nonhuman animal chimeras capable of human gamete production and human pregnancy.

The dignity-related issues and the organ transplant-related issues fall within the scope of (1), while the gametes and pregnancy issues fall within the scope of (3). It is true that, depending on how the human/great-ape chimeras were created, they might or might not possess human cells in their brains. However, even if the number of human brain cells was small, or if there were none, the case for killing such chimeras for their human organs will still fall within (1) because it becomes a discussion about the moral duties we have towards persons and borderline persons – a category which encompasses human/great ape chimeras. The fourth paper of this thesis, 'Killing Human/Pig Chimeras for Their Human Organs: Exploring the Welfare Issues', revolves around issues of moral status and the species overlap argument, and therefore is

relevant to (1). Accommodating the fourth paper in this way might seem artificial, but I contend that the issue of moral status is fundamental for the discussion of (1) and thus this fourth paper fits well within that discussion.

In the final section of the introduction I presented the abstracts and detailed summaries of the four papers that form the main body of this text in order to facilitate the reading of these papers.

10.2 THE ARTICLES

In the first paper, 'Human Dignity and the Creation of Human/Nonhuman Chimeras', I explored the dignity-based arguments advanced by Karpowicz et al. (2004, 2005), Johnston and Eliot (2003), de Melo-Martín (2008), and MacKellar and Jones (2012) against the creation of human/nonhuman animal chimeras that could possess human-like mental capacities, or that could possess certain mental capacities that we would not be able to properly classify. I am the first to examine Johnston and Eliot's, de Melo-Martín's, and MacKellar and Jones's dignity based arguments. In order to make sense of the discussion, I started by examining the definitions of 'human' dignity that have been advanced within the chimera ethics literature. Examining these definitions filled an important gap within this literature, as different authors had been using different definitions of 'human' dignity. These authors often caused confusion and talked at odds with each other by referring to different things when talking about 'human' dignity. It is worth mentioning that throughout this paper I only worked with the 'human' dignity definitions present in the chimera ethics literature. I did so because undertaking a comprehensive examination of the concept of 'human' dignity would have required much more space than was available, and because exploring the richness of that topic would have shifted the focus of this dissertation.

When considering the 'human' dignity concept, I concluded that a definition that has at its core the idea that being human is a *necessary condition* for possessing dignity is deeply problematic when assessing chimera research for two reasons. First, because it is speciesist and neglects the work done in animal ethics. Second, because it is impossible to operationalise in order to argue that the creation of *all* human/nonhuman animal chimeras with human-like mental capacities would violate 'human' dignity. It is impossible because certain chimeras cannot be regarded *in a strict sense* as being members of the *Homo sapiens* species. This finding is important for the second paper ('The Ethics of Killing Human/Great-ape Chimeras for their Organs: A Reply to Shaw et al.') because I discussed the case of killing human/great ape chimeras for their human

organs, chimeras that would be borderline persons but that could not be regarded, in all instances, as belonging to the *Homo sapiens* species.

Having identified the problem of a definition of 'human' dignity that held that being member of *Homo sapiens* is a necessary condition for possessing it, I moved on to explore what would come of a species-neutral psychological capacities account of 'human' dignity. From this I concluded, alongside most animal ethicists, that if what is important are the cognitive capacities that an entity possesses then we can do without the 'human' element of the definition. This finding in turn throws light onto the issue of whether the subsidiarity principle, discussed in the second and fourth papers, requires us to kill human/pig chimeras, human/great-ape chimeras *or humans* that possess similar cognitive capacities. This question is inescapable once we accept that belonging to the *Homo sapiens* species cannot be a necessary condition for possessing dignity. Until now, the link between chimera ethics and the argument from species overlap had been underexplored.

In the main section of this paper I examined, in detail, eleven objections that are present in the academic literature on this topic against the creation of human/nonhuman animal chimeras that have at their base the concept of 'human' dignity. I did so from a species neutral position; in order to accomplish this I occasionally reformulated the objections to fit this species neutral stance. I believe I have convincingly shown that all eleven arguments are found wanting because each argument commits one or more of the following mistakes: (i) they fail to properly distinguish between the moral problems that arise from creation acts and the moral problems that arise from how chimeras would be treated once they exist; (ii) they misconstrue what it is to be treated solely as a means towards others' ends; (iii) they fail to properly show how humanity's dignity would be debased by the creation of human/nonhuman animal chimeras; and finally (iv) they do not stress the moral duties that moral agents would have towards human/nonhuman animal chimeras with human-like mental capacities, regardless of the intention for which they were created. I concluded that, so far, all dignity-based arguments against the creation of human/nonhuman animal chimeras with human-like cognitive capacities are found wanting. This paper, as a whole, contributes to the area of chimera ethics in an important negative way: it shows that all the 'human' dignity arguments advanced so far fail to make their case. This means that these authors have to either retreat to an argument against the creation of human/nonhuman animal chimeras that possess human-like mental capacities that has at its base the concept of dignity, or they have to come up with new arguments.

In the second paper, 'The Ethics of Killing Human/Great-ape Chimeras for their Organs: A Reply to Shaw et al.', I examined the morality of killing human/great ape chimeras for their human organs. This paper is a detailed response to Shaw et al.'s 2014 paper 'Using Non-Human Primates to Benefit Humans: Research and Organ Transplantation'. After introducing the topic of the human organ shortage crisis, I reconstructed Shaw et al.'s position on *nonhuman animal research* and moral status. On moral status they adopt, although they do not say so explicitly, a non-speciesist cognitive capacities account. On *nonhuman animal research*, Shaw et al. assume the mainstream position: in principle it is morally justified to experiment on nonhuman animals. To this they add two caveats. First, there are morally worthy aims and morally unworthy aims for which to carry out nonhuman animal research. Second, there are morally relevant distinctions between killing and harming certain nonhuman animals and killing and harming others. The more sophisticated the cognitive capacities a nonhuman animal has, the higher regard we should have for its interests. This section regarding the morally worthy aims and the morally unworthy aims of nonhuman animal research directly impacts the ethical discussion of the animal welfare objections in the fourth paper. It does so because the answer to the question of whether certain medical nonhuman animal research is morally permissible establishes, in principle, if research on human/nonhuman animal chimeras with human-transplantable organs is morally permissible or not.

After presenting the authors' position concerning nonhuman animal research and moral status, I explained why they think that neither a cognitive capacities account of moral status nor McMahan's time-relative interest account are capable of answering the question of whether it is morally permissible to kill *human/primate* chimeras for their human organs. In other words, whether it is morally permissible to kill partially-human creatures with slightly less psychological capacity than normal human adults for the sake of humans. According to Shaw et al., the sliding-scale nature of *both accounts* cannot tell us if killing such creatures is as morally problematic as killing innocent normal human adults.

Given this, Shaw et al. rely on the proportionality and subsidiarity principles in order to provide us with a *clear-cut* answer to the question 'in what circumstances would it be morally permissible to kill human/primate chimeras for their human organs?' According to them, both of these principles allow for the *killing of human/primate* chimeras when the purpose of doing so was to save human lives. In fact, the subsidiarity principle also allows for the killing of human/pig chimeras for their human organs when we aim to save human persons. This topic is explored in the fourth paper. While discussing the proportionality principle, I noted how Shaw

et al.'s position would also apply to the case of *killing human/great-ape* chimeras for their human organs. Although they do not say this *explicitly*, it follows logically from their arguments: great apes possess slightly fewer psychological capacities than normal adult humans, and furthermore Shaw et al. accept, when discussing the subsidiarity principle, that sacrificing a great ape in order to save a human life seems appropriate.

Having reconstructed their position I revisited the discussion on moral status, and specifically addressed the question of what moral status great apes possess. Contrary to the introduction, where I explored *the grounds of moral status*, I here focused on the issues relating to personhood and borderline personhood. I concluded that great apes should be regarded as *borderline persons* and not as paradigmatic persons. I also explored whether the degree of respect that should be shown to persons should be *proportional* to their cognitive capacity, or if there is a cognitive capacities *threshold* above which everyone must be equally respected. After I noted some of the problems with a proportional account, I opted for a two-tier moral theory. A two-tier moral theory holds that above a certain threshold *a morality of equal respect should dictate* our interactions with other creatures that are also above the threshold. The question that was then left to answer was whether great apes and human/great-ape chimeras (i.e. borderline persons) should be treated according to the time-relative interest account (i.e. as we treat sentient beings), or if they in fact pass the threshold and should be respected just as we respect normal human adults.

Before presenting my case *against* killing human/great ape chimeras in order to use their human organs, I pointed out that in fact McMahan's two-tier moral theory does not have the sliding-scale-nature problem as Shaw et al. claimed. Finally, I advocated a *level-up solution* to the problem of borderline persons, and presented what I hope is a convincing case for doing so. The level-up solution, simply put, is that the differences between borderline persons and persons are so faint that in fact we should treat them as if they were non-existent. Thus I defended the idea that in principle it is immoral to kill human/great apes so that humans may use their organs. This conclusion also entails that under certain conditions killing human/pig chimeras for their human organs is morally permissible; a conclusion that coincides with that presented in the fourth paper. These finds add to the current literature by showing, contrary to Shaw et al.'s position (or what follows from their position), that killing human/great ape chimeras for their human organs is morally impermissible. This is important because great apes, due to their evolutionary closeness to humans, seem to be, biologically speaking, the ideal nonhuman animals for creating human organs within. This work further adds to the current

chimera ethics debate by presenting and exploring the consequences of *a level-down* solution to the problem of borderline persons. Although neglected by Shaw et al., this topic is truly vital for the correct assessment of when it is morally permissible to kill a human/nonhuman animal chimera for its human organs.

Three logical implications follow from adopting *a level-down stance* to the problem of borderline persons: (i) it would be morally permissible to kill borderline human and human nonpersons for their human organs, (ii) it would be morally unjustifiable to kill human/great-ape chimeras for the sake of human borderline persons and human nonpersons, and (iii) instead of waiting years for scientists to develop human/great-ape chimeras whose organs we could use for transplantation, we should start using human nonpersons and human-borderline persons for their organs today. If Shaw et al. rejected my level-up solution, they would need to address the implications for their case of using human/great ape chimeras for their human organs in order to be regarded as plausible.

In the third paper, 'Ethical Aspects of Creating Human/Nonhuman Chimeras Capable of Human Gamete Production and Human Pregnancy', I covered two topics. The first topic concerned the moral problems arising from the creation of majorly-nonhuman human/nonhuman animal chimeras capable of human gamete production. The second concerned the moral problems generated if a sentient nonperson human/nonhuman animal chimera that is predominantly nonhuman were to become pregnant with a human conceptus.

Given that so far nobody has advanced an argument against the creation of human/nonhuman animal chimeras that could produce human gametes, despite most researchers and groups agreeing that this research raises special ethical concerns, I departed from a hypothetical normative stance against their creation and then tried to justified it. My stance is that it is morally wrong to create human/nonhuman animal chimeras that could produce human gametes. I examined three arguments to support this. The first argument is a *general* argument against the creation of human/nonhuman animal chimeras. If we can prove that the creation of *any* human/nonhuman animal chimera is immoral, then we by extension prove that the creation of human/nonhuman animal chimeras capable of human gamete production is immoral. Given that all of the arguments so far advanced against the creation of chimeras in general fail, as I explained in depth in the introduction, I moved on to examine whether human gametes have an intrinsic value that would be debased by being generated within human/nonhuman animal chimeras. An argument with the intrinsic value of human gametes at its centre would assert

that we should not create chimeras capable of human gamete production because the intrinsic value of human gametes would be debased. The main problem with this argument is that human gametes do not possess intrinsic value, and therefore this claim cannot be used as the foundation of an argument against the creation of such creatures. Next I examined whether human gametes could have instrumental value and whether this value could be debased by being generated within human/nonhuman animal chimeras, in which case we should not create this kind of creature. The problem with this argument is that if something's instrumental value depends on the completion of a certain task, then, as long as chimera-generated human gametes can complete this task within the same range of effectiveness, it is simply not true that the instrumental value of chimera-generated human gametes is debased. I concluded that there is no sound argument to support the hypothetical normative stance about the creation of chimeras capable of producing human gametes.

I then examined three arguments in support of the creation of chimeras capable of producing human gametes: the saving persons argument, the unburdening women argument, and the restoration of fertility argument. Of these three arguments the strongest is the saving persons argument. This argument allows for the creation, harming and killing of such chimeras. While there are good grounds for accepting that the other arguments (the unburdening women argument and the restoration of fertility argument) successfully posit a case for *harming* chimeras as part of therapy aimed at reducing the suffering of human persons, I left whether these arguments are strong enough to establish that it would be morally permissible to kill sentient nonperson human/nonhuman animal chimeras as an open question.

In the second part of this paper I examined some of the ethical problems that could emerge from the reproduction, or insemination, of nonperson human/nonhuman animal chimeras that produce human gametes. Given that this topic has never been explored, I tried to present *a taxonomy* of possible problematic issues regarding the human pregnancy of a nonperson human/nonhuman animal chimera. I specifically addressed the question of whether we are morally required to terminate a human pregnancy that occurs within a partiality human interspecific chimera. My answer to this question was that *we are not morally obliged to terminate such pregnancies*, with the notable exception of wrongful life cases. The moral problems that emerge from a nonperson human/nonhuman animal chimera becoming pregnant with a human conceptus mirror the moral problems that emerge from pregnancies in fully incompetent familyless women. Therefore labelling this specific case as particularly novel and problematic is unwarranted. This specific issue links to both the discussion of moral status in

the second paper and the discussion of whether all humans possess dignity or not, which is the main topic of the first paper.

Finally, I assessed how the interests of the nonperson human/nonhuman animal chimeras could be affected by carrying human pregnancies, and I established the moral duties researchers would have towards those creatures. This article adds to the literature in two important ways. First, I showed that it is morally permissible to create nonperson human/nonhuman animal chimeras that could produce human gametes. I then showed that it is morally permissible to harm and kill such creatures when their gametes are to be used as tools for saving persons. Second, I was the first person to explore the moral issues that emerge from the human pregnancy of a nonperson human/nonhuman animal chimera.

In the fourth and final paper, 'Killing Human/Pig Chimeras for Their Human Organs: Exploring the Welfare Issues', I examined the welfare issues around killing human/pig chimeras for their human organs. The paper is divided into two sections. In the first section I draw attention to the methodological shortcomings of Shaw et al.'s (2015) "Creating Human Organs in Chimaera Pigs: An Ethical Source of Immunocompatible Organs?" This section shows that these authors failed to take into account the pre-existing literature on chimera ethics, which had already dealt with the objections (the risk of zoonosis objection, the 'human features' objection, and the human dignity objection) to the creation and use of human/pig chimeras that they examine in their paper.

The second section of the paper further examines the animal welfare issues that relate to the creation and use of human/pig chimeras for their human organs. I build upon Shaw et al.'s discussion of four objections to the creation and use of human/pig chimeras for their human organs: the meat-eating objection, the unfairness objection, the overall wellbeing objection, and the numbers objection. Here, I establish links between classic animal ethics issues and chimera ethics.

The meat-eating debate is relevant to chimera ethics because it shows that under specific circumstances, such as when the person's life depends on doing so and there is no alternative, it is morally permissible to kill nonhuman animals that are sentient but that are nonpersons. This topic relates to the discussion of moral status in the second paper, as we are discussing how to weigh the lives of different individuals that possess different cognitive capacities.

The unfairness objection points out that not all humans donate their organs, and it is therefore unfair to kill human/pig chimeras for their human organs. I noted that we need to collect

empirical data in order to assess whether Shaw et al.'s claim that even if everybody donated their organs there would still be a shortage for transplantation is true. Whether it is fair or not to kill human/pig chimeras for their human organs in allogeneic transplantation scenarios depends, largely, on the answer to this question. Shaw et al. further support the case for killing human/pig chimeras for their organs by pointing out that chimera organs would be preferable to 'standard' donation because if we rely on the patient's own iPS cells to produce the organs then we avoid the problems related to organ rejection. In response to this point, I clarified that only if the organ(s) increase the patient's interests to the point that they outweigh the chimera's interest in remaining alive is it morally permissible to kill chimeras for their organs.

The third objection I examined is the overall wellbeing objection. This establishes that whereas, for example, pigs can be farmed in an ethical way, human/pig chimeras' wellbeing would be negatively affected because of the conditions we would have to keep them in in order for them to be used for transplantation. Thus it would be immoral to use them for this purpose. To address this objection, I questioned whether it would be necessary to kill the chimeras after harvesting the organs. I concluded that to minimise harm we should not terminate the chimeras if afterwards they could live worthwhile lives. I also contended that unless it is necessary to do otherwise, we should allow chimeras to live in groups to increase their wellbeing.

The final objection that I examined was whether it would be better not to pursue this research, given the total number of nonhuman and part-human creatures that we would need to create and to kill to achieve the goal of creating human-transplantable organs within chimeras. I pointed out that in order to reduce the number of chimeras that we would need to kill and harm to obtain human organs we could move to an opt-out organ donation system. I then examined whether it would be morally permissible to kill human/pig chimeras for the sake of non-sentient nonperson human beings and nonperson sentient human beings. This relates to the discussion about whether we should kill human/great ape chimeras to benefit humans that are nonpersons. I concluded that if we *only compare the interests of these two creatures* we would have to accept that it would be morally impermissible to kill such chimeras to benefit such humans.

10.3 CONTRIBUTIONS TO EXISTING LITERATURE ON CHIMERA ETHICS

In this section I presented in a more detailed fashion how the four papers that form the main body of this thesis add to the existing literature on chimera ethics

My examination of the topic of 'human' dignity and the creation of human/nonhuman animal chimeras contributes to the literature on chimera ethics in at least four important ways. First, I presented in detail the main definitions of 'human' dignity that have been used in the debate around the creation of human/nonhuman animal chimeras. This fills an important gap in the current literature on chimera ethics because what we understand by dignity, or 'human' dignity, is the foundation upon which arguments in this area are dependent. In showing that a cognitive capacities account of dignity can in fact accommodate the supposed problems regarding our moral obligations towards human/nonhuman animal chimeras with human-like mental capacities I cleared the way for the discussion to move on.

I contributed further to this area by showing that all dignity-related arguments advanced to date fail to make a *principled case* against the creation of human/nonhuman animal chimeras with human-like mental capacities. I conducted the most extensive research, by engaging with all the current literature on the topic, and the most in depth one. My arguments are novel in bringing to light that our moral evaluations of cases where *humans* are chimerised with nonhuman components and those where nonhuman animals are chimerised with human components must be symmetrical when we discuss the morality of the creation of chimeras. If what I defend is true, then I have clearly shown that the arguments advanced by Karpowicz et al. (2004, 2005), Johnston and Eliot (2003), de Melo-Martín (2008), and MacKellar and Jones (2012) are problematic because they assume that the creation of human-to-human or nonhuman-to-human chimeras must be assessed in a qualitatively different manner than the creation of human-to-nonhuman chimeras.

I made another relevant addition to the literature in the first paper by proving that the main dignity-based arguments against the creation of human/nonhuman animal chimeras with human-like mental capacities confuse how a chimera could be wronged or harmed *by coming into existence* with the wrongs and harms that would be imposed, *after creation*, upon them in biological research contexts. Finally, I have shown that the arguments that have at their base 'human' dignity in fact misunderstand and misrepresent how a being could be treated solely as means towards others' ends. Given that in Kantian ethics this point is fundamental in order to understand when someone's dignity is violated, in clarifying this I have allowed for future research to depart from a clearer stance.

A general contribution of the paper 'The Ethics of Killing Human/Great-Ape Chimeras for Their Organs: A Reply to Shaw Et Al.' to the literature on chimera ethics is to have shown that

medical ethics, when dealing with human/nonhuman animal chimeras, must look to animal ethics in order for the discussion to be pertinent and informed – a point that I remake in the fourth paper. It would be philosophically obtuse to investigate the topic of chimera research from a medical ethics perspective alone. The discussion of our moral duties towards nonhuman animals is paramount for a proper ethical assessment of chimera ethics to take place.

Furthermore, this paper contributes to the field of medical ethics in a more specific way by showing that *it is morally impermissible to kill human/great ape chimeras for their human organs*. This is particularly relevant as scientists move forward with empirical research into how to create solid human organs within nonhuman animals. I accomplished this, partially, by proving that the arguments advanced by Shaw et al. (2014) to show that killing such chimeras would be morally permissible in order to save a human life are in fact erroneous.

Another addition I make to the field is the conclusion that the proportionality and subsidiarity principles cannot be invoked to justify the killing of human/great ape chimeras. This is so because a theory of moral status that distinguishes between sentient beings, borderline persons and persons can be coupled with a two-tier moral theory in order to properly differentiate the morality of killing sentient beings to benefit persons from that of killing borderline persons or persons to benefit other persons. Such an account would rule out, all things being equal, killing human/great ape chimeras to save human lives.

The final contribution I make to the literature in this second paper is to show that non-speciesist cognitive capacities accounts of moral status also need to deal with the consequences of claiming that a sentient nonperson can be morally sacrificed for their organs; a topic that was also explored in the fourth paper. This is important because there are humans that are sentient nonpersons, and thus such a conclusion would apply to them. It would be easy to endorse a *relational account of moral status* to avoid this conclusion, but ultimately not even this would solve *all* 'problematic' instances. This means that there would always be certain humans that could be morally sacrificed for their organs. Here we have two options: either we bite the bullet and accept this conclusion, or we try to find a different argument to show that we should not sacrifice these humans for their human organs.

My third paper, 'Ethical Aspects of Creating Human/Nonhuman Chimeras Capable of Human Gamete Production and Human Pregnancy', contributes by being the first *thorough* examination of the ethical aspects of creating human/nonhuman chimeras capable of human

gamete production and human pregnancy. It bears mentioning that, in a small section of a book chapter, Greely (2013) also marginally examined both topics.

Two important contributions made in this work are as follows: initially, I show that so far there is no successful *principled* argument against the creation of human/nonhuman animal chimeras that could produce human gametes. The strategy used to prove this is threefold. First, I show that there is no principled argument against the creation of *all* chimeras, and thus this reason cannot be invoked to rule out the creation of human/nonhuman animal chimeras that could produce human gametes. Second, I show that human gametes do not possess intrinsic worth and thus this cannot be used to construct an argument against the creation of interspecific chimeras capable of human gamete production. Third, if we accept that human gametes *only* possess instrumental value then it is easy to see how chimera-produced gametes could possess identical value to human-produced gametes, and thus no argument claiming that human gametes' instrumental value would be debased by being produced within an interspecific chimera would succeed. These three arguments are *completely novel* to the literature on chimera ethics.

Next, I show that *there are three reasons to create chimeras capable of human gamete production*: unburdening women, saving persons, and restoring fertility. As I defended previously, the saving persons argument is the only one that is strong enough to justify harming and killing nonperson human/nonhuman chimeras capable of human gamete production. This conclusion is also novel to the chimera ethics discussion, and it is important in terms of morally justifying real biological research.

The second major contribution of this paper is to prove that *there is no moral duty to terminate a human pregnancy within a human/nonhuman animal chimera that is primarily nonhuman*. In fact, such pregnancies should be treated just as we treat the pregnancies of fully incompetent familyless women. Despite the academic literature treating this case as particularly novel and problematic, there is no morally relevant difference from cases that we currently encounter within human pregnancies.

The final paper, 'Killing Human/Pig Chimeras for Their Human Organs: Exploring the Welfare Issues', adds to the current literature on chimera ethics by showing that classic topics in animal ethics have substantial relevance when discussing the ethics of killing sentient human/nonhuman animal chimeras for their human organs. In the second paper I relied on animal ethics to examine the ethics of killing human/great ape chimeras, whereas here I

specifically draw from the meat-eating debate and the discussion of nonhuman animal wellbeing to examine in more depth the ethical issues surrounding the killing of human/pig chimeras for their organs.

A novel conclusion reached in this thesis is that we can draw an analogy between killing nonhuman animals to eat their meat, when our lives depend on it, and killing human/pig chimeras for their organs when our lives depends on it. A second novel conclusion is that the first holds, even if the wellbeing of the chimera would suffer because of the conditions in which it must be kept for the transplantation procedure to be carried out safely.

10.4 FURTHER RESEARCH ON CHIMERA ETHICS

Finally, I presented future research avenues that could be explored in the area of chimera ethics, which depart from the findings of my four papers.

One aspect that remains open for further research is how to treat cases where it is not clear if the created chimera is a person, a borderline person, or a sentient nonperson. In this thesis I have assumed that we would be able, with a high degree of certainty, to properly identify the moral status of the chimera we were dealing with. While this assumption is valid for the cases I examined, there could be cases (and it could be the majority of them) where we would be unable to properly establish the moral status of the chimera. Should we be guided, for example, by something akin to the precautionary principle? In recent work Julian Savulescu notes that much more research must be done on the epistemological aspect of chimera research (Savulescu 2013), and while Matthew Haber and Bryan Benham (2012), Monika Piotrowska (2014) and Sarah Chan (2014) have done some work on this topic the question of what morality requires from us when we are unsure about the moral status of a chimera is still an unresolved issue.

A topic outside the sphere of applied ethics that could also be explored with the help of human/nonhuman animal chimera research is whether being a person is proper sortal or phase sortal (Gómez-Lobo, 2004, 2005). Although in this work I have aligned myself with the interpretation that being a person is phase sortal (i.e. humans are not persons during the whole course of our biological existence), more work needs to be done on this problem. If, for example, being a person is proper sortal (i.e. humans are persons during the whole course of our biological existence) then my conclusion that human/nonhuman borderline person chimeras should not be killed for the sake of other human borderline persons or human sentient nonpersons fails, because all humans are persons. The same would happen with the conclusion

that we should not kill sentient nonperson human/nonhuman chimeras for the sake of sentient nonperson humans. These two implications, obviously, suppose that the chimeras are not human in the relevant sense of the term, and thus that they are nonpersons.

A third possible avenue of research is an investigation of Insoo Hyun's (2013) objection to the possibility of creating human-to-nonhuman animal chimeras that could become persons by virtue of human engrafted cells. He argues that the biological configuration and development of the human brain is such that the creation of human-to-nonhuman animal chimeras with human-like mental capacities is unfeasible. While this is an empirical claim, I suggested that it could be philosophically challenged in two ways. First, by examining whether the similarities between human and great-ape brains could allow for the creation of human/nonhuman paradigmatic person chimeras that are predominantly great-ape and, second, by distinguishing between how primary chimeras and secondary chimeras are created. The creation of a human/great ape chimera by embryo fusion, if feasible, would put into doubt Hyun's claims.

The topic of chimera research and organ transplantation is a fertile one for future research. First, we could research the moral distinction between the creation of human/nonhuman animal chimeras for autologous transplantations and the creation of human/nonhuman animal chimeras for allogenic transplantations. Although Shaw et al. (2014) mention this point, they do not examine it thoroughly and it warrants special attention. A second topic is whether we should allow individuals to pay to create human/nonhuman animal chimeras with the sole intention of providing themselves with a needed organ, or if we should centralise the creation of such chimeras to *maximise* the production of human organs and benefit multiple patients at the same time? This research would encompass issues of distributive justice, animal ethics and medical ethics.

Another interesting investigation would be to ask what moral issues would arise if chimera-based organ transplantation carried the risk of xenozoonosis. Specifically, how should we morally proceed given that such transplants would be limited to people in the first world, at least initially? Chimera ethics would again intersect with issues of distributive justice, but also with the risk of xenozoonosis, and the duties we have towards the developing world. A first step towards exploring these issues was made by Robert Sparrow (2009) when discussing xenotransplants, however the relation between xenozoonosis and chimera-based organ transplantation has not been addressed in the academic literature.

Finally, further research into transplantation could explore the morality of creating nonperson human/nonhuman animal chimeras capable of human gestation and using them to produce congenitally-caused anencephalic humans. This would be useful for providing human organs for human infants that need them. It would be stimulating to explore this case because we could 'surgically' remove the problems associated with the potentiality argument. In principle, it seems, both opposing groups in the abortion debate (the pro-life group and the pro-choice group) would have to accept the conclusions that we reached while exploring this issue.

BIBLIOGRAPHY

Abbott, A., and David C. (2001). China Plans "Hybrid" Embryonic Stem Cells. *Nature* 413 (6854): 339–339. doi:10.1038/35096722.

Alter, J. S. (2007). The Once and Future "Apeman" Chimeras, Human Evolution, and Disciplinary Coherence. *Current Anthropology 48*(5): 637–52. doi:10.1086/520133.

Arregui, L., & Dobrinski, I. (2014). Xenografting of testicular tissue pieces: 12 years of an in vivo spermatogenesis system. *Reproduction*, *148*(5), R71–R84. http://doi.org/10.1530/REP-14-0249.

Ashcroft, R. E. (2005). Making Sense of Dignity. *Journal of Medical Ethics* 31 (11): 679–82. doi:10.1136/jme.2004.011130.

Austriaco, N. P. G. (2011). Complete Moles and Parthenotes Are Not Organisms. In A. Suarez & J. Huarte (Eds.), *Is this Cell a Human Being?* (pp. 45–54). Springer Berlin Heidelberg.

Bailey L. L., Nehlsen-Cannarella S. L., Concepcion W., & Jolley W. B. (1985). Baboon-to-human cardiac xenotransplantation in a neonate. *JAMA*, *254*(23), 3321–3329. http://doi.org/10.1001/jama.1985.03360230053022

Balaban, E., Teillet, M. A., & Le Douarin, N. (1988). Application of the quail-chick chimera system to the study of brain development and behavior. *Science (New York, N.Y.)*, *241*(4871), 1339–1342.

Barker JH, Polcrack L. (2001). Respect for persons, informed consent and the assessment of infectious disease risks in xenotransplantation. *Medicine Health Care and Philosophy*, *4*(1),53–70.

Baylis, F. (2008). Animal Eggs for Stem Cell Research: A Path Not Worth Taking. *The American Journal of Bioethics*, *8*(12), 18–32. http://doi.org/10.1080/15265160802559161.

Baylis, F., & Fenton, A. (2007). Chimera Research and Stem Cell Therapies for Human Neurodegenerative Disorders. *Cambridge Quarterly of Healthcare Ethics*, *16*(2), 195–208.

Baylis, F., & Robert, J. S. (2006). Primer on Ethics and Crossing Species Boundaries. Retrieved 1 September 2015, from http://www.actionbioscience.org/biotechnology/baylis_robert.html.

Baylis, F., & Robert, J. S. (2007). Part-Human Chimeras: Worrying the Facts, Probing the Ethics. *The American Journal of Bioethics*, *7*(5), 41–45. http://doi.org/10.1080/15265160701290397.

Behringer, R. R. (2007). Human-Animal Chimeras in Biomedical Research. *Cell Stem Cell 1*(3): 259–62. doi:10.1016/j.stem.2007.07.021.

Bennett, R. (2009). The fallacy of the Principle of Procreative Beneficence. *Bioethics*, *23*(5), 265–273. http://doi.org/10.1111/j.1467-8519.2008.00655.x

Bennett, R. (2014a). There Can Be No Moral Obligation to Eradicate All Disability. *Cambridge Quarterly of Healthcare Ethics*, *23*(01), 30–40. http://doi.org/10.1017/S0963180113000418

Bennett, R. (2014b). When Intuition is Not Enough. Why the Principle of Procreative Beneficence Must Work Much Harder to Justify Its Eugenic Vision. *Bioethics*, *28*(9), 447–455. http://doi.org/10.1111/bioe.12044

Bentham, J. 2007. *An Introduction to the Principles of Morals and Legislation*. Mineola, N.Y: Dover Publications Inc.

Beyleveld, D., and Roger B. (2002). *Human Dignity in Bioethics and Biolaw*. 1 edition. Oxford ; New York: Oxford University Press.

Bhan, A., Singer, P. A., & Daar, A. S. (2010). Human-animal chimeras for vaccine development: an endangered species or opportunity for the developing world? *BMC International Health and Human Rights*, *10*, 8. http://doi.org/10.1186/1472-698X-10-8.

Bok, H. (2003). What's Wrong with Confusion? *The American Journal of Bioethics*, *3*(3), 25–26. http://doi.org/10.1162/15265160360706471.

Boonin, D. (2008). How to Solve the Non-Identity Problem. *Public Affairs Quarterly 22*(2): 129–59.

Brännström, M., Johannesson, L., Bokström, H., Kvarnström, N., Mölne, J., Dahm-Kähler, P., … Nilsson, L. (2015). Livebirth after uterus transplantation. *Lancet*, *385*(9968), 607–616. http://doi.org/10.1016/S0140-6736(14)61728-1.

Brem, S. K., & Anijar, K. (2003). The Bioethics of Fiction: The Chimera in Film and Print. *The American Journal of Bioethics*, *3*(3), W22-W24.

Brennan, S. (2015). New opt-out system in Wales aims to revolutionise organ donation. *The Guardian*. 25 November. http://www.theguardian.com/society/2015/nov/25/organ-donation-wales-pioneers-opt-out

Brophy, B., Grant S., Thomas W., David W., L'Huillier P., and Laible G. (2003). Cloned Transgenic Cattle Produce Milk with Higher Levels of β-Casein and κ-Casein. *Nature Biotechnology 21*(2), 157–62. doi:10.1038/nbt783.

Chan, S. (2014). Hidden Anthropocentrism and the 'Benefit of the Doubt': Problems With the 'Origins' Approach to Moral Status. *The American Journal of Bioethics*, *14*(2), 18–20. http://doi.org/10.1080/15265161.2013.868958.

Charland, L. C. (2003). Are There Answers? *The American Journal of Bioethics*, *3*(3), 1–2. http://doi.org/10.1162/15265160360706697.

Chen, D., Duan-Cheng W., Ya-Ping Z., Qing-Yuan S., Zhi-Ming H., Zhong-Hua L., Peng S., et al. (2002). Interspecies Implantation and Mitochondria Fate of Panda-Rabbit Cloned Embryos. *Biology of Reproduction 67*(2): 637–42.

Chen, Y., Zhi X., Ailian L., Kai W., Wen W. M., Jian X. C., Yong L., et al. (2003). Embryonic Stem Cells Generated by Nuclear Transfer of Human Somatic Nuclei into Rabbit Oocytes. *Cell Research 13*(4): 251–63. doi:10.1038/sj.cr.7290170.

Chong, J. J. H., Xiulan Y., Creighton W. D., Elina M., Yen-Wen L., Jill J. W., Mahoney W. M., et al. (2014). Human Embryonic-Stem-Cell-Derived Cardiomyocytes Regenerate Non-Human Primate Hearts. *Nature* 510 (7504): 273–77. doi:10.1038/nature13233.

Clark, M. A. (1999). This little piggy went to market: the xenotransplantation and xenozoonose debate. *The Journal of Law, Medicine & Ethics*, *27*(2), 137–152.

Cobbe, N. (2011). Interspecies Mixtures and the Status of Humanity. In A. Suarez & J. Huarte (Eds.), *Is this Cell a Human Being?* (pp. 129–155). Springer Berlin Heidelberg.

Cohen, C. B. (2007). *Renewing the Stuff of Life: Stem Cells, Ethics, and Public Policy* (1 edition). Oxford ; New York: OUP USA.

Comstock, G. L. (2012). *Vexing Nature?: On the Ethical Case Against Agricultural Biotechnology* (2000 edition). Boston, MA: Springer.

Cooley, D. R. (2008). Genetically Engineering Human-Animal Chimeras and Lives Worth Living. *Between the Species*, *13*(8), 1–19.

Dannemann, M., Aida M. A., and Janet K. (2016). Introgression of Neandertal- and Denisovan-like Haplotypes Contributes to Adaptive Variation in Human Toll-like Receptors. *The American Journal of Human Genetics 98*(1): 22–33. doi:10.1016/j.ajhg.2015.11.015.

Davis, P. H., & Stanley, S. L. (2003). Breaking the species barrier: use of SCID mouse–human chimeras for the study of human infectious diseases. *Cellular Microbiology*, *5*(12), 849–860. http://doi.org/10.1046/j.1462-5822.2003.00321.x.

de Melo-Martín, I. de. (2008). Chimeras and Human Dignity. *Kennedy Institute of Ethics Journal*, *18*(4), 331–346. http://doi.org/10.1353/ken.0.0268.

DeGrazia, D. (1997). Great Apes, Dolphins, and the Concept of Personhood. *The Southern Journal of Philosophy*, *35*(3), 301–320. http://doi.org/10.1111/j.2041-6962.1997.tb00839.x.

DeGrazia, D. (2005). On the Question of Personhood beyond Homo sapiens. In P. Singer (Ed.), *In Defense of Animals: The Second Wave* (2nd Revised edition, pp. 40–53). Malden, MA: Wiley-Blackwell.

DeGrazia, D. (2007). Human-Animal Chimeras: Human Dignity, Moral Status, and Species Prejudice. *Metaphilosophy*, *38*(2-3), 309–329. http://doi.org/10.1111/j.1467-9973.2007.00476.x.

DeGrazia, D. (2008). Moral Status as a Matter of Degree? *The Southern Journal of Philosophy* XLVI: 181–98.

DeGrazia, D. (2014). On the Moral Status of Infants and the Cognitively Disabled: A Reply to Jaworska and Tannenbaum. *Ethics 124*(3): 543–56. doi:10.1086/675077.

DeGrazia, D & Sebo, J. (2015). Necessary Conditions for Morally Responsible Animal Research. *Cambridge. Quarterly of Healthcare Ethics*, *24*(04), 420-430. http://dx.doi.org/10.1017/S0963180115000080

Deschamps, J. Y., Francoise A. R., Pierre S., and Edouard G. (2005). History of Xenotransplantation. *Xenotransplantation 12*(2): 91–109. doi:10.1111/j.1399-3089.2004.00199.x.

Deutscher Ethikrat. (2011). *Human-animal mixtures in research Opinion*. Berlin: German Ethics Council.

Devolder, K. (2005). Creating and sacrificing embryos for stem cells. *Journal of Medical Ethics*, *31*(6), 366–370. http://doi.org/10.1136/jme.2004.008599.

Devolder, K. (2015). *The Ethics of Embryonic Stem Cell Research*. Oxford: OUP Oxford.

Devolder, K., & Harris, J. (2007). The Ambiguity of the Embryo: Ethical Inconsistency in the Human Embryonic Stem Cell Debate. *Metaphilosophy*, *38*(2-3), 153–169. http://doi.org/10.1111/j.1467-9973.2007.00480.x.

Dombrowski, D. A. (2006). Is the argument from marginal cases obtuse? *Journal of Applied Philosophy*, *23*(2), 223–232.

Douarin, N. L., and McLaren A., eds. (1984). *Chimeras in Developmental Biology*. London; Orlando: Academic Press Inc.

Douglas, P. M. (2002). *Purity and Danger: An Analysis of Concepts of Pollution and Taboo* (1 edition). London; New York: Routledge.

Eberl, J. T., & Ballard, R. A. (2008). Exercising restraint in the creation of animal-human chimeras. *The American Journal of Bioethics: AJOB*, *8*(6), 45–46. http://doi.org/10.1080/15265160802248286

Eberl, J. T., & Ballard, R. A. (2009). Metaphysical and Ethical Perspectives on Creating Animal-Human Chimeras. *Journal of Medicine and Philosophy*, *34*(5), 470–486. http://doi.org/10.1093/jmp/jhp035.

Engelhard, M., Kristin H., Matthias B., and Louis-Marie H., eds. (2010). Methods to Generate Transgenic Animals. In *Genetic Engineering in Livestock: New Applications and Interdisciplinary Perspectives*, 31–48. Berlin: Springer-Verlag.

Fehilly, C. B., Willadsen, S. M., & Tucker, E. M. (1984). Interspecific chimaerism between sheep and goat. *Nature*, *307*(5952), 634–636. http://doi.org/10.1038/307634a0.

Feinberg, J. (1984). *Harm to Others (The Moral Limits of the Criminal Law Volume I)*. Oxford: Oxford University Press.

Feinberg, J. (1986). Wrongful Life and the Counterfactual Element in Harming. *Social Philosophy & Policy 1*(4): 145–78.

Fessenden, M. (2015, May 10). Turning the American Chestnut into a GMO Might be the Only Way to Save it. Retrieved 5 September 2015, from http://www.smithsonianmag.com/smart-news/wheat-genes-could-save-american-chestnut-180955216/

Gardner, M. (2015). A Harm-Based Solution to the Non-Identity Problem. *Ergo, an Open Access Journal of Philosophy* 2: 427–44.

Geens, M., De Block, G., Goossens, E., Frederickx, V., Van Steirteghem, A., & Tournaye, H. (2006). Spermatogonial survival after grafting human testicular tissue to immunodeficient mice. *Human Reproduction (Oxford, England)*, *21*(2), 390–396. http://doi.org/10.1093/humrep/dei412.

Gewirth, A. (1982). *Human Rights*. University of Chicago Press.

Glover, J. (2006). *Choosing Children: Genes, Disability, and Design: Genes, Disability, and Design*. Oxford University Press, UK.

Glover, J. (2015). On moral nose. In J. Coggon, S. Chan, S. Holm, & T. Kushner (Eds.), *From Reason to Practice in Bioethics: An Anthology Dedicated to the Works of John Harris*. Manchester University Press.

Gómez-Lobo, A. (2004). Does respect for embryos entail respect for gametes? *Theoretical Medicine and Bioethics*, *25*(3), 199–208.

Gómez-Lobo, A. (2005). On potentiality and respect for embryos: a reply to Mary Mahowald. *Theoretical Medicine and Bioethics*, *26*(2), 105–110; discussion 111–113.

Grau, C. (2010). Moral Status, Speciesism, and Liao's Genetic Account. *Journal of Moral Philosophy 7*(3): 387–96. doi:10.1163/174552410X511518.

Greely, H. T. (2003). Defining Chimeras... and Chimeric Concerns. *The American Journal of Bioethics*, *3*(3), 17–20.

Greely, H. T. (2013). Human/Nonhuman Chimeras: Assessing the Issues. In T. L. Beauchamp & R. G. Frey (Eds.), *The Oxford Handbook of Animal Ethics* (Reprint edition, pp. 671–698). Oxford; New York: Oxford University Press.

Greely, H. T., Cho, M. K., Hogle, L. F., & Satz, D. M. (2007). Thinking About the Human Neuron Mouse. *The American Journal of Bioethics: AJOB*, *7*(5), 27–40. http://doi.org/10.1080/15265160701290371.

Greek, R., and Menache A. (2013). Systematic Reviews of Animal Models: Methodology versus Epistemology. *International Journal of Medical Sciences 10*(3): 206–21. doi:10.7150/ijms.5529.

Greene, M., Schill, K., Takahashi, S., Bateman-House, A., Beauchamp, T., Bok, H., … Dennett, D. (2005). Moral issues of human-nonhuman primate neural grafting. *SCIENCE*, *309*(5733), 385–386.

Haber, M. H., & Benham, B. (2012). Reframing the ethical issues in part-human animal research: the unbearable ontology of inexorable moral confusion. *The American*

Journal of Bioethics: AJOB, *12*(9), 17–25. http://doi.org/10.1080/15265161.2012.699139.
Habermas, J. (2003). *The Future of Human Nature*. (H. Beister, M. Pensky, & W. Rehg, Trans.) (1 edition). Cambridge, UK: Polity.
Han, X., Chen, M., Wang, F., Windrem, M., Wang, S., Shanz, S., … Nedergaard, M. (2013). Forebrain Engraftment by Human Glial Progenitor Cells Enhances Synaptic Plasticity and Learning in Adult Mice. *Cell Stem Cell*, *12*(3), 342–353. http://doi.org/10.1016/j.stem.2012.12.015
Hayry, M. (2004). There is a difference between selecting a deaf embryo and deafening a hearing child. *Journal of Medical Ethics*, *30*(5), 510–512. http://doi.org/10.1136/jme.2002.001891

Douglas, H., Wagner, E. F. and Palmiter, R. D. (2007). The Origins of Oncomice: A History of the First Transgenic Mice Genetically Engineered to Develop Cancer. *Genes & Development 21*(18): 2258–70. doi:10.1101/gad.1583307.
Hanser, M. (2008). The Metaphysics of Harm. *Philosophy and Phenomenological Research 77*(2): 421–50. doi:10.1111/j.1933-1592.2008.00197.x.
Harris, J. (1985). *The Value of Life*. New York: Routledge.
Harris, J. (1998). *Clones, Genes, and Immortality: Ethics and the Genetic Revolution*. Oxford University Press.
Harris, J. (2001). One Principle and Three Fallacies of Disability Studies. *Journal of Medical Ethics 27*(6): 383–87. doi:10.1136/jme.27.6.383.
Harris, J. (2002). Law and regulation of retained organs: the ethical issues. *Legal Studies*, *22*(4), 527–549. http://doi.org/10.1111/j.1748-121X.2002.tb00667.x.
Harris J. (2006). *The Value of Life: An Introduction to Medical Ethics*. London: Routledge.
Harris, J. (2010). Transhumanity: A Moral Vision of the Twenty-First Century. In N. A. Davis, R. Keshen, & J. McMahan (Eds.), *Ethics and Humanity* (pp. 257–276). Oxford: Oxford University Press.
Harris, J. (2011). Taking the 'Human' Out of Human Rights. *Cambridge Quarterly of Healthcare Ethics*, *20*(01), 9–20. http://doi.org/10.1017/S0963180109990570.
Hendriksen, C. F. (1996). A Short History of the Use of Animals in Vaccine Development and Quality Control. *Developments in Biological Standardization* 86: 3–10.
Hesiod. (1914). *Hesiod, the Homeric Hymns, and Homerica*. (H. G. Evelyn-White, Trans.) (Revised edition). Cambridge, Mass. : London: Loeb Classical Library.
Höflinger, L. (2012). In the Land of the Pizzly: As Arctic Melts, Polar and Grizzly Bears Mate. *SPIEGEL ONLINE*. October 3. http://www.spiegel.de/international/world/polar-bears-and-grizzlies-producing-hybrid-offspring-as-arctic-melts-a-859218.html.
Holden, C. (2005). Korean Cloner Admits Lying about Oocyte Donations. *Science (New York, N.Y.) 310*(5753): 1402–3. doi:10.1126/science.310.5753.1402.
Homer. (1836). *The Iliad of Homer*. (A. Pope, Trans.) (Vol. 1). New York: Harper & Brothers.
Horta, O. (2014). The Scope of the Argument from Species Overlap. *Journal of Applied Philosophy*, *31*(2), 142–154. http://doi.org/10.1111/japp.12051.
Houdebine, L-M. (2009). Production of Pharmaceutical Proteins by Transgenic Animals. *Comparative Immunology, Microbiology and Infectious Diseases 32*(2): 107–21. doi:10.1016/j.cimid.2007.11.005.
Hughes, J. (2007). Justice and Third Party Risk: The Ethics of Xenotransplantation. *Journal of Applied Philosophy*, *24*(2), 151–168. http://doi.org/10.1111/j.1468-5930.2007.00357.x.

Human Fertilisation and Embryology Authority. (2007a). Hybrids and Chimeras: A Consultation on the Ethical and Social Implications of Creating Human/animal Embryos in Research.

Human Fertilisation and Embryology Authority. (2007b). Hybrids and Chimeras: Findings of the Consultation. http://www.hfea.gov.uk/docs/AM_Item_08_Sep07.pdf.

Human Fertilisation and Embryology Authority. (2007c). Hybrids and Chimeras: A Report on the Findings of the Consultation.

Humphreys, K. (2014). An organ shortage kills 30 Americans every day. Is it time to pay donors? *The Washington Post*. Retrieved from http://www.washingtonpost.com/blogs/wonkblog/wp/2014/10/20/an-organ-shortage-kills-30-americans-every-day-is-it-time-to-pay-donors/.

Humphreys, A., and Payne E. (2015). Ottawa Senators Owner Eugene Melnyk's Plea for Liver Donor Answered but Ethical Questions Raised. *National Post*, May 16. http://news.nationalpost.com/news/canada/ottawa-senators-owner-eugene-melnyks-plea-for-liver-donor-answered-but-ethical-questions-raised.

Huther C. (2009). Chimeras: The ethics of creating human-animal interspecifics [Doctoral thesis]. *Ludwig-Maximilians-Universitat Munchen*. Available from: http://edoc.ub.uni-muenchen.de/10022/1/Huther_Constanze.pdf

Hyun, I. (2013). *Bioethics and the Future of Stem Cell Research*. New York, NY: Cambridge University Press.

Hyun I, Taylor P, Testa G, Dickens B, Jung KW, McNab A, et al. (2007). Ethical standards for human-to-animal chimera experiments in stem cell research. *Cell Stem Cell, 1*(2), 159–63.

Isotani, A., Hatayama, H., Kaseda, K., Ikawa, M., & Okabe, M. (2011). Formation of a thymus from rat ES cells in xenogeneic nude mouse↔rat ES chimeras. *Genes to Cells: Devoted to Molecular & Cellular Mechanisms*, *16*(4), 397–405. http://doi.org/10.1111/j.1365-2443.2011.01495.x.

Izpisua Belmonte, J. C. (2016). Tissue Mash-Up: a Q&A with Juan Carlos Izpisua Belmonte - Scientific American. http://www.scientificamerican.com/article/tissue-mash-up-a-q-a-with-juan-carlos-izpisua-belmonte/.

Jaworska, A, and Tannenbaum J. (2013). The Grounds of Moral Status. In *The Stanford Encyclopedia of Philosophy*, edited by Edward N. Zalta, Summer 2013. http://plato.stanford.edu/archives/sum2013/entries/grounds-moral-status/.

Jaworska, A, and Tannenbaum J. (2014). Person-Rearing Relationships as a Key to Higher Moral Status. *Ethics 124*(2): 242–71. doi:10.1086/673431.

Jaworska, A, and Tannenbaum J. (2015). Who Has the Capacity to Participate as a Rearee in a Person-Rearing Relationship? *Ethics 125*(4): 1096–1113. doi:10.1086/680905.

Jones, D. (2010). Is the Creation of Admixed Embryos "an Offense against Human Dignity"? *Human Reproduction & Genetic Ethics 16*(1): 87–114. doi:10.1558/hrge.v16i1.87.

John, J. St., and Lovell-Badge R. (2007). Human–animal Cytoplasmic Hybrid Embryos, Mitochondria, and an Energetic Debate. *Nature Cell Biology 9*(9): 988–92. doi:10.1038/ncb436.

Johnston, J., & Eliot, C. (2003). Chimeras and 'Human Dignity'. *The American Journal of Bioethics*, *3*(3), W6-W8.

Kahane, G., and Savulescu J. (2012). The Concept of Harm and the Significance of Normality. *Journal of Applied Philosophy 29*(4): 318–32. doi:10.1111/j.1468-5930.2012.00574.x.

Kamm, F. M. (2007). *Intricate Ethics: Rights, Responsibilities, and Permissible Harm*. Oxford ; New York: OUP USA.

Kant, I. (1963). *Lectures on Ethics*. Translated by Louis Infield. New York: Harper Torchbooks.

Kant, I. (1998). *Kant: Groundwork of the Metaphysics of Morals*. Cambridge University Press.
Karpowicz, P., Cohen, C. B., & van der Kooy, D. (2004). It is ethical to transplant human stem cells into nonhuman embryos. *Nature Medicine*, *10*(4), 331–335. http://doi.org/10.1038/nm0404-331.
Karpowicz, P., Cohen, C. B., & van der Kooy, D. (2005). Developing human-nonhuman chimeras in human stem cell research: ethical issues and boundaries. *Kennedy Institute of Ethics Journal*, *15*(2), 107–134.
Kaufman, F. (1998). Speciesism and the Argument from Misfortune. *Journal of Applied Philosophy*, *15*(2), 155–163. http://doi.org/10.1111/1468-5930.00083.
Kim, S. S., Kang, H. G., Kim, N. H., Lee, H. C., & Lee, H. H. (2005). Assessment of the integrity of human oocytes retrieved from cryopreserved ovarian tissue after xenotransplantation. *Human Reproduction (Oxford, England)*, *20*(9), 2502–2508. http://doi.org/10.1093/humrep/dei099.
Kittay, E. F. (2005). At the Margins of Moral Personhood. *Ethics*, *116*(1), 100–131. http://doi.org/10.1086/454366.
Kittay, E. F. (2009). The Personal Is Philosophical Is Political: A Philosopher and Mother of a Cognitively Disabled Person Sends Notes from the Battlefield. *Metaphilosophy*, *40*(3-4), 606–627. http://doi.org/10.1111/j.1467-9973.2009.01600.x.
Kobayashi, T., Kato-Itoh, M., & Nakauchi, H. (2014). Targeted Organ Generation Using Mixl1-Inducible Mouse Pluripotent Stem Cells in Blastocyst Complementation. *Stem Cells and Development*. http://doi.org/10.1089/scd.2014.0270.
Kobayashi, T., Yamaguchi, T., Hamanaka, S., Kato-Itoh, M., Yamazaki, Y., Ibata, M., … Nakauchi, H. (2010). Generation of rat pancreas in mouse by interspecific blastocyst injection of pluripotent stem cells. *Cell*, *142*(5), 787–799. http://doi.org/10.1016/j.cell.2010.07.039.
Korsgaard, C. M. (2012). A Kantian Case for Animal Rights. In *In Animal Law: Tier Und Recht*, edited by Margot Michel, Daniela Kühne, and Julia Hänni, 3–27. Zurich: Dike Verlag.
Lapidot, T. (2001). Mechanism of human stem cell migration and repopulation of NOD/SCID and B2mnull NOD/SCID mice. The role of SDF-1/CXCR4 interactions. *Annals of the New York Academy of Sciences*, *938*, 83–95.
Le Douarin, N. M., & Teillet, M.-A. M. (1974). Experimental analysis of the migration and differentiation of neuroblasts of the autonomic nervous system and of neurectodermal mesenchymal derivatives, using a biological cell marking technique. *Developmental Biology*, *41*(1), 162–184. http://doi.org/10.1016/0012-1606(74)90291-7.
Lepp, Heino. (2011). What Is a Lichen? *What Is a Lichen?* March 7. https://www.anbg.gov.au/lichen/what-is-lichen.html.
Legrand, N., Ploss, A., Balling, R., Becker, P. D., Borsotti, C., Brezillon, N., … Ziegler, P. (2009). Humanized Mice for Modeling Human Infectious Disease: Challenges, Progress, and Outlook. *Cell Host & Microbe*, *6*(1), 5–9. http://doi.org/10.1016/j.chom.2009.06.006.
Liao, S. M. (2010). The Basis of Human Moral Status. *Journal of Moral Philosophy 7*(2): 159–79. doi:10.1163/174552409X12567397529106.
Liao, S. M. (2012). The Genetic Account of Moral Status: A Defense. *Journal of Moral Philosophy 9*(2): 265–77. doi:10.1163/174552412X625718.
Liechty, K. W., Tippi C. MacKenzie, Aimen F. Shaaban, Antoneta Radu, AnneMarie B. Moseley, Robert Deans, Daniel R. Marshak, and Alan W. Flake. (2000). Human Mesenchymal Stem Cells Engraft and Demonstrate Site-Specific Differentiation after in Utero Transplantation in Sheep. *Nature Medicine 6*(11): 1282–86. doi:10.1038/81395.

Locke, J. 1964. *An Essay Concerning Human Understandig*. Edited by Peter H. Nidditch. Oxford: Clarendon Press.

Loi, P., G. Ptak, B. Barboni, J. Fulka, P. Cappai, and M. Clinton. (2001). Genetic Rescue of an Endangered Mammal by Cross-Species Nuclear Transfer Using Post-Mortem Somatic Cells. *Nature Biotechnology 19*(10): 962–64. doi:10.1038/nbt1001-962.

MacKellar C. (2007). Chimeras, hybrids and 'cybrids'. *Christian Medical Fellowship Files*, 34, 1-3. http://admin.cmf.org.uk/pdf/cmffiles/34_hybrids.pdf (accessed 6 Oct 14).

MacKellar, C., & Jones, D. A. (Eds.). (2012). *Chimera's Children. Ethical, Philosophical and Religious Perspectives on Human-Nonhuman Experimentation*. London: Bloomsbury Continuum.

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

Maher, B. (2008). Egg shortage hits race to clone human stem cells. *Nature News*, *453*(7197), 828–829. http://doi.org/10.1038/453828a.

Manninen, B. A. (2007). Revisiting the Argument from Fetal Potential. *Philosophy, Ethics, and Humanities in Medicine* 2 (May): 7. doi:10.1186/1747-5341-2-7.

Matsunari, H., Nagashima, H., Watanabe, M., Umeyama, K., Nakano, K., Nagaya, M., … Nakauchi, H. (2013). Blastocyst complementation generates exogenic pancreas in vivo in apancreatic cloned pigs. *Proceedings of the National Academy of Sciences*, *110*(12), 4557–4562. http://doi.org/10.1073/pnas.1222902110.

Maxwell, K. N., Cholst, I. N., & Rosenwaks, Z. (2008). The incidence of both serious and minor complications in young women undergoing oocyte donation. *Fertility and Sterility*, *90*(6), 2165–2171. http://doi.org/10.1016/j.fertnstert.2007.10.065.

McMahan, J. (2003). *The Ethics of Killing: Problems at the Margins of Life: Problems at the Margins of Life*. Oxford University Press.

McMahan, J. (2008). Eating animals the nice way. *Daedalus, 137*(1): 66–76.

McMahan, J. (2009). Cognitive Disability and Cognitive Enhancement. *Metaphilosophy*, *40*(3-4), 582–605. http://doi.org/10.1111/j.1467-9973.2009.01612.x.

Melo, H., Brandao, C., Rego, G., & Nunes, R. (2001). Ethical and legal issues in xenotransplantation. *Bioethics*, *15*(5-6), 427–442.

Moyes, J. (1997). Art Lovers Savaged by a Mutated Sheep. *The Independent*, August 29. http://www.independent.co.uk/news/art-lovers-savaged-by-a-mutated-sheep-1247901.html.

Muotri, A. R., Nakashima K., Toni N., et al. (2005). Development of Functional Human Embryonic Stem Cell-Derived Neurons in Mouse Brain. *Proceedings of the National Academy of Sciences of the United States of America 102*(51): 18644–48. doi:10.1073/pnas.0509315102.

Murray, J. E., Merrill J. P., and Hartwell H. J. (1958). Kidney Transplantation Between Seven Pairs of Identical Twins. *Annals of Surgery 148*(3): 343–57.

National Academies of Science. (2005). *Guidelines for Human Embryonic Stem Cell Research. Committee on Guidelines for Human Embryonic Stem Cell Research, National Research Council*. Washington, D.C.: National Academies Press.

NHS. (2014). NHSBT - The Organ Donation Register. Retrieved 1 December 2014, from http://www.organdonation.nhs.uk

NHS Blood and Transplant. (2015). 'NHS Blood and Transplant Reveals Nearly 49,000 People in the UK Have Had to Wait for a Transplant in the Last Decade'. November 20. https://www.organdonation.nhs.uk/news-and-campaigns/news/nhs-blood-and-transplant-reveals-nearly-49-000-people-in-the-uk-have-had-to-wait-for-a-transplant-in-the-last-decade/.

Norcross, A. (2004). Puppies, Pigs, and People: Eating Meat and Marginal Cases. *Philosophical Perspectives 18*(1): 229–45. doi:10.1111/j.1520-8583.2004.00027.x.

Norton, A. T., & Zehner, O. (2008). Which Half is Mommy?: Tetragametic Chimerism and Trans-Subjectivity. *WSQ: Women's Studies Quarterly*, *36*(3-4), 106–125. http://doi.org/10.1353/wsq.0.0115.

Ourednik, V., Ourednik J., Flax J. D. W., Zawada M, Hutt C., Yang C., Kook I. Park, et al. (2001). Segregation of Human Neural Stem Cells in the Developing Primate Forebrain. *Science 293*(5536): 1820–24. doi:10.1126/science.1060580.

Palacios-González, C. (2015). Human Dignity and the Creation of Human-Nonhuman Chimeras. *Medicine, Health Care and Philosophy*, *18*(4), 487–499. http://doi.org/10.1007/s11019-015-9644-7.

Palacios-González, C., Harris, J., & Testa, G. (2014). Multiplex parenting: IVG and the generations to come. *Journal of Medical Ethics*, *40*(11), 752–758. http://doi.org/10.1136/medethics-2013-101810.

Parfit, D. (1984). *Reasons and Persons*. Oxford: Clarendon Press.

Pasqualino, L., Galli, C., and Ptak, G. (2007). Cloning of Endangered Mammalian Species: Any Progress? *Trends in Biotechnology 25*(5): 195–200. doi:10.1016/j.tibtech.2007.03.007.

Piotrowska, M. (2011). Part-Humans: How Human Are They and Does It Matter? PhD Thesis, US: The University of Utah.

Piotrowska, M. (2014). Transferring Morality to Human–Nonhuman Chimeras. *The American Journal of Bioethics*, *14*(2), 4–12. http://doi.org/10.1080/15265161.2013.868951.

Pluhar, E. B. (2006). Experimentation on humans and nonhumans. *Theoretical Medicine and Bioethics*, *27*(4), 333–355. http://doi.org/10.1007/s11017-006-9009-6.

Pray, L. 2008. Recombinant DNA Technology and Transgenic Animals. *Nature Education 1*(1): 51.

Purshouse, C. (2015). A Defence of the Counterfactual Account of Harm. *Bioethics*, October, n/a – n/a. doi:10.1111/bioe.12207.

Rashid, T., Kobayashi, T., & Nakauchi, H. (2014). Revisiting the Flight of Icarus: Making Human Organs from PSCs with Large Animal Chimeras. *Cell Stem Cell*, *15*(4), 406–409. http://doi.org/10.1016/j.stem.2014.09.013.

Ravelingien, A., Braeckman, J., & Legge, M. (2006). On the Moral Status of Humanized Chimeras and the Concept of Human Dignity. *Between the Species*, *13*(6).

Reardon, S. (2015). New Life for Pig-to-Human Transplants. *Nature* 527 (November): 152–54. doi:10.1038/527152a.

Regalado, A. (2015). Surgeons Smash Records with Pig-to-Primate Organ Transplants. *MIT Technology Review*. August 12. https://www.technologyreview.com/s/540076/surgeons-smash-records-with-pig-to-primate-organ-transplants/.

Regan T. (2004). *The Case for Animal Rights*. First Edition, Updated with a New Preface edition. Berkeley; University of California Press.

Rendu, W., Beauval C., Crevecoeur I., Bayle P., Balzeau A., Bismuth T., Bourguignon L., et al. (2014). Evidence Supporting an Intentional Neandertal Burial at La Chapelle-Aux-Saints. *Proceedings of the National Academy of Sciences 111*(1): 81–86. doi:10.1073/pnas.1316780110.

Resnik, D. B. (2003). Patents on Human-Animal Chimeras and Threats to Human Dignity. *The American Journal of Bioethics*, *3*(3), 35–36. http://doi.org/10.1162/15265160360706534.

Rizzo, A. (2010, May 21). Vatican: Scientists shouldn't play God. Retrieved 8 September 2015, from http://www.nbcnews.com/id/37285047/ns/technology_and_science-science/t/vatican-scientists-shouldnt-play-god/.

Robert, J. S. (2006). The science and ethics of making part-human animals in stem cell biology. *Federation of American Societies for Experimental Biology*, *20*(7), 838–845. http://doi.org/10.1096/fj.05-4286lsf.

Robert, J. S., & Baylis, F. (2003). Crossing species boundaries. *The American Journal of Bioethics: AJOB*, *3*(3), 1–13. http://doi.org/10.1162/15265160360706417.

Rossiianov, K. (2002). Beyond Species: Il'ya Ivanov and His Experiments on Cross-Breeding Humans with Anthropoid Apes. *Science in Context 15*(02): 277–316. doi:10.1017/S0269889702000455.

S. 1373, 109th Congress. (2005, July). A bill to amend Title 18, United States Code, to prohibit human chimeras. Retrieved 8 September 2015 from http://www.gpo.gov/fdsys/pkg/BILLS-109s1373is/pdf/BILLS-109s1373is.pdf.

Sacci Jr., J. B., Alam, U., Douglas, D., Lewis, J., Tyrrell, D. L. J., Azad, A. F., & Kneteman, N. M. (2006). Plasmodium falciparum infection and exoerythrocytic development in mice with chimeric human livers. *International Journal for Parasitology*, *36*(3), 353–360. http://doi.org/10.1016/j.ijpara.2005.10.014.

Sagoff, M. (2007). Further Thoughts About the Human Neuron Mouse. *The American Journal of Bioethics*, *7*(5), 51–52. http://doi.org/10.1080/15265160701290447.

Sanal, M. G. (2011). Future of liver transplantation: Non-human primates for patient-specific organs from induced pluripotent stem cells. *World Journal of Gastroenterology : WJG*, *17*(32), 3684–3690. http://doi.org/10.3748/wjg.v17.i32.3684.

Sankararaman, S., Mallick S., Dannemann M., Prüfer K., Kelso J., Pääbo S., Patterson N., and Reich D. (2014). The Genomic Landscape of Neanderthal Ancestry in Present-Day Humans. *Nature 507*(7492): 354–57. doi:10.1038/nature12961.

Savulescu, J. (2003). Human-animal transgenesis and chimeras might be an expression of our humanity. *The American Journal of Bioethics: AJOB*, *3*(3), 22–25. http://doi.org/10.1162/15265160360706462

Savulescu, J. (2013). Genetically Modified Animals: Should There Be Limits to Engineering the Animal Kingdom? In T. L. Beauchamp & R. G. Frey (Eds.), *The Oxford Handbook of Animal Ethics* (Reprint edition, pp. 641–670). Oxford; New York: Oxford University Press.

Schroeder, D. (2010). Dignity: One, Two, Three, Four, Five, Still Counting. *Cambridge Quarterly of Healthcare Ethics*, *19*(01), 118–125. http://doi.org/10.1017/S0963180109990302.

Scottish Council on Human Bioethics. (2006). Ethics of animal-human mixtures. Embryonic, Fetal and Postnatal Animal-Human Mixtures: An ethical discussion. *Scottish Council on Human Bioethics*. Available from: http://www.schb.org.uk/downloads/publications/ethics_of_animal-human_mixtures.pdf

Scott, C. T. (2006). Chimeras in the crosshairs. *Nature Biotechnology*, *24*(5), 487–490. http://doi.org/10.1038/nbt0506-487.

Shaw, D. (2014). Creating chimeras for organs is legal in Switzerland. *Bioethica Forum*, *7*(1), 24–26.

Shaw, D., Dondorp, W., & de Wert, G. (2014). Using non-human primates to benefit humans: research and organ transplantation. *Medicine, Health Care, and Philosophy*, *17*(4), 573–578. http://doi.org/10.1007/s11019-014-9565-x.

Shaw, D., Dondorp, W., Geijsen, N., & de Wert, G. (2015). Creating human organs in chimaera pigs: an ethical source of immunocompatible organs? *Journal of Medical Ethics*, *41*(12),970-974 http://doi.org/10.1136/medethics-2014-102224.

Shultz, L. D., Ishikawa, F., & Greiner, D. L. (2007). Humanized mice in translational biomedical research. *Nature Reviews Immunology*, *7*(2), 118–130. http://doi.org/10.1038/nri2017.

Simonti, C. N., Vernot B., Bastarache L., Bottinger E., Carrell D. S., Chisholm R. L., Crosslin D. R., et al. (2016). The Phenotypic Legacy of Admixture between Modern Humans and Neandertals. *Science 351*(6274): 737–41. doi:10.1126/science.aad2149.

Singer, P. (1993). *Practical Ethics* (2nd edition). Cambridge; New York: Cambridge University Press.

Singer, P. (2001). *Animal Liberation*. New York: HarperCollins.

Singer, P. (2009). Speciesism and Moral Status. *Metaphilosophy*, *40*(3-4), 567–581. http://doi.org/10.1111/j.1467-9973.2009.01608.x.

Singer, P. 2011. *Practical Ethics*. 3 edition. New York: Cambridge University Press.

Skidmore, J. A., M. Billah, R. V. Short, and W. R. Allen. (2001). Assisted Reproductive Techniques for Hybridization of Camelids. *Reproduction, Fertility, and Development 13*(7-8): 647–52.

Smajdor, A. (2014). How useful is the concept of the 'harm threshold' in reproductive ethics and law? *Theoretical Medicine and Bioethics*, *35*(5), 321–336. http://doi.org/10.1007/s11017-014-9302-8.

Sparrow, R. (2009). Xenotransplantation, Consent and International Justice. *Developing World Bioethics*, *9*(3), 119–127. http://doi.org/10.1111/j.1471-8847.2009.00251.x.

Steinbock, B. (2011). *Life Before Birth: The Moral and Legal Status of Embryos and Fetuses, Second Edition* (2 edition). Oxford: OUP USA.

Stier, M., & Schoene-Seifert, B. (2013). The Argument from Potentiality in the Embryo Protection Debate: Finally 'Depotentialized'? *The American Journal of Bioethics*, *13*(1), 19–27. http://doi.org/10.1080/15265161.2012.743619.

Stout, J. (2001). *Ethics after Babel: The Languages of Morals and Their Discontents*. Princeton University Press.

Streiffer, R. (2003). In defense of the moral relevance of species boundaries. *The American Journal of Bioethics: AJOB*, *3*(3), 37–38. http://doi.org/10.1162/15265160360706543

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

Streiffer, R. (2010). Chimeras, moral status, and public policy: Implications of the abortion debate for public policy on human/nonhuman chimera research. *The Journal of Law, Medicine & Ethics*, *38*(2), 238–250.

Streiffer, R. (2014). Human/Non-Human Chimeras. In E. N. Zalta (Ed.), *The Stanford Encyclopedia of Philosophy* (Fall 2014). Retrieved 1 September 2015 from http://plato.stanford.edu/archives/fall2014/entries/chimeras/

Sun, Y., Xiao, D., Pan, X.-H., Zhang, R.-S., Cui, G.-H., & Chen, X.-G. (2007). Generation of human/rat xenograft animal model for the study of human donor stem cell behaviors in vivo. *World Journal of Gastroenterology: WJG*, *13*(19), 2707–2716.

Tam, P. P. L., & Rossant, J. (2003). Mouse embryonic chimeras: tools for studying mammalian. *Development*, *130*(25), 6155–6163. http://doi.org/10.1242/dev.00893.

The Academy of Medical Sciences. (2011). *Animals containing human materials*. The Academy of Medical Sciences. Retrieved 1 September 2014 from http://www.acmedsci.ac.uk/p47prid77.html.

Tippett, P. (1983). Blood Group Chimeras: A Review. *Vox Sanguinis*, *44*(6), 333–359. http://doi.org/10.1111/j.1423-0410.1983.tb03657.x.

U.S. Department of Health & Human Services. (2011). Donate the Gift of Life. Html. April 11. http://www.organdonor.gov/index.html.

Usui, J., Kobayashi, T., Yamaguchi, T., Knisely, A. S., Nishinakamura, R., & Nakauchi, H. (2012). Generation of kidney from pluripotent stem cells via blastocyst complementation. *The American Journal of Pathology*, *180*(6), 2417–2426. http://doi.org/10.1016/j.ajpath.2012.03.007.

Vernot, B., and Akey J. M. (2014). Resurrecting Surviving Neandertal Lineages from Modern Human Genomes. *Science 343*(6174): 1017–21. doi:10.1126/science.1245938.

Wade, N. (1998). Researchers Claim Embryonic Cell Mix of Human and Cow. *The New York Times on the Web*, November, A1, A26.

Warren, M. A. (2000). *Moral Status – Obligations to Persons and Other Living Things*, Oxford: Oxford University Press.

Weissman, A., Gotlieb, L., Colgan, T., Jurisicova, A., Greenblatt, E. M., & Casper, R. F. (1999). Preliminary experience with subcutaneous human ovarian cortex transplantation in the NOD-SCID mouse. *Biology of Reproduction*, *60*(6), 1462–1467.

Williams, N. J. (2013). Possible Persons and the Problem of Prenatal Harm. *The Journal of Ethics*, *17*(4), 355–385. http://doi.org/10.1007/s10892-013-9149-7.

Williams, N. J. (2014). Pre-Implantation and Pre-Natal Selection of Offspring: Can There Be a Duty to Select Against Disability? PhD Thesis, Manchester: The University of Manchester.

Williams, N. J., & Harris, J. (2014). What is the harm in harmful conception? On threshold harms in non-identity cases. *Theoretical Medicine and Bioethics*, *35*(5), 337–351. http://doi.org/10.1007/s11017-014-9303-7.

Wilmut, I., A. E. Schnieke, J. McWhir, A. J. Kind, and K. H. S. Campbell. (1997). Viable Offspring Derived from Fetal and Adult Mammalian Cells. *Nature 385*(6619): 810–13. doi:10.1038/385810a0.

Wyns, C., Langendonckt, A. V., Wese, F.-X., Donnez, J., & Curaba, M. (2008). Long-term spermatogonial survival in cryopreserved and xenografted immature human testicular tissue. *Human Reproduction*, *23*(11), 2402–2414. http://doi.org/10.1093/humrep/den272.

Xiang, A. P., Mao, F. F., Li, W.-Q., Park, D., Ma, B.-F., Wang, T., … Lahn, B. T. (2008). Extensive contribution of embryonic stem cells to the development of an evolutionarily divergent host. *Human Molecular Genetics*, *17*(1), 27–37. http://doi.org/10.1093/hmg/ddm282.

Yauch, L. E., & Shresta, S. (2008). Mouse models of dengue virus infection and disease. *Antiviral Research*, *80*(2), 87–93. http://doi.org/10.1016/j.antiviral.2008.06.010.

Zhang, J., Li L., Cai Y., et al. (2008). Expression of Active Recombinant Human Lactoferrin in the Milk of Transgenic Goats. *Protein Expression and Purification 57*(2): 127–35. doi:10.1016/j.pep.2007.10.015.