BVA British Veterinary Association | Policy statement

BVA Policy Position on Gene Editing of Animals

1. Introduction

The passing of the Genetic Technology (Precision Breeding) Act 2023 ('The Precision Breeding Act')[1] was the first step in UK law towards allowing the use of genetic technology in commercial agriculture. The UK Precision Breeding Act applies to both plants and animals. It applies only to England. The devolved nations continue to outlaw all forms of genetic modification.

The Precision Breeding Act permits the genetic editing of all organisms in the taxonomic group Metazoa, other than a human (or a human admixed embryo). Funding and demand for research and development is likely to come initially from large-scale commercial agriculture, with a focus on production animals. In planning the regulatory framework to support the Precision Breeding Act, DEFRA are focussing initially on pigs, poultry and salmon as the priority species. Until the secondary legislation has been passed and that regulatory framework is in place, gene edited animals should not be found in England outside a laboratory environment regulated under the Animals (Scientific Procedures) Act (1986, as amended) (A(SP)A)[2].

This BVA policy focuses on gene editing of animals. It is already legal to import animal feed containing crops that have been gene edited from countries where this is permitted, and the only change brought about by the Precision Breeding Act is that such feed could now be manufactured domestically.

BVA's Gene Editing Working Group looked at the potential uses for the gene editing technology which will be permitted by the Precision Breeding Act, and whether or not such uses are ethically justifiable given their potential animal health and welfare impacts. Food labelling and consumer choice were considered beyond the remit of this position. Potential uses for gene editing include improving resistance to disease, curing congenital conditions, changing the physiology or appearance of an animal, improving productivity, and adapting an animal to thrive in different conditions.

2. What is Gene Editing: Definitions

For the purposes of this policy position, terms are defined as follows.

- Gene editing is changing an organism's DNA by making alterations to its genetic code.
- Genetic modification is the process of changing the DNA of an organism by introducing elements of exogenous DNA from a different organism or artificial sequence.
- Selective breeding is the strengthening of specific characteristics through sexual or asexual reproduction.

This is in line with the wording of the Precision Breeding Act. However, it should be noted that, from a technical perspective, there is little or no distinction between gene editing and genetic modification. That said, the Precision Breeding Act only allows gene editing which does not

[1] The Genetic Technology (Precision Breeding) Act 2023: https://bills.parliament.uk/bills/3167/publications

[2] The Animals (Scientific Procedures) Act (1986, as amended): https://assets.publishing.service.gov.uk/media/5a82438440f0b6230269bb57/ConsolidatedASPA1Jan2013.pdf

introduce DNA from another organism, and which makes a change that could theoretically have occurred through traditional selective breeding.

Advocates for gene edit note that selective breeding for a desired trait can result in the loss of other desirable traits which take many generations to recover, whereas gene editing allows the swift removal of undesirable material without removing nearby genetically linked material[3].

Most of the changes introduced with gene editing are limited to somatic cells, which are cells other than egg and sperm cells (germline cells). These changes are isolated to only certain tissues and are not passed from one generation to the next. However, changes made to genes in egg or sperm cells or to the genes of an embryo could be passed to future generations[4]. Although heritable changes are less common, this position considers multiple generations in all cases, as this then covers both changes to individual animals and changes to the germline.

3. Risks of Gene Editing

Off target side effects and failed experiments. Any genetic experiment is likely to result in multiple failed experiments, some of which may impact live animals, whose welfare needs must be safeguarded. Even partially successful attempts risk off-target side effects, such as more rapid growth, increased risk of splayed legs, or limb deformities, which will need to be treated to safeguard the animal. In the experimental stages, animals on whom gene editing is being undertaken are safeguarded in the UK by A(SP)A. Once permission is given under the Precision Breeding Act for animals to move from an experimental setting to a commercial setting their welfare should be safeguarded by the Animal Welfare Act (2006) and by the Precision Breeding Act and associated secondary legislation. That secondary legislation has yet to be proposed/enacted. Ensuring that genetically edited animals remain fully traceable within commercial settings, and that a robust, centralised and mandatory mechanism for reporting on their health and welfare is established and independently run, is a necessary prerequisite for the ethical use of genetically edited animals.

Reduced standards. There is a concern that developing more resilient animals will lead to reduced focus on animal health and welfare practices. For example, if a strain is created that is resistant to a highly contagious disease, some may see the reduced risk of infection as an opportunity to increase stocking densities or relax biosecurity precautions.

Homogeneity and limited gene pool There is a risk that a strain with a desirable trait (such as a flu-resistant hen) will come to predominate in the commercial sphere to the exclusion of other breeds. The consequence of this could be that development of vaccines and treatments for that disease will attract significantly reduced funding, limiting options for treating other breeds. With the example of avian influenza, this would affect our ability to control the spread of the disease in rare breeds, backyard flocks, and wildfowl.

There is also a resultant reduction in genetic diversity if the vast majority of a breed comes to be descended from the same limited breeding stock. This will have a particularly serious impact in breeds with an already small genetic pool. Lack of genetic diversity can itself have negative impacts on health and welfare and, once lost, it is impossible to recover unless preserved in a gene bank.

Future generations Health and welfare is not only a concern for the animal that has itself been gene edited. Where a trait can be passed down to future generations, this progeny also needs to be monitored for adverse impacts that may not be apparent in the original animal. Legislation needs to clarify for how many generations an animal should be considered gene edited, and welfare reporting should continue. This will not be the same for all species due to the variation in reproduction rates – five generations of prawns could take place in matter of months and give insufficient time for assessment, whereas five generations of cattle would be a much longer time period – perhaps excessive for a monitoring purposes.

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[3] UK Parliament Brief: Genome Edited Animals, 1.4 Pg 14

[4] Definition from the US National Library of medicine: What are Genome Editing and CRISPR-Cas9?

4. Potential uses of Gene Editing: Opportunities.

Gene editing has the potential both to improve animal health and welfare, if the potential deleterious effects (intended or unintended) can be successfully mitigated. As with any selective breeding, there are also commercial uses to which is could be put, but the ethics of these would need to be carefully considered.

Disease eradication. It may be possible to isolate a gene sequence that confers increased resistance to infectious diseases, for example avian influenza or indeed Bovine Tuberculosis. Pigs are being developed in the US that are resistant to Porcine Reproductive and Respiratory Syndrome (PRRS), through the removal of a section of a gene responsible for making a protein that enables the virus to enter the pig's cells[5]. Such increased resistance would be economically advantageous for industry, and would have health and welfare benefits for the livestock. Generally, increased disease resistance in non-human animals has the potential to have positive effects on One Health and One Welfare. For example, genetically editing cattle to be resistance to trypanosomiasis carried by the Tsetse fly has the potential to improve not only the health and welfare of cattle but also the wellbeing of the humans who are dependent upon those cattle. Genetic editing to increase resistance to disease could reduce the use of medicines and, in some cases, help in tackling antimicrobial and anthelmintic resistance (which has knock-on benefits for sustainability). However, it will be necessary to ensure that increased disease resistance doesn't lead to a lowering of welfare standards, as noted above. There is also at least a theoretical risk that genetic editing for increased disease resistance increases selection pressure for pathogens to mutate to avoid the genetic edit and thus become harder to treat when they do cause disease - which could of course also be zoonotic. This would apply equally to non-genetic treatmenhts, but the speed and scale of the change potentially amplifies the impact.

Congenital conditions. Gene editing could present a method of breeding out, or treating, common deleterious conditions - for example deafness in Dalmatians - which are difficult to eradicate through traditional selective breeding methods. Such eradication could improve the health and welfare of animals although it could be argued whether the negative impact of, for example, deafness, is sufficient to justify the risks.. However, caution is needed when using genetic editing for breeds which are already small in numbers to avoid reducing an already small gene pool and therefore genetic diversity, which could in itself have negative health welfare consequences.

Increased productivity It is likely that there will be a commercial imperative to use gene editing to improve productivity, as has been the case with non-genetic selective breeding. Gene editing offers a means of improving production traits more quickly and more accurately than traditional selective breeding methods. However, the relative speed of the change could make it more difficult to mitigate unintended consequences. Any changes made using gene editing should be stable and should not have an adverse impact on animal health or welfare or human or environmental health. For example, improving the productivity of a dairy cow by increasing longevity, and therefore the number of lactations, could be preferable to improving productivity through increased milk yield per lactation. Environmentally, keeping the same cow in production for longer is significantly more sustainable as it reduces the overheads associated with disposal and the inputs needed for raising additional numbers of replacement heifers.[6]

Altered physiology. Gene editing could be used to alter the appearance or physiology of an animal. There are cases where such changes could have the potential to improve animal welfare. A strain of hornless cattle has been developed, which many would welcome as it

[5] UK Parliamentary Brief op cit pg 27

[6] Grandl, F., Furger, M., Kreuzer, M., & Zehetmeier, M. (2019). Impact of longevity on greenhouse gas emissions and profitability of individual dairy cows analysed with different system boundaries. *Animal*, *13*(1), 198-208.

avoids the risk of injury to animals and humans, and the alternative pain of de-horning or disbudding. Indeed, BVA's position[7] already recommends selection of polled sires for this reason. Furthermore, gene editing could be used more efficiently than conventional selective breeding methods to start to correct extreme conformation in companion animals, for example in the brachycephalic breeds, and in production animals, such as fast-growing broiler chickens. However, many health issues are multifactorial and polygenetic and may not therefore be amenable to full correction using gene editing.

Gene editing could however also be used to alter the appearance or physiology of an animal not to improve animal welfare, but to satisfy human aesthetic demands – for example to produce a particular colour of coat. While there are instances where gene editing for colour could be justifiable on health and welfare grounds, for example selecting for darker-eyed cattle to reduce the risk of SCCS associated with white eyes, use of gene editing for aesthetics alone confers no health or welfare advantage on animals. In a utilitarian analysis, given the potential harms associated with gene editing (for example unpredictable off-target effects), such uses would not be ethically justifiable.

There are also cases where the argument is less clearcut. For example, genetic edits could be made in a racehorse that increase skeletal density, reducing the risk of fractures. This would have a demonstrable benefit to welfare, but many might argue that it would be more responsible to focus on other measures that are already being undertaken such as the structure of courses, or the number of runners amongst other. Some in the industry may also have concerns that such a genetic change would confer a competitive advantage, giving a financial motivation aside from any welfare benefit.

These more borderline/complex examples perhaps need to be decided case by case, but the fundamental principle of any licensed gene edit is that there should be a demonstrable benefit to health and welfare that would be sufficient to outweigh any adverse impact or unforeseen risks of the process. This should be one of the roles of the review body that Defra intends to set up to consider applications for market authorisations.

Gene editing should not be used in an attempt to compensate for poor management practices. The risk of disease resistance leading to increased stocking densities has been noted above. There is also the potential to select sheep with shorter tails. While this could avoid the need for docking, there are now less invasive ways to reduce the risk of flystrike, without interfering with the animal's natural use of its tail.

Adaptation to changing environment Some researchers are suggesting that gene editing could be used to alter existing breeds to better adapt to the changing climate. Work is ongoing in the US to breed cattle with shorter, thinner coats, resulting in greater heat tolerance and therefore greater milk production at higher temperatures. However, given the potential risks associated with gene editing, there is also the option to move to breeds which are already adapted to hotter conditions, or to revert to tougher older breeds which are less sensitive to changing conditions. This would however, have an impact on economic viability and environmental sustainability as such breeds are generally less productive, and are also drawing on a narrower gene pool with the risks outlined earlier.

5. Regulation

There are legislative matters surrounding the use of genetic editing which are of importance to animal health and welfare but which are not risks arising from the use of gene editing

[7] BVA Policy Position on Analgesia in Calves: https://www.bva.co.uk/media/1172/analgesia-in-calves.pdf

technology itself. These should be prioritised in BVA's discussions and lobbying efforts as the regulatory framework is developed -see conclusions and recommendations below.

Devolved nations and cross border issues. As the Precision Breeding Act applies only to England, there are clear issues to be tackled with the governments of the devolved nations around the labelling and identifying of gene edited food products. It is essential that there is an efficient and effective mechanism in place to ensure ongoing co-operation and collaboration across the UK. Such a mechanism must ensure a degree of parity so as not to disadvantage producers in any particular region at any given time, yet allow sufficient flexibility to progress animal health and welfare, and food safety, and avoid stifling or slowing progress by a requirement to avoid divergence. There are currently no guidelines for farmers, vets, and hauliers on the movement of animals across borders. For those farming near the border, their holding may fall under two jurisdictions, or the nearest market or abattoir may be in Wales or Scotland. There will therefore need to be a pragmatic solution for cross-border holdings that does not unnecessarily complicate grazing patterns or animal movements. Beyond the remit of BVA, but there may also be an issue for supermarkets and wholesalers around the distribution of food products across the UK. There is currently no indication from the government about labelling of genetically edited animal produce to facilitate informed consumer choice.

Traceability. There is no way, within the terms of the Precision Breeding Act, to put a genetic marker on a gene edited animal as this would involve introducing exogenous DNA. While BVA notes that Defra and FSA are confident that existing tracing systems will suffice for tracking gene edited animals and carcases, this remains to be tested. Although traceability for commercial livestock is better established and more stringent than for companion animals and equines, there is currently no legislative provision for tracing the progeny of such gene edited animals. There also needs to be agreement on how many generations will require to be so traced (this may differ between species), and whether animals arising from cross-breeding with gene-edited animals will be traced. All such detail will be essential for reporting health and welfare impacts throughout the life of the animals and, if appropriate, their progeny.

Imports from lower welfare systems. There is a risk that animals which have undergone gene editing outside the UK, under less stringent legislative and regulatory regimes with lower standards of animal welfare protection will be imported into the UK. Defra has said that the same criteria will apply for marketing authorisations whether an animal is bred in the UK or abroad, but it is unclear how genetically edited animals would be identified and stopped at the border, and there is some anecdotal concern amongst stakeholders that such animals may already be entering the UK. There is currently also no system for identifying and tracing imported genetically edited animals, who could potentially go into commercial setting and be used for cross-breeding with non-genetically edited animals, thus creating offspring whose health and welfare would not fall withing any system of mandatory monitoring and reporting.

Oversight Defra intends to create a welfare advisory body to review marketing authorisations and oversee post-market health and welfare reporting. No assurances have yet been given that body needs will include veterinary expertise or have the powers necessary to enforce standards and to deal appropriately with any adverse welfare reports post-market.

6. Conclusion and Recommendations

Gene editing has the potential to be a very useful tool in improving animal health and welfare through tackling susceptibility to disease, hereditary conditions, and poor conformation. However, it is only one tool, and should not be the default or first resort mechanism for dealing with any of these issues. Gene editing will remain expensive and experimental for some years to come, and as with any new technology, may carry unforeseen and potentially large risks, which we cannot yet clearly mitigate.

The government has the opportunity, when legislating in a new area, to ensure that this technology is used responsibly and where it can have the most positive effects on animal and

human health and welfare and on sustainability. Over the coming years, BVA will need to work closely with Defra, Parliament and other partners to shape the legislation accordingly.

The fundamental principles which should govern the use of gene editing in non-human animals are:

- That any gene edit should have a demonstrable health or welfare benefit to the animal being edited, and/or its progeny, where the trait is heritable.
- That gene editing should not be used to compensate for poor management or reduced welfare standards.

On considering the above points, the working group reviewed what BVA should want to see in the legislative framework to protect animal health and welfare and give clarity to vets and owners as to the breeding and management of gene edited animals. The working group concluded that the ideal regulatory framework should:

1. Ensure that he impact on animal welfare of any gene editing should be comparable or better than current high-welfare methods of production.
2. Insist gene editing should only be licensed where it results in a positive health or welfare benefit to the animal; or has a neutral impact on the animal and potentially a positive One Health benefit. Gene editing should not be used to alter an animal's appearance for aesthetic reasons or to facilitate poor management practices.
3. Prevent gene editing being licensed where the primary aim is to improve the performance of an animal athlete to achieve sporting success.
4. Recommend that licensing of gene editing aimed at preventing or reducing disease through reduced susceptibility, is considered in the context of welfare impacts on other breeds, the need to maintain genetic diversity, the danger of provoking mutations, and to the availability of vaccines and medicines.
5. Ensure that applications for a market authorisation include an assessment of impacts on biodiversity, the environment, and the ecosystem. Any efficiency gains should not outweigh environmental considerations.
6. Clarify at which stage (e.g. experimental; nucleus herd; commercial) animals pass from the protection of the A(SP)A to being regulated under the Precision Breeding Act.
7. Design and implement animal welfare assessment protocols for all genetically edited animals which include a statutory requirement for vets, owner, and responsible abattoir staff to report impacts to an independent authority for analysis. That authority should include veterinary expertise.
8. Create clear mechanisms for tracing genetically edited animals over prolonged periods of time or multiple generations, both those imported from overseas, and movements within the UK, where the Precision Breeding Act relates only to England.
9. Ban the import of genetically edited animals or their offspring from countries where legislation around gene editing of animals requires lower welfare standards than the A(SP)A and the Precision Breeding Act.
10. Establishment of a gene bank to allow the unpicking of edits should side effects develop over time.