U.S. pork producers see tremendous potential in biotechnology including gene editing to address animal health issues such as porcine reproductive and respiratory syndrome, as well as assisting the industry to improve areas such as animal welfare, responsible antibiotic use, and sustainability.

With that, the regulatory environment can't be a barrier to innovation, development and adoption which it has proven to be for decades. The rest of the world is taking off in this space. The US needs to stay competitive and continue to meet our domestic and international demands.

Survey questions:

What are your primary concerns about current oversight for biotechnology products? For example, you might share information about length or cost of different regulatory processes.

NPPC's concerns with the current oversight include but are not limited to the time to approval, the narrow scope of the approval itself, the cost, and the lack of expertise of the current regulatory agency when it comes to livestock. Livestock biotech (specifically genetically engineered) approvals have been minimal under FDA for decades, while USDA oversight of genetic technologies in plants has flourished. The amount of time required to move through the approval process (along with cost), has resulted in companies seeking approvals in other countries. This also means that international competitors such as Argentina, Australia, Brazil, Canada, and China are moving forward while the U.S. industries lag behind. Even the European Union, long viewed as a country against agricultural genetic innovation, is having meaningful discussion about accessing the benefits of gene editing. The current regulatory process is placing U.S. livestock and poultry producers at a disadvantage. The FDA also has very limited expertise across the agricultural production chain. This is where USDA has expertise. Further, no other country is attempting to regulate agricultural applications of genetic technologies in animals as "drugs". A genome that had been subject to gene editing qualifies that animal, and its offspring, as an animal drug in perpetuity. This means that millions of animal drugs would be moving in commerce? How would you classify a drug residue from an animal with a modified genome? What would qualify as an adverse event reporting? How does this classification impact trade if we are exporting "animal drugs"? How does this influence day-to-day activities of a farm if they are now considered drug manufacturing facilities? This is an inefficient and unnecessary way to regulate this technology that will limit advancement and adoption of science that can have huge, positive, impacts for animal health, welfare and food security. Public and private agricultural research institutions and innovators are hesitant to conduct work in this area because they do not see a path forward to commercialization. In a recent conversation with an academic researcher, approval of five genetically engineered swine cost $300,000 and took three years. The U.S. government can do better for our agriculture industries.

How would you describe an ideal oversight system for biotechnology products? For example, you might share how products could enter the system; how reviews could occur and by whom; or the appropriate role, if any, for outside advisory panels.

USDA regulating agricultural applications of animal genetic technology under the Animal Health Protection Act (AHPA), the Federal Meat Inspection Act (FMIA), and the Poultry Products Inspection Act (PPIA) is a very sound proposal. It would allow the USDA to bring the full breadth of its expertise and authority to bear in ensuring their safe and appropriate use in animals while fostering these new technologies as it has done for plants for years. The AHPA contains all the tools necessary to effectively regulate agricultural animals bred utilizing new genetic technologies. The FMIA and the PPIA contain all the tools needed to ensure that the meat

products they produce are safe. These bodies of law are robust and well-able to address concerns about the application of genetic technologies to livestock and poultry populations used for the production of food. Furthermore, it must be acknowledged that the Secretary of Agriculture has far better authorities to control the movement and marketing of animals and animal products should the need arise. The USDA has a long history of working with state and tribal animal health and food safety authorities, and industry, to address situations concerning the health of animals, and the safety or wholesomeness of food products. In the unlikely event that an approved (or for that matter unapproved) application of a genetic technology leads to a negative consequence, the USDA is well poised to take any necessary actions. The FDA is not—it is not reasonable to presume that they could effectively manage such situations under drug recall authority.

Regardless of the regulatory agency overseeing biotechnology, NPPC supports using the 2017 National Academies of Sciences, Engineering and Medicine publication "Preparing for the Future Products of Biotechnology" (NAS Report) as direction. The NAS Report offers a clear and elegant pathway, consistent with the Coordinated Framework for the Regulation of Biotechnology (the Coordinated Framework), that if FDA were the regulatory agency could utilize to determine what, if any, approval under the FD&C Act is required for gene edited animals not intended to produce biopharmaceuticals or medical devices. This regulatory approach would utilize the NAS Report's elegant classification system of new biotechnology products as "familiar and noncomplex," "unfamiliar or complex," and "unfamiliar and complex." Rather than require a new animal drug application for each gene edit to animals.

1. **Familiar and Noncomplex: The nature of the gene edit is such that it either corresponds to a genotype found in the subject or a sexually compatible species, could reasonably occur in the subject species through mutagenesis, or is a deletion of any size.** Animals produced through gene editing techniques that meet these criteria should not be subject to regulation under the FD&C Act. The inserted or deleted genetic sequences, or the resultant genome, cannot be defended as an "article" under the FD&C Act. Animals derived from gene edits that fall into this category would have a genome indistinguishable from non-genome edited animals that share the relevant genotype through inheritance or mutagenesis. Therefore, they and the products they produce pose no novel risks. The consideration of their genome as a new animal drug—in perpetuity under the FDA's draft guidance—cannot be defended on scientific, practical, or public health grounds. <u>The genotype resulting from gene edits determined to be "familiar and noncomplex" could legitimately and reasonably be achieved through current animal breeding techniques.</u> Gene editing offers the animal agriculture community incredible promise to rapidly disseminate desirable characteristics through animal populations. Gene edits that are familiar and noncomplex either mimic genetic sequences known to exist in the species of interest, or that are very reasonably likely to exist or to develop through mutagenesis with or without selection pressure. These genes could be propagated without gene editing techniques—though at a much slower rate and not in isolation, thereby compromising years of selective breeding—throughout the species. Given the known nature of this genetic material—or in the case of a deletion, the high predictability of the result—there is no new or novel element being introduced into the genetic library of the subject species. There is, therefore, no new or novel risk or threat to animal health, human health and food safety, or the environment. The use of gene editing in this context should not be viewed in a regulatory capacity as any different from those already in use and developed over millennia of domestication. Any special scrutiny or labelling would be without scientific or legal merit.

2. **Unfamiliar or Complex: The inserted genetic material is limited to one or a few genes that are not reasonably likely to occur in the subject species or consists of multiple and interacting familiar genes.** Animals produced through gene editing techniques that meet these criteria should be subject to a test to determine the appropriateness of regulation under the FD&C Act. The FDA should develop a modified approval process whereby the novelty of the edit can be assessed against previous applications, and the safety of the edit can be demonstrated as appropriate. The "article" under the FD&C Act in this circumstance should be limited solely to the genetic information inserted into animals subject to the gene editing technique—the genetic inheritance of their offspring and further descendants should not be considered an "article" under the FD&C Act, and they or their products should not be subject to any special consideration or labelling under such.

3. **Unfamiliar and Complex: The inserted genetic material is not reasonably likely to occur in the subject species and consists of multiple interacting genes.** Animals produced through gene editing techniques that meet these criteria may be the proper subject of regulation under the FD&C Act under a framework like that proposed by the FDA in the draft guidance. However, the FDA should develop a clear pathway that allows, after a defined number of generations reasonable to demonstrate safety and efficacy, those animals' descendants to not have their genomes considered an article of interest under the FD&C Act, or their products subject to any additional scrutiny or labelling under such.

What are beneficial aspects of biotechnology oversight? For example, you might share what is successful about current oversight for biotechnology products, in the United States or in other countries.

There are advantages with regard to consumer acceptance of the products. In a recent (2021) Food Marketing Institute survey evaluating consumer attitudes, trust and acceptance of bioengineered and gene-edited food, the results showed that federal agencies including USDA, FDA, and UN FAO are the most trusted organizations for information. Respondents also prefer federal decision makers for labeling issues related to bioengineered or gene-edited food over state-based ones, with 69% of respondents choosing the U.S. Food and Drug Administration as their preferred decision-maker for such labels.

How can Federal agencies better prepare researchers and new companies to enter the regulatory system? For example, you might share how the Federal government could better connect oversight of biotechnology research (such as the NIH Guidelines for rDNA research) with oversight and regulation of biotechnology products.

Federal agencies should seek opportunities to collaborate with researchers and industry in as many ways as possible. The National Academy of Sciences, Engineering and Medicine committee on heritable genetic modification in food animals, is one example.