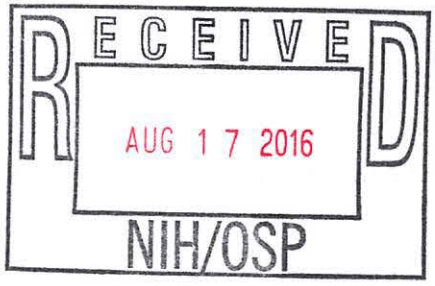
August 12, 2016



Office of Science Policy
National Institutes of Health
6705 Rockledge Drive, Suite 750,
Bethesda, MD 20892
Re: Notice Number: NOT-OD-16-128

And via the on-line form at http://grants.nih.gov/grants/rfi/rfi.cfm?ID=57

I am writing with regard to NIH consideration of certain research proposals involving human-animal chimera models. As per the request and invitation to comment on the scope of a steering committee's recommendations and specific proposed policy revisions, I am commenting on each.

Scope

The scope of the NIH steering committee's programmatic input with regard to the creation of human-nonhuman animal chimeras should be expansive. The committee could unintentionally overlook ethical problems that could arise if it begins its considerations with the belief that it need not or should not consider some areas of NIH activity that may lead to, promote, support, or regulate the creation or use of any human-nonhuman animal chimeras.

NIH has already proposed, without explanation, that the NIH steering committee's scope should not include the use of rodents. This suggested limitation should be eliminated. It would be ironic for NIH to require the committee to disregard research previously funded by NIH. Panksepp, Jules B., and Garet P. Lahvis. "Rodent empathy and affective neuroscience." *Neuroscience & Biobehavioral Reviews* 35.9 (2011): 1864-1875 is a worthwhile review. NIH funds projects which rely on the claim that humans, monkeys and rats suffer similarly from early adversity. Rats, according to the funded researchers, "recapitulating" the human condition. (Singh-Taylor, Akanksha, et al. "Synaptic rewiring of stress-sensitive neurons by early-life experience: a mechanism for resilience?" *Neurobiology of stress* 1 (2015): 109-115, which was funded in part by National Institute of Health grants NS28912, MH73136, and P50 MH096889.)

It seems presumptive and unscientific of NIH to preclude consideration of rat-human chimeras given the probable cognitive/emotional similarities across Mammalia.

Changes to Sections IV and V of the Guidelines

It appears that Sections IV and V would be combined into Section IV and that Section V would be deleted.

The prohibition on the use non-human primate embryos is appropriate but shortsighted and has little scientific evidence to support its limited scope. The question of sentience was discussed very briefly at the NIH Workshop on Research with Animals Containing Human Cells on November 6, 2015. The brief nature of the discussion was due to an acknowledgement by the panelists and participants that next to nothing is known about the nature of sentience.

There is no scientific evidence that a monkey suffers more than a mouse or less than a human. All such rankings are based entirely on unwarranted supposition.

This matter deserves more discussion. Humans readily and broadly believe that we ought not cause other humans serious suffering when used in research, and particularly not if the benefits that might accrue will be enjoyed by someone other than the research subject. A large body of regulations and guidance documents make informed consent the keystone of research using humans. Humans unable to provide informed consent are usually represented by an advocate or guardian. Other animals are not afforded similar protections or safeguards.

The current question and fear implied in the NIH recommended limitations on the creation of monkey-human chimeras is that animals being experimented on and kept in bleak conditions might suffer like humans would if they were similarly used and caged. There is little evidence that they do not do so already.

The NIH Steering Committee

The NIH Workshop on Research with Animals Containing Human Cells did not give me much faith that the NIH will be able to fairly evaluate the ethics involved in the creation of animal-human chimeras. It appeared that nearly all of the many panelists were financially biased in favor of animal experimentation and that many were eager to see NIH funding for the use of nonhuman-human chimeras.

The last session was nominally about animal welfare. The speakers and those who engaged in discussion consistently said that the current system of animal welfare oversight was robust and working well. They were generally in agreement that current rules and oversight are adequate. They may have believed what they said, but they must have been unfamiliar with the weight of evidence to the contrary.

Audits by USDA's Office of Inspector General have consistently found that the USDA's oversight of animal care is woefully ineffective and that USDA has failed repeatedly to fix problems documented in the Audits. The only blinded evaluation of the Animal Care And Use Committee system was published in 2001. No one in the industry has tried to test its conclusion that IACUCs decision-making reliability is no better that the flip of a coin. (Plous, Scott, and Harold Herzog. "Reliability of protocol reviews for animal research." *Science* 293.5530 (2001): 608-609.) Many cases of needless suffering, neglect, and frivolous harmful NIH-funded research can be pointed to. The panelists seemed uniformed about the well-documented failings of oversight of NIH-funded animal experimentation.

On August 5, I requested a roster of the proposed NIH internal Steering Committee and was told by Ryan Bayha, Director of Strategic Engagement, that the members had not been selected. I worry that the committee will be staffed by those vested in some professional or financial way in the use of animals in research. A case in point is Carrie Wolinetz, associate director for science policy at NIH, and a participant in the NIH Workshop. Her previous position with the Federation of American Societies for Experimental Biology points to her matter-of-fact bias. FASEB

strongly and unabashedly promotes the increased use of animals. The conclusions of the steering committee will be foregone and of little merit if members are so plainly biased.

I worry too that NIH will select committee members who may not have the perquisite knowledge needed to contribute to an informed recommendation. Panelists at the NIH Workshop on Research with Animals Containing Human Cells admitted that there was scant science on the nature of sentience but then asserted that animals with smaller and morphologically different brains were not sentient; an obvious logical and factual error. They seemed to use *sentience* to mean "human-like consciousness," a term with no clear meaning. They also seemed to believe that intelligence was indicative of the potential for suffering, another plain error. These mistaken beliefs are akin to urban myth, they seem to be part of a paradigm at NIH that limits the scope of consideration for animals being used in funded research.

Those charged with making ethical decisions for the public at large about the ways sentient beings can be imprisoned or harmed or killed in the name of science must be conversant with current knowledge about animals' minds; they must be conversant with the realities of the laboratory environment, the problems with current oversight, the peer-viewed reviews of the poor translation of animal-based research to clinical improvement, and they absolutely must not have a vested interest in the committee's recommendations.

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