Office of the General Counsel

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September 2, 2016

Filed Electronically

Office of Science Policy
National Institutes of Health
6705 Rockledge Drive, Suite 705
Bethesda, MD 20892

Re: Proposed Changes to the NIH Guidelines for Human Stem Cell Research and the Proposed Scope of an NIH Steering Committee's Consideration of Certain Human-Animal Chimera Research

Dear Sir or Madam:

On behalf of the United States Conference of Catholic Bishops ("Conference"), we submit the following comments on a proposal by the National Institutes of Health ("NIH") to authorize federally funded human/animal chimera research, published at 81 Fed. Reg. 51921 (Aug. 5, 2016).

Interest of the United States Conference of Catholic Bishops

The Conference is a nonprofit corporation organized under the laws of the District of Columbia. The Catholic bishops in the United States are members of the Conference. The Catholic Church, the largest religious denomination in the United States, has over 68 million adherents in over 17,000 parishes throughout the country. The Conference advocates and promotes the pastoral teaching of the bishops in such diverse areas as education, family life, health care, social welfare, immigration, civil rights, and the economy. The Conference participates in rulemaking proceedings of importance to the Catholic Church and its people in the United States. Rulemaking that concerns the protection of unborn human life and the ethical integrity of science and medicine is of paramount concern to the Conference.

In the Conference's view, the dignity and inviolability of human life at every stage of development is a foundational principle of any truly civilized society. The core ethical norms protecting human research subjects, affirmed in the Nuremberg Code and many subsequent documents, reflect this principle. The right not to be subjected to harmful experimentation

without one's express and informed consent is an innate human right, belonging to each and every member of the human family by his or her very nature as a human being. Thus it does not belong to government to recognize this right for some human beings and not for others, or to set aside protection of this right in the name of expanded knowledge or the good of society. Laws or regulations which fail to give full recognition to this fundamental right do not succeed in nullifying the right in question, but only call into question their own moral legitimacy. It is in light of this moral conviction that we offer the following comments.

General Comments

NIH has announced that it plans to rescind the moratorium it initiated on September 23, 2015 forbidding federal funding of human/animal chimera embryo research. In place of the moratorium, NIH proposes to make minor changes to its existing regulations on human embryonic stem cell research. While a very few research proposals in making part-human, part-animal organisms will be subject to an extra level of review by an NIH-controlled steering committee, the bottom line is that the Federal government will begin expending taxpayer dollars on the creation and manipulation of new beings whose very existence blurs the line between humanity and animals such as mice and rats. In doing so, the government is ignoring the fact that federally funded research of this kind is prohibited by Federal statute and is also grossly unethical.

The government has already crossed a significant moral line by treating the destruction of human beings, at a very early stage of development, as the raw material for allegedly useful human embryonic stem cell ("ESC") research. Such research has failed to produce treatments for human ailments over the last 17 years, and morally noncontroversial avenues such as adult stem cell and induced pluripotent stem cell research have surpassed ESCs in scientific and clinical benefits.[1] The government now proposes running roughshod over another basic moral principle, however, by injecting human embryonic stem cells into the embryos of various animal species to create beings who do not fully belong to either the human race or the host animal species.

Among the experiments eligible for federal funding under this proposal are:

1. Introducing human pluripotent stem cells into non-human primate embryos after the blastocyst stage;
2. Introducing such human cells into *any* animal species "where the introduction of human cells may contribute to the germ line," as long as the resulting being is not allowed to engage in "breeding";
3. Introducing these human cells into non-human mammalian embryos "such that there could be either a substantial contribution or a substantial functional modification to the animal brain by the human cells."

[1] "In fact, no field of biotechnology has promised more and delivered less in the way of treatments than embryonic stem cells. Only a handful of human studies has ever been carried out, without significant results." A. Bajak, "Will Embryonic Stem Cells Ever Cure Anything?", *MIT Technology Review*, Aug. 12, 2016, at https://www.technologyreview.com/s/602143/will-embryonic-stem-cells-ever-cure-anything/.

Research in category #3, says NIH, will merely require extra review by a steering committee made up of NIH staff—staff who presumably have endorsed the legitimacy of such research—*except* when the mammal engineered to have a human or mostly human brain is a "rodent," in which case it may proceed and receive federal funds after receiving only routine peer review. With a stroke of the pen, the "mouse with a human brain" that some researchers have proposed—prompting widespread public controversy and the introduction of federal legislation to prohibit such abuses—will be a matter of routine federal policy.[2] This raises grave moral as well as legal issues.

1. **Moral Considerations**

When NIH issued its moratorium in September 2015, it pledged to review "the state of the science in this area, *the ethical issues that should be considered*, and the relevant animal welfare concerns associated with these types of studies." Yet NIH apparently held only one meeting on this complex and controversial issue, in November 2015, and its task was to "review the state of the science and discuss animal welfare issues." 81 Fed. Reg. at 51922. It seems there was no discussion of "ethical issues" involved in producing partly human animals.

The Catholic Church's ethical objection to research involving the destruction of human life at an early stage of development is well known, stated at many levels and in many forums, and will not be revisited here. Suffice it to say that even federal advisory bodies engaged in approving or recommending destructive human embryo research have acknowledged that the human embryo is a form of human life that deserves respect.[3] Such respect has been absent from the Administration's actions regarding human embryonic stem cell research.

While we continue to have a moral objection to any research that uses the destruction of live human embryos as a source of "raw material" for further research, the new proposal for producing human/animal hybrids raises new and troubling questions of its own. This was even recognized by NIH's own Human Embryo Research Panel in 1994, which authorized a wide array of destructive human embryo research – but declared the production of human/animal chimeras "unacceptable for federal funding."[4]

Catholic morality does not object in principle to the respectful use of animals in research that can benefit humanity. But because of the unique dignity of the human person, there are limits to what can morally be done along this line.

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[2] *See* M. Fessenden, "Half the Cells in This Mouse's Brain Are Human," *Smithsonian Magazine*, Dec. 3, 2014, at http://www.smithsonianmag.com/smart-news/half-cells-mouses-brain-are-human-180953520/; S. 1373, the Human Chimera Prohibition Act of 2005 (109th Cong.), at https://www.govtrack.us/congress/bills/109/s1373.

[3] "The preimplantation human embryo warrants serious moral consideration as a developing form of human life." National Institutes of Health, *Report of the Human Embryo Research Panel* (Sept. 1994), p. 2. "[M]ost would agree that human embryos deserve respect as a form of human life." National Bioethics Advisory Commission, *Ethical Issues in Human Stem Cell Research* (September 1999), vol. I, p. ii.

[4] "The Panel *unanimously opposes*, on ethical and scientific grounds, the creation of heterologous, or human-nonhuman chimeras, with or without transfer [to a womb]." *Report*, op. cit., p. 95 (emphasis added). Again, this Panel unanimously *supported* federal funding of harmful experiments using human embryos generally.

One respected Catholic ethicist, reflecting official Catholic teaching, has succinctly described the moral limits this way:

> • The procedures must not involve the creation or destruction of human embryos.
> • They must not involve the replication of major pillars of human identity in animals, such as the brain system.
> • They must not involve the production of human gametes, meaning the basic building blocks of human reproduction.[5]

Of course, NIH's new proposal violates *all three* of these principles. It relies on the destruction of human embryos; it contemplates producing entities with partly or wholly human brains (without any additional level of scrutiny in the case of rodents); and it allows for producing living entities who have human gametes (though researchers will be told to take precautions so these entities do not engage in "breeding").

Does the proposal involve the *creation* of human embryos? In reality, the proposal sets no effective limits to prevent this research from producing entities whose species membership is at least ambiguous. The extent to which human cells contribute to the final organism will depend on factors such as the number of cells introduced and the stage of development of the host embryo, and no research has established parameters for these variables to ensure that researchers remain on the "safe" side of the species boundary.

Herein lies the key moral problem involved in this proposal, beyond the already grave problem of exploiting human embryos as cell factories for research. For if one cannot tell to what extent, if any, the resulting organism may have human status or characteristics, it will be impossible to determine what one's moral obligations may be regarding that organism. If this is an animal, one may ultimately destroy that animal once it has served its research use – many would say one *must* do so, to prevent any possibility of breeding that may produce more human/animal hybrids. If this being may have some claim on membership in the human family, then morally one *must not* take such action – and that is true legally as well, for any federally funded research covered by the Dickey amendment. We submit that producing new organisms, regarding whom our fundamental moral and legal obligations are inevitably confused and even contradictory, is itself immoral.[6] NIH should give far more serious consideration to this and other moral problems before seeking to fund human/animal chimera research.

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[5] Rev. Tad Pacholczyk, cited in J. Allen, "Pope didn't endorse animal/human hybrids, but expert says 'We can talk'," *Crux*, Feb. 6, 2016, at https://cruxnow.com/church/2016/02/06/pope-didnt-endorse-animalhuman-hybrids-but-expert-says-we-can-talk/. As one Catholic teaching document points out, there are even limits to the kinds of cells or organs that can morally be transplanted between two humans: "Ethically, not all organs can be donated. The brain and the gonads may not be transplanted because they ensure the personal and procreative identity respectively. These are organs which embody the characteristic uniqueness of the person, which medicine is bound to protect." Pontifical Council for Pastoral Assistance to Health Care Workers, *Charter for Health Care Workers* (1995), no. 88. Exchanging such cells or organs between humans and non-human animals is even more problematic. Cf. *id.*, no. 89.

[6] For a secular version of this concern, see J. Robert and F. Baylis, "Crossing species boundaries," 3 (3) *American Journal of Bioethics* 1-13 (2003).

2. Legal Objections

NIH has also issued this proposal without attending to a threshold legal question: Does the research conform to the governing statutory language, the Dickey amendment to annual Labor/HHS appropriations bills which has forbidden federal funding of destructive research involving human embryos since 2005? NIH guidelines and regulatory proposals must first of all conform to what Congress has enacted into law.

The Dickey amendment forbids the use of federal funds to create a human embryo for research purposes, or to support any part of a research project in which a human embryo is destroyed, discarded, or subjected to risk of injury or death greater than that permitted for research involving live children in their mother's wombs.[7] For purposes of this statutory provision, a "human embryo" is defined to include "any organism, not protected as a human subject under 45 CFR 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, *or any other means* from *one or more human gametes or human diploid cells*" (emphasis added).

The embryos to be produced in this research are certainly not protected now under federal regulations on human subject research at 45 CFR 46 – those regulations are applicable beginning with implantation in a mother's womb. They will certainly be "derived" by one of the "other means" referenced here, by introduction of "one or more … human diploid cells" (that is, human pluripotent stem cells). Therefore, by the governing statute, NIH may not fund the production of such embryos, or any research in which they are destroyed, discarded or subjected to significant research risks. In other words, it is unlawful for NIH to conduct or fund such research.[8]

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[7] The current text of the amendment is Sec. 508 of Division H of Public Law 114-113, the Consolidated Appropriations Act of 2016:

> Sec. 508. (a) None of the funds made available in this Act may be used for— (1) the creation of a human embryo or embryos for research purposes; or (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 CFR 46.204(b) and section 498(b) of the Public Health Service Act (42 U.S.C. 289g(b)).
>
> (b) For purposes of this section, the term "human embryo or embryos" includes any organism, not protected as a human subject under 45 CFR 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells.

[8] The Administration may wish to argue that this research involves not the "creation" of human embryos under Sec. 508(a)(1), but the modification of embryos already in existence. The argument is weak. Producing a creature who may not even clearly belong to the same species as the initial embryo is surely making something new – especially when, as here, this could include producing a nonhuman animal with a human or partly human brain or gametes. But that argument is of no relevance in any case. The new entity is "derived" (Sec. 508(b)) by combining the initial animal embryo and human diploid cells, so research that subjects such embryos to substantial risks is forbidden under Sec. 508(a)(2). By dictionary definition, to "derive" something is to "acquire," "obtain," or "extract," "to take or get (something) from (something else)." It is significantly broader than "create," and was intentionally used by Congress in this broader sense.

This is no accident. Congress's reference to "one or more" human gametes or human diploid cells was intentionally incorporated into the amendment in response to researchers' proposals for cloning human embryos for research – including proposals for inserting human diploid genetic material into the eggs of other species such as cows.[9] Forbidding the production of mixed human/animal embryos was exactly what Congress intended by this language. NIH's proposal is contrary to this provision.[10]

Conclusion

The proposed research in human/animal chimeras raises all the ethical problems of human embryonic stem cell research in general, and serious additional problems of both ethics and legality. The current NIH proposal would not prevent the most egregious abuses, such as the production of non-human animals with substantially human brains or gametes – in fact, it explicitly contemplates funding some of these abuses. Finally, NIH does not indicate that sufficient research has been conducted using solely animal sources, such as stem cells from non-human primates, before funding research that could definitively blur the boundary between human beings and non-human animals. As such, even by longstanding NIH policy, and aside from the moral objections we raise herein, the current proposal is seriously flawed. For all these reasons, the proposal should be set aside.

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[9] R. Hotz, "Cow Egg Used as Incubator in Cloning Boon," *Los Angeles Times*, Jan. 19, 1998, at http://articles.latimes.com/1998/jan/19/news/mn-9920. For a critique of this approach, see Testimony of Richard M. Doerflinger on behalf of the Committee for Pro-Life Activities, National Conference of Catholic Bishops before the Senate Appropriations Subcommittee on Labor, Health and Education, Dec. 2, 1998, at http://www.usccb.org/issues-and-action/human-life-and-dignity/stem-cell-research/ethical-concerns-regarding-new-developments-in-embryo-research.cfm. The Catholic Church has stated: "From the ethical standpoint, such procedures represent an offense against the dignity of human beings on account of *the admixture of human and animal genetic elements capable of disrupting the specific identity of man.*" Congregation for the Doctrine of the Faith, "Instruction *Dignitas Personae* on Certain Bioethical Questions" (2008), no. 33 (emphasis in original), at http://www.vatican.va/roman_curia/congregations/cfaith/documents/rc_con_cfaith_doc_20081208_dignitas-personae_en.html.

[10] In our view, this is not the first time NIH has ignored the text of the Dickey amendment. The amendment forbids funding "research in which" human embryos are destroyed, discarded or subjected to substantial risk. NIH has held that this only forbids funding the *act* of destroying embryos for their stem cells. NIH's new proposal continues this strained interpretation, saying that Dickey forbids only "NIH funding of the derivation of stem cells from human embryos." Along with the prime sponsor of the Dickey amendment and many others, we hold that federal law already forbids NIH to use the destruction of human embryos as a source of stem cells for its research. This would make NIH's new proposal doubly illegal. See "Bishops' Conference Comments on NIH Guidelines for Embryonic Stem Cell Research," Jan. 31, 2000, at http://www.usccb.org/issues-and-action/human-life-and-dignity/stem-cell-research/guidelines-for-embryonic-stem-cell-research.cfm.

Respectfully submitted,

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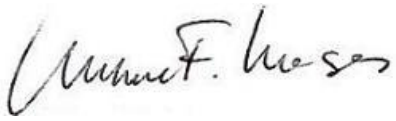

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