

# MEAT OF THE MATTER

## Gene Editing Holds Tremendous Promise, but FDA Hampering Progress

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Gene editing in livestock is an emerging technology that promises significant animal health benefits. It accelerates genetic improvements, reduces the need for antibiotics and lowers the financial risk for farmers. However, gene editing's potential is being hampered by what is essentially a regulatory land grab by the U.S. Food and Drug Administration (FDA). The National Pork Producers Council has called on the U.S. Department of Agriculture to assert its proper oversight over livestock on America's farms and take the reins on this issue.

### Health Benefits:

Gene editing accelerates genetic improvements that could be realized over long periods of time through breeding: It offers an approach to precisely introduce useful genetic variation into food animal breeding programs. Gene editing is distinct from genetic engineering because it is targeted and does not necessarily involve the introduction of foreign DNA. Emerging applications include raising pigs resistant to Porcine Reproductive and Respiratory Syndrome (PRRS), a highly contagious swine disease that causes significant animal suffering and costs pork producers worldwide billions of dollars.

PRRS is a devastating disease to the U.S. pork industry, and gene editing offers a solution. However, the FDA's approach to regulating gene editing will cause approval to be lengthy, costly and should the gene edit be approved, few if any producers will be able to utilize it. Simply put, the U.S. cannot regulate the genome of animals as drugs and remain globally competitive.

### Economic Impact of PRRS:

- PRRS is the most economically important disease of domestic swine in North America, Europe and Asia. This devastating viral disease leads to reproductive failure, reduced growth, suffering and premature death, with a mortality rate of 12-15%.
- The total cost of PRRS to the U.S. pork industry is estimated to be \$664 million annually, due to productivity losses of both breeding and growing pig herds. Additionally, the total costs attributed to PRRS for veterinary, biosecurity and other outbreak-related costs are \$477 million annually.
- Vaccines have not been effective against the disease, and although genetic selection for natural resistance is an option, success to date has been limited, possibly because of the genetic diversity of the PRRS virus. Not surprisingly, the virus has become established in most swine-producing regions of the world, with only a few exceptions.

### However, gene editing offers a solution to PRRS:

- Gene editing can be utilized to make pigs resistant to PRRS, virtually eliminating all production losses specifically related to the virus. Critically, this will also make the pigs less susceptible to secondary bacteriological infections that can require antibiotics.
- This gene editing solution works by utilizing CRISPR/Cas9 to knock out a single gene (CD163) in the pig's genome, which makes its macrophage cells (the cells PRRS targets) resistant to PRRS infection.
- This is not transgenic. No new genetic material is added. One simple change is made to an existing gene.
- The accuracy and efficacy of this gene edit has worked in lab experiments. There is absolutely no reason to doubt that the edit will work in any member of the porcine species.

### FDA is Blocking Progress on Gene Editing:

- The FDA's regulatory approach is not risk based. It is using the same strategy that was utilized for the incredibly lengthy and costly approval process for the AquaAdvantage® Salmon, which is transgenic and developed using older gene modification techniques. While the FDA's approach may still be appropriate for transgenic applications of gene editing technology, it is not for changes within the animal's own genome.
- The FDA is currently requiring significant numbers of at least three generations of descendants of the actual gene-edited animals to be reared to adulthood and evaluated as part of the approval process. This not only doesn't take into account the dynamics of animal breeding; it also creates considerable waste. This approval process will take at least five years for every gene edit proposed for pigs. For cattle, it will be even longer—at least 10 years.
- Crucially, once an edit has been approved, FDA has signaled that the edit is only approved for the lineage of animals that has gone through the approval process and not for the species generally. This will either lead to an extreme narrowing of the gene pool, or hundreds if not thousands of lengthy and expensive approval applications. These are unacceptable outcomes—this alone should indicate that the approval process is broken.
- Meanwhile, other countries are rapidly moving ahead with risk-based approval processes that ensure that most non-transgenic edited animals are not considered GMOs. This will simultaneously drive elite animal breeding out of the U.S.—long the international leader—and place U.S. producers at a potentially catastrophic competitive disadvantage with foreign competitors.

### Even if the PRRS edit is approved, producers will not want to use it if the animal's genome is considered an animal drug.

- The FDA's insistence that the altered genome be considered an animal drug (regulated article) rather than the much more reasonable and rationale consideration of the gene editing construct (for example the CRISPR/Cas9 molecule with associated genetic information unique to the edit) will have a chilling effect on this technology.

- The FDA's statements that this is not regulating the animal and that there are no practical consequences are naïve at best. Any living organism is indistinguishable from its genetic material. Therefore, the descendants of an edited animal will be subject to regulation as animal drugs in perpetuity. If, despite all these obstacles, gene editing is widely adopted, this means that the FDA could claim regulatory jurisdiction at whim over the entire U.S. livestock population.
- Consideration of an animal as a drug could have real and significant consequences to the international trade in animals and animal products. This is in effect a drug that cannot leave the animal or the products it produces. The potential trade barriers are massive.
- Producers are not confident that the FDA will respect its assertion that it will use regulatory discretion to exempt producers from most requirements of the Food, Drug and Cosmetic Act. The FDA could, at will, decide to consider every farm that has livestock descended from a gene-edited animal a drug manufacturing facility, and inspect it and take enforcement actions for any perceived violations of the FDCA.

Other diseases are currently the subject of very promising gene editing research, but these are unlikely to even enter the approval process under the current FDA protocol.

#### **Transmissible gastroenteritis (TGE)**

- TGE is another viral disease of swine that causes production losses. It was just announced that another simple gene knockout can make pigs resistant to this virus.
- TGE, though consequential, does not cause the same magnitude of financial losses as PRRS. Therefore, it is highly unlikely that this edit will ever move forward for approval under the current paradigm. The costs and obstacles are too high, especially if the edit is not approved for use in all pigs (not just descendants of those going through an approval process).

#### **African Swine Fever (ASF)**

- ASF is an extremely virulent and lethal viral disease of pigs. There is no vaccine or other treatment. It is not currently in the U.S., but Europe and Asia are experiencing outbreaks. Should ASF come to the U.S., it would devastate the pork industry overnight.
- The European Union and China are devoting a lot of resources to exploring gene editing as a way of making pigs resistant to ASF. Should they be successful, they could simultaneously protect their pigs and reduce or even stop efforts to eradicate the virus.
- If the EU and China are successful in their efforts, this would place the U.S. in an untenable position. The FDA would preclude use of a gene editing solution across the U.S. pig herd even if it were approved under a legitimate process in another country. Faced with an outbreak, U.S. pork producers would need to put each one of the hundreds of breeds, genetic lines, and even breeding herds of pigs into a five-year approval process before the industry could protect itself.
- Additionally, this scenario could also create a dangerous dynamic in which the Secretary of Agriculture—who needs to have all authority over animal movements and dispositions in an animal health emergency—and the FDA Commissioner make competing claims of authority over livestock. This would be untenable.

*In summary, gene editing offers a tremendous opportunity for the U.S. pork industry, but oversight over edited animals and their descendants on farms should be transferred from FDA to USDA. The agency has already established the right regulatory framework by adopting a risk-based approach to reviewing potential genetic changes in plants. It easily could adapt that approach for livestock and regulate gene-edited animals under the Animal Health Protection Act. We will continue to urge FDA to relinquish its current proposed oversight of gene edited animals on farms and instead place that authority where it belongs, at USDA.*

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