Nuffield Council on Bioethics
Call for Evidence on the Use of Genome Editing in Farmed Animals

Responses submitted by Beyond GM
September 20, 2019

Summary

- Our response to this call for evidence is based substantially on a synthesis of views expressed at a recent roundtable convened by our organisation (in partnership with Compassion in World Farming) in June 2019. This roundtable included individuals representing a wide range of perspectives on this issue. These views were summed up in our report *Gene-edited Animals in Agriculture*, which we believe represents one of the most current exchanges of views on the subject.
- There is inevitably crossover between the subject headers being polled here. It is especially important for everyone – the research establishment, regulators, NGOs etc – to understand that how, and why, gene editing (GE) is advancing is often linked to other areas of inquiry such as ethics, socioeconomic impact and regulation.
- As an organisation we are concerned with the speed of development in this field, and the much publicised (though theoretical) 'no limits' narrative that lies behind its application. In the rush to bring the first commercialised GE animals to market we believe that robust efforts to ensure the welfare of the animals and the safety of the product intended for the food chain, and to understand and mitigate negative environmental impacts, are not being consistently made by developers. This puts extra pressure on regulatory authorities either to find ways to 'put the brakes on' or to follow the path of least resistance and acquiesce to deregulation. Responsible regulation is a middle ground between these two extremes.
- Much of the new research in this field is aimed at addressing health deficits in farmed animals – and in particular those that are reared in intensive, industrial systems. The question arises whether these health deficits are primarily the result of a genetic 'glitch' in the animal or whether they arise due to the system in which the animal is reared and can, therefore, be addressed in other effective ways.
- There are calls to remove regulatory bottlenecks that might prevent commercialising GE animals. It is worth noting, however, that although there has been much fanfare around the development of GE animals, no actual GE farm animals have been developed and/or commercialised in the UK or in the rest of the EU. This means much of this discussion remains in the realm of the theoretical and academic.
- The potential speed with which such animals can be brought to market may be limited less by the technology itself than by the consequences of that technology (i.e. unanticipated adverse effects, increasingly complex regulation) as well as by resistance from the public, civil society and, in some cases, farmers and breeders.

- In the main, animals developed using GE are intended for intensive industrial farming systems. There is a large body of opinion suggesting that whichever yardstick is used – welfare, sustainability, environment, nutrition etc – this type of farming system is damaging and outdated.
- The issue of gene edited farm animals has touchpoints with other types of animals (and insects) that are considered future candidates for gene editing. We would urge you not to look at the issue of genome-edited farm animals in isolation but in the context of the bigger horizon of genome editing events which are being proposed in order to 'fix' the natural world.

1. Current research

What kinds of innovation does genome editing make possible (or practical) that selective breeding or transgenic modification techniques do not?

1.1 Gene editing has been proposed as a way of meeting a variety of needs within the livestock sector such as protecting animals from disease, e.g. PRRS (Porcine Reproductive and Respiratory Syndrome) and ASFv (African Swine Fever) and, in farmed salmon, ISA (Infectious Salmon Anaemia, or 'salmon flu') by altering their immune response; creating animals with desirable commercial attributes such as producing more muscle mass (meat) while consuming less feed; and adapting animals to their environments, such as cattle with 'slick' coats that protect them from extreme heat.

1.2 These problems are real, but many of them are also 'man-made' – a consequence of the conditions in which the animals are raised and the spread of industrial livestock farming into geographical areas (e.g. tropical climates) not well suited to this endeavour. We are not aware of any 'modification' that can be made with gene editing that can't be made through a combination of selective breeding and good animal husbandry.

Are there any technical constraints or bottlenecks holding up genome editing research in this field?

What are the expected timescales within which we might expect to see particular genome editing applications being used on farms?

1.3 The argument for gene editing is that it can make such modifications more quickly – potentially avoiding 15 years of backcrossing in order to produce desirable traits in farm animals. This notion of speed, however, may be misleading.

1.4 Although gene editing is promoted as a fast technology with limitless possibilities, we have yet to see any gene-edited animals appear on farms or in the food chain. In part, this is because the results in animals thus far are not as predictable or reliable as hoped. For example, a recent Wall St Journal investigation also reported on unintended effects of gene-edited animals including enlarged tongues and extra vertebrae. Brazil's plans to breed hornless dairy cattle, gene-edited with TALENs, were recently scrapped when a study by the US Food and Drug Administration revealed that one of the experimental animals contained a sequence of bacterial DNA including a gene conferring antibiotic resistance. In theory, this

antibiotic resistance gene could be taken up by any of the billions of bacteria present in a cow's gut or body and from there be spread beyond the farm.

1.5 Delays in bringing gene-edited animals quickly to market are also due, in part, to the fact that regulators are having difficulty keeping up with the speed of development and increasing complexities of the field. Some regulatory authorities are erring on the side of caution with regard to the regulation/deregulation issue, others are not. As noted in our roundtable report, diverse approaches to regulation alongside emerging unintended consequences mean that gene-editing is subject to multiple limitations and may not be the 'fast' solution it is made out to be.

2. The Socioeconomic Context

What are the societal, production, environmental and policy challenges to which genome editing applications in farmed animals might offer a response?

2.1 There is broad agreement amongst NGOs, policymakers and food producers that, in a variety of ways, our food system is no longer functioning optimally, that it needs to change and is, in fact, changing. These changes are responses to a range of problems including climate change, land use changes, high levels of non-communicable diseases (which are linked to available food choices) and illness linked to resistant bacteria (some of which can be traced back to antibiotics use on farms) and a growing awareness of the poor welfare in many livestock operations.

2.2 Gene-editing is proposed as one way to address some of these issues, for instance by re-engineering animals to have innate resistance to specific bacteria, or to have no tails or horns, (thus avoiding inhumane procedures like tail docking and dehorning), or to be more productive whilst consuming less feed. If we are not willing to change the food system then adapting the animal to the system via gene editing may be seen as our best or only option.

2.3 In our roundtable it was recognised that certain diseases in farm animals, some of which can be devastating to entire herds, are becoming more common and need to be addressed. Increased use of antibiotics and vaccines has drawbacks and may be inappropriate, ineffective or have knock on consequences for human health. Again, in these limited instances, and in an assumed context of a more industrialised system, some uses of genome editing may be appropriate.

How might genome editing technologies help to address these challenges, and what practical benefits and drawbacks would genome editing applications have over existing or envisaged alternative approaches?

2.4 Much of the current focus is on health deficits in farmed animals – and in particular those that are reared in intensive, industrial systems. At least half of current projects focus on viral disease resistance. Gene editing is especially important here as viruses operate within the cell and damage the host through that mechanism. For this reason, they can be much harder to deal with than, for example, a bacterial infection of the gut. This does raise the question, however, of whether these health deficits are primarily the result of a genetic 'glitch' that needs to be fixed or do they come from somewhere else?

2.5 Our conversations around this topic suggest that many of the issues which genome editing is being used to address are context specific. Poor health in animals often arises as a result of the systems in which they are kept and gene editing should not be used to address diseases that primarily result from keeping animals in stressful, crowded conditions. Such diseases can, and some argue, should be tackled by improving housing, husbandry and hygiene.

What groups or organisations are likely to benefit most from the use of genome editing in farmed animals and what groups or organisations might be disadvantaged?

2.6 It is difficult, at this stage, to predict where the benefits/disbenefits will be. Historically, the products of genetic engineering have tended to benefit those in high volume industrial systems who can afford to invest in the technology and who are able make the necessary royalty payments.

What do you think are the broader social, economic and political drivers that will facilitate, impede or otherwise shape the development and use of genome editing applications in farmed animals, and what effect do you think these will have?

2.7 Much depends on how we envisage our future farming system. There is now a large body of opinion suggesting that, by whichever yardstick is used – welfare, sustainability, environment, nutrition etc – this type of farming system is damaging and outdated. The recent IDDRI report *An Agroecological Europe in 2050: Multifunctioning Agriculture for Healthy Eating* presents an achievable, alternative vision of farming for crops and animals.

2.8 If we envisage the future of farming as largely agroecological, and invest in and work conscientiously towards that kind of system change, then it is possible that gene editing will not have much of a role – or may only have a very limited role – in livestock farming. However, if we envisage that the industrial model will continue to prevail then genome editing – with its attendant, complex regulatory and socioeconomic implications – may take on a more prominent role.

How might differing regional social, economic and political drivers influence the likely development and adoption of genome editing applications in the UK, the EU and the rest of the world?

2.9 There are now calls to deregulate the products of genome editing, including animal products. The arguments for this are largely economic/political. Developers believe that regulations interfere with innovation and policymakers have been persuaded that deregulation will open up the 'ideas economy' in the UK and elsewhere. In other words, they are less concerned about selling the products (animals) created by gene editing than they are about selling the technology, which is deemed far more valuable.

2.10 It is important to note, however, that the economic benefits of older-style genetic engineering have never been thoroughly investigated and are therefore neither proven nor disproven. Gene-edited livestock continues in this tradition garnering praise, investment and priority in terms of policy-making on the basis of assumptions and promises rather than hard facts. In a farming culture where the economics are already unpredictable, we believe the economic case for genome edited animals should be more robustly and independently assessed.

2.11 Deregulation also brings other consequences with it. Many countries are grappling with how to regulate such a new technology and the conclusions being drawn are anything but uniform. Differing approaches to regulation between different countries could have a negative impact on trade, which has yet to be fully articulated.

2.12 In any case we would argue that economics/politics is the wrong starting point for any discussion on the production of food and that there is sufficient uncertainty about gene editing, on a variety of levels, to preclude deregulation.

What effect do you think public attitudes will have on innovation in this field (in the UK, the EU and internationally) and how should researchers and policy makers take account of these?

2.13 The spectre of 'public good' is very often raised in the argument for gene-edited animals. It is not clear, however, just what that public good is or how much real weight it might be given set against economic aspirations of government and industry.

2.14 Public attitude towards genetically engineered food is traditionally negative. Public understanding of gene editing is not well researched. Although the European Court of Justice has ruled that gene editing is genetic engineering, it is not clear that the majority of citizens are even aware of this decision or whether they even know what the term 'gene editing' refers to.

2.15 Results of the recent Eurobarometer survey, were widely interpreted by industry as showing a more positive attitude amongst citizens towards gene editing than to older style genetic engineering ('GMOs'). However, the fine print of the survey noted that in 2010 respondents were asked about GMOs while in 2019 respondents were asked a completely different question about gene editing and that the two questions/results were not directly comparable.

2.16 More often than not, our experience, is that members of the public want to know why we are using extreme technologies to produce food and whether there is any better, simpler alternative.

3. Ethics

Are there any categorical ethical objections to genome editing farmed animals and if so on what grounds are they based?

3.1 Animal welfare advocates contend that animals are sentient beings, with needs and intrinsic value beyond their value in a commercial livestock system. This is in direct contrast to the approach of the business/biotechnology sector which, arguably, focuses more on animals' productivity. Some worry that directly altering an animal's genome may also alter its essential nature or 'animalness'. From a welfare perspective, it is also argued that gene editing treats the animal like a machine rather than a sentient being and that this is ethically unacceptable.

3.2 Organic breeders have a philosophical objection/resistance to the idea of altering the organism at the cellular level because this is seen as an assault on the integrity of the

organism. Some also worry about genetic ‘contamination’. This is more than a philosophical/ethical concern, however, since such contamination could mean they lose their organic certification and therefore income.

3.3 It is interesting there are many complex and high level arguments around gene-editing humans and how this might affect our ‘humanness’ and whether it disturbs our genetic integrity in some way – but gene edited farm animals have yet to benefit from the same level of detailed discussion.

What, if any, are the ethical differences between using genome editing and deliberately altering an animal’s physiology in other ways, for example, by using hormones, surgical procedures or drugs?

3.4 Our recent report noted that any discussion about ethics is really a discussion about consequences and our willingness and ability to look further down the line at the potential results of our actions. In that respect the ethical questions around for example, drugs vs gene editing are similar.

3.5 The drugs that we currently use to treat sick animals have widespread knock on consequences. Antibiotics, for example, can encourage resistant strains that are harder to treat and that can spread beyond the farm. For this reason, it is argued that irresponsible use of antibiotics on the farm is unethical. At this moment in time, gene editing an animal to be resistant to a specific bacterial or viral disease is represented as a better ethical choice since it could help reduce the use of antibiotics and vaccines. However, there is no iron-clad guarantee that these genetic tweaks will confer long-term immunity.

3.6 With herbicide-resistant and pesticide-producing GMO plants, for example, it has been shown that plants, insects and microbes can evolve in ways that can relatively quickly make the genetic change ineffective and which require the farmer to use ever more potent herbicides, insecticides and fungicides.

3.7 In bacteria and viruses pressure from antibiotics and even vaccines can force evolution in the microbial community that produces more virulent strains that can quickly become dominant. Increasingly potent treatments are, thus, necessary to fight disease.

3.8 With animals bred to be resistant to certain diseases, we need much better and more conclusive evidence of the consequences in the microbial community as a result of this change.

What, if any, are the ethical differences between using genome editing and using alternative methods such as traditional selective breeding methods, or marker assisted selection to alter the characteristics of a breed of farmed animals?

3.9 It’s difficult to present a definitive answer to this question because there is not enough comparative research on gene-edited animals to say whether the consequences of this type of breeding are the same, better or worse than selective breeding.

3.10 Genome editing, in the main, does not take into account the systemic nature of farming, but instead treats ‘problems’ (horns in cows, rising levels of respiratory infections in pigs and chickens etc) as single, isolated problems. Given that agriculture is a deeply connected

system, there is an argument that denying this connection opens the door to negative consequences and is therefore irresponsible and unethical.

3.11 Selective breeding has been shown to have a negative impact on animal health, notably skeletal and metabolic diseases, lameness, reproductive issues and mastitis – and here too it could be argued that the line between what is an ethical issue and what is a welfare issue is very thin. These impacts can certainly be magnified or minimised depending on the systems in which farm animals are kept. This is likely to be true for gene-edited animals as well.

Are some but not other applications of genome editing in farmed animals acceptable and, if so, on what does their acceptability depend (for example, improving animal welfare, meeting objectives of importance for animals or humans, etc.)?

3.12 While an agroecological approach to farming is widely believed to be the better, healthier, more ethical systems of crop and livestock production, progress towards this ideal is slow. At our recent roundtable it was argued that for some intractable diseases that are impacting farmers right now gene editing could provide a 'bridge' during a period of system change. How that bridge is managed has intersections with how we regulate the products of gene editing and with post-market surveillance.

4. Law, regulation and policy

Are there reasons to think that genome editing approaches are inherently more likely than alternative approaches to result in adverse outcomes, or to result in outcomes that are potentially more harmful; what are the major risks or uncertainties that regulation should seek to manage?

4.1 Our knowledge of genome functioning is still very incomplete. Unexpected and concerning consequences of gene editing are being discovered very rapidly now (see 1.4) and the severity and irreversibility of some of the risks posed by genetically engineering animals is unknown.

4.2 This may be one reason why, contrary to the publicity around gene-edited animals, we have not found many on any side of the argument who promote wholesale deregulation of plants and animals produced using genome editing technologies. Regardless of any individual's personal views, EU law is clear that gene editing is genetic engineering. Genetic engineering, like any 'disruptive' technology (e.g. driverless cars, artificial intelligence), is fraught with uncertainties and as such requires regulation.

4.3 In the EU regulation is structured around the Precautionary Principle, which is not only concerned with the probability of the risks, both known and unknown, but the severity of the consequences and their irreversibility. The Precautionary Principle provides a method for dealing with uncertainty by saying if there is risk, even if the probability of negative impacts is or seems low, we should either not proceed or proceed with extreme caution.

What are the roles of policy and markets in shaping livestock farming practices and what should be the key policy objectives in this area?

4.4 In order to give markets a say in regulation it is now being proposed that the Precautionary Principle in the EU (and by implication Post-Brexit UK) should be replaced by the Innovation Principle – one which favours deregulation and is aimed at helping new technologies into the market faster. This change flies in the face of the core purpose of regulation. We contend that regulation is intended to provide protection, either to individuals, or to the environment, and not to promote markets. Further, we contend that our regulators should act as gatekeepers rather than doormen in order to provide the public with sufficient confidence in the regulatory process.

Do you think that the existing EU regulatory framework for the production and sale of GMOs is appropriate for genome editing applications in farmed animals and, if not, what alternatives might be considered?

4.5 Europe has been called a regulatory 'superpower'. In the landscape of regulation – from persistent and potentially toxic chemicals, to the tightening online privacy laws and in the approval and regulation of agricultural biotechnology – European standards are widely regarded as comprehensive and ambitious. With the advent of new genome editing techniques, biotechnology companies argue that the current approach to GMO regulation is out of date, that it is too restrictive and damaging to innovation and, moreover, that it is out of line with evolving standards elsewhere in the world. This point of view is fiercely contested by others who believe that there are significant risks in liberalising GMO regulation.

4.6 Given the escalating disagreements in this area, it is likely inevitable that EU regulations will be opened up and revised. The question is what shape will that revision take? At a minimum, our report concluded that government, research and policy agencies and industry bodies should work with civil society bodies in the following ways:

> **4.6a** Government should give more careful consideration to how we assess the creation and introduction of new genetic engineering technologies for breeding animals (and plants). This process needs to begin with questions such as what problems are we trying to solve and what kind of food system do we want. It requires a much more rigorous and nuanced evaluation of evidence, of benefits as well as risks and of viable alternatives. It should include (among others) scientific, social, environmental, welfare and ethical considerations.
>
> **4.6b** Citizens must be involved. The recent international IPES report *Towards a Common Food Policy for the EU* prioritises a participatory process for assessing technological innovations, that involves citizen stakeholders and allows the precautionary principle to be consistently applied in regard to food and farming systems. We agree this is the direction of travel for regulations worldwide and would not want to see the UK left behind. This involvement could take the form of an independent expert group and ideally a citizen-centred process to explore the issues as well as hold key players (including government) to account. At present there is no structure for this so it needs to be built from the ground up.
>
> **4.6c** Market development pathways should also be regulated to ensure that all of the above considerations are taken into account.

5. Finally

Is there any important question that you think we should have asked or an area that we ought to have covered, or any other information that you would like to bring to our attention in order to help us with this inquiry?

5.1 This inquiry focuses on farmed animals – an indeed this is the area of research which seems most advanced. However, other animals are also becoming targets for gene editing. A recent IUCN report, for example, suggests that gene editing can be used to resurrect extinct species, or improve health and resilience in at-risk species that are being, directly or indirectly, impacted by things like climate change or loss of habitat. Farm animals – in both extensive and intensive systems – do come into contact with wild animals. It is only short step from re-engineering wild animals to conserve them to re-engineering them for other purposes. Geese, badgers and bison, for example, are all implicated in infecting farm animals with various diseases. What are the potential consequences of genetically 'editing' these wild animals so they don't impact farm animals?

5.2 The recent release of gene-edited, gene drive mosquitoes in Brazil provides another example. These insects were supposed to breed with native mosquitoes and produce weak offspring that would die quickly without passing on their altered genome. However, the offspring have proved to be robust and are now breeding well beyond their original breeding grounds. Mosquitoes are vectors for all kinds of disease in humans and animals – and for diseases that can be transferred from animals to humans – so this is potentially concerning.

5.3 We are not aware of any research that looks at possible interactions between gene-edited farm animals and gene-edited wild animals/insects. This, however, is on the horizon and is just one example of how the R&D around gene edited farm animals needs to be looked at through a wider and longer-term lens.