Wary of the rapid pace and direction of developments in human biology and biotechnology, Stuart Newman took an unusual action. A cell biologist and professor at the New York Medical College, Newman applied to the U.S. Patent and Trademark Office on December 18, 1997, for what has been dubbed the “humanzee” patent. The patent application abstract described the invention as

a mammalian embryo developed from a mixture of embryo cells, embryo cells and embryonic stem cells, or embryonic stem cells exclusively, in which at least one of the cells is derived from a human embryo, a human embryonic stem cell line, or any other type of human cell, and any cell line, developed embryo, or animal derived from such an embryo.¹

The authors are grateful to Stuart Newman for providing them with documents supporting the various submissions to the U.S. Patent and Trademark Office. Newman was not involved in the preparation of this article, but he did verify factual claims after it was submitted. For funding support of related research, J. S. Robert thanks the Stem Cell Network (a member of the Networks of Centres of Excellence Programme in Canada). Address correspondence to: Jason Scott Robert, School of Life Sciences, Arizona State University, Box 874501, Tempe, AZ 85287-4501; e-mail: jason.robert@asu.edu.

¹ The initial application from 1997 (08/993,564), the second application from 2002 (10/308,135), and many of the supporting documents are available online on the U.S. Patent and Trademark Office Web site, http://www.uspto.gov, under “Status and IFW.”
Newman, supported by anti-biotechnology activist Jeremy Rifkin, aimed to secure the patent and then restrict the application of this technology for a period of twenty years, during which they hoped to foster a social debate about moral boundaries.²

The application contained thirty-six claims encompassing four general kinds of invention—embryos, stem cell lines derived from the embryos, animals developed from the embryos, and descendants of animals developed from the embryos. The summary of the invention section of the application read in part:

Applicant has developed a strategy to create innovative chimeric embryos, cell lines, and animals for use in research, medicine, drug development, and disease prevention. Applicant has also developed a strategy to create chimeric embryos, cell lines, and animals which can be used as organ and/or tissue donors for other animals to include humans.³

The application specifications explained how chimeric embryos had been created using various nonhuman cells, and extrapolated those methods to the use of human cells; but the application did not contain any diagrams, nor did it allege that Newman had actually created any human-nonhuman chimeras using the methods described.

Before the patent office took action on the application, Newman filed a petition asking for clarification of whether cloned or genetically modified human embryos were patentable. This was done in response to comments by then-Commissioner Bruce A. Lehman that neither human beings nor half-human “monsters” were patentable.⁴ Newman’s petition argued that human embryos at the stage envisioned for use in creating the chimeras he wished to patent were not considered human beings under the law, and asked for confirmation of this position. The patent office refused to answer this critical question. Procedural rules provided a way out, and the petition was dismissed. (“It would clearly be inappropriate to issue a general statement in a decision on petition, as to the patentability of an entire class of claims in the abstract.”⁵) During the fall of 1998, Commissioner Lehman made further public statements on the matter, so Newman filed a second petition that again asked for clarification on this subject, and questioned the propri-


⁴ Quoted in Dowie, “Gods and Monsters,” 48. In 1987, then-Commissioner Donald J. Quigg issued a memo opening the door for patents to be granted for man-made animals, but he cited the Thirteenth Amendment’s prohibition against slavery as the reason patents could not be issued for human beings. (“A claim directed to or including within its scope a human being will not be considered to be patentable subject matter.”) Shortly thereafter, a patent was issued for the Harvard OncoMouse.

ety of Lehman’s comments regarding the pending application. The second petition was dismissed for the same reason as the first. Shortly thereafter, the patent office finally took action on the pending application.

On March 18, 1999, the patent office issued its first of nine rejections. Explanations for rejection were expanded and modified over the next five years while Newman filed numerous amendments and a second application, which modified existing claims and expanded the total number of claims to well over one hundred. The four general categories of rejection were that the claims “embraced a human being” and were therefore not patentable subject matter, that there was a lack of written description and enablement that would inform others how to create and use the invention, that some of the claims were anticipated by prior work and therefore not novel, and that the invention had no utility. In essence, the patent office threw everything but the kitchen sink at the application, giving no ground on any potential reason for allowing a patent.

While the patent office probably exaggerated the application’s deficiencies, there was some validity to the various rejections. We will discuss each one in turn, on the basis of the rationale stated for the final rejection in August 2004. We will then briefly discuss some of the ethical issues raised by this endeavor, especially given Newman’s intention to spur vigorous public debate on the social acceptability of part-human chimeras.

**Non-patentable Subject Matter**

The presence of some nonhuman primate cells does not make a human embryo nonhuman…. Contrary to the argument that the claimed animal was never exclusively human in origin, i.e., that the chimeric embryo never existed as a human embryo, the specification states: “the invention relates to chimeric embryos and chimeric animals created from human embryos.”… The Office does not agree that humans are patentable subject matter.\(^6\) The patent office used this rationale for rejection of the embryo, animal, and descendant claims, but not for the stem cell claims.

Discussion of this topic in the various patent office filings and rejections involved Supreme Court cases such as *Roe v. Wade* over whether the human embryo is rightly considered a human being under the law.\(^7\) Presumably, if the embryo is merely a component of a human being, like a liver cell or a genetic sequence, for example, then a patent could be issued, and indeed some patents have been issued for similar inventions. Newman argued that the embryo he wished to patent was a chimera that contained human cells, but was not a human being. The patent office never expressly stated its position on this topic, but ruled as though it considered a human embryo to be a human being, not a component part for purposes of obtaining a patent.

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The next step was more difficult to take, because the patent office does not have express authorization to deny patent applications for inventions that embrace a human being. In fact, the Supreme Court decision in Diamond v. Chakrabarty arguably prohibits them from doing so.\(^8\) Relying on assumptions derived from statutory language, and constitutional issues like the Thirteenth Amendment’s prohibition against slavery, the patent office simply asserted that it has the authority to deny patents on this basis. This decision was tentatively supported by Congress when it passed the Consolidated Appropriations Act of 2004 (sec. 634: “None of the funds appropriated or otherwise made available under this Act may be used to issue patents on claims directed to or encompassing a human organism”).\(^9\) Identical language was included in the Consolidated Appropriations Act of 2005, and the timing makes it appear to have been passed for the unarticulated purpose of rejecting Newman’s application for a patent. Still, this was hardly a strong endorsement of the patent office’s decision, inasmuch as appropriation acts only govern the fiscal year’s budget, and expire thereafter if not renewed.

It remains difficult to determine exactly what the patent office decided, given the variation in language used—“embracing” and “encompassing” are not very specific words, and “human,” “human embryo,” “human being,” and “human organism” seem to have been used interchangeably at times. Certainly, there was something about the early-stage embryo that the patent office felt uneasy about. One probably valid evaluation of this decision is that they just wanted to leave the issue for another day, and another decision maker.

**Lack of Written Description and Enablement**

Neither the art at the time of filing nor the present specification provide the requisite guidance as to the methodology that would lead to the production of these chimeric embryos or their use … without an undue amount of experimentation or with a predictable degree of success.\(^10\)

There is no description of chimera that conveys to the skilled artisan exactly what type of chimerism applicant envisions as the invention. Furthermore, the specification fails to demonstrate possession of the invention by actual reduction to practice, clear depiction of the invention in a detailed drawing, or description with sufficient relevant identifying characteristics of the invention as a whole such that a person skilled in the art would recognize that the inventor had possession of the claimed chimeric animals.\(^11\)

The patent office used this rationale for rejection of all claims.

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Discussion of the issue of description and enablement of the invention began with questions about the relative percentage of human cells in the chimera, and devolved into considerable detail about the cellular makeup of individual organs. The evidence Newman presented of existing chimeras, such as the sheep-goat (geep) chimera,\textsuperscript{12} was not specific as to the cellular composition of the resulting embryo or animal. Newman contended that it did not matter whether the organism was composed of 1 or 99 percent human cells, nor what the cellular composition of component parts were—in either case, it would still be a human-nonhuman chimera that his patent would cover. However, the patent office insisted that a proper description of the invention required a detailed depiction of which parts would be human and which parts would be nonhuman and to what extent. Unfortunately, the ability to control development in that manner is currently beyond scientific capabilities. Newman’s inability to explain a method for making a chimera with specific qualities or cellular composition was taken by the patent office to mean he had neither described his invention adequately, nor enabled others to make the invention. The patent office apparently was not concerned that such a description might remain forever unavailable, given the contingencies of embryonic development, nor did it matter to them that, again given developmental contingencies, even if two chimeras are created simultaneously from identical materials, they will almost certainly develop into creatures with different proportions of cells.

Furthermore, the patent office repeatedly stated that there was no reduction to practice that would show, through appropriate experiments, the embodiment of what Newman claimed to have invented. Had Newman actually created a human-nonhuman chimera, presumably he could have overcome this reason for rejection, at least in applying for a patent for that specific kind of chimera. Of course, creating a chimera would have flown in the face of Newman’s objective for obtaining the patent in the first place.

The patent office thus put Newman into a difficult position. There is some validity to this rejection when one considers the history of similar kinds of embryonic experimentation. Dr. Ian Wilmut led the team that successfully cloned Dolly the sheep in 1997 only after considerable experimental work,\textsuperscript{13} and cloning a human embryo appears to be proving at least as challenging. When the patent office argued that Newman’s specifications were insufficient to enable someone to create a human-nonhuman chimera without an undue amount of experimentation, they probably had a good point in that considerable experimentation would be involved (although a lot hinges on the meaning of “undue”). Had Newman truly been interested in creating such a chimera, he might have been able to do so, but how much additional time and effort would have been required, and what the ultimate methodology would have been, we cannot say. Moreover, his aversion to actually making part-human chimeras was part of Newman’s motivation for seeking the patent.


\textsuperscript{13} Ian Wilmut et al., “Viable Offspring Derived from Fetal and Adult Mammalian Cells,” \textit{Nature} 385.6619 (February 27, 1997): 810–813.
Lack of Novelty

A person shall be entitled to a patent unless the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.14

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The descendant of the chimeric animal is not necessarily any different from one of the source species…. Individual germ cells would represent only one species…. Therefore, the descendants would not be any different from humans, or nonhuman primates found in nature.15

The patent office used this rationale for rejection of the stem cell and descendant claims, but not the embryo and animal claims.

Newman’s claim that his chimeric stem cells were novel was based on their purported immune tolerance when used in either originating species.16 That is, he could create a chimera from human and nonhuman primate materials, obtain stem cells from the chimeric embryo, and use those stem cells in either a human or a nonhuman primate without the problem of immune rejection. The patent office decided that the alleged immune tolerance was insufficient to establish that Newman’s stem cells were novel.17 The cells would undeniably be either human or nonhuman primate because there was no subcellular chimerism claimed. The patent office contended there was nothing novel about Newman’s proposed stem cells, and that they were anticipated by work done by others more than one year before the application was filed, so no patent on the stem cells could issue.18 Also, the claim on descendants of chimeric animals was rejected because the germ cells, sperm and egg, from the chimeric animal would necessarily be either human or nonhuman primate, not themselves chimeric.19 Therefore, the descendants could be fully human or fully nonhuman primate, and no patent can be issued on such beings. Had Newman actually

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18 Ibid.

19 Interestingly, in a recent National Academies publication, it has been recommended that the breeding of chimeras be prohibited, presumably because the committee doubted the validity of this claim, or instead were worried about (i) two part-human chimeras producing human gametes, mating, and thereby creating a human embryo developing in a chimeric uterus, or (ii) a single part-human chimera producing human gametes and mating with another part-human chimera that produced non-human gametes, thereby creating a part-human hybrid developing in a chimeric uterus. See Committee on Guidelines for Human Embryonic Stem Cell Research, Guidelines for Human Embryonic Stem Cell Research (Washington, D.C.: National Academies Press, 2005), 99. For discussion, see Jason Scott Robert and Françoise Baylis, “Stem Cell Politics: The NAS Prohibitions Pack More Bark than Bite,” Hastings Center Report 35.6 (November–December 2005): 15–16.
created stem cells from a human-nonhuman primate chimeric embryo, it is possible he could have described the biological differences between his invention and existing stem cell lines. But, again, that would have obviated the purpose of his application.

**Lack of Utility**

Even assuming toxicology studies are a critical step in the development of new drugs, there is no specific explanation showing that observing developmental disorders in chimeras would have any practical utility.\(^2\)

The patent office used this rationale for rejection of the animal and descendant claims, but not the embryo and stem cell claims.

The lack of utility rejection seems to have the least justification. Newman argued the chimeric animals could be used in experiments that would reveal information about human biology. This is the rationale for all biological experiments using human cells with nonhuman animals, and its utility has much support in the literature and in common sense.\(^2\) Of course, Newman had no specific evidence that his invention could be used for any specific purpose. The patent office hung its hat on this seemingly unreasonable requirement of specificity.

**The Ethics of Creating Part-Human Chimeras**

It is worth setting our discussion of Newman’s humanzee patent quest within the context of the small but suggestive ethical literature on creating part-human chimeras. The first publication to explore this issue was co-authored by one of us (J.S.R.), in a target article in the *American Journal of Bioethics.*\(^2\) Our argument was a simple one, although it has been misinterpreted: of the many possible objections to crossing the human species boundary in stem cell research—such as concerns about the naturalness of species boundaries and the unnaturalness of transgression of those boundaries, concerns about playing God, and concerns about violating human dignity—none of these has been well-developed enough to justify a prohibition on such research. However, we argued, the amorphous worry that something precious was at stake in the prospect of making part-human animals might be more appropriately articulated through the concept of *moral confusion.* While we did not say that such research was indeed morally confusing, we suggested that those who were worried about such research might well be worried that it would introduce a further degree of unacceptable confusion into our moral relationships with each other.

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and with nonhuman animals, let alone with novel creatures brought to term. We did not develop this point, but rather placed the burden for its elucidation on those who would prohibit such research.

Since then, in addition to the two dozen commentaries on our article, a few more have addressed the morality of creating part-human animals. Karpowicz, Cohen, and van der Kooy have published one short opinion piece and one longer article claiming that there is nothing wrong with creating part-human animals in stem cell research, but that certain kinds of stem cell chimeras would indeed violate human dignity, and so should not be created. Their concern is that transplanting human cells into especially receptive nonhuman hosts (e.g., early embryos of closely related nonhuman primates) might confer some of the complex psychological characteristics of humans on these chimeras. Mark Greene and coauthors have made the same argument, although they avoid the phrase “human dignity.” The voluntary guidelines for human embryonic stem cell research proposed by the National Academy of Sciences include several restrictions on chimera research for apparently the same reasons. One of us (J.S.R.) has explored these and related proposals in a more philosophical way.

So where do we stand? First, whether creating part-human animals in stem cell research is morally objectionable remains to be decided. While it is evident that there are substantive scientific reasons for wanting to create such animals, the moral objections that are beginning to be articulated may lead to more widespread prohibitions. Second, whether the patent office will issue a patent on a humanzee itself remains to be decided. Newman’s patent application was finally denied in 2004, and he allowed the six-month appeal period to lapse in February 2005. Newman interpreted this as a partial victory, explaining that the patent office had deemed part-human chimeras to be unpatentable. But this is not so clear-cut—that Newman’s patent application was unsuccessful says nothing about future applications, as the patent office does not work by precedent, and a future application may overcome the stated objections to the humanzee patent application.

Accordingly, the issue of utility and the concern about novelty may be overcome in the creation and characterization of part-human animals, which would also permit for a more detailed written description, thus providing sufficient specifics to

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25 Committee, *Guidelines*.

26 Robert, “Model Systems” and “Science and Ethics.”

27 Ibid.

28 Kittredge, “Question of Chimeras,” 54.
enable replication. This leaves the patent office with only the concern about non-statutory subject matter—the concern that a part-human chimera somehow “embraces a human” and so should remain unpatentable. It is questionable whether the patent office will continue to endorse this line, however. As former Commissioner Lehman has remarked, “Stuart Newman is promoting an effort that will make it difficult to engage in biological research and commercialize the fruits of that research. It’s not funny or cute; it is profoundly wrong. Every attempt to stop science has been characterized by darkness.”29 If that particular perspective is widespread in the patent office, and Congress does not take action to deal with the issue, then we can expect patents on part-human chimeras in the near future.

29 As quoted in Dowie, “Gods and Monsters.”