

**A Greener World-American Anti-Vivisection Society-Animal Legal Defense Fund
Animal Welfare Institute-Center for Food Safety-Food and Water Watch
Food Animal Concerns Trust-Friends of the Earth-Institute for Agriculture and Trade Policy
International Center for Technology Assessment-National Family Farm Coalition
Northwest Atlantic Marine Alliance-World Animal Protection**

Secretary Xavier Becerra
U.S. Department of Health and Human Services
200 Independence Ave SW
Washington, DC 20201

April 5, 2021

Sent by mail and email

Dear Secretary Becerra:

RE: USDA MOU on the Movement of Animals Modified or Developed by Genetic Engineering

Congratulations on your long-delayed confirmation by the U.S. Senate. As you and your staff review and prioritize how to respond both to the legacy issues from the previous administration and to emerging issues under Health and Human Services (HHS) authorities, we request that your office respond expeditiously to clarify the Food and Drug Administration's regulatory authority over genetically engineered (GE) animals.

We are representatives of consumer, animal welfare, food safety, agriculture trade policy, and environmental groups concerned about the public health, environmental, and animal welfare effects of genetically engineering food animals.

We wish to bring to your attention an administrative action by outgoing USDA Secretary Sonny Perdue to withdraw most of FDA's regulatory authority over genetically engineered animals and fish and transfer that authority to USDA's Animal and Plant Health Inspection Service (APHIS). The administrative action takes the form of a Memorandum of Understanding (MOU) signed on January 13, 2021 by Secretary Perdue and Dr. Brett Giroir, HHS Assistant Secretary for Health, and posted on the APHIS website.¹ However, although HHS did sign the MOU, the MOU has not been posted on the FDA website, which means that the MOU is not in effect since it states, "This agreement will become effective when signed by both parties and made publicly available on the USDA and FDA websites."²

On January 11, FDA Commissioner Hahn told HHS leadership that he refused to sign the MOU, according to *Politico*, "amid concerns about its legality and the potential health repercussions of relaxing oversight of certain genetically altered products . . . One senior administration official

¹ MEMORANDUM OF UNDERSTANDING BETWEEN THE UNITED STATES DEPARTMENT OF AGRICULTURE AND THE FOOD AND DRUG ADMINISTRATION, DEPARTMENT OF HEALTH AND HUMAN SERVICES, available at:

<https://www.aphis.usda.gov/biotechnology/downloads/mou-usda-fda.pdf>

² Ibid. p. 4

told POLITICO that the White House was behind the sudden push for approval.” Career FDA lawyers opposed the MOU, but they were overruled by HHS political appointees.³ The MOU is part and parcel of other Trump administrative initiatives to weaken FDA’s authority to protect public health.

We share Commissioner Hahn’s concerns and urge you to ask Secretary Vilsack to instruct USDA officials to remove the MOU from the APHIS website, since it is not in effect. We further ask that you order the HHS Office of the General Counsel to evaluate the legality of the MOU in the context of FDA’s statutory authorities and scientific capacity to regulate and conduct pre-market and post-market risk assessment of genetically engineered animals and fish.

Secretary Perdue, in announcing the MOU, repeated animal and meat industry arguments that FDA’s safety-oriented regulatory approach impedes rapid commercialization of GE animals. The industry demands, in the words of the National Pork Producers Council, “regulatory certainty” to expedite investment in and commercialization of GE animals, especially swine.⁴ However, reassigning regulatory authority to an agency avid to market GE animal products world-wide is very likely to compromise the scientific integrity of the risk assessment of GE animals.

FDA has found compelling grounds for stringent oversight of newer GE techniques. For example, consider the case of the “hornless” dairy cow developed by the Minnesota firm Recombinetics. USDA had touted the gene editing used to produce the “hornless” (polled) cow as being just like conventional breeding, only faster. In 2016, the company insisted that it had examined the genomic sequence of the animal and found no unintended effects. Fortunately, FDA scientists examined the sequence of the animal and found that the engineering had left a full copy of a plasmid and a second copy of the repair template sequence in the genome.⁵ The plasmid, which contained genes for resistance to antibiotics, ampicillin, neomycin and kanamycin, was used to edit the DNA but should not have been left behind in the genome of the animal. Why hadn’t Recombinetics found this inserted genetic material which FDA scientists found? A Recombinetics executive admitted that the company had never bothered to look for the genetic sequence of the plasmid, since they did not think that it would be integrated into the genome of the cow.⁶

USDA and Recombinetics both should have known that gene editing techniques, such as use of engineered nucleases, are known to cause off-target and on-target mutations. Studies with

³ Sara Oweremohl and Adam Cancryn, “FDA fights for independence in Trump administration’s final days,” *Politico*, January 13, 2021. <https://www.politico.com/news/2021/01/12/fda-independence-hhs-458515>

⁴ Dan Flynn, “Perdue exits the building after getting USDA jurisdiction over gene-edited livestock,” *Food Safety News*, January 22, 2021. <https://www.foodsafetynews.com/2021/01/perdue-exits-the-building-after-getting-usda-jurisdiction-over-gene-edited-livestock/>

⁵ Norris AL, Lee SS, Greenlees KJ, Tadesse DA, Miller MF and H Lombardi. 2020. Template plasmid integration in germline genome-edited cattle. *Nature Biotechnology*, 38: 163-164.

⁶ “It was not something expected, and we didn’t look for it” says Tad Sontesgard, CEO of Acceligen, a subsidiary of Recombinetics that owns the animals.

Regaldo, A. 2019. Gene-edited cattle have a major screwup in their DNA. MIT Technology Review. At: <https://www.technologyreview.com/2019/08/29/65364/recombinetics-gene-edited-hornless-cattle-major-dna-screwup>

mouse cells have shown that CRISPR-Cas9 not only causes off-target mutations,⁷ it also can lead to on-target mutations that can lead to large deletions and complex chromosomal rearrangements.⁸ Another mouse study using CRISPR-Cas9 found large on-target mutations that resulted in immune dysregulation.⁹ In June 2020, *Nature* published a story about three peer-reviewed studies involving human embryos. All the studies found large unwanted on-target mutations involving large deletions and chromosomal rearrangements, and even referred to these effects in the headline as “chromosomal mayhem.”¹⁰ Clearly, gene editing techniques can cause both on-target and off-target effects, with potentially adverse consequences. Fortunately, FDA’s draft guidance on new kinds of genetic engineering would at least have the GE animal product developer demonstrate with relevant data and studies that there are no “off target” effects in the GE animal.¹¹

USDA’s track record in pre-market safety review and risk assessment of GE products also testifies against investing it with regulatory authority over GE animals and fish. First, APHIS has declined to develop relevant GE animal regulations. Instead, APHIS developed only limited protocols to govern scientists’ research on GE animals and insects, despite explicit recommendations from the USDA Inspector General to develop GE animal regulations. Moreover, in its response to the Inspector General, USDA staff said that the FDA review of GE animals was scientifically robust, “*We wish to emphasize that the Food and Drug Administration (FDA) now has a rigorous mandatory approval process for GE animals that examines, among other things, the health of the animal. As described in the OIG report, FDA published Guidance to the Industry which describes how FDA’s New Animal Drug Authority will be used to evaluate the safety of GE animals.*”¹²

FDA scientists have demonstrated that they are able and willing to take a more fulsome approach to reviewing GE animals. FDA has adopted a scientifically sound definition of genetic engineering that includes newer gene-editing techniques – bucking the pressure from industry players to have gene-editing declared exempt from GE regulation.¹³ This definition is also in

⁷ Yee J-K. 2016. Off-target effects of engineered nucleases. *The FEBS Journal* 283:3239-3248. At: <https://febs.onlinelibrary.wiley.com/doi/pdf/10.1111/febs.13760>

⁸ Kosicki M, Tomberg K and A Bradley. 2018. Repair of double-strand breaks induced by CRISPR-Cas9 leads to large deletions and complex rearrangements. *Nature Biotechnology*. Doi:10.1038/nbt.4192. At: https://www.researchgate.net/publication/326429946_Repair_of_double-strand_breaks_induced_by_CRISPR-Cas9_leads_to_large_deletions_and_complex_rearrangements

⁹ Simeonov DR, Brandt AJ, Chan AY, Cortez JT et al. 2019. A large CRISPR-induced bystander mutation causes immune dysregulation. *Communications Biology* 2:70. At: <https://www.nature.com/articles/s42003-019-0321-x.pdf>

¹⁰ Ledford, H. 2020. CRISPR gene editing in human embryos wreaks chromosomal mayhem. *Nature* 583: 17-18. At: <https://www.nature.com/articles/d41586-020-01906-4>

¹¹ FDA. 2017. Draft Guidance for Industry #187 Regulation of Intentionally Altered Genomic DNA of Animals. At: <https://www.fda.gov/media/74614/download>

¹² https://www.aphis.usda.gov/biotechnology/downloads/audits/USDA_OIG_50601-16-Te.pdf

¹³ FDA. 2019. Guidance for Industry: Voluntary Labeling Indicating Whether Foods Have or Have Not Been Derived from Genetically Engineered Plants. At: <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-voluntary-labeling-indicating-whether-foods-have-or-have-not-been-derived>

line with that of many other nations, including those of the European Union¹⁴, promoting regulatory harmonization with key trade partners.

In brief, FDA clearly has far more of the expertise and “safety first” perspective needed to regulate novel GE animals. Stringent regulation is required not only to ensure safety, but also to avoid blowback from the “rush-to-market, consequences be damned” mentality of some regulation-haters. That said, FDA needs to shore up its regulatory regime. Guidance documents for GE animal regulation should be recast as formal regulations capable of addressing, with enforcement measures as necessary, the food safety and the environmental safety challenges posed by these new kinds of GE organisms.

With such improvements, FDA is the clear choice for regulating GE animals.

We urge you to request Secretary Vilsack to order APHIS to remove the MOU from its website. The continued presence of the inoperative MOU may give the inaccurate impression that FDA agrees to transfer most aspects of GE food animal pre-market safety reviews to USDA.

We also ask for a meeting with the new FDA Commissioner and the staff responsible for overseeing the risk assessment and regulation of GE Animals.

Sincerely,

Jaydee Hanson

Policy Director, Center for Food Safety jhanson@centerforfoodsafety.org

On behalf of the following groups:

**A Greener World
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Animal Welfare Institute
Center for Food Safety
Food and Water Watch
Food Animal Concerns Trust (FACT)
Friends of the Earth
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International Center for Technology Assessment
National Family Farm Coalition
Northwest Atlantic Marine Alliance (NAMA)
World Animal Protection**

¹⁴ Center for Food Safety, Comments on USDA’s regulatory changes, August 6, 2019. https://www.centerforfoodsafety.org/files/part-340-comments--center-for-food-safety--2019-08-06_34160.pdf.

