



Secretary Tom Vilsack
U.S. Department of Agriculture
1400 Independence Ave., SW
Washington, DC 20250

February 26, 2021

Dear Secretary Vilsack,

Sent by mail and posted to the docket

RE: [Docket No. APHIS–2020–0079] RIN 0579–AE60 Advanced Notice of Proposed Rulemaking (ANPR): Request for comment on Regulation of the Movement of Animals Modified or Developed by Genetic Engineering

We wish to bring to your attention and to that of Secretary of HHS nominee Xavier Becerra an administrative action by outgoing Secretary of Agriculture Sonny Perdue to withdraw most of FDA’s regulatory authority over genetically engineered animals and fish and transfer that authority to the Department of Agriculture’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

On January 11, FDA Commissioner Hahn told HHS 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 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.² 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 Secretary Vilsack to instruct USDA officials to remove the MoU from the APHIS website and to halt any budgetary, regulatory, organizational or personnel activities, including transfer of current regulatory submission information, to implement the MoU’s provisions. We further ask that Attorney General Becerra, following his confirmation as HHS Secretary, order the HHS Office of the Inspector General to evaluate the legality of the MoU in the context of FDA’s statutory authorities and scientific

¹ <https://www.aphis.usda.gov/biotechnology/downloads/mou-usda-fda.pdf>

² Sara Owerwohl 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>

capacity to regulate and conduct pre-market and post-market risk assessment of genetically engineered (GE) 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.³ 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 novel GE animals.

FDA found compelling grounds for stringent oversight of newer GE techniques. For example, in the case of the "hornless" dairy cow developed by the Minnesota firm Recombinetics. The USDA had been touting 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 "off target" effects. Fortunately, a FDA scientist 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.⁴ The plasmid, which contained genes for resistance to the antibiotics both 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? Because the CEO of the Recombinetics subsidiary of Recombinetics that owned the hornless cattle 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.⁵ In other words, they took a "don't look, don't find" strategy.

USDA should have known that gene editing techniques, such as use of engineered nucleases, are known to cause off-target mutations. Studies with mouse cells have shown that CRISPR-Cas9 not only causes off-target mutations,⁶ it also can lead to on-target mutations that can lead to large deletions and complex chromosomal rearrangements.⁷ Another mouse study using

³ 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/>

⁴ 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.

⁵ "It was not something expected, and we didn't look for it" "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>

⁶ 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>

⁷ 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

CRISPR-Cas9 found large on-target mutations that resulted in immune dysregulation.⁸ In June 2020, *Nature* published a story on 3 studies involving human embryos that all found large unwanted on-target mutations involving large deletions and chromosomal rearrangements, and even referred to these effects in the headline as “chromosomal mayhem.”⁹ 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 producer of a new animal demonstrate that there are no “off target” effects.¹⁰

These unsettling and unanticipated safety issues underscore both how much there is yet to learn about manipulating the genomes of animals, as well as the need for “safety first” regulation. Undoubtedly, the nation’s food and drug safety authority is better equipped to fulfill this role than USDA, whose primary mission has been to advance the interests of U.S. agribusiness.

USDA’s track record in this arena also speaks against investing it with regulatory authority over GE animals and fish. First, the Department’s Animal and Plant Health Inspection Service (APHIS) declined to develop extensive regulations to oversee genetically engineered animals and developed only limited protocols to govern scientists’ research on GE animals and insects, despite explicit recommendations from the USDA Inspector General to develop regulations. Moreover, in its response to the Inspector General, the USDA staff said that the FDA review of GE animals was adequate, *“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.”*¹¹

Second, this same USDA agency has a checkered history in regulating GE plants: from losing track of pharmaceutical-producing crops,¹² to rubber-stamp approval of herbicide-resistant soybeans and cotton that have enabled devastating drift damage across millions of crop acres.¹³ USDA has failed its duties even on narrowly economic grounds. Its lax regulation of GE crop field trials has led to export market rejection of GMO-contaminated grain shipments on

⁸ 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>

⁹ 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>

¹⁰ FDA. 2017. Draft Guidance for Industry #187 Regulation of Intentionally Altered Genomic DNA of Animals. At: <https://www.fda.gov/media/74614/download>

¹¹ https://www.aphis.usda.gov/biotechnology/downloads/audits/USDA_OIG_50601-16-Te.pdf

¹² U.S. Government Accountability Office. Genetically Engineered Crops: Agencies are Proposing Changes to Improve Oversight, but Could Take Steps to Enhance Coordination and Monitoring. GAO-09-60, November 2008.

¹³ Brandon Keim. Monsanto’s newest GM crops may create more problems than they solve. *Wired*, February 2, 2015. <https://www.wired.com/2015/02/new-gmo-crop-controversy/>. See also: Emily Unglesbee. When Drift Hits Home: Dicamba Moves Beyond the Bean Fields and INto the Public Eye. *The Progressive Farmer*, July 20, 2018. <https://www.dtnpf.com/agriculture/web/ag/crops/article/2018/07/20/dicamba-moves-beyond-bean-fields-eye>.

numerous occasions, costing U.S. agriculture billions in lost revenue. ¹⁴ And the USDA's recent overhaul of its GE plant regulatory regime will only make matters worse. Not only will GE plant developers be permitted to "self-regulate" in many respects; USDA need not even be notified prior to testing or commercial introduction of many GE plant types. Besides potential safety issues, this radical deregulatory initiative pushed through by Secretary Perdue's USDA cannot fail to saddle U.S. farmers and agriculture with still more losses as GMO-sensitive export markets reject shipments contaminated with GMOs that USDA may not even know exist.

Clearly, GE animals must not be permitted to "run wild" under a similarly lax, USDA-style regulatory regime.

In contrast, FDA scientists have demonstrated that they intend to take a more fulsome approach to reviewing GE animals. For one, 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. This definition is also in line with that of many other nations, including those of the European Union ¹⁵, promoting harmonization with key trade partners.

In brief, we believe it is absolutely clear that FDA 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 teeth, the food safety and the environmental safety challenges posed by these new kinds of genetically engineered organisms.

With such improvements, FDA is the clear choice for regulating GE animals. **Secretary Becerra and Secretary Vilsack should withdraw the Memorandum of Understanding that would transfer GE animal review to the USDA.**

Sincerely,

Jaydee Hanson
Policy Director

William Freese
Senior Scientist

¹⁴ U.S. Government Accountability Office, Genetically Engineered Crops: Agencies are Proposing Changes to Improve Oversight, but Could Take Steps to Enhance Coordination and Monitoring. GAO-09-60, November 2008. See also: Rick Weiss. Gene-Altered Profit-Killer. The Washington Post, Sept. 21, 2006.

¹⁵ 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.