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Mice, Men, and Monsters: Opposition to Chimera Research and the Scope of Federal Regulation

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INTRODUCTION

In Western traditions, part-human, part-animal entities—sirens, Minotaurs, and Gorgons—have been perceived as threats to humanity. These amorphous creatures are often portrayed as luring humans into the underworld, bridging the gap between human civilization and the animal kingdom, and acting as intermediaries between this world and the next. Interspecies creatures, which transgress traditional boundaries between the human and animal realms, continue to challenge contemporary Western society, particularly in the wake of biotechnology capable of introducing entities possessing human and animal tissues.¹

When President George W. Bush delivered the State of the Union address on January 31, 2006, he called upon Congress “to pass legislation to prohibit the most egregious abuses of medical research . . . [which include] creating human-animal hybrids.” ² President Bush found the topic of national importance, warning the American public that human-animal chimera research threatens to devalue the Creator’s gift of human life.³

In recent years, stem cell science⁴ has begged society to consider where to
draw the line between human embryonic cells and human beings. Less well known is that the boundary between humans and animals is also becoming surprisingly blurred in light of advancing stem cell technology. Stem cells facilitate the production of human-animal chimeras, organisms that are a composite of human and animal cells.

As the production of interspecies chimeras becomes more prevalent in cutting-edge scientific research, the public response has been mixed. Some have responded with excitement at the potential of chimeras to hasten the advent of stem cell therapies. Others have responded with moral outrage and disgust at the willingness of researchers to blur the line between human and animal. Across the board, widespread confusion about the state of the science and the purpose of these creations has resulted in a political wildfire.

Chimera research has garnered such a strong response because it blurs the boundary between what is human and what is animal, implicating the moral question: how “human” are animals that contain human stem cells? There is no consensus in the scientific community on how many human cells it should be permissible to implant into a nonhuman animal. As one chimera researcher explains, “it comes down to what percentage of human cells starts making you squirm.”

Furthering the controversy, most recent research has focused on implanting human neural cells into nonhuman brains. The National Academy of Sciences (NAS) has stated that “[p]erhaps no organ that could be exposed to [human embryonic stem] cells raises more sensitive questions than the animal brain, whose biochemistry or architecture might be affected by the presence of human cells.” Both the public and the scientific community seem to correlate stem cells in the brain with what it means to be human, raising a series of ethical questions.

The lack of centralized regulation in the United States and the advancing state of science has created palpable anxiety. In 2005, Republican Senator Sam Brownback of Kansas introduced the Human Chimera Prohibition Act (HCPA)

specialized cells, such as those in the heart, brain or bone. The predominant way to produce human stem cells is to take them from a recently fertilized human embryo, destroying the embryo in the process. See National Institutes of Health, Glossary [Stem Cell Information], http://stemcells.nih.gov/STEMCells/TEMPLATES/STEMCellContentPage.aspx?NRMODE=Published &NRNODEGUID=%7b3C35BAB6-0FE6-4C4E-95F2-2CB61B58D96D%7d&NROriginalURL=%2finfo%2fglossary%2easp&NRACHEHINT=NoModifyGuest#stemcells (last visited Jan. 22, 2008); see also Gina Kolata, Scientists Bypass Need For Embryo To Get Stem Cells, N.Y. TIMES, Nov. 21, 2007, at A1.


6. Id. at 2.

to restrict the creation of chimeras. Also in 2005, the President's Council for Bioethics twice addressed the ethical problems implicated by chimeras, while the NAS issued guidelines regarding the types of chimera experiments it deemed acceptable in the context of the proper use of human stem cells.

This Comment will explore the various responses that have emerged to regulate chimera research. Section I outlines the current state of chimera technology. Section II evaluates several moral arguments in opposition to the creation of human-animal chimeras. Section III explores the basis and purpose of the HCPA in the context of other proposed regulatory measures. Finally, Section IV examines alternatives to broad federal regulation, focusing on the benefits of a localized, committee-based approach to regulating cutting-edge science.

I
THE SCIENCE OF CHIMERAS

A. Vocabulary

The word “chimera” has its origin from a mythological creature that was part lion, part serpent, and part goat, slain by the hero of Greek mythology Bellerophon, considered the greatest slayer of monsters. In modern times, the term “chimera” has been used rather loosely.

On a broad scale, modern biotechnology construes “chimera” to include organisms “comprised of at least two genetically distinct populations of cells originating from independent embryos,” but not existing as a result of sexual reproduction. Each branch of the biological sciences has refashioned the definition, so that “chimera” has been used broadly to describe inter- and intra-species combinations of molecules, cells, and even whole organs. For example, geneticists sometimes use “chimera” to describe a single DNA sequence that combines sequences originating from two separate individuals. Embryologists frame chimeras in terms of both inter- and intra-species prenatal combinations of cells that originally were derived from two different zygotes. In the world of transplantation research, a chimera could describe the

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9. See id.
10. See Shreeve, supra note 5, at 1; see also ROBERT GRAVES, THE GREEK MYTHS (rev. ed. 1960).
11. D. Scott Bennett, Comment, Chimera and the Continuum of Humanity: Erasing the Line of Constitutional Personhood, 55 EMORY L.J. 347, 347-48 (2006). It is important to note that chimeras are not hybrids, which are created as a result of sexual reproduction across species and contain recombined genes throughout their bodies. See Francois Baylis & Jason Scott Robert, Part-Human Chimeras: Worrying the Facts, Probing the Ethics, 7 AM. J. BIOETHICS 41 (2007).
13. See id. at 110.
14. See id. A zygote is a cell formed by the union of an egg cell and sperm cell.
There are several categories of chimeras, but human-animal embryonic chimeras are the most novel creations that transgress species boundaries. For the purposes of this Comment and unless otherwise specified, a "chimera" is a single entity that results from the transplantation of human embryonic stem (hES) cells into a prenatal (embryonic or early fetal stage) nonhuman host. This definition distinguishes chimeras from "hybrids," genetic combinations resulting from the fertilization of an egg from one species by the sperm of another species. In the case of a hybrid, such as a mule, each cell contains DNA from two species so that genetic mixing has occurred, which is not the case in a chimera.

B. Science of Chimera Production

Understanding the methods scientists use to create chimeras is a crucial step towards grasping the implications of the HCPA or any similar regulation of chimera research and the limitations it would impose. There are four basic methods used to produce chimeras. First, the most common method is by hES cell injection, which calls upon scientists to inject hES cells into an early embryo of another species. The hES cells are then able to differentiate inside the nonhuman embryo and theoretically integrate into all tissue types. The resulting chimera contains a mix of cells of two species. At the time of publication, scientists in the United States have refrained from injecting animal cells into a human embryo. However, Britain's Human Fertilisation and Embryology Authority (HFEA) has approved injecting animal cells into a human embryo so long as the embryo is destroyed after fourteen days and is never implanted into a human being. It has also been proposed to insert hES cells into an animal embryo. The Bush administration has restricted federal funding for stem cell research and would not approve this type of experiment.

15. See id.
17. See Karpowicz, supra note 12, at 110.
18. There are three sources of hES cells. The first is to pluck them from an early stage human embryo, destroying the embryo in the process. The second is to use adult stem cells found in differentiated human tissue. The newest method is to insert a retrovirus into human skin cells which reprograms the cells, causing them to behave like stem cells. The risks involved in the last method are yet to be determined. See National Institutes of Health, supra note 4; see also Kolata, supra note 4, at A1.
19. See Bennett, supra note 11, at 351.
20. See id.
for a federal grant, though it could be pursued through private funding.\(^2\)

A second technique, which has been less popular but has also had some success, is embryonic mixing—combining embryos of two organisms at a very early stage.\(^3\) In 1984, this technique produced the much-discussed "geep," a goat-sheep chimera which exhibited attributes of both animals.\(^4\)

A third technique, human-nonhuman nuclear transfer, which entails transferring the nucleus of a cell from one species into the de-nucleated cell of another species, has also been attempted in some laboratories utilizing cloning technology.\(^5\) In 2003, scientists in China used this cloning technology to insert human DNA into de-nucleated rabbit eggs and allowed the cells to develop for fourteen days before terminating the experiment, raising ethical ire amongst some in the international scientific community.\(^6\)

Finally, transplants have also proved a fruitful avenue for the production of chimeras. This process involves engrafting tissues, such as organs or valves, from one organism into an organism of a different species.\(^7\) For example, in 1988, researchers transplanted regions of a quail brain into the brain of a baby chicken.\(^8\) The resulting chimeric brain contained cells from the chicken and the quail, allowing researchers to observe the positions of the host and donor cells.\(^9\) Throughout embryonic development and post-hatching, scientists noted the cell movements in brain morphogenesis. Some of the chimeric chicks were later reported to have made crowing noises characteristic of quails, raising questions about the transferability of species-specific traits.\(^10\)

C. Use and Misuse of Chimeras

"We're too big. We cost too much. You can't slice us up at will."

—Hank Greely, Professor of Law at Stanford, explaining why chimeras are more suitable lab animals in hES cell research than humans.\(^11\)

1. Current Uses of Chimeras

Another important step in contemplating future government regulation of chimeras is to survey the history of chimera production to distinguish between the type of scientific experimentation currently enabled by the existing

\(^{22}\) See Shreeve, supra note 5, at 111-12.
\(^{23}\) See Bennett, supra note 11, at 351-52.
\(^{24}\) See id.
\(^{25}\) See id.
\(^{26}\) See id.
\(^{27}\) See id.
\(^{28}\) See Karpowicz, supra note 12, at 334.
\(^{29}\) Id.
\(^{30}\) See Karpowicz, supra note 12.
technologies described above and the research contemplated by science fiction.

One current use of chimera research is to aid scientists in researching human diseases. In 1988, Dr. Irving Weissman and his colleagues at Stanford made the first breakthrough in chimera technology when they configured a mouse with a fully human immune system to study the development of AIDS.\textsuperscript{32} That same year, researchers performed the quail brain transplant described in Section I.B. \textit{supra}.  

Scientists also use chimera research to study the intricacies of human anatomy. Several years ago, Esmail Zanjani, hematologist at the University of Nevada’s College of Agriculture, Biotechnology, and Natural Resources, began contemplating using sheep as models to examine the human blood system.\textsuperscript{33} The team injected lambs with human stem cells, derived mostly from human bone marrow, hoping that the hES cells would develop into blood cells.\textsuperscript{34} While some scientists doubt Zanjani’s results, Zanjani claims that when he examined the chimeric sheep he found that the human cells had migrated throughout the sheep’s body and developed into all types of cells, such as those in the blood, bone, liver and heart, providing insight into the workings of the human blood system.\textsuperscript{35} 

Most recently, in 2004, researchers at the Mayo Clinic injected hES cells into forty-day old fetal pigs.\textsuperscript{36} Since the hES cells were transferred late in development, the chimeras have the outward appearance of pigs.\textsuperscript{37} Unlike a human with an animal tissue transplant, the chimera has human and porcine cells throughout its body.\textsuperscript{38} 

Some of the most controversial research involves the insertion of human neural stem cells into the brains of animals, particularly primates.\textsuperscript{39} For example, Dr. Eugene Redmond of Yale University’s recent experiments on the Caribbean Island of St. Kitts has drawn attention, as he has implanted immature human stem cells into the region of a monkey’s brain that produces dopamine, a neurochemical that is depleted in the brains of people with Parkinson’s disease.\textsuperscript{40} The experiment is an attempt to uncover the factors that control the differentiation of stem cells and their propensity to form tumors.\textsuperscript{41} 

In addition, Dr. Weissman and his colleagues at Stanford have proposed inserting human neural stem cells into the fetal brain of a mouse whose own neurons happen to die off just before birth.\textsuperscript{42} This would result in a living

\begin{itemize}
\item[32.] \textit{See} Shreeve, \textit{supra} note 5.
\item[33.] \textit{See} id. at 2.
\item[34.] \textit{See} id.
\item[35.] \textit{See} id.
\item[36.] \textit{See} Bennett, \textit{supra} note 11.
\item[37.] \textit{See} id.
\item[38.] \textit{See} id.
\item[39.] \textit{See} Shreeve, \textit{supra} note 5 at 1.
\item[40.] \textit{See} id.
\item[41.] \textit{See} id.
\item[42.] \textit{See} id. at 5.
\end{itemize}
mouse whose brain was composed only of human neural cells.\textsuperscript{43} Weissman sought the help of his colleague at Stanford, law professor Hank Greely, who assembled a committee to review the ethical questions involved with such a project. The most complex issue the ethics review committee faced was the "nontrivial chance of conferring significant aspects of humanness on the nonhuman organism."\textsuperscript{44} The committee concluded that the risk alone was not sufficient to prevent the experiment from continuing, so long as sufficient check points were established. As of the time of publication, Weissman had yet to produce a human neural mouse though he had produced a mouse with a 1% human brain.\textsuperscript{45}

2. Potential Beneficial Uses of Chimeras

While there are a myriad of potential uses for research chimeras, there are four broad positive applications which have been presented as justifications for the creation of human-animal chimeras. First, the production of chimeras may improve the development of pharmaceutical drugs by allowing for the testing of the benefits, side-effects, and drug interactions on human cells without subjecting human subjects to unknown risks.\textsuperscript{46} It has been suggested that chimeras would provide a more accurate representation of the effects of drugs on humans than testing drugs on animals because the impact on human cells could be noted directly, as the transplanted human cells could be tagged inside the host organism for clear observation.\textsuperscript{47} This could speed up the slow process of drug approval and reduce the compounded costs of pre-clinical and subsequent clinical trials.

Chimeras also present a potential model in which to grow more viable organs for transplantation into humans. Each year millions of people suffer from diseases that could be aided by organ transplantation and many die while waiting for donations.\textsuperscript{48} Coupled with the problem of inadequate supply, a significant barrier is posed by the lack of organs that are compatible with the immune systems of patients.\textsuperscript{49} As a result of this widespread unmet need, tissue engineering has been developed with the aim of creating off-the-shelf tissue-

\begin{thebibliography}{99}
\bibitem{43} See id.
\bibitem{44} Id. at 4-5 (quoting Greenley's statement to National Academy of Sciences panel).
\bibitem{46} See Bennett, \textit{supra} note 11, at 353.
\bibitem{47} Id.
\bibitem{49} See id.
\end{thebibliography}
engineered organs.  

Chimeras potentially present one solution to this problem. One suggested method would entail extracting stem cells from a recipient’s bone marrow and injecting the sample into a sheep at either the embryonic or fetal stage. Once the sheep was born, much of the animal’s organs would consist of the recipient’s own cells and would be ready for harvesting. The premise is that the recipient’s immune system would more readily accept the chimeric organ than an organ from another human or animal, though compatibility is not ensured. It has been surmised that the possibility of the host rejecting the animal cells in the chimeric organ could be overcome, and optimists such as Alan Flake of the Children’s Hospital in Philadelphia, have suggested that chimeric transplants of this sort could be available in the next ten to fifteen years.

More broadly, chimeras can be used as tools to study human growth and development. Chimeric models provide insight because some developmental studies cannot be done on humans but may be brought to fruition through living chimera embryos. Through chimeras, researchers have the potential to create models that more closely resemble a human system without exposing human subjects to unknown risks. For example, transplanting stem cells derived from the bone marrow of adult humans into postnatal animals allows researchers to track the dispersion of human stem cells, examine their migration, and observe how they specialize and interact with other cells. Consequently, scientists are provided with the means to explore the potential for repairing or replacing damaged tissues in a human organism, as they can observe cells migrating to areas in need of repair.

Human-animal chimeras can play several critical roles in the advancement of stem-cell research. Effective preclinical trials are particularly necessary given the unique set of unknowns surrounding hES cells. First, scientists can use chimeras to evaluate hES cells without endangering human test subjects. Moreover, early in utero transplants of hES cells into animals would satisfy

50. See id.
52. See id.
53. For ethical reasons, certain experiments—such as grafting human neural cells into humans solely for experimental purposes—are prohibited even if they would lead to human treatments, making research on chimeras more attractive. See Mark Greene et al., Moral Issues of Human-Nonhuman Primate Neural Grafting, 309 SCI. MAG. 385, July 15, 2005, available at http://www.sciencemag.org/cgi/content/full/309/5733/385; see also Bennett, supra note 11, at 353.
55. See id.
57. See Karpowicz, supra note 12, at 331.
FDA requirements, which mandate that scientists test hES cells in animals prior to clinical trials. Chimeras could thus be used as vehicles to examine stem cells' propensity to form tumors and to demonstrate that stem cells can survive and differentiate successfully after transplantation.

Human-animal chimeras may provide insight into neurodegenerative and psychiatric diseases, such as Parkinson's and Alzheimer's. As "it is currently unknown whether hES [cells] can differentiate into authentic human neurons in vivo," the chimeric-mouse model illustrates the "differentiation and migration potential of hES in vivo." Chimeric-mouse models have already produced insights into neurodegenerative diseases such as amyotrophic lateral sclerosis, commonly known as "Lou Gehrig's Disease." Experiments have demonstrated that human embryonic stem cells implanted into the brain of an embryonic mouse can differentiate into functional neural lineages and generate mature, active human neurons that successfully integrate into the adult mouse's forebrain. These results can guide scientists as to which therapies may be effective in humans.

Human-animal chimera research may also prevent the direct use of human embryos for research purposes. Scientists may be able to implant adult stem cells found in many living organs and tissues throughout the human body within animal embryos to produce human tissue and organs. If so, they can "eliminate[] the need to use human stem cells from embryos for the same purpose." Thus, human-animal chimera research might circumvent the divisive debate surrounding the destruction of human embryos and the beginning of human life.

3. Potential Misuses of Chimeras

Opponents of chimera research have suggested several possible negative appropriations of chimeras. Some opponents of chimera research fear that unrestrained scientific experimentation could lead to the exploitation of chimeras. For example, critics have suggested that future human-animal chimeras could be used for non-therapeutic purposes, such as to delay the aging process.

The most nightmarish of these objectionable uses has been that human-
primate chimeras would be created for commercial exploitation and used as slaves. Mark Dowie of the University of California at Berkeley has sketched a world in which quasi-human “flesh robots” threaten to “erase taboos we still embrace, like bestiality, or reintroduce practices we’d hopefully sloughed off, like slavery.” He asked, “[c]ould one animal cell make a being suitable for ownership, forced labor, and medical experimentation, just as ‘one drop’ of black blood once did?” There also exists anxiety about the rights allocated to this class of “lesser humans” and the ramifications this stratification would have on human civilization.

On the one hand, this horrific vision is reminiscent of scenarios found in works of science fiction. One critic has described this rhetoric as “over-the-top” and countered by pointing out that an E. coli bacterium is not made human because it possesses a gene for human insulin. On the other hand, Dowie’s vision resonates with more forceful concerns that society would misuse human-animal chimeras. Indeed, several moral objections to the “beneficial” uses involving human stem cells have arisen in support of a ban on human-animal chimera production. The following Part will assess a range of objections from the public and from within the scientific community.

II
OBJECTIONS TO CHIMERA RESEARCH

The progression of biotechnology research has given rise to many concerns. Most of these concerns stem from moral objections to the implications of such research. Some of the most vocal opponents to hES cell research believe that destroying embryos to extract stem cells is morally objectionable. Additionally, some animal-rights activists base their efforts on protecting the moral rights of animals used in biomedical research. Nevertheless, most biomedical research and advisory boards support both hES cell research and biomedical research performed on animals.

It is therefore surprising that human-animal chimera research, which synthesizes both human and animal research, draws widespread concern from within the scientific community. Geron, the company that funded James Thomson’s original derivation of stem cells, mandated that an ethics advisory

66. See Dowie, supra note 64.
67. See Bailey, supra note 62.
68. See Streiffer, supra note 54, at 347.
69. See id.
70. See id.
71. See id.
board review any project involving "any creation of chimeras." Even more stringently, WiCell Research Institute, the organization that manages the University of Wisconsin's stem-cell research, has stipulated that recipients of Wisconsin hES cell lines shall not engage in "(i) the mixing of [hES cell lines] with an intact embryo, either human or nonhuman; implanting [hES cell lines] or products of [hES cell lines] in a uterus; and (iii) attempting to make whole embryos with [hES cell lines] by any method." These requirements suggest that the creation of chimeras poses a novel set of moral problems. However, not all chimeras have provoked the same moral stir. For example, the transfer of human material, such as embryonic stomachs, tracheas, and lungs, into the bodies of mice has failed to raise ethical ire. In addition, surgeons routinely transplant pig valves into the hearts of humans suffering from coronary disease—the former U.S. Senator Jesse Helms being just one of those who benefited from this procedure—without eliciting great moral inquiry. Cynthia B. Cohen of the Kennedy Institute of Ethics at Georgetown University has argued that the only ethically questionable research involves implanting stem cells derived from the brain or eye into animal embryos. These opinions suggest that people become most uncomfortable with chimera research when it blurs the boundaries between what is human and what is animal.

The rest of Part II will explore the possible sources that underlie the moral malaise caused by the creation of chimeras through an examination of the objections articulated by the research community and the public. Parts III and IV will then assess the coherence of those arguments and whether the Brownback bill adequately addresses the most persuasive of these concerns.

A. "Yuck" Factor

"We all know a human when we see one, but, really, that is all that is known about our identity as a species." Some people experience an "instinctive hostility" when contemplating the creation of a human-animal chimera. Investigators have dubbed this response the "yuck" factor. Some scientists, such as bioethicist Dr. Leon Kass, current chairperson of the President's Council of Bioethics, have identified instinctive queasiness or repugnance toward human-animal chimeras as a sign that chimera research is

72. See id. at 350.
73. Id.
74. See Shreeve, supra note 5.
75. See Karpowicz, supra note 12, at 108.
76. See id. at 7 (citing J. HARRIS, CLONES, GENES, AND IMMORALITY: ETHICS AND THE GENETIC REVOLUTION 177 (1998)).
77. Id. at 7.
78. See id.
morally wrong. Kass has explained:

Repugnance . . . revolts against the excesses of human willfulness, warning us not to transgress what is unspeakably profound. Indeed, in this age in which . . . our given human nature no longer commands respect . . . repugnance may be the only voice left that speaks up to defend the central core of our humanity. According to this view, intuition and revulsion alone provide a sufficient basis for concluding that chimera research is morally unacceptable.

However, emotions are a questionable basis for moral decision making if there is no articulation of the underlying emotion, as is the case when someone experiences disgust. Consider a few generally shared human emotional responses: for example, the horror at a child being raped or the indignation at a person being wrongfully convicted. These scenarios elicit anger and compassion and there are underlying reasons accompanying these emotional responses that justify their influence on public policy. In contrast, a person experiencing disgust has no underlying rationale for his emotion and therefore has difficulty persuading others to share his sentiment. For example, a woman who is angered by the murder of her child can persuade someone to share her reasons and consequently her emotions. In comparison, a person disgusted by a homosexual can provide no reasoning that would convince someone to share that emotion.

Human intuition is a similarly unreliable basis upon which to determine policy. Some will argue that an intuitive response, in contrast to a purely emotional one, does not require further justification because it represents an authoritative "inner voice." However, intuitive reactions often conflict. Consider the reactions that arise from witnessing someone in distress: the intuition to help a fellow human may provide the impetus to rescue, while the intuition for self-preservation may prevent a person from intervening. Consequently, an intuitive response may be no better than an emotional response when making a moral choice.

Therefore, the "yuck" that some experience when contemplating a chimera—whether it be emotional or intuitive—is not sufficient to support an ethical judgment without an explanation of the reasons underlying the reaction.

79. See Shreeve, supra note 5.
81. See Karpowicz, supra note 12, at 110-11.
82. See id.
84. See id.
1. Aversion to "Visible" Chimeras

Because we cannot accept an unsupported intuitive or emotional response as a sufficient basis for moral objection, we must examine what underlies the instinctive repugnance that some experience. One explanation is that the appearance of "visible chimeras"—animals with features that appear human—educes instinctive disgust. Dr. William Hurlbut, a physician, consulting professor at Stanford, and member of the President's Council for Bioethics, concludes that the creation of visible chimeras is unethical because "human appearance is something we should reserve for humans."85

The public response to Dr. Charles Vacanti and Yilin Cao's 1997 experiment supports this theory that the "yuck" factor is a response to aesthetics. Their team inserted a polymer template under the skin of a mouse's back to determine whether such a template could help grow cartilage in the shape of a three-year-old child's auricle.86 The result was a mouse carrying what appeared to be a human ear on its back. Anti-biotechnology groups successfully used these images to elicit strong public responses of discomfort.87

However, there are two primary flaws with the argument that an aversion to visible chimeras provides sufficient grounds for prohibiting chimera research. First, experiments such as the Vacanti mouse are an important step towards aiding children who suffer from certain deformities. If the scientific community explained the purpose of this type of experimentation, the public would need to weigh the advantages of enhanced medical aptitude against the effect of superficially conferring a human appearance onto a nonhuman host.88

The second weakness of this argument becomes apparent in the context of an experiment in which scientists create a normal-looking mouse that contains a handful of human brain cells or a human-animal embryo, but the public never sees it.89 In these cases, the claim that conferring human traits on nonhuman animals is the source of the moral disgust does not apply. In the majority of experiments that involve implanting hES cells into nonhuman animals, too few cells have been transferred to generate human traits, and the experimental subject does not grow beyond the Petri dish, rendering this argument moot.

2. Reproductive Issues and Aversion to Hybrids

Another facet of the "yuck" factor is that an animal containing human sperm or eggs would have the potential to mate with another animal possessing

85. Streiffer, supra note 54, at 351.
86. Yilin Cao et al., Transplantation of Chondrocytes Utilizing a Polymer-Cell Construct to Produce a Tissue-Engineered Cartilage in the Shape of a Human Ear, 100 PLASTIC RECONSTRUCTIVE SURGERY 297, 297-302 (1997).
87. See Streiffer, supra note 54, at 351.
88. See id. at 352 ("It is not remotely plausible to think that the mere visual appearance of the mouse makes such research wrong.").
89. See Shreeve, supra note 5.
human gametes\textsuperscript{90} thereby producing a human with animal parentage. Although this scenario gives rise to a slew of problematic hypothetical situations, the argument can be readily dismissed at this stage. First and foremost, the scientific community largely recognizes that this type of chimera experimentation is not desirable. As expressed by Dr. Norman Fost, "[I]nvariably nobody wants to see an experiment where two mice that have eggs and sperm of human origin have the opportunity to mate and produce human offspring . . . That's beyond anybody's wildest nightmare."\textsuperscript{91} Even the most controversial scientists have refrained from crossing this line. For example, Dr. Ali Brivanlou, one of the few scientists proposing to insert hES cells in an animal embryo, has no plans to take the embryo to term. Rather, he expects to terminate the embryos after one week.\textsuperscript{92}

Furthermore, this scenario relies upon the success of several unlikely variables. Scientists would need to bring two chimeras to term and then the two chimeras would have to mate. This presumes that there are scientists interested in undertaking this endeavor and that existing institutional oversight bodies would approve this experiment. Both conditions are theoretically possible, but currently unlikely. As Robert Lanza, Vice President for medical and scientific development at Advanced Cell Technology in Worcester, Massachusetts, said, "I personally don't want to engage in those kinds of experiments, and I won't have any of my scientists do that work . . . Sure, we could reach our endpoints quicker that way. But it takes you into very murky water."\textsuperscript{93}

Even if scientists did undertake this endeavor, fertilization of a human embryo in an animal host is not guaranteed. For example, scientists are unsure whether the environment inside the host cell—in particular the host cell's cytoplasm and mitochondria—could adversely affect the viability of human gametes. In addition, even if fertilization were to be successful, it would be "biologically impossible for a human fetus to be delivered from a rodent uterus."\textsuperscript{94} As seen from these hypothetical scenarios, this type of "nightmare" situation is far from a viable threat.

\textbf{B. Public Policy Objections}

\textit{1. Concern for Animal Welfare}

Opposition to human-animal chimera research also comes from animal-rights activists who claim that implanting hES cells into animals has potentially harmful effects on these hosts. While human-animal chimera research invokes traditional concerns in animal ethics, it also sparks new concern for the impact

\begin{itemize}
  \item Gametes are eggs and sperm.
  \item Shreeve, \textit{supra} note 5, at 4.
  \item Id. at 3.
  \item Id. at 4.
  \item Id. at 4.
\end{itemize}
on an animal’s neural tissue.\textsuperscript{95} This issue is most prevalent in the context of experimentation that involves transplanting human neural cells into the brains of animals, particularly into the brains of primates in early embryonic or fetal stages. Complicating the issue is the fact that human subjects receive greater protection than animal subjects, leaving the degree of protection for chimeras unresolved.\textsuperscript{96}

In this vein, animal welfare proponents put forth two primary objections. First, some fear that human neural cells may confer increased mental aptitude to the animal subjects, which might in turn lead to greater capacities to experience pain. Groups such as the University of Wisconsin’s Bioethics Advisory Committee have suggested that the development of human neural tissue in an animal host “raises at least the theoretical possibility that such tissue could become integrated in a way that human experiences become possible.”\textsuperscript{97} This is problematic because sacrificing a chimera capable of experiencing human pain would be morally equivalent to sacrificing the interests of a fully human adult, which would be unacceptable.\textsuperscript{98} Though it is unknown to what extent the introduction of hES cells may impact cognitive capacities, this possibility has lead some critics concerned for animal welfare to completely reject human-animal chimera experimentation.\textsuperscript{99}

Second, animal-welfare proponents contend that current conditions may be inadequate to protect chimeras if they were to experience human-like pain. Animal research oversight committees generally forgo even the most basic interests of animals to pursue valid research objectives.\textsuperscript{100} By contrast, human research oversight committees presume that humans have a moral status that entitles them to a stringent prohibition on harmful research without informed consent.\textsuperscript{101} If the standard of protection for chimeric animals was raised to meet the bar required for human subjects, this new standard would almost certainly stifle certain research objectives, such as the testing of pharmaceutical drugs.\textsuperscript{102}

It is not necessary to reject chimera research on the grounds of animal-welfare concerns for two primary reasons: (1) the state of the science does not require more than a case-by-case analysis; and (2) the existing regulatory system has jurisdiction to oversee chimera technology.

First, the risk of conferring “human experiences” on animal hosts is extremely remote unless the mixing of cells occurs at a very early stage in the animal’s embryonic development.\textsuperscript{103} Even if a primate’s entire thalamocortical

\textsuperscript{95} See Streiffer, supra note 54, at 352.
\textsuperscript{96} See id. at 362.
\textsuperscript{97} Id. at 353.
\textsuperscript{98} See id. at 362.
\textsuperscript{99} See id.
\textsuperscript{100} See id.
\textsuperscript{101} See id.
\textsuperscript{102} See id.
\textsuperscript{103} See id. at 353.
system consisted of human cells, the chimera is unlikely to gain human consciousness because its neurons would lie in anatomically different networks. It is also uncertain whether the hES cells could overcome constraints such as an animal’s skull size or the influence of the surrounding nonhuman cellular environment.

As of the time of publication, no experiment has been performed that introduced a large number of hES cells into a nonhuman primate at an early embryonic stage and then brought the primate to term. Hence, the impact of this type of experimentation on the cognitive function of a nonhuman animal has yet to be ascertained. It seems sufficiently prudent to assess each experiment proposing to implant hES cells or human neural cells into an embryonic animal’s brain on a case-by-case basis. Implementing a ban on all chimera research that may not enhance an animal’s cognitive ability would be premature, given the nascent state of the technology. Section IV will delve further into why a case-by-case approach may provide the best means of regulating chimera research.

Second, the federal government regulates animal welfare, thereby addressing both this objection to chimera research and the call for further legislation. Since 1985, the Animal Welfare Act has required research facilities that work with higher mammals to establish Institutional Animal Care and Use Committees (IACUCs). The amended legislation mandates that each institution elect at least three members, and that “[s]uch members shall possess sufficient ability to assess animal care, treatment, and practices in experimental research as determined by the needs of the research facility and shall represent society’s concerns regarding the welfare of animal subjects used at such facility.” The law endowed the IACUCs with a broad scope of authority, creating a flexible regulatory system specifically designed to respond to “society’s concerns” regarding animal welfare. The IACUCs are best situated to review chimera research conditions because these bodies are already supervising the conditions in which animals are being used in experimentation. The argument that too few safeguards will be adopted to address a chimera’s enhanced ability to experience pain is weakened in the presence of these oversight committees, as these concerns fit squarely within their jurisdiction.

104. The thalamocortical system constitutes the majority of the mammalian brain.
105. See Karpowicz, supra note 12, at 334.
106. See Streiffer, supra note 54, at 355.
107. Further, when asked about the effects of introducing neural hES cells into an animal early in development, Dr. Fred Gage, specialist of neuroplasticity and neural stem cells at the Salk Institute, has said “we don’t know the answer to [this] question because the experiment hasn’t been done, that I know of.” Id. at 356.
108. See id.
110. Id. at § 1752(c).
111. Animal-rights supporters could also argue that creating human-nonhuman chimeras purely to benefit humans constitutes animal cruelty. However, IACUCs are equipped to monitor
2. Concern for Public Health

Another public policy justification for banning chimeras rests on the idea that mixing human and animal cells will make humans more susceptible to disease. The fear that retroviruses lurking in animal DNA could mutate and infect humans has led to an opposition to xenotransplantation—the transplantation of live cells, tissues, or organs from a nonhuman animal source to a human—in countries such as the United Kingdom and Canada. This concern has become particularly relevant in the context of the avian flu virus and the SARS epidemic, which brought international attention to diseases transmitted to humans via animals. On the domestic front, the Centers for Disease Control and Prevention reported twelve human cases of monkeypox, a virus that belongs to the same group of diseases as smallpox, resulting from human contact with prairie dogs. In the HCPA, Senator Brownback echoes this concern for public health, arguing that the creation of chimeras makes it easier for diseases to infect humans.

Indeed, diseases that threaten to cross species barriers pose a viable threat because hosts' immune systems have not previously encountered these diseases and the hosts may be particularly vulnerable to them. For example, the 1918 flu epidemic that killed an estimated fifty million people around the globe is believed to have sprung from an avian flu virus. However, critics must balance this threat against the potential medical benefits of allowing chimera research, such as faster drug and stem-cell development. Given the medical promise that chimeras present, prohibiting their use based on isolated outbreaks of disease may not be justifiable.

C. Other Objections

1. Social Taboo

Another theory is that the creation of chimeras is simply a moral taboo, akin to cannibalism or incest. In Western culture, mixing two types of

the conditions of chimera experimentation to ensure the ethical treatment of chimeras.

112. See Bennett, supra note 11, at 354.
113. See Westphal, supra note 51.
115. See Human Chimera Prohibition Act, supra note 8.
118. See Karpowicz, supra note 12, at 110.
Theme has been interpreted as a symbol of evil. Along the same lines, modern society is generally hostile to the idea of human and nonhuman sexual activity and both law and custom have traditionally prohibited bestiality. Some have suggested that chimera research evokes images of bestiality, which accounts for a portion of the public’s reservations.

Although maintaining social taboos plays an important role in preserving core social values, the taboo argument does not provide a sufficient basis for prohibiting chimera studies. First, the taboo against mixing human and nonhuman animals is not universally accepted, weakening the argument as a basis upon which to prohibit research. For example, the Egyptians traditionally depicted their gods with nonhuman animal heads, and certain Native American communities portrayed sacred images that combined human and nonhuman animal features. Second, taboos fluctuate according to social norms. In Western society, blood transfusions and organ donations have historically been the subject of social taboos, yet today are generally accepted practices. Cultural inconsistency and variability render taboos an unreliable basis for determining whether the government should prohibit chimera research.

2. Religious Rationale

Opposition to human-animal chimera research is also voiced by religious critics, who question whether creating chimeras is a form of manipulating life. These opponents of chimeras base their view on the belief that all God’s creatures reflect Divine perfection and that all possible creatures are already in existence. From this point of view, creating human-animal chimeras amounts to “playing God.” Further, opponents of chimera production have emphasized that Jesus Christ came to Earth specifically as a human, not an animal, highlighting the distinction between the two worlds and the unique dignity of human beings, as well as human stewardship over animals.

However, proponents of chimera research also invoke the Divine, arguing that God “left the world in a state of imperfection so that we become His

119. See id. at 331.
120. See Robert, supra note 16, at 7.
121. Id.
122. See Karpowicz, supra note 12, at 111-12.
123. See id. at 112.
124. See id.
125. See id. at 112-113.
126. See Bennett, supra note 11, at 354.
128. See Bennett, supra note 11, at 354.
partners.”130 This interpretation suggests that humans should engage in research that has the potential to provide cures for diseases afflicting fellow human beings. Though each of these arguments is premised on a different theological tenet, each can be supported by selective reading and interpretation of scripture. Consequently, adopting a religious rationale as grounds for banning chimera experimentation would necessitate prioritizing one religious teaching over another. Further, reasoning based solely on religious beliefs does not provide the best basis for federal legislation that seeks to reflect moral consensus.

3. Preserving Mankind’s Moral Status

Another concern is that implanting hES cells into nonhuman animals could result in animals with human consciousness. This brings to mind the image of a human metamorphosing into an animal, or a human trapped inside an animal’s body. In response, Dr. Evan Snyder, a stem cell researcher at the Burnham Institute in San Diego, has reassured the public that they “will never ever have a little human trapped inside a mouse or monkey’s body.”131 Furthermore, scientists who use chimeras affirm that they have no desire to confer human consciousness upon their research subjects.132

While this Comment has addressed the prohibition of chimera production in the context of animal welfare,133 research of this nature also impinges upon society’s conception of the relative moral status of humans. Some have argued that chimeras should be banned because animals with enhanced moral status threaten the superior moral rights of humans.134 The moral superiority of humans has traditionally been grounded in three principles. First, ancient Abrahamic tradition delineates separate codes of conduct for animals and humans, bestowing on humans the duty to act as stewards of the animal kingdom.135 Second, the influential philosopher Kant suggested that man can be distinguished from nonhuman animals because of his ability to act as a rational agent and be conscious of the principles which guide his actions.136 Lastly, it has been suggested that humans’ greater cognitive capacity gives

132. See Shreeve, supra note 5, at 2 (“We have to be sure we are not creating beings with consciousness,” Francoise Baylis, a bioethicist at Dalhousie University in Halifax, Nova Scotia.).
133. See supra Section II.B.i Concern for Animal Welfare.
134. See Streiffer, supra note 54, at 354 (suggesting that the “moral status principles” is the strongest rationale in opposition of chimera research).
them an elevated moral status.\textsuperscript{137} On any of these grounds, equating two morally disparate individuals is problematic.\textsuperscript{138} Specifically, producing human-animal chimeras challenges our existing relationships with nonhuman animals as well our potential dealings with chimeras.\textsuperscript{139}

The basis of the "moral status principle" suffers from some of the flaws plaguing previously discussed grounds for opposition. If it is accepted that humans are morally superior based on an Abrahamic conception, then the same inadequacies that permeated the religious arguments discussed in Section II.C.ii recur. Alternatively, if moral superiority is rooted in higher cognitive capacity or reasoning, then the strength of the argument in support of prohibiting research hinges on two issues: the viability of transferring human consciousness and the cost or benefit of this activity.

While many are skeptical about animals' potential to develop human characteristics as a byproduct of hES cell transfer, some suggest that even increased cognitive capacity would not result in an immediate and radical change in the current relationship between animals and humans. For example, some in the scientific community underestimate similarities in mental capacity, and hence corresponding moral status, between humans and nonhuman primates.\textsuperscript{140} A multidisciplinary working group consisting of twenty-three researchers from universities across the United States (hereinafter "the Greene Working Group") has suggested that the challenge of introducing human cells into the brains of nonhuman primates should be viewed as a means to understand the mental capabilities of engrafted animals and how they should be treated, rather than as an "ethical ill."\textsuperscript{141} Correspondingly, the development of more humanlike cognitive capacities need not be viewed purely as a risk to avoid.

4. Species Integrity

Some critics are uncomfortable with the idea of human-animal chimeras because they believe that the boundaries between species should not be crossed, and that creating interspecies entities is patently unnatural.\textsuperscript{142} Biotechnology critic Jeremy Rifkin espouses this viewpoint and posits that the production of chimeras undermines "species integrity."\textsuperscript{143} Commentators who share this perspective base their argument on various essentialist theories of what constitutes human identity and belonging to the \textit{homo sapien} species.\textsuperscript{144}

\begin{enumerate}
\item \textsuperscript{137} See Streiffer, \textit{supra} note 54, at 353-54.
\item \textsuperscript{138} See id.
\item \textsuperscript{139} See Robert, \textit{supra} note 16, at 9.
\item \textsuperscript{140} See generally Greene, \textit{supra} note 53.
\item \textsuperscript{141} See id.
\item \textsuperscript{142} See Robert, \textit{supra} note 16, at 2 (discussing the view that "species identity is fixed and that species boundaries are inappropriate objects of human transgression.").
\item \textsuperscript{143} See Bennett, \textit{supra} note 11, at 354.
\item \textsuperscript{144} See Robert, \textit{supra} note 16, at 5.
\end{enumerate}
The "species integrity" argument is further supported by the teleological principle that nature should be undisturbed so that life can follow its natural course. Thus, creating interspecies chimeras is deemed unethical because it blurs the lines between species, and produces results antithetical to the natural ordering of the species.

The species integrity argument is based on tenuous premises and does not justify prohibiting chimera research. Those espousing the species integrity argument believe that species identity is fixed and that species are clearly demarcated. However, this premise has yet to be affirmed by genetic or biological studies. While biologists have been able to isolate a particular string of nucleotides as distinctly human, the unique identity of *homo sapiens* has not been established through comparative genomic research. In fact, there is evidence to the contrary, such as the revelation that 99% of the human genome is shared with chimpanzees.

Further, there is considerable debate in the scientific community as to whether biological species are real. Some have even suggested that there is no current scientific theory that justifies species boundaries. For example, the Greene Working Group confirmed that the idea of fixed species is not scientifically valid or philosophically supported. The group did not find the species integrity argument persuasive on moral grounds because the creation of human-animal chimeras has already taken place without moral objection through xenografting.

It is also noteworthy that the species integrity argument relies on indefinite terminology. The teleological principle can be readily dismissed because an entity's "natural path" is speculative to the point of "confus[ing] biological description with the justification of ethical norms." It may be concluded that scientific theories do not support the existence of species boundaries in a way that makes chimera research morally problematic and appropriate for prohibition.

Though the species integrity argument lacks viability when gauged by scientific accuracy, it is worth acknowledging that the notion of a fixed species remains prevalent in our society. The popularly held notion that a species boundary is fixed reflects the underlying moral problem regarding the creation

145. See Karpowicz, supra note 12, at 332.
147. Chemical compounds which are the structural units of DNA.
148. See id. at 4.
149. See Shreeve, supra note 5.
150. See Karpowicz, supra note 12, at 333; see also Robert, supra note 16, at 6.
152. See id. (explaining that "the safety and efficacy of engrafting fetal pig cells has been studied in people with Parkinson's disease and Huntington's disease without moral objection."). A xenograft is a transplant of cells, tissues or organs taken from a donor of one species and implanted into a recipient of another species.
of chimeras: the notion of a fixed species exists as a moral construct, and an ethical issue arises when human classification schemes are transgressed. This argument has some force because the inclination to divide the world into easily distinguishable categories has been described as a “fundamental organizing principle of civilization.”

Arguably, a special “human dignity” distinguishes humans as a separate class of species. The argument proposes that species should not be mixed because humans possess functional and psychological capacities that indicate that they are worthy of respect. However, it is precisely humans’ ability to make moral choices and our respect for human dignity that should encourage society to support medical research to alleviate human suffering.

Most arguments presented against chimera research can be dismissed due to internal inconsistencies, lack of scientific support, or in light of the fact that current oversight is sufficient. However, a common thread of moral disquietude runs through the voices of opposition: society is fundamentally uncomfortable when socially acknowledged boundaries are transgressed. This unease stems not just from mixing animal and human parts; there seems to be no taboo or intuitive unease in response to implanting pig valves in human hearts.

Rather, this social aversion appears to stem from disturbing the categories of animal and human. Nonetheless, while human-animal chimeras may not be morally problematic in terms of stem cell research or a scientific demarcation of “species,” the possibility remains that chimeras could be prohibited because a majority believes that human dignity is threatened when accepted categories are muddled. Whether the HCPA addresses this underlying moral objection and whether protecting society’s preference for clearly demarcated categories provides a sufficient basis for federal prohibition are the subjects of the remainder of this Comment.

III

THE HUMAN CHIMERA PROHIBITION ACT

A. Basis and Purpose of the Proposal

Given this framework, I now examine the purpose of the legislation Senator Sam Brownback proposed for congressional consideration. This section will identify the moral concerns the bill and its proponents purport to assuage and how the law addresses those goals. The next section will then analyze whether the law as intended and written would alleviate the core of society’s moral concern.

154. Shreeve, supra note 5, at 110-11.
155. See Karpowicz, supra note 12, at 333.
156. See id.
157. See Shreeve, supra note 5, at 2-3 (explaining that “the Senator may not trigger a yuck.”).
On April 15, 2005, Senator Brownback addressed Harvard Law School, explaining his vision of the federal government’s role in emerging biotechnology. His opening remarks on the broader purpose of legislative biotechnology regulations revealed his ideological framework. Brownback made it clear that biotechnology regulations should be implemented to enforce the professional moral code regulating scientific research. The senator explained that this is particularly relevant today because the ethical code guiding the scientific profession is threatened by emergent “[s]kepticism about God; Skepticism about the sacredness of human life . . . Skepticism about the very ethical code—the Hippocratic Oath—that has guided medical professionals and researchers for more than two millennia.” While Brownback stated that a scientist does not need to be religious to be ethical, his rhetoric reflects his conservative, pro-life agenda. Brownback’s contention is that “life begins at the beginning” and that without a doubt, “[s]cience affirms that the young human, at his or her earliest moments of life, is a human.” This ideology underlies Brownback’s legislative proposals and reappears as a basis for the HCPA.

The Act puts forth three specific reasons why the federal government should prohibit the creation of chimeras. First, the purpose of the HCPA is to prohibit the most “ethically challenging human-animal hybrids.” Second, Brownback warns that chimeras provide an optimal means of genetic transfers that would facilitate the transfer of infectious diseases, both domestically and abroad, from animal populations to humans and vice versa. The text of the Act explicitly includes the emerging threat of animal disease infection as a reason for the proposed ban.

Most significantly, the bill is intended to “prohibit science that compromises human dignity by blurring the lines between animals and humans.”


159. The moral code Brownback refers to stems from the Hippocratic Oath: “As to diseases, make a habit of two things—to help, or at least do no harm.” Id. at 1.

160. See id.

161. Id. at 2.

162. The only exception to Brownback’s 100% rating from the National Right to Life Committee occurred when he supported the McCain-Feingold campaign-finance bill (which the NRLC deemed hostile not because it favored abortion, but because it restricted the activities of political advocacy groups). Brownback is also the author of the Unborn Child Pain Awareness Act. See John Miller, Saint Sam: Senator Brownback of Kansas is one of the Country’s Leading Virtuecrats, NAT’L REV., May 8, 2006, available at http://www.findarticles.com/p/articles/mi_m1282/is_8_58/ai_n16359554/pg._3.


164. Id. at 5.

165. Id. at 6.

166. See id.

167. See id.
humans.” As Brownback has explained: “To create a human that is less than fully human or to create an animal that possesses particularly unique human aspects—such as a human brain or human reproductive organs—is a violation of this dignity.” However, this premise requires further explanation, for it begs the question why creating an entity that is not “fully human” constitutes a violation of “human dignity.” A human who has a pig valve implanted in his heart is not likely to be considered “less than fully human.” Is the distinction a question of the type of organ implanted (such as the heart and the brain noted by Brownback) or the number of cells transferred from another species, or is there another basis for a transgression of human dignity? One answer can be found in the text of the HCPA: “[S]erious ethical objections are raised to some types of chimeras because they blur the lines between human and animal, male and female, parent and child, and one individual and another individual.”

This justification embodies the “blurring the boundaries” principle, reiterating that the crossing of lines between any two categories creates moral discomfort and provides grounds for prohibition. The debates emerging from the public forum and scientific communities have this principle at their core.

According to Brownback, the scope of the legislation is modest, prohibiting only certain types of unethical research. Brownback intended the bill to be “consensus” legislation, designed to complement the senator’s ban on all forms of human cloning. The legislation purports to ban the creation of only “the most egregious chimeras,” which Brownback contends fall into eight categories, including:

(a) human embryos that are not fully human, (b) human eggs fertilized with animal sperm, (c) animal eggs fertilized with human sperm, (d) human eggs with an animal nucleus, (e) animal eggs with a human nucleus, (f) eggs with both human and animal chromosomes, (g) animals with human reproductive organs, and (h) animals with human brains.

B. Impact and Scope of Legislation

The rationale underlying the HCPA thus reflects the prevalent “blurring of the boundaries” principle, mirroring concerns voiced in the public sphere. However, the text of the bill suffers from ambiguous and overly inclusive terminology that could have consequences antithetical to the public’s best interest. Brownback states that the draft legislation only prohibits the “most egregious” types of chimera, but a closer inspection reveals that a wide range of chimera fall within the ambit of the law as presently drafted. The bill’s

168. Id.
169. Id.
170. Human Chimera Prohibition Act, supra note 8, at § 2.
171. See Brownback, supra note 158, at 5.
172. Id.
173. Id. at 7.
FEDERAL REGULATION OF CHIMERA RESEARCH

The definition of chimera is scientifically vague and differs from biotechnological definitions prevalent in scientific literature. Further, it departs from what scientists in general and the NAS have defined as chimeras.

First, most accepted definitions limit chimera to entities produced by tissue transplants, not fertilization, but the bill defines "chimeras" to include hybrids. Section 301(1)(C)-(D) of the Act prohibits the creation of a chimera as a product of a human egg fertilized by a nonhuman sperm or a nonhuman egg that has been fertilized by a human sperm. Yet chimeras refer to organisms with genetically distinct cell populations originating from different embryos. In contrast, each hybrid cell contains DNA from both species.

The proposed bill also includes mixed species produced by Somatic Cell Nuclear Transfer (SCNT) as chimeras. These "cybrids" are produced when a cell nucleus from a somatic cell is transferred into an egg whose nucleus has been removed and the somatic cell and the egg belong to different species. The creation of cybrids would facilitate cloning research because it is easier to collect eggs from nonhuman animals than it is from humans.

Last, the bill's language lacks biological sophistication. The bill draws a sharp line between animal and human and does not acknowledge research suggesting that animals and humans are part of the same spectrum. Genetic research suggests there are few "human genes" and that animals and humans share both genes and DNA retroviruses. For example, human DNA is only 1.2 to 1.6% different from that of chimpanzees.

The implications of this expansive definition are two-fold. The Joint Steering Committee for Public Policy fears that the scientifically confused definition of chimeras would ban valuable research. For example, Irv Weissman's proposal to create a fully human neural mouse would be banned under section 301(1)(I), which specifically prohibits "a nonhuman life form engineered such that it contains a human brain or a brain derived wholly or predominantly from human neural tissues."

Second, the use of vague terminology in reference to chimera further obfuscates the role of research chimera. The bill's language, which lumps chimeras and hybrids together, precludes research that allows scientists to ensure that stem cells do not form tumors even though this does not involve any genetic mixing.

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175. See id.
176. See Human Chimera Prohibition Act, supra note 8, at §301(1)(C)-(D).
177. See id. at §301(1)(E)-(F).
178. A somatic cell is any cell in the body other than an egg or sperm cell.
180. Id.
181. See The Joint Steering Comm., supra note 56.
182. Human Chimera Prohibition Act, supra note 8, at § 301(1)(I).
183. See The Joint Steering Comm., supra note 56.
could be misled into thinking that all chimeras involve genetic mixing and the role of research chimeras might be overlooked.

The core concern expressed in the HCPA is a desire to avoid blurring the boundary between animal and human. To ensure this demarcation at all costs, the bill has sacrificed a nuanced analysis of the scientific relationship between human and animal and adopted oversimplified, if not inaccurate, terminology.

C. Possible Constitutional Barrier

Central to the discussion of the viability of any legislation aimed at codifying moral opposition to the use of chimeras in scientific research is whether legislation premised purely on moral distaste or the invocation of “morality” is sufficient to justify federal legislation. A court has yet to consider whether in the absence of other harm, moral disapproval alone constitutes a legitimate state interest that justifies a statute criminalizing specific scientific research. However, the Supreme Court has addressed whether the power of the State could be used to enforce moral and ethical principles on the whole of society through the operation of criminal law.

In Lawrence v. Texas, the Supreme Court considered the appropriate relationship between legislation and morality, holding that a Texas statute prohibiting homosexual sodomy violated the Due Process Clause of the Fourteenth Amendment. In defining the issue, the majority cited Planned Parenthood of Southeastern Pa. v. Casey for the proposition that “our obligation is to define the liberty of all, not mandate our own moral code.” As the Court noted in Lawrence, Planned Parenthood affirmed that the Constitution affords protection to personal decisions central to human dignity because these choices are critical to the liberty provided by the Fourteenth Amendment. The Lawrence Court highlighted the assertion in Planned Parenthood that “at the heart of liberty is the right to define one’s own concept of existence, of meaning, of the universe, and of the mystery of human life. Beliefs about these matters could not define the attributes of personhood were they formed under compulsion of the state.” Justice O’Connor contributed a highly persuasive concurrence, advocating that the anti-sodomy law was unconstitutional based on equal protection grounds. Explaining the basis of her rationale, she stated that “we have never held that moral disapproval, without any other asserted state interest, is a sufficient rationale under the Equal Protection Clause to justify a law that discriminates among groups of

184. See Human Chimera Prohibition Act, supra note 8, at § 2(2) (citing “serious ethical objections” as a premise for the bill).
186. See id. at 578.
187. Id. at 571 (quoting Planned Parenthood of Southeastern Pa. v. Casey, 505 U.S. 833, 850 (1992)).
188. See id. at 574.
189. Id. (quoting Casey, 505 U.S. at 851).
persons."

The precedent elucidated in *Lawrence v. Texas* may have implications regarding whether the articulated basis for the HCPA or any other similar legislation is within the ambit of the federal government. Both the majority’s opinion and Justice O’Connor’s concurrence suggest that a law branding either one type of activity or one class of persons as criminal based solely on the state’s moral disapproval of that class or action defies the values of the Constitution. If the articulated premise for the Brownback bill is primarily that the creation of human-animal chimeras threatens human dignity and morality, this rationale may not be sufficient to sustain criminal enforcement by the state. Absent demonstrable, tangible harm to the public, the constitutionality of the HCPA could come into question, particularly if the Court viewed its purpose as to enforce a particular code of morality upon the scientific community and on society at large.

While proponents of the law may raise public health concerns as a legitimate federal interest, the Court would need to determine whether the increased risk of disease posed by human-animal chimeras created in laboratories would be sufficient to warrant restrictive legislation. A narrow reading of *Lawrence* might suggest that the holding only applies when there is no other asserted state interest, and therefore the public health concern stated as a rationale for the HCPA might be sufficient to escape the application of *Lawrence*. However, if a broader reading of the case is adopted, the Court may view the HCPA as merely a subterfuge for the government’s moral disapproval of specific scientific research which would likely not be sustainable under *Lawrence v. Texas*.

**D. Policy Rationale**

Beyond the constitutional question of whether legislators can make specific research guidelines such as those in the HCPA, scientists and lawmakers have hotly debated whether legislators should make such specific guidelines. On the one hand, some commentators argue that legislators are not equipped to make specific laws regulating scientific research because lawmakers lack the requisite scientific knowledge. In light of rapidly changing science, these commentators believe that Congress should focus on the process and not the subject of the experimentation. On the other hand, some fear that as the science to create human-animal chimeras and hybrids advances, scientists will be unable to stop from producing entities with more and more
human parts irrespective of society's moral concerns, necessitating independent legislative regulation. 193

IV
ALTERNATIVES TO BROAD FEDERAL LEGISLATION

The key question that emerges in response to the HCPA is whether comprehensive legislation is necessary to alleviate society's moral concerns, or are less restrictive mechanisms available to regulate research? The following Part discusses existing regulatory recommendations and proposes general guidelines for future research.

A. Recommendations for the Regulatory Landscape

Superimposing Brownback's legislation upon current biotechnology regulation in the United States is helpful for determining the best strategy for ensuring appropriate ethical supervision. Both the NAS and the President's Council on Bioethics have set forth ethical guidelines for scientists engaging in chimera research.

1. National Academy of Sciences

In 2005, the NAS published guidelines recommending permissible types of hES cell research. 194 In regards to chimeras, the NAS suggested that the transfer of hES cells into nonhuman animals at any stage of embryonic, fetal, or prenatal development should require the approval of an independent ethics committee. 195 This case-by-case approach to each proposed experiment suggests that the NAS recognizes the need for close scrutiny of chimera research, yet allows for the possibility that some work could proceed with appropriate ethical supervision.

The final guidelines recommend that an ethics committee pay particular attention to the effects of differentiation and integration of human cells into nonhuman tissues. 196 The NAS Committee proposed that an Embryonic Stem Cell Research Committee (ESCRO) address specific concerns regarding inserting hES cells into developing animals. This committee would consider the amount of hES cells to be transferred and the sites to which the transfer


195. See HUMAN EMBRYONIC STEM CELL RESEARCH ADVISORY COMMITTEE, supra note 7, at 7.

196. See id. at 7 § (b)(ii).
cells would be implanted. This suggests one way in which ethics review boards could monitor the progress of an experiment while ascertaining whether the experiment should proceed at different stages.

While the implementation of an ethics committee allows for some flexibility and case sensitivity, the NAS made two black-and-white recommendations. First and foremost, experiments that would introduce hES cells into nonhuman primate blastocysts or, more broadly, inject embryonic stem cells into a human blastocyst, should be prohibited at this time. The specific reference to primates suggests that the NAS recognizes the heightened ethical risk caused by the close proximity of the species. Second, no animal that has been implanted with hES cells should be allowed to breed. This stipulation recognizes the risks breeding of chimeras poses and expresses a normative judgment that this type of research has no justifiable purpose at this point.

2. President's Council on Bioethics

The President's Council on Bioethics has also proposed regulatory measures, yet has proscribed targeted congressional legislation rather than the NAS's more nuanced, case-sensitive approach. The Council recommended that Congress enact legislative measures to demarcate certain types of chimera research as unethical and thereby prohibited. Interestingly, the Council based this demarcation on the purpose of the research rather than the type of science involved. The Council stated that the transplantation of animal organs to benefit human recipients is acceptable and that the use of vaccines and drugs produced from animals should be encouraged. The Council went so far as to suggest that in the future, they "do not see any overriding objection to the insertion of animal-derived genes or cells into a human body—or even into human fetuses—where the aim would be to treat or prevent a dread disease in the patient or the developing child."

The Council thus made clear that in the context of therapy and preventative medicine, chimera research is morally acceptable, indicating that it does not find the mixing of human and animal materials in and of itself problematic.

However, the Council deemed unacceptable the creation of human-animal chimeras for the purposes of procreation. The Council drew two bright-line

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197. A blastocyst is a pre-implantation embryo consisting of 50-250 cells depending on its age.
198. See Human Embryonic Stem Cell Research Advisory Committee, supra note 7, at 8.
199. See id.
201. Id.
202. See id. at 8-9.
rules involving the mixing of human and nonhuman gametes or blastomeres at the very earliest stages of biological development. A human embryo may not be implanted into the body of a nonhuman species and a hybrid human-animal embryo may not be produced by fertilizing a human egg with animal sperm or by fertilizing an animal egg with human sperm. The Council’s rationale is “[p]reserving a [r]easonable [b]oundary between the [h]uman and the [n]onhuman (or, between the [h]uman and the [a]nimal) in [h]uman [p]rocreation.” In the eyes of the Council, human-animal hybrids are threatening because their creation would require a judgment of the humanity or moral worth of an ambiguous entity. From the Council’s perspective, creating the likes of a “humanzee,” a hypothetical ape/human hybrid, creates a moral status inquiry that is too complex for current undertaking. The Council is primarily uncomfortable with the premise that a part-human entity would have other-than-human progenitors, as this impliedly threatens the image of the traditional family.

B. Recommendations for Prudential Limits

Rather than implementing broad legislative bans on chimeras, hybrids and cybrids, government should appoint oversight committees or charge existing committees to review chimera research. In prescribing a framework for the evaluation of proposals that seek to create human-animal chimeras, Congress may want to delineate certain outer moral boundaries of chimera research.

Broad federal legislation may not be the best means of regulating this field for several reasons. First, as previously explained, Lawrence v. Texas may bar regulatory legislation that carries criminal penalties and is premised solely on preserving human dignity. As previously explained, it is uncertain whether a bill such as the HCPA premised primarily on preserving human dignity and carrying criminal penalties will be upheld. Moreover, broad federal legislation is unnecessary because the NAS already prohibits many activities involving chimera research, and scientific communities, as well as research institutions, widely adhere to these mandates. In addition, some states that fund stem cell initiatives and chimera research, such as California, have similar guidelines that prevent funding of certain objectionable chimera research activities. For example, the California Institute for Regenerative Medicine (CIRM) suggested standards for all research institutions supported in whole or part by state funds.

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203. A blastomere is a type of cell produced by division of the egg after fertilization and prior to the cell differentiation of the inner cell mass and the outer-layer of cells (trophectoderm).
204. See President’s Council for Bioethics, supra note 200, at 9.
205. See id.
206. Id. at 8.
207. See id. at 9.
208. See Lawrence, 539 U.S. at 582.
209. See The Joint Steering Comm., supra note 56.
In 2006, proposed CIRM regulations would deny funding to experiments introducing stem cells into nonhuman primate embryos, introducing any stem cells (human or nonhuman) into human embryos, and breeding any animal that has been implanted with stem cells from a covered stem cell line.

However, in order to provide guidelines for oversight committees, Congress may still need to delineate the outer-bounds of morally acceptable scientific experimentation. This author recommends that Congress address only the most controversial aspects of chimera research and allow oversight committees, who possess greater scientific prowess to evaluate research proposals, to balance the particular risks posed by each experiment. The following parts propose areas that would be appropriate for limited government regulation.

1. Early Termination Policy for Chimeric Embryos

A general ban on the introduction of pluripotent human stem cells into nonhuman primate blastocysts is overly restrictive. If the NAS sanctions an early termination policy in regards to human embryos, the same should apply to chimeric embryos. An early termination policy for chimeric embryos would be preferable because it would allow early-stage research, yet would restrict chimeras to the Petri dish. An early termination policy for chimeric embryos would also circumvent many of the moral objections to chimera research because it would prevent "visible chimeras" and prohibit chimeric embryos from possessing the psychological and cognitive characteristics associated with the human brain. While an outright ban like the one proposed in the HCPA is overly restrictive, prudential limits, such as an early termination policy in regards to chimeric embryos, are appropriate.

2. Limitation on Neural Transplants

Protections of the sanctity of the "human brain" are vague and require specification. For example, the Act prohibits the creation of a nonhuman life that contains a "human brain or brain derived wholly or predominantly from human neural tissues." Yet it is unknown to what extent the development of

211. See id. at § 10030: Activities Not Eligible for CIRM Funding (c)-(e).
212. A pluripotent cell is a single cell with the capability of developing into cells of all germ layers (endoderm, ectoderm, and mesoderm).
213. See Streiffer, supra note 54, at 365.
214. See id. at 366.
215. See Karpowicz, supra note 12, at 334.
216. Human Chimera Prohibition Act, supra note 8, at § 301(1)(I).

human neural tissues in a nonhuman would be limited by the architecture of the host’s body. If the nonhuman who had received the implant demonstrated no change in cognitive capacities, would we still say it possessed a “human brain?”

At this stage, the prudential limit would be to prohibit the engraftment of human neural cells into great apes, particularly early in their neural development.\(^{217}\) Since the category of great apes includes chimpanzees, our closest living relative, the risk of transferring human cognitive functions is highest and engraftment of human neural cells should be prohibited.\(^{218}\) Engrafting neural tissues into other nonhuman primates could proceed with a high degree of monitoring by review committees.

3. Limitation on Chimeras with Human Physical Features

Congress should limit the creation of nonhuman animals with human physical features because the production of these types of chimeras blurs the lines between human and animal. In 1997, Dr. Charles Vacanti and a team of plastic surgeons at the University of Massachusetts grew an exterior human ear and attached it to the back of a mouse to demonstrate a method of creating cartilage structures for transplantation in humans.\(^{219}\) The photo of the mouse caused public unrest amongst animal rights advocates and anti-genetics groups. The mouse was mistakenly thought to have been genetically engineered to grow an ear on its back.\(^{220}\) In reality, the mouse’s DNA had not been altered and the ear had been grafted. The mouse was a chimera, not a human/mouse hybrid. The unrest the Vacanti mouse unleashed strongly suggests that this type of experiment blurs the lines between species beyond what is morally acceptable and thus should be subject to restriction.

4. Limitation on Hybrids

Legislation should distinguish chimeras from hybrids. This Comment has focused on the moral implications of chimeras, but has touched upon the problematic scenario of two chimeras breeding, possibly resulting in a genetic hybrid. While the regulation of hybrids is beyond the scope of this Comment, the NAS, the President’s Council on Bioethics, and the HCPA\(^ {221}\) have all

\(^{217}\) See Greene, supra note 53.


\(^{221}\) See HUMAN EMBRYONIC STEM CELL RESEARCH ADVISORY COMMITTEE, supra note 7, at 6 ("Other types of studies should not be permitted at this time (such as . . . breeding of any
included some prohibition on the creation of hybrids, suggesting that the subject merits attention if Congress were to undertake new regulation of the creation of human-animal entities.

5. Oversight Committees

Within these contours of limited federal legislation, Congress should empower ethical review committees to assess chimera research on a case-by-case basis. Oversight committees are best equipped to engage in a dialogue with local scientific communities, which would encourage a system of participatory regulation rather than pitting the knowledge of scientists against the right of legislators to protect public morality. Committees would also allow for a more flexible approach, as the moral issues implicated by each case could be evaluated, providing the best opportunity for monitoring experimentation. In fact, several advisory organizations already endorse committees as the best means of reviewing the production of human-animal chimeras.222

Currently, Institutional Review Boards (IRBs) have implicit jurisdiction over chimera research and would be well-suited to oversee experimentation. These committees, associated with universities, medical facilities, or for-profit bodies, are designed to review and monitor biomedical and behavioral experiments involving human subjects. In accordance with the Food and Drug Administration (FDA) and the Health and Human Services (HHS) regulation, local IRBs must approve a research project involving a human subject, which includes human tissue, to access federal funds.223 IRBs are charged with ensuring that risks are counterbalanced by benefits to either the subjects themselves or society at large. Institutions may also require university researchers to comply with IRB standards in exchange for federal support, and the FDA and HHS have the authority to mandate compliance.224 As evidenced by the widespread establishment of IRBs and the strong motivation for researchers to comply, a local infrastructure is prepared to review research on interspecies chimeras.

222. See, e.g., HUMAN EMBRYONIC STEM CELL RESEARCH ADVISORY COMMITTEE, supra note 7, at 6 ("for example the creation of a chimera might involve both an Institutional Review Board (IRB), if cells are to be obtained from human donors for research, and an Institutional Animal Care and Use Committee (IACUC), if animals are to be used in the research.").

223. See 45 C.F.R. § 46.109 (2005), available at http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.109 (explaining that an IRB must review human subject research); see also Office for Human Research Protections Department of Health and Human Services, Guidance for Investigators and Institutional Review Boards Regarding Research Involving Human Embryonic Stem Cells, Germ Cells and Stem Cell-Derived Test Articles (2002) (stating that "[a]ll clinical research involving... biological products... is also subject to FDA regulations.").

224. See 45 C.F.R. § 46.122 (stating that "[f]ederal funds administered by a department or agency may not be expended for research involving human subjects unless the requirements of [IRB review] have been satisfied.").
various classes of chimera.

The NAS has supported a similar framework and has recommended the use of Embryonic Stem Cell Research Oversight Committees (ESCROs) to approve stem cell research. NAS guidelines on human embryonic research endorse creating committees of both scientists and non-scientists to review a proposal in a context where the advantages and disadvantages of a specific experiment are known. The production of chimeras would be within the scope of their explicit authority. Likewise, the International Society for Stem Cell Research (ISSCR) has proposed that all research involving generating chimeric animals, for example, by implanting various types of human cells into animals, be subject to review by specialized oversight bodies. The proposed Stem Cell Research Oversight (SCRO) process is not designed to replace mandated IRB review.

A concern with implementing ethics committees is that project approval would not be consistent throughout the United States, and that consequently, investigators would be subject to different standards. However, advocates of a case-by-case approach suggest a framework of factors that could be used to evaluate proposals to create chimeras, thereby diminishing the problem of inconsistency. To begin with, the ISSCR recommends that investigators express a scientific rationale for using human embryonic material, totipotent or pluripotent cells and explain the merit of their proposal. Second, the relevant expertise of investigators, including their prior experience with embryonic stem cell derivation in animal systems, would need to be explained. Lastly, researchers should articulate the ethical permissibility of their proposal in light of their research goals.

In addition to these guidelines for assessment, ethics committees should evaluate ethical risks that chimera research poses based on specific factors. For example, the Greene Working Group recommends six factors to guide ethics committees in determining whether a specific proposal involving the transfer of human cells into a nonhuman entity should proceed. Committees should consider: 1) the proportion of engrafted human cells, 2) the neural development of the nonhuman animal, 3) the species of the nonhuman animal, 4) the brain

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225. See Human Embryonic Stem Cell Research Advisory Committee, supra note 7, at 5 (suggesting that "the [ESCRO] committee should include representatives of the public and persons with expertise in developmental biology, stem cell research, molecular biology, assisted reproduction, and ethical and legal issues in hES cell research.").


227. See id. at 8.

228. See, e.g., Greene, supra note 50, at 386 (suggesting six factors that research oversight committees should consider).

229. See International Society for Stem Cell Research, supra note 226. at 5, §8.3(a)-(b).

230. See id. at 5, § 8.3 (c).
size of the nonhuman animal, 5) the site of integration, and 6) the brain pathology of the nonhuman animal.\textsuperscript{231} Another important factor that should be added to this list is the nonhuman's stage of development, because the functional influence of engrafted cells will be markedly greater at the very early stages of development.\textsuperscript{232}

The findings of the committee arranged at Stanford to review the ethical implications of Irv Weissman's proposal to create a human neural mouse exemplify the benefits of such a committee-based approach. The multidisciplinary committee comprised of law professors and scientists concluded that the risk alone was not sufficient to prevent the experiment from continuing, but that the committee should implement a series of "stopping points" to monitor the progress of the neural mouse.\textsuperscript{233} For example, if the implanted human neural cells appeared to be reshaping the architecture of the mouse's neural edifice or causing other "disquieting and disturbing results," early-termination of the experiment would be required.\textsuperscript{234} Barring such results, the mouse could be brought to term.\textsuperscript{235} This step-by-step risk analysis would ensure sufficient safeguards while leaving decision making to scientists who are most knowledgeable about the state of the science.

**CONCLUSION**

Many Americans find the notion of scientists creating part-human, part-animal entities frightening. Opponents of the advancement of this branch of stem cell science have couched their arguments in terms of protecting religion, human moral superiority, integrity of the species, animal welfare, and public health. After stripping away the inconsistencies, scientific inaccuracies, and political motivations of each argument, there remains a core moral value that underlies all these views: blurring the boundaries between human and animal creates discomfort because it erodes the classification system that brings society stability and coherence.

In response to this prevalent moral concern, Senator Brownback introduced the HCPA of 2005. While the Act seeks to protect human dignity by preserving a clear line between humans and animals, it further confuses the issue by broadly defining chimeras in a way that is scientifically questionable. If enacted, this overly broad definition will stifle the progress of stem cell research.

The flaws in the drafting of the Act reflect the inherent weaknesses of broad federal legislation banning chimera research, as well as the necessary

\textsuperscript{231} See Greene, \textit{supra} note 53, at 386.
\textsuperscript{232} See \textit{id.} at 3 (claiming that the "potential for engrafted cells to have significant functional influence will be markedly greater for engraftment at very early stages of development.")
\textsuperscript{233} See Shreeve, \textit{supra} note 5, at 6.
\textsuperscript{234} See \textit{id.}
\textsuperscript{235} See \textit{id.}
participation of scientists in the regulation of new biotechnologies. Legislators have limited knowledge about the implications of emerging technologies. Further, lawmakers may not have the constitutional right to enact legislation based solely on enforcing morality without clearly identifying an independent state interest worthy of federal protection.

A preferable solution would come in the form of limited legislation combined with new or expanded ethics committees with the authority to oversee chimera research. A localized approach would allow for a more nuanced appraisal of each experiment based on the advantages and disadvantages of each project. Oversight review boards would also comprise a multidisciplinary undertaking that could better account for the views of the scientific community, while addressing public concerns.

While a discussion of chimeras quickly gives way to horrific images of gruesome monsters, of men with tails, and of beasts reemerging from a mythic past, society should not lose sight of the primary subject at issue: the human patient. Perhaps Congress should consider that stifling the advancement of chimera research and stem cell therapies is also a viable threat to our human dignity.