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DRAFT STUDY ON GENOME EDITING IN LIVESTOCK AND POTENTIAL RAMIFICATIONS FOR GENETIC RESOURCES

Note by the Secretariat

1. In endorsing the outline of *The Third Report on The State of the World's Animal Genetic Resources for Food and Agriculture* (Third Report) at its Nineteenth Regular Session,¹ the Commission on Genetic Resources for Food and Agriculture (Commission) approved, subject to the availability of the necessary resources, the coverage of “special topics”, including: (i) vulnerability of animal genetic resources in the face of climate change and the role of genetic diversity in adaptation and resilience; (ii) establishment and scaling-up of breeding programmes in challenging environments; and (iii) genomic measures of genetic variation and the future use of the breed concept in the formation of new breeds. The Twelfth Session of the Intergovernmental Technical Working Group on Animal Genetic Resources for Food and Agriculture also suggested addressing the topics of gene editing and other emerging technologies, if possible.²

2. In response to these recommendations, FAO commissioned the preparation of thematic studies covering the three topics approved by the Commission, as well as on genome editing and emerging technologies in animal phenotyping, as suggested by the Working Group. These studies are at various stages of development and will be made available online for commenting by countries along with sections of the draft Third Report.

3. Genome editing is a novel technology that allows for the introduction of changes in the genomic sequence of an organisms, and hence the observable phenotype of the resulting individual. The objective of this technique’s application is to improve the ability of the individual to serve its purpose to humankind, and an edited gene represents new diversity. However, potential ramifications on genetic resources are not universally favourable. Therefore, increasing and disseminating knowledge on this technology are imperative for its proper utilization in the management of animal genetic resources for food and agriculture.

¹ CGRFA-19/23/Report, paragraph 107.

² CGRFA/WG-AnGR-11/21/Report, paragraph 21.

4. In 2023, FAO collaborated with student participants in the Dean's Global Agriculture and Food Leadership Program of the Iowa State University to undertake an in-depth literature review and series of expert interviews on genome editing. The students were directed by Professors Steven Lonergan and Elisabeth Huff-Lonergan. On this basis, a draft report was prepared. This report was then reviewed, elaborated and revised through the input of an international expert and FAO staff members.

5. The document has been prepared by Gillian Anderson, Jennifer Holliday, Abbie Sesker, and Amy Taylor, of the Iowa State University, Ames, United States of America; and Mike McGrew of the Roslin Institute and Royal (Dick) School of Veterinary Studies, University of Edinburgh, The United Kingdom of Great Britain and Northern Ireland; and FAO staff members. The content of the review is entirely the responsibility of the authors and does not necessarily represent the views of FAO or its Members.

Genome editing in livestock and potential ramifications for genetic resources

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INTRODUCTION

Genetic selection for specific traits in livestock is a practice that has been used for thousands of years in many different cultures and contexts. All around the world, livestock keepers have been using selective breeding to enhance specific animal traits. The selective breeding process allows humans to enhance particular characteristics by pairing male and female individuals who display these traits with complementary mates and then subsequently selecting the offspring inheriting the favourable trait. The practice of breeding for specific traits can help humankind solve various increasing global food issues with solutions that were once theoretical but are now genetically possible. Because of the power of genetic selection, today nearly all agricultural production utilizes genetically improved seeds and animals in some manner (Dace, 2021). However, infrastructure, money, and generations of breeding are required to achieve a population with the desired characteristics.

Genome editing is a novel method of genetic intervention that enables scientists to directly and precisely modify the deoxyribonucleic acid (DNA) of an organism and can be applied to both plants and animals. The ability to locate, modify, or replace a precise area of DNA within a genome is a complicated process. This process starts with genomic and bioinformatics genome analyses, which allow scientists to identify a gene and DNA sequence of interest. In such a case, the identified gene is of interest because it, (i) biochemically influences an important trait, (ii) differs in DNA sequence among individuals – that is, different alleles, and (iii) the sequence differences lead to variation in the trait. The traits inherited by organisms are acquired through their gene variants, so changing a gene's nucleic sequence can change the physical characteristics of the animal. A population is genetically improved by increasing the frequency of animals with the favourable sequence/allele from one generation to the next.

Traditionally, breeding programmes will increase the frequency of a favourable DNA sequence as a consequence of aiming to improve the overall mean genetic value of the population. Breeding programmes using DNA data would try to increase the frequency by identifying individuals possessing this DNA sequence and breeding them to produce more offspring. Genome editing allows scientists to obtain the same endpoint more quickly, by complementing traditional breeding with new biotechnologies to edit the target gene to yield more individuals with the preferred DNA sequence. Genome editing is accomplished by creating a double-stranded break in the DNA, after which the natural DNA repair mechanism is triggered within that cell at that area of the genome. During the repair process, scientists can edit the sequence of or cut nucleotides from that section of DNA, thus creating a permanent genetic change (O.T.S., 2023). Methods for genome editing that have been used in livestock species include the clustered, regularly interspaced, short palindromic repeat/Cas system (CRISPR/Cas9), transcription activator-like effector nucleases (TALENs), and Zinc Finger Nucleases (ZFNs). Box 1 briefly summarizes these techniques.

BOX 1

Genome-editing technologies

Three main techniques have been used to edit the genome of livestock, (i) Zinc finger nucleases (ZFNs); (ii) transcription activator-like effector nucleases (TALENs), and (iii) the clustered, regularly interspaced, short palindromic repeat/Cas system (CRISPR/Cas9). These three approaches differ in the way that they target and bind to organism's DNA, and the nuclease used to cut the gene

for editing. The properties of these three approaches determine the ease of their application, and consequent success and cost.

Zinc fingers are small proteins that are stabilized through coordination with Zinc atoms, which provide stability. In ZFNs, three to six ZN domains are fused with a FokI restriction nuclease. Each of the ZN domains is engineered to bind to a specific 3-basepair sequence, allowing for precise targeting within the genome, while the FokI nuclease cuts the DNA after dimerization.

The transcription activator-like effectors of TALENs are proteins secreted by *Xanthomonas* bacteria. By engineering the amino acids of the DNA binding domains, TALEs can be made to bind a specific DNA sequence. Fusion with a FokI nuclease results in a molecule that can target, bind to and cut double-stranded DNA, thus providing a tool for genome-editing.

The CRISPR/Cas9 system is based on a DNA molecule of “clustered regularly interspaced short palindromic repeats” and a “CRISPR-associated protein 9” molecule, which naturally allow bacteria to destroy invading viruses by cutting their DNA. By delivering CRISPR/Cas9 into eukaryotic cells along with a synthesized strand of “guide” RNA that is complementary to the DNA sequence of a target gene, the genome of an individual cell can be cut in a specific place.

For all three technologies, the actual *editing* occurs during the “repair” of the DNA cut, which relies on the cell’s natural mechanisms and does not differ among the techniques. Repair occurs through one of two approaches: (i) non-homologous end joining, whereby the cut ends are resealed, and (ii) homology-directed repair, which uses a specific DNA template. Homology-directed repair allows the introduction of a synthesised DNA template for making a predictable and desired change in the DNA sequence and function, whereas non-homologous end joining is unpredictable and results in short DNA deletions or insertions and is thus primarily used in cases where the goal of the genome editing is to lose or “knock-out” gene function.

Genome editing via the CRISPR/Cas9 system is the least technically demanding of the three approaches, mainly because synthesizing a single guide RNA is simpler and faster than engineering the DNA constructs encoding ZFNs and TALENs. This renders CRISPR/Cas9 system faster, cheaper and more easily scalable. Therefore, although both ZFNs (e.g. Yang *et al.*, 2011) and TALENs (e.g. Cui *et al.*, 2015) have been used for genome editing in livestock, CRISPR/Cas9 is currently the most commonly used technique (Ledesma and Van Eenennaam, 2024).

These recent genome technological developments make understanding, adapting, and creating DNA material much more accessible. Genome editing has already been used to help us not only alter but better understand genetics (Yeadon, 2014). The technology of CRISPR/Cas9 allows scientists to make edits in DNA more quickly and accurately than ever before, opening doors for many future applications. (Balch, 2021).

Genome editing is often compared to and confused with transgenesis. Both are approaches to modify the genetic material of organisms. These biotechnological techniques differ, however, in their methods and outcomes. Transgenic methods entail the introduction of foreign DNA, referred to as a “transgene”, from one organism to another. The foreign DNA is usually a sequence from a different species and carries a specific gene that will encode a desired phenotype, usually by promoting the expression of a protein not naturally produced by the host organism. The methods are used to generate a new phenotype, but the precise location of integration of the foreign DNA into the host genome is unpredictable and not easily controlled. Consequently, transgenic methods tend to be complicated. In contrast, genome editing is a simple method that precisely modifies an organism's genome at specific locations within the genome. This approach makes targeted changes to existing genetic material, usually without introducing any foreign DNA. A deeper understanding of cellular biology and physiology is necessary to correctly use this application.

Genome editing is the process of making subtle changes, such as deletions, insertions, or sequence modifications, to a specific location of the DNA of an organism by using advanced biotechnologies.

Genome editing technology permits DNA modification in a living organism's genome without needing to inherit this modification from the parents. Since no foreign DNA is introduced to the initial DNA of the organism during genome editing, any variation in the genes that are made could occur through natural processes of mutation. In the case of agriculture, genome editing has been used to improve productivity, food safety, animal health, and plant and animal welfare. New technologies, specifically the CRISPR-Cas9 system, are relatively easy to use, allow precise genetic modifications, and can provide for relatively high throughput.

EXAMPLES OF GENES THAT HAVE BEEN TARGETS FOR GENOME EDITING

Genome editing has already been applied to animal species used for agricultural production, although to a lesser degree than with plants. Examples of livestock traits for which genome editing has been proposed include increased productivity, decreased susceptibility to pathogens, disease and pathogens, and enhanced climate adaptability (Karavolias *et al.*; 2021; Tait-Burkard *et al.*, 2018). A few specific cases are presented in detail in the subsequent sections.

Resistance to porcine reproductive and respiratory syndrome

Porcine reproductive and respiratory syndrome (PRRS) is a panzootic disease of pigs and is responsible for major economic losses worldwide (Montaner *et al.*, 2019). The symptoms of PRRS are mainly late-term abortions and stillbirths in sows and severe respiratory disease in piglets. PRRS has a very narrow host range, and within the host, its primary cellular target is porcine alveolar macrophages (PAMs) (Burkard *et al.*, 2017). The PRRS virus (PRRSV) is a single-stranded RNA virus that infects host porcine cells by interacting with specific cellular receptors on PAMs and is subsequently taken into the cell via endocytosis to complete its life cycle and impact its host tissues and organs. A transmembrane glycoprotein named CD163 acts as a fusion receptor for PRRSV and is exclusively expressed on the cell surface of PAMs. The CD163 receptor contributes to mediating immune response and to scavenge free heme proteins and other components of damaged cells (Kristiansen *et al.*, 2001; Moestrup and Møller, 2004). PAMs express the CD163 scavenger receptor containing a cysteine-rich domain 5 (SRCR5) that is known to be an interaction site for the PRRS virus. Once the virus binds to the SRCR5 binding site, it can be included in an uptake vesicle through the process of vesicle endocytosis (Burkard *et al.*, 2017). Once internalized, the vesicle releases the viral genome into the cytosol to initiate virus infection. As stated above, the CD163 receptor protein is expressed at high levels on the surface of PAMs and the SRCR5 domain has been determined to be the site of interaction with the virus and thus route through which PRRSV infects the cell (Xu *et al.*, 2020).

CD163 is encoded by 16 exons, with the SRCR5 domain encoded by exon 7. Studies of the CD163 receptor *in vitro* (Van Breedam *et al.*, 2010) led scientists to the hypothesis that disabling this gene would result in a complete loss of function of the protein and thus confer resistance to PRRS infection (Whitworth *et al.*, 2016; Whitworth *et al.*, 2022). The first PRRS-resistant, genome-edited pigs were developed by introducing small genetic changes (specifically indels, which is the addition or deletion of one or more nucleotides in a DNA sequence, in the first exon of CD163. Those pigs showed complete resistance to the PRRS virus but were smaller in size than wild-type pigs. The second group of PRRS resistant pigs were CRISPR edited to lack only exon 7, retaining all the other functions of CD163. Using confocal microscopy, Burkard *et al.* (2017) revealed the absence of replication structures in the SRCR5 CD163 deletion macrophages, indicating inhibition of infection before gene expression at the entry, fusion, or unpacking stages, resulting in these pigs completely resistant to PRRS virus.

Many examples have been reported of using genome editing to create models for understanding and addressing the susceptibility of livestock to viruses (Söllner *et al.*, 2021). The model and success of the PRRSV-resistant pigs through the editing of the CD163 gene provide a roadmap for future applications to yield disease resistance without the need for vaccines.

Another virus that significantly threatens global swine production is the African swine fever virus (ASFV). This virus has already cost swine producers billions of dollars, significantly decreased pork production, and caused a loss of valuable resources globally (You *et al.*, 2021). The ASFV enters cells through clathrin-mediated endocytosis, but this process does not require CD163. In fact, CD163 is not essential for ASFV infection, even though CD163 has been reported as one possible receptor (Sanchez *et al.*, 2017). This observation implies that other receptors mediate endocytosis of ASFV. Therefore, ongoing fundamental investigations to define the specific mechanism of infection will inform scientists and potentially identify genome editing targets to yield ASFV-resistant pigs (Wang *et al.*, 2021).

Incentives to consider genome editing to improve disease resistance in livestock are substantial, especially in intensive systems. Improving resistance is imperative for diseases with no vaccines available or poor immunization following vaccinations. In addition, the use of genome editing for disease resistance has potential applications and benefits in conserving local and endangered breeds, as an outbreak in such a population would decrease genetic diversity and overall numbers of animals in that breed, increasing its risk of extinction.

SLICK Gene

Given the generally increasing mean ambient temperature associated with global climate change, it is critical to maintain or improve the ability of livestock to perform efficiently under environmental conditions causing heat stress. Heat stress can negatively impact milk and meat quality, disrupt animal production and fertility and interrupt homeostasis (e.g. Collier and Gebremedhin, 2014; Das *et al.*, 2016; Rojas-Downing *et al.*, 2017). On the population level, heat stress can also increase parasite prevalence and disease occurrence and progression. Different breeds and individuals within breeds differ in their ability to tolerate high temperatures, suggesting a genetic component to heat stress (Brown-Brandl *et al.*, 2006). For example, the SLICK phenotype in cattle, commonly found in several breeds of African origin, is a genetically inherited trait characterized by shorter hair with a lower follicle density across the animal coat, allowing animals to dissipate more heat and maintain lower body temperatures when compared to wild-type animals.

The Senepol breed is a synthetic breed of cattle that was developed in the West Indies by crossing N'Dama cattle imported from Senegal with Red Poll cattle imported from England. The Senepol is an example of cattle that naturally express the phenotype of the SLICK mutation. Porto Neto *et al.* (2018) characterized the genome of the Senepol breed, and they identified a frameshift deletion within the last exon of the prolactin receptor, which resulted in the truncation of a portion of the cytoplasmic domain of the protein. Cattle with the SLICK phenotype have greater thermotolerance and higher milk production in tropical and subtropical regions (Dikmen *et al.*, 2014). Prolactin (PRL) is a hormone responsible for milk production but is also very important for hormonal regulation. The prolactin receptor (PRLR) plays a big role in mammary development, is expressed in many tissues and is now known to regulate hair length and coat characteristics (e.g. Craven *et al.*, 2006; Littlejohn *et al.*, 2014). However, it should be noted that there are other breeds of cattle with a SLICK coat phenotype that do not have the PRLR mutation (Porto Neto *et al.* 2018).

Researchers at the University of Florida were the first scientists to report attempts to introgress the SLICK-coated phenotype into highly productive breeds, by inseminating Holstein cows with Senepol semen (Dikmen *et al.*, 2014). However, genome editing is an option to introduce the causative mutation into a new population, which would be faster and more precise than through traditional introgression via crossbreeding and subsequent selection. The SLICK mutation can thus be introduced in the gene pools of high producing but thermo-sensitive breeds to reduce heat stress in breeds that do not perform well in high-temperature and humidity environments (Hansen *et al.*, 2020).

Recognition of this naturally occurring mutation provided fundamental knowledge that informed an approach for a single gene edit to produce increased heat-tolerant cattle. The timeline to produce SLICK gene edited cattle included recognition and documentation of the valuable phenotype,

identification and characterization of the causative mutation, and application of methods to yield the desired edit in a high value animal. Fundamental research that links naturally occurring genetic variation directly to a beneficial phenotype is crucial as it identifies targets for genomic editing or selective breeding programmes. The case of the SLICK gene provides an example of how genome editing could benefit a livestock species in a changing climate.

PRODUCER AND CONSUMER WILLINGNESS AND ACCESS

For technology to be accepted and utilized, many dimensions of the application must be considered. One factor that will substantially impact the willingness to adopt or use genome-editing technology is economics. Financial considerations must be taken into account for numerous stakeholders. Economics will influence implementation by technology companies, livestock producers, accessibility of technology due to patents, and consumer willingness to pay are all variables that will affect adoption of genome editing applications.

Implementation regarding livestock producers

It can be argued that the attitudes of livestock producers toward genome editing and their willingness or ability to adopt the technology by raising genome-edited animals are among the most critical factors for investors in the research and development of the technology. If producers and breeders are unwilling to invest in required breeding changes needed on their farms or cannot begin to consider incorporating edited animals in their breeding practices due to policy, financial, or even cultural and religious reasons, then there is little incentive for other stakeholder to invest in the research and development of genome-edited animals.

The economic implications for implementing this technology into a producer's breeding operation must be carefully considered. The ability of the products of gene-edited animals to positively impact their livelihoods is critical. Ufer *et al.* (2022) studied the considerations that livestock producers make when deciding to implement new technologies such as genome editing in their operations. In the study, dairy farmers in the United States of America were asked how likely they would purchase genome-edited dairy cattle that resist Bovine paratuberculosis, commonly known as Johne's disease, a bacterial infection primarily in the small intestine of ruminants that leads to wasting, lost productivity and mortality. Among dairy farmers in the United States, 68 percent of herds have had at least one cow affected (USDA APHIS | Johne's Disease, 2013). Estimated annual losses due to Johne's Disease in the late 2010s were USD198 million in the United States, USD75 million in Germany, USD56 million in France, and USD54 million in New Zealand (Rasmussen *et al.*, 2021). Therefore, economics are an important issue for control of Johne's disease. Currently no selective breeding programme or genome-edited option for Johne's disease-resistant dairy cattle exists, so the study conducted was purely hypothetical.

Ufer *et al.* (2022) surveyed farmers on their hypothetical willingness to include genome-edited cattle resistant to Johne's disease in their breeding programme under different scenarios, including a reduction by 10 percent in the price farmers would receive when selling their milk. As expected, willingness to use genome-edited cattle decreased in scenarios where milk price decreased by 10 percent. In fact, 31.8 percent of respondents would "absolutely reject" the adoption of this technology in their herds if it meant a 10 percent reduction of milk sale price, regardless of other factors under consideration (Ufer *et al.*, 2022). Conversely, increased profit was a necessary, but not sufficient prerequisite for adopting genome editing technologies. Adoption rate was also found to depend on the effectiveness of the genome editing, advice provided by veterinarians, and the level of adoption among peers.

Whereas the Johne's disease survey was completed on a hypothetical genome edit, some inference can be drawn from adoption of transgenic crops by producers in low- and middle-income countries. An example with high economic impact on producers in Bangladesh is the adoption of Bt brinjal, a type of

eggplant (Shelton *et al.*, 2018) genetically modified to produce Bt delta endotoxin, which kills insect pests that attempt to feed off the plant. In Bangladesh, brinjal producers experience severe losses to eggplant fruit and shoot borers (EFSB) (Shelton *et al.*, 2018). The caterpillars of this variety of moths damage the shoots and flowers of the plants and eventually cause intense damage to the fruit by boring into it, causing the produce to become unmarketable (Shelton *et al.*, 2018). Consequently, farmers consistently spray insecticides, sometimes up to twice daily, to ensure these pests are not infesting their fields. This can lead to more than 100 rounds of insecticide application per season, resulting in high residue amounts on the fruits. Moreover, the insecticide is not fully effective, and farmers regularly lose 30 to 60 percent of their yields, even when applied. (Shelton *et al.*, 2018). Insecticide applications account for 35 to 40 percent of input costs for brinjal farmers (Shelton *et al.*, 2018). Since the implementation of the Bt brinjal began in 2014, net profits for producers have increased six-fold. Producers growing non-Bt brinjal in the 2016-2017 season received a net return of US\$357/ha (Shelton *et al.*, 2018). In comparison, producers raising Bt brinjal in the same growing season received a net profit of US\$2,151/ha (Shelton *et al.*, 2018). Farmers growing the Bt brinjal also observed a 61 percent decrease in the cost of pesticide inputs compared to the non-GMO varieties (Shelton *et al.*, 2018).

Although not directly comparable to genome-editing in animals, the Bangladesh study demonstrates the enormous potential of genetically modifying genomes, whether by genome editing or transgenesis. Therefore, under an ideal context, farmers in other low-and-middle-income countries (LMIC) may also benefit economically from genome editing in livestock. Hamm and Welham (2022) proposed that farmers in LMIC would benefit from animal genome editing that increases tolerance to environmental changes and by spreading elite genetics more efficiently. Their conclusions were drawn from a public dialogue workshop on the ethics of genome-editing of farmed animals in the United Kingdom; participants stated that they believed that climate change was the most prominent issue for farmers in LMIC. Participants discussed how climate change coupled with a lack of water resources created conditions that would impact the livestock sector. Specifically, climate change would decrease grazing opportunities. Improving adaptability through genome editing could thus enhance animal welfare. The workshop participants also noted that genome editing could increase the affordability of meat products through increased efficiency, and thus improve food security and nutrition for the general population of LMIC.

Implementation regarding consumer willingness to pay

Regardless of the cost, new technologies such as genome editing can only be implemented and used by farmers if policy allows. Similarly, consumers cannot purchase products from genome-edited livestock unless policies allow. The ability of consumers to purchase genome edited products in a given country may not align with the policy regarding use by breeders. For example, a given country may restrict production of genome-edited animals but allow consumption of their products if imported from another country; the opposite may also be true (Genetic Literacy Project, 2023). However, if or when a country's policy allows the sale of genome-edited livestock products, consumers will consider more than just their presence on the store shelf.

Consumer perception of genome-edited animal products, however, has not been well studied. Research carried out on crops may provide some insight. A recent study in China examined consumers' willingness to pay for rice grown by using different breeding technologies: (i) conventional, (ii) genetically modified, and (iii) genome-edited (Ding *et al.*, 2023). To learn about the three breeding technologies in the study, participants first had to watch a three-minute instructional video. In the study, consumers considered the different rice products' effects on the environment, their health, ethical concerns, regulations, and price comparisons. The consumers were more concerned about the effects of genetically modified products compared to genome-edited products, but consumers were most willing to pay for conventionally bred products (Ding *et al.*, 2023). Forty percent of respondents in the study were willing to pay any premium to avoid all genetically modified or genome-edited products. When excluding those willing to pay a premium for conventional

products, the remaining consumers were more willing to pay for a genome-edited product than for a conventionally bred products (Ding *et al.*, 2023).

A similar study was done on genome-edited apples in the United States and France. In that study, consumers' willingness to pay was associated with their level of education on genome editing and genetic modification (Marette *et al.*, 2021). The experiment involved five rounds of willingness-to-pay surveys. The first round focused only on conventionally bred apples to gain an understanding of the baseline. The remaining rounds compared different combinations of conventional, genome-edited or genetically modified apples. Education on genome editing and genetic modification began with round four. Various groups were provided differing amounts of instruction. Excluding any prior knowledge participants may have had, data from rounds four and five suggested that providing background information on the breeding technologies resulted in a significant decrease in consumer willingness to pay for products from the genetic technologies, in both the United States and France, compared to the data from rounds two and three (Marette *et al.*, 2021). The decrease in willingness to pay was greater in France than in the United States, and the information provided on genome editing had a smaller effect on the willingness to pay than did information on genetic modification (Marette *et al.*, 2021). Certain consumers were classified "boycotters" or "indifferent" based on their answers before and after receiving information and education. Boycotters were those whose willingness to pay dropped to zero upon receiving information on the technologies used. The proportions of boycotters were 42.6 and 19.3 percent in France and the United States, respectively (Marette *et al.*, 2021). Indifferent participants were those with a consistently positive outlook on genome editing and genetic modification both before and after receiving information. Of the United States participants, 32.5 percent were indifferent, versus 13 percent for France (Marette *et al.*, 2021). Thus, there is a subset of consumers adamantly opposed to genetic technologies in both countries.

With little data available on genome-edited livestock products and consumer willingness to pay, it is difficult to accurately decipher how this sector may be affected by consumer choice. Information about consumer behaviour for GMOs or other technologies may provide an indication, but leave room for uncertainty. Overall, studies on producer and consumer decision-making show that it is important to consider that both producers and consumers are working to make the best choice for themselves or their operations. Business decisions are an important and impactful factor in adopting genome-editing technologies, but it is not the only factor that decision-makers need to keep in mind.

POLICY AND PUBLIC PERCEPTION OF GENOME EDITING

The regulations surrounding plant and animal genome-edited products are complex. In many countries, genome-edited products are regulated based on where they fall in one of three site-directed nuclease (SDN) classifications (FAO, 2023). In order of level of alteration, these are small base-pair insertions/deletions or changes (SDN-1), small, specific changes by homologous recombination (SDN-2), and precise insertion of DNA elements of foreign origin (SDN-3). SDN-1 and SDN-2 types are virtually indistinguishable from natural variants and variants produced by mutagenic agents (Schmidt *et al.*, 2020). This manner of classification is based on both the degree of difference from the consensus genotype of the organism and whether these changes could have occurred naturally. However, in some countries, all three categories of genome-edited products are regulated with blanket legislation, no matter the genetic technique used. An example of this is seen in the 2018 European Court of Justice (CJEU) ruling, stating that "all genome-edited organisms must be categorized as genetically modified organisms and are therefore subject to significant regulatory burdens under the EU GMO Directive" (Schmidt *et al.*, 2020). This ruling applies to all European Union member states and has significantly impacted genome editing research in these countries, with some research companies moving their research operations outside of the European Union. Most genomic editing applications and research are now found in the United States and China. According to Schmidt *et al.* (2020), reactions to this decision were varied, and it was followed up by a study commissioned by the European Council. The European Council study did not use the SDN terminology, but instead used the broader term "new genetic technologies" (NGT). The NGT were defined as "techniques capable of

altering the genetic material of an organism and that have emerged or have been mainly developed since 2001" (Laaninen, 2021). The primary conclusion of the study was that there were "limitations as to the capacity of the [CJEU] legislation to keep pace with scientific developments" (Schmidt *et al.*, 2020). According to the scientists, rejecting NGT entirely could limit opportunities for improving the sustainability of the agri-food system and reaching climate-change targets. Rejection would also limit the ability of livestock producers to enter the market and for further innovation to occur in Europe. Although the CJEU ruling is an example of regulation of genome editing in high-income countries, it highlights the barriers genome-edited organisms face to enter the mainstream market. It is also important to consider that these rulings were primarily concerned with plants, not animals, suggesting the path forward for animals may face further unknown challenges.

While the CJEU ruling directly impacts the EU member states, the decisions high-income countries make impact producers in LMICs through avenues such as trade and market access. As stated by Pixley *et al.* (2022):

“The EU stance on transgenics in the past discouraged developing countries that traded foods with the EU from using such varieties.....As a result, smallholders in many LMICs have been unable to access transgenic technology and are becoming less competitive with farmers in countries that approved and adopted the technology. The same could happen with genome-edited crops.”

After the CJEU ruling, nine countries signed a statement in the World Trade Organization stating the plant varieties created by genome editing should be regulated in the same way cultivars from traditional methods are regulated. (Pixley *et al.*, 2022).

Argentina was one of these nine countries and is an example of a middle-income country with well-developed genome editing legislation. The Argentinian government took a "new regulations for genome editing" approach, meaning they regulate genome-edited or modified organisms based on the breeding approach. This specific regulatory approach for genome-edited organisms is in direct contrast to the blanket legislation of the European Union (Friedrichs *et al.*, 2019). According to Schmidt *et al.* (2020), Argentina does not regulate plant products if there is no foreign DNA in them. Colombia, Brazil, and Chile followed suit with similar interpretations in 2015. In other LMICs such as Nigeria, Kenya, India, Paraguay, Bangladesh, the Philippines, and Indonesia, the discussions about the regulation of GE products are ongoing, and for the most part, products are regulated on a case-by-case basis (Schmidt *et al.*, 2020).

TABLE 1
Regulation of genome edited organisms in selected countries as of June 2023

Site-directed nuclease (SDN) classification		
SDN-1	SDN-2	SDN-3
European Union New Zealand	European Union New Zealand	Argentina, Australia, Brazil, Chile, Colombia, China, European Union New Zealand, United States of America

Source: Schmidt *et al.*, (2020).

Regulatory landscapes are among the drivers of innovations within a country, but public perception is a key driver of legislation. Agencies and individuals charged with the development of regulation, policy, and commercialization of genomic techniques must consider the opinions of the populace if there will be synergy between the public and science. In a qualitative study completed by Naab *et al.* (2021) that took place shortly after the CJEU decision, 38 participants in the United Kingdom of Great Britain and Northern Ireland were split into five focus groups and answered questions about their perceptions towards genome technologies applied to breeding farm animals. In this study "genome technologies" comprised six different technologies, including genome editing. The topics of the focus groups ranged from ranking different types of genomic technologies, giving participants information

about the different techniques, and ethical dilemmas that could arise from utilization of the technologies.

The main themes from the case study were benefits versus harms, regulation, animal welfare, food production, health, sustainability, and the environment. Some participants said they could see potential benefits of genome technologies if there were a consistent and precautionary framework, but at the same time, they recognized that would be difficult to establish. Some participants opposed using the technologies for food production but were more favourable about using them for medical research and health care, while others held the opposite opinion. Using technologies to conserve animal species was a popular sentiment among most participants. Generally, participants in the focus groups were favourable towards genomic techniques being used to improve animal health and welfare. For some participants, the most important potential impact of genomic technologies was environmental sustainability, "leading to greater productivity, safer human food, improved animal health and welfare, and the preservation of ecosystems," (Naab *et al.*, 2021). Other discussions included lower costs, greater productivity, and the naturalness and temperament of animals. Ethical concerns raised by the participants included the natural purpose of keeping livestock and how it will or will not be maintained when using the technologies, the need to reduce meat consumption, overall concerns about the use of genomic technologies in the animal production system, and the fear of motivation driven solely by financial interests (Naab *et al.*, 2021). While this qualitative study involved only a small number of people, it offers insight into the public perception of genome editing in animals specifically. One impact on public perception of genome editing not highlighted in the above study is public confusion over scientific terminology. Pixley *et al.* (2022) argued that clear and precise terminology must be used consistently in relation to genome editing "to transparently explain the process, products, benefits and potential risks and mitigation strategies ... to build public trust and consistent regulatory oversight of technologies." Consistent usage of terminology would ease public confusion regarding genome editing and make information clearer and more understandable. However, as the National Academies of Sciences, Engineering, and Medicine of the United States of America (2016) indicate, neither science nor human innovation are confined to "neat boxes", making generalizations about genome editing difficult.

Another point of uncertainty regarding genome editing of livestock is the patent and ownership landscape, in a context where animal genetic resources are often considered both as public and private goods (Boettcher *et al.*, 2023). According to Scheinerman and Sherkow (2021), the term "intellectual property" is a broad term, but patents fall under its umbrella. Multiple high-income countries have patents for many varieties of CRISPR technology. However, most of these are found in the United States and China, which is logical considering the 2018 CJEU ruling and its impact on where genome editing innovations occur. CRISPR technology evolves quickly, increasing the number of related patents and stakeholders. When technological development resides in the private sector, it can be more difficult for others to access it. However, with a legislating body that is representative of its constituents, governments can ensure public concerns are considered. This is a reason for which government-set licenses could be a logical approach for genome editing (Scheinerman and Sherkow, 2021). Licenses could serve as "a form of democratic oversight that gives the public the capacity to prevent purely private interests from superseding their own, especially in ways that are dominating, oppressing, or otherwise harmful or unjust" (Scheinerman and Sherkow, 2021). With representative governments setting policies for patents, the public can be protected. However, we are not aware of such an approach currently being taken for genome editing.

International agreements that govern ownership, use, and access to biological genetic resources under the Convention of Biological Diversity (CBD) are in place to protect the genetic biodiversity of the Global South from exploitation (Nehring, 2022). One primary agreement is the Nagoya Protocol. The Nagoya Protocol on Access and Benefit sharing is an international treaty adopted in 2010 that "covers genetic resources and traditional knowledge (TK) associated with genetic resources, as well as the benefits arising from their utilization" (Secretariat of the Convention on Biological Diversity, 2011). It applies to commercial and non-commercial sectors and provides greater legal certainty regarding genetic resources. Users of genetic resources must receive prior informed consent from the country

where the genetic resource is found. The user and country of origin must negotiate and agree upon mutually agreed terms of access and use of the resource. The Nagoya Protocol establishes clear and non-arbitrary guidelines for how genetic resources can be used and ensures the equal distribution of benefits to the rightful parties. Including traditional knowledge, the Nagoya Protocol protects information and resources held by indigenous and local communities, preventing exploitation. However, the Nagoya Protocol only applies to material genetic resources, not digital resources, which are more prominent in genome technology and genome-editing (Nehring, 2022).

Given the changing landscape and technological advances, it is now possible to utilize sequence information (digital information, not specifically biological information) as a basis for making genetic modifications and improvements. For example, with genome editing technologies, it is possible that simply having the DNA sequence associated with a trait could allow the editing of genomes to achieve a specific breeding goal rather than relying on traditional breeding techniques that require biological material to achieve the same goal. There is disagreement over whether the existing agreements such as the Nagoya Protocol under the CBD cover digital sequence information (DSI). DSI data on the composition of genetic resources exists in databases, and these could be used by institutions or agencies that have no contractual relationship with the country of origin of the biological genetic resource from which the digital data were derived. Under this circumstance, it has been proposed that there is no legal requirement to acknowledge the benefit sharing with the country of origin – potentially putting LMICs at risk for exploitation, as these countries often lack access to technological resources to the extent high-income countries do. Proposals have been made to amend the Nagoya Protocol to include DSI in the agreement and thus increase the opportunity for benefit-sharing. The controversy over inclusion of DSI is ongoing, and there are sound legal arguments for both the inclusion and exclusion of DSI. A negotiated agreement will be required and any decisions made regarding DSI's inclusion or exclusion will have significant implications for the future of genome editing and how access and benefit sharing apply to DSI (Bond *et al.*, 2020).

Policy relating to genome editing of animals is complicated and ever-evolving. While some countries have developed protocols and regulations for genome editing, others are still in the development phase or currently have no regulations in place. Public perception plays a critical role in the development of policies and is influenced by many factors, including environmental, ethical, and social concerns. Confusion over terminology and the patent landscape also contribute to the perception of genome editing. Equitable access to and benefit sharing of genetic resources is crucial to safeguard against inequality, while not unduly impeding research and development. In addition to the CBD and Nagoya Protocol, decisions must be made regarding DSI to provide clarity on the future of genetic resources.

FUTURE CONSIDERATIONS FOR GENOME EDITING OF LIVESTOCK AND GENETIC DIVERSITY

Genome editing has the potential to favourably impact how future generations of livestock producers efficiently utilize natural resources, adapt to climate change and combat disease issues through innovative farming practices.

Researchers aim to develop livestock breeds with new traits. Many of the applications discussed herein are aimed toward intensive agricultural practices but have the potential, within the confines of an enabling context, including the policy environment, to be useful across many countries, regardless of income level.

The protection of agrobiodiversity is crucial and urgent, especially when considering the possible future effects of climate change. As previously discussed, disease is one of the largest contributors to the loss of farm incomes and can threaten entire populations of genetic resources. When looking further into the potential of genome editing, it is important to ask questions that advance our understanding of biological and metabolic pathways that influence livestock. For instance, can scientists contribute to building resistance to diseases like African Swine Fever and Avian influenza?

Answers to such questions require additional fundamental information regarding cellular and organismal responses to stress and disease.

On the other hand, the application of genome editing could lead to population genetic “bottlenecks,” when the genetic variation within a given gene is reduced during one or more generations of genome editing. Subsequently, the traits encoded by the underlying genetic alleles carried by the generations subject to editing will be replicated and inherited by the entire population. This decrease in population size can result in a loss of genetic variation due to random genetic drift. In the context of genome editing, this occurs when a newly introduced gene allele becomes more prominent in the genome, essentially phasing out the original version and thus decreasing the diversity of the organism's original DNA. However, this loss of variation is not limited to the edited gene. For economic and practical reasons, genome editing would presumably be done in a relatively small sample of animals within a given population, and then subsequent generations of conventional breeding and selection would be required to disseminate the edited gene throughout the population. If not managed very carefully, this process will result in a population of animals whose genomes are dominated by the genetic content of the small number of originally edited animals, resulting in the loss of many alleles from the large proportion of the population that was not subjected to genome editing. A general decrease in genetic variation can cause a decrease in ability to adapt to new selection pressures, like climate change, since many of the alleles that would facilitate climate adaptability would be lost through genetic drift.

Another important consideration for the future of animal genome editing is the feasibility of applying this technology to smaller populations and local breeds. In addition to the challenges posed by bottlenecks, there is the issue of whether or not all livestock-keeping communities will embrace these technologies. Cultural perspectives will play an important role in the adoption of genome editing. The deeply rooted ethical values and concerns of biotechnology on animal welfare, breed preservation, and ethical considerations of many communities determine policy and consumerism. (Hudson *et al.*, 2019).

Economic factors will also play a major role in selecting agricultural breeds for genome editing. These technologies are being developed for application to transboundary commercial breeds and thus benefit intensive production systems. Applying these technologies to native and local breeds will be more difficult. Undertaking genome editing requires extensive research, from identifying interesting alleles, to perfecting the advanced reproductive biotechnologies to make the editing and dissemination process as efficient as possible. According to Menchaca *et al.* (2020), “Once presumptive genome-edited animals are born, an exhaustive genotypic analysis in addition to the phenotypic one is necessary” to determine if the edit was successful. For LMICs, this intensive analysis may not be possible for their native breeds, making subsequent dissemination difficult. The large size and economic interests of producers using commercial transboundary breeds mean that more funding is available for research and development of these populations. This provides more opportunities to efficiently and effectively exploit novel and expensive technologies such as genome editing, on these breeds. Another concern for local breeds in LMICs is that even if an initial generation of genome-edited animals can be made available, disseminating the genome edit through relevant breeds and lines will likely be costly and laborious. Propagating the edited allele throughout a population will require infrastructure including facilities for applying reproductive technologies such as artificial insemination and embryo transfer, genotyping to track the transmission of the edited allele, and data recording to allow selection for a comprehensive selection goal, not simply the presence of the new gene. The absence of proper infrastructure and resources is one reason for the current livestock production and efficiency gaps between high- and low-income countries, ultimately emphasizing its potential advantages if adapted by local breeds in LMICs.

OUTLOOK AND CONCLUSION

Genome editing in animals is evolving quickly, and in the near future, some of the biggest challenges will be social and political. Currently, some LMICs are developing policies and legislation around genome editing; this process takes time and mindful deliberation. These policies will be formed

around public perception, which will continue to evolve as more genome edits occur in animals, although following different cultural and social considerations. Climate change requires more robust livestock carrying disease-resistance and heat tolerance traits to maintain efficiency. Genome editing has the potential to aid producers in LMICs in combating the effects of climate change on their livestock. However, this depends on equitable policy formulation, addressing technical barriers like population bottlenecks, maintaining existing biodiversity, and ensuring the providing of balanced information to producers and consumers.

REFERENCES

- Boettcher, P., Baumung, R., Leroy, G., & Besbes, B.** 2023. The role of animal genetic resources in the sustainable livestock transformation. *Proceedings of the Association for the Advancement of Animal Breeding and Genetics*, 25:1-4.
<https://www.cabidigitallibrary.org/doi/pdf/10.5555/20230390453>
- Bond, M.R. and Scott, D.** 2020. Digital biopiracy and the (dis)assembling of the Nagoya Protocol. *Geoforum*, 117. <https://doi.org/10.1016/j.geoforum.2020.09.001>
- Brown-Brandl, T.M.; Nienaber, J.A.; Eigenberg, R.A.; Mader, T.L.; Morrow, J.L.; Dailey, J.W.** 2006. Comparison of heat tolerance of feedlot heifers of different breeds. *Livestock Science*, 105: 19–26. <https://doi.org/10.1016/j.livsci.2006.04.01>
- Burkard, C., Opriessnig, T., Mileham, A.J., Stadejek, T., Ait-Ali, T., Lillico, S.G., Whitelaw, C.B. A. and Archibald, A.L.** 2018. Pigs lacking the scavenger receptor cysteine-rich domain 5 of CD163 are resistant to porcine reproductive and respiratory syndrome virus 1 infection. *Journal of Virology*, 92(16). <https://doi.org/10.1128/jvi.00415-18>
- Collier R.J. and Gebremedhin K.G.** 2015. Thermal biology of domestic animals. *Annu Rev Anim Biosci.* 3:513-32. <https://doi.org/0.1146/annurev-animal-022114-110659>
- Craven, A.J., Nixon, A.J., Ashby, M.G., Ormandy, C.J., Blazek, K., Wilkins, R.J. and Pearson, A.J.** 2006. Prolactin delays hair regrowth in mice. *J Endocrinol.* 191(2):415-25.
<http://doi.org/10.1677/joe.1.06685>
- Cui, C., Song, Y., Liu, J. et al.** 2015. Gene targeting by TALEN-induced homologous recombination in goats directs production of β -lactoglobulin-free, high-human lactoferrin milk. *Sci Rep* 5, 10482.
<https://doi.org/10.1038/srep10482>
- Dace, H.** 2021. *Gene Editing in Food Production: Charting a Way Forward*. [Accessed 18 May 2023]
<https://www.institute.global/insights/tech-and-digitalisation/gene-editing-food-production-charting-way-forward#an-introduction-to-gene-editing>
- Das, R. , Sailo, L., Verma, N., Bharti, P., Saikia, J., Imtiwati, & Kumar R.** 2016. Impact of heat stress on health and performance of dairy animals: A review. *Veterinary World*, 9(3): 260-268.
<https://doi.org/10.14202/vetworld.2016.260-268>
- Dikmen, S., Khan, F. A., Huson, H.J., Sonstegard, T.S., Moss, J.I., Dahl, G.E. and Hansen, P.J.** 2014. The SLICK hair locus derived from Senepol cattle confers thermotolerance to intensively managed lactating Holstein cows. *Journal of Dairy Science*, 97(9), 5508–5520.
<https://doi.org/10.3168/jds.2014-8087>
- Ding, Y., Yu, J., Sun, Y., Nayga, R. M. and Liu, Y.** 2023. Gene-edited or genetically modified food? The impacts of risk and ambiguity on Chinese consumers' willingness to pay. *Agricultural Economics*.
<https://doi.org/10.1111/agec.12767>

FAO. 2023. *Gene editing and food safety – Technical considerations and potential relevance to the work of Codex Alimentarius*. <https://doi.org/10.4060/cc5136en>

Friedrichs, S., Takasu, Y., Kearns, P., Dagallier, B., Oshima, R., Schofield, J. and Moreddu, C. 2019. An overview of regulatory approaches to genome editing in agriculture. *Biotechnology Research and Innovation*, 3(2), 208–220. <https://doi.org/10.1016/j.biori.2019.07.001>

Genetic Literacy Project. 2023. *Where are GMO crops and animals approved and banned?* Genetic Literacy Project. <https://geneticliteracyproject.org/gmo-faq/where-are-gmo-crops-and-animals-approved-and-banned/>

Hamm, D. and Welham, M. 2022. *Public dialogue on genome editing in farmed animals*. <https://www.nuffieldbioethics.org/assets/images/Nuffield-BBSRC-Sciencewise-dialogue-topic-guides-Oct2022.pdf>

Hansen, P.J. 2020. Prospects for gene introgression or gene editing as a strategy for reduction of the impact of heat stress on production and reproduction in cattle. *Theriogenology*, 154:190–202. <https://doi.org/10.1016/j.theriogenology.2020.05.010>

Hudson, M., Mead, A.T.P., Chagné, D., Roskrige, N., Morrison, S., Wilcox, P.L. and Allan, A. C. 2019. Indigenous perspectives and gene editing in Aotearoa, New Zealand. *Frontiers in Bioengineering and Biotechnology*, 7. <https://doi.org/10.3389/fbioe.2019.00070>

Innovative Genomics Institute (IGI). 2022. *CRISPR in Agriculture*. <https://innovativegenomics.org/crisprpedia/crispr-in-agriculture/>

Karavolias, N.G., Horner, W., Abugu, M.N. and Evanega, S.N. 2021. Application of Gene Editing for Climate Change in Agriculture. *Frontiers in Sustainable Food Systems*, 5. <https://doi.org/10.3389/fsufs.2021.685801>

Kristiansen, M., Graversen, J.H., Jacobsen, C., Sonne, O., Hoffman, H.J., Law, S.K. and Moestrup, S.K. 2001. Identification of the hemoglobin scavenger receptor. *Nature*. 409: 198–201. <https://doi.org/10.1038/35051594>

Laaninen, T. 2021. *New genomic techniques: European Commission study and first reactions*. European Parliament. [https://www.europarl.europa.eu/RegData/etudes/BRIE/2021/698760/EPRS_BRI\(2021\)698760_EN.pdf](https://www.europarl.europa.eu/RegData/etudes/BRIE/2021/698760/EPRS_BRI(2021)698760_EN.pdf)

Ledesma A.V. and Van Eenennaam, A.L. 2024. Global status of gene edited animals for agricultural applications. *The Veterinary Journal*, 305:106142. <https://doi.org/10.1016/j.tvjl.2024.106142>

Littlejohn, M.D., Henty, K.M., Tiplady, K., Johnson, T., Harland, C., Lopdell, T., Sherlock, R.G., Li, W., Lukefahr, S.D., Shanks, B.C., Garrick, D.J., Snell, R.G., Spelman, R.J. and Davis, S. R. 2014. Functionally reciprocal mutations of the prolactin signaling pathway define hairy and slick cattle. *Nature Communications*, 5(1). <https://doi.org/10.1038/ncomms6861>

Marette, S., Disdier, A.-C., and Beghin, J. C. 2021. A comparison of EU and US consumers' willingness to pay for gene-edited food: Evidence from apples. *Appetite*, 159, 105064. <https://doi.org/10.1016/j.appet.2020.105064>

Menchaca, A., dos Santos-Neto, P.C., Mulet, A.P. and Crispo, M. 2020. CRISPR in livestock: From editing to printing. *Theriogenology*, 150, 247–254. <https://doi.org/10.1016/j.theriogenology.2020.01.063>

- Moestrup, S.K. and Møller H.J.** 2004. CD163: a regulated hemoglobin scavenger receptor with a role in the anti-inflammatory response. *Annals of Medicine*, 36(5):347-354. <https://doi.org/10.1080/07853890410033171>
- Montaner-Tarbes, S., del Portillo, H.A., Montoya, M. and Fraile, L.** 2019. Key gaps in the knowledge of the porcine respiratory reproductive syndrome virus (PRRSV). *Frontiers in Veterinary Science*, 6. <https://doi.org/10.3389/fvets.2019.00038>
- Naab, F.Z., Coles, D., Goddard, E. and Frewer, L.J.** 2021. Public perceptions regarding genomic technologies applied to breeding farm animals: A qualitative study. *BioTech*, 10(4), 28. <https://doi.org/10.3390/biotech10040028>
- Nehring, R.** 2022. Digitising biopiracy? The global governance of plant genetic resources in the age of digital sequencing information. *Third World Quarterly*, 43(8), 1970–1987. <https://doi.org/10.1080/01436597.2022.2079489>
- Oligonucleotide Therapeutics Society.** 2023. *Innovation, Versatile Gene Editing Technologies, and Patent Battles*. <https://www.oligotherapeutics.org/innovation-versatile-gene-editing-technologies-and-patent-battles/>
- Oluwakemi, H.O., Rauf, R.I., Seyi, E.A., and Harry, K.** 2020. Readiness of the Nigerian public for the introduction of genetically modified crops into the food market. *African Journal of Biotechnology*, 19(7), 426–438. <https://doi.org/10.5897/ajb2020.17136>
- Pixley, K.V., Falck-Zepeda, J.B., Paarlberg, R. L., Phillips, P.W.B., Slamet-Loedin, I.H., Dhugga, K. S., Campos, H. and Gutterson, N.** 2022. Genome-edited crops for improved food security of smallholder farmers. *Nature Genetics*. <https://doi.org/10.1038/s41588-022-01046-7>
- Rasmussen, P., Barkema, H.W., Mason, S., Beaulieu, E., and Hall, D. C.** 2021. Economic losses due to Johne's disease (paratuberculosis) in dairy cattle. *Journal of Dairy Science*, 104(3), 3123–3143. <https://doi.org/10.3168/jds.2020-19381>
- Rojas-Downing, M.M., Nejadhashemi, A.P., Harrigan, T., and Woznicki, S.A.** 2017. Climate change and livestock: Impacts, adaptation, and mitigation. *Climate Risk Management*, 16(16), 145–163. <https://doi.org/10.1016/j.crm.2017.02.001>
- Scheinerman, N., and Sherkow, J.S.** 2021. Governance choices of genome editing patents. *Frontiers in Political Science*, 3. <https://doi.org/10.3389/fpos.2021.745898>
- Schmidt, S.M., Belisle, M., and Frommer, W.B.** 2020. The evolving landscape around genome editing in agriculture. *EMBO Reports*, 21(6). <https://doi.org/10.15252/embr.202050680>
- Secretariat of the Convention on Biological Diversity.** 2011. *The Nagoya Protocol on Access and Benefit-sharing: What is the Nagoya Protocol?* Secretariat of the Convention on Biological Diversity. <https://www.cbd.int/abs/infokit/revise/web/factsheet-nagoya-en.pdf>
- Shelton, A.M., Hossain, M.J., Paranjape, V., Azad, A.K., Rahman, M.L., Khan, A.S.M.M. R., Prodhan, M.Z.H., Rashid, M.A., Majumder, R., Hossain, M.A., Hussain, S.S., Huesing, J.E., and McCandless, L.** 2018. Bt Eggplant Project in Bangladesh: History, Present Status, and Future Direction. *Frontiers in Bioengineering and Biotechnology*, 6. <https://doi.org/10.3389/fbioe.2018.00106>
- Söllner, J.H., Mettenleiter, T.C., and Petersen, B.** 2021. Genome editing strategies to protect livestock from viral infections. *Viruses*, 13(10), 1996. <https://doi.org/10.3390/v13101996>

- Tait-Burkard, C., Doeschl-Wilson, A., McGrew, M.J., Archibald, A.L., Sang, H.M., Houston, R.D., Whitelaw, C.B. & Watson, M.** 2018. Livestock 2.0 – genome editing for fitter, healthier, and more productive farmed animals. *Genome Biology*, 19(1). <https://doi.org/10.1186/s13059-018-1583-1>
- Ufer, D., Ortega, D.L., Wolf, C.A., McKendree, M. & Swanson, J.M.** 2022. Getting past the gatekeeper: Key motivations of dairy farmer intent to adopt animal health and welfare-improving biotechnology. *Food Policy*, 112, 102358–102358. <https://doi.org/10.1016/j.foodpol.2022.102358>
- University of California Berkley.** (n.d.). *Bottlenecks and founder effects*. Evolution.berkeley.edu. [Accessed 5 June 2023] from <https://evolution.berkeley.edu/bottlenecks-and-founder-effects/>
- USDA APHIS.** 2013. *USDA APHIS | Johne's Disease*. Usda.gov. <https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/nvap/NVAP-Reference-Guide/Control-and-Eradication/Johnes-Disease>
- Van Breedam, W., Delputte, P.L., Van Gorp, H., Misinzo, G., Vanderheijden, N., Duan, X. & Nauwynck, H.J.** 2010. Porcine reproductive and respiratory syndrome virus entry into the porcine macrophage. *Journal of General Virology*, 91(Pt 7):1659-67. <https://doi.org/10.1099/vir.0.020503-0>. Epub 2010 Apr 21. PMID: 20410315.
- Van Eenennaam, A.L. and Young, A.E.** 2018. Gene editing in livestock: promise, prospects and policy. *CAB Reviews: Perspectives in Agriculture, Veterinary Science, Nutrition and Natural Resources*, 13(027). <https://doi.org/10.1079/pavsnmr201813027>
- Wang, S., Qu, Z., Huang, Q., Zhang, J., Lin, S., Yang, Y., Meng, F., Li, J. and Zhang, K.** 2022. Application of gene editing technology in resistance breeding of livestock. *Life*, 12(7), 1070. <https://doi.org/10.3390/life12071070>
- Whitworth, K.M., Green, J.A., Redel, B.K., Geisert, R.D., Lee, K., Telugu, B.P., Wells, K.D. and Prather, R.S.** 2022. Improvements in pig agriculture through gene editing. *CABI Agriculture and Bioscience*, 3(1). <https://doi.org/10.1186/s43170-022-00111-9>
- Whitworth, K.M., Rowland, R.R.R., Ewen, C.L., Tribble, B.R., Kerrigan, M.A., Cino-Ozuna, A.G., Samuel, M.S., Lightner, J.E., McLaren, D.G., Mileham, A.J., Wells, K.D. and Prather, R.S.** 2016. Gene-edited pigs are protected from porcine reproductive and respiratory syndrome virus. *Nature Biotechnology*, 34(1), 20–22. <https://doi.org/10.1038/nbt.3434>
- WOAH - World Organisation for Animal Health.** 2023. *African swine fever (ASF) – Situation report 32*. (n.d.). Retrieved June 7, 2023, from <https://www.woah.org/en/document/african-swine-fever-asf-situation-report-32/>
- World Bank.** 2022. *New World Bank country classifications by income level: 2022-2023*. Blogs.worldbank.org. <https://blogs.worldbank.org/opendata/new-world-bank-country-classifications-income-level-2022-2023>
- Xu, H., Liu, Z., Zheng, S., Han, G., and He, F.** 2020. CD163 Antibodies inhibit PRRSV infection via receptor blocking and transcription suppression. *Vaccines*, 8(4), 592. <https://doi.org/10.3390/vaccines8040592>
- Yang, D., Yang, H., and Li, W. et al.** 2011. Generation of PPAR γ monoallelic knockout pigs via zinc-finger nucleases and nuclear transfer cloning. *Cell Res*, 21: 979–82. <https://doi.org/10.1038/cr.2011.70>

Yeadon, J. 2014. *Pros and cons of ZNFs, TALENs, and CRISPR/Cas*. The Jackson Laboratory. <https://www.jax.org/news-and-insights/jax-blog/2014/march/pros-and-cons-of-znfs-talens-and-crispr-cas>

You, S., Liu, T., Zhang, M. et al. 2021. African swine fever outbreaks in China led to gross domestic product and economic losses. *Nature Food* 2, 802–808. <https://doi.org/10.1038/s43016-021-00362-1>

Zhang, Q., and Yoo, D. 2015. PRRS virus receptors and their role for pathogenesis. *Veterinary Microbiology*, 177(3-4), 229–241. <https://doi.org/10.1016/j.vetmic.2015.04.002>