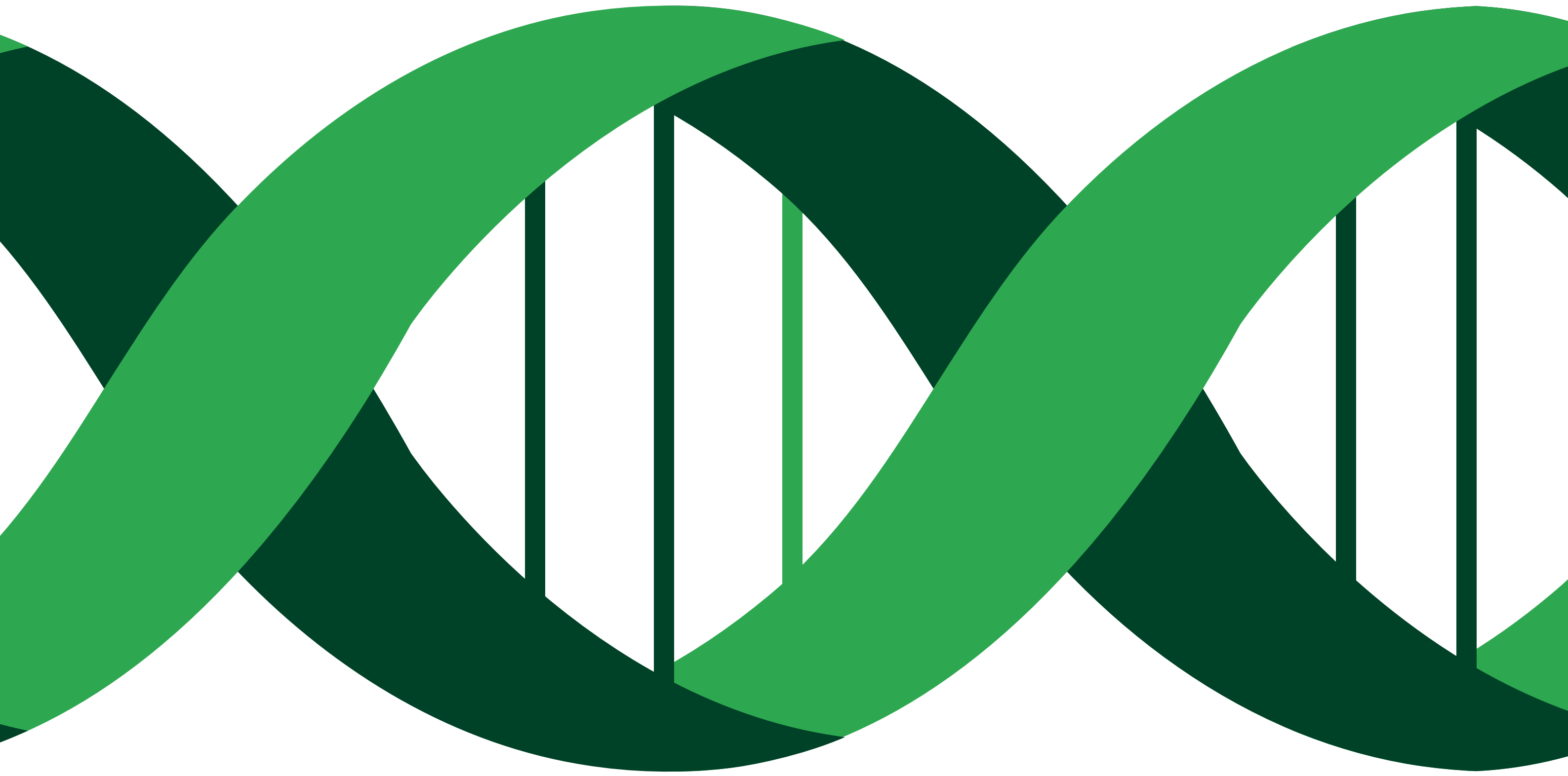
Genome Editing and Agriculture:
Policy, Practices and Public Perceptions (GEAP3)
Policy Briefing 1

GENOME EDITING IN AGRICULTURE: ISSUES FOR POLICY AND REGULATION



Introduction

Genome editing, also known as gene editing, is a technique of genetic engineering that involves the alteration of an organism's genetic structure by adding, deleting, changing or replacing individual nucleotides or sequences of DNA. Genome editing includes several different methods and tools, which can be used by breeders to alter the traits of crop plants and livestock animals. Genome-edited crops and food products are beginning to be commercialised, which raises questions around how the techniques and products of genome editing should be governed.

This briefing explains why the governance of genetic engineering is a topic of public interest and concern. It considers whether genome editing raises new issues relating to environmental and food safety, intellectual property rights or trade, and why genome editing applications may provoke public controversy. In particular, it discusses whether regulations and policies to govern the techniques, applications and products of genome editing should be any different from those applied to the previous generation of genetic engineering technology.

Background

Within the past 25 years, several powerful new techniques of genome editing have emerged, which promise to have a significant impact on the genetic manipulation of crops and livestock. Most genome-editing techniques use nucleases, a type of enzyme that repairs genetic damage or performs immune functions in living organisms, to cut and reconnect targeted sections of DNA. Researchers have developed ways to exploit this capability to cut out or insert selected genetic sequences, or to 'knock out' or modify the expression of specific genes. These novel techniques of genetic engineering may be used, either to generate mutations (i.e. to induce genetic variation that could be a source of valuable traits), or to insert or replace individual genes or sequences of interest (which could be transgenes taken from another organism).

In 2012, a paper in the journal Science reported that a tool known as CRISPR-Cas9 could be used as a versatile and efficient genome-editing tool. CRISPR stands for Clustered Regularly Interspaced Short Palindromic Repeats. The technique uses an endonuclease or 'restriction enzyme' to cut the genome in a specific location. These restriction enzymes are known as Cas (CRISPR-associated) proteins. While the CRISPR tool recognises the sequences of interest, the Cas proteins cut the DNA strands. Experiments using the restriction enzyme Cas9 have stimulated a rapidly growing body of research studies, but other numbered Cas proteins are also being investigated.

Genome editing, genetic engineering, genetic modification...

Should the techniques and products of genome editing be considered essentially the same as, or in specific respects different from, previous generations of modern biotechnology? Do CRISPR and other genome-editing methods raise new societal concerns or different public policy issues, compared to other methods of genetic engineering or mutation breeding? These questions are already lively topics of debate. In this briefing note, we examine reasons why genome editing could warrant special considerations from the perspectives of biology, political economy and geopolitics.

A key frame of comparison is with the way that societal stakeholders, policy frameworks and legal arrangements have treated a previous generation of genetic engineering, which is often referred to in public debate by the shorthand term GMOs, or genetically modified organisms. However, some stakeholders might argue that it would be more appropriate to compare the genetically engineered organisms produced using new genome editing techniques with ones developed using mutation breeding. Mutation breeding is an established technique used in crop breeding, which uses radiation or chemicals to stimulate genetic mutations. These alternative frames for comparison could have material consequences in the real world: in some jurisdictions, genetic modification has attracted special regulations that have not been applied to mutation breeding techniques.

Differences in biology?

In practice and in legal frameworks, the term GMO has come to refer to organisms produced using some specific techniques, which incorporate genetic material transferred from another organism. Some people referred to GMOs as transgenics, because they contained these transferred genes or 'transgenes'.

Before the methods of genome editing were developed, the principal techniques used to create transgenic organisms involved physically smashing genetic material together in living cells – a technique known as 'biolistics'; or using a bacterium (usually *Agrobacterium tumefaciens*) to carry genes into plant cells and splice them into the genome of the host.

An example of a commercial GMO is 'Bt cotton', a type of cotton that incorporates genes originally obtained from a soil bacterium called *Bacillus thuringiensis* (Bt). A famous experimental case involved introducing genes from a flounder (a type of fish) into a strawberry, in the hope that the transferred genes would allow the strawberries to resist frost. As these examples illustrate, a factor that attracted much attention and caused some concern was that these techniques could be used to transfer DNA between organisms that were unrelated genetically. They produced types of genetic recombination that could not have happened without human intervention.

It is widely understood that public concerns about GMOs have to do with the perceived 'unnaturalness' of these novel genetic mixtures. To help overcome these misgivings, some scientists have proposed new terminology to distinguish between different products of genetic engineering, based on the origin of the introduced DNA. Alongside *transgenesis* (where the introduced genes originated in a sexually incompatible organism), the terms *intragenesis* and *cisgenesis* have been proposed to designate specific types of genetic recombination, where the genes or sequences concerned originated in the same organism or from a sexually compatible gene pool. The idea is that intragenic and cisgenic organisms ought to provoke less concern among the public and consumers – and therefore should attract more permissive regulation.

Genetic engineers and regulatory scientists have categorised genome editing processes into three types: SDN-1, SDN-2 and SDN-3 (the abbreviation SDN stands for 'site-directed nuclease'). The distinction depends on the mechanism used to reconnect the genome after it has been cut by the restriction enzyme. With SDN-1, the organism's own cellular repair mechanisms make the repair: this process is prone to create random mutations, thereby generating genetic variation that could prove useful in a breeding programme. With SDN-2 and SDN-3, the genetic engineers construct a template which tells the organism how to repair itself. When the changes to the genome are quite small, the modification is classified as SDN-2. Genetic engineers argue that the small genetic changes that result from SDN-1 and SDN-2 procedures are similar to mutations that could have occurred in nature, so that less stringent regulation is appropriate for these organisms. SDN-3 is the label given to procedures that involve the introduction of longer genetic sequences, which could come from a sexually incompatible organism.

Evidently, the transgenic–cisgenic–intragenic and SDN-1, -2 and -3 schemas can help to distinguish conceptually between products of genetic engineering based on whether they incorporate new genetic material. However, they might not help society to distinguish genome editing from older genetic engineering techniques. While genome editing can be employed, as its name implies, only to delete or rearrange individual bases or short segments of existing DNA, it can also be used to introduce genetic material from another organism, which could include a sexually incompatible species. This implies that scientists can use genome editing to create organisms that might be considered intragenic/cisgenic or transgenic, according to the above schema. Yet the technique used (employing nucleases to cut and reconnect genetic sequences) is certainly different from the biolistics- and *Agrobacterium*-mediated methods that were used to create earlier generations of GMOs. It still remains to be teased apart which aspects of genome editing biology (if any) might be thought to matter from scientific, societal and regulatory points of view: the specific techniques employed; the sources of genetic material used, transferred and/or transformed; the nature and extent of the transformations made; or some combination of these three.

Some commentary on genome editing addresses another issue that is believed to be a source of public concern about GMOs: namely, that genetic engineering using biolistics or *Agrobacterium* produces random, unpredictable changes in DNA. (The same concern worries some critics of mutation breeding too.) While it is true that the sites of genetic recombination using these methods are unpredictable, in practice the transformation is replicated multiple times, and the mass of transformed material that results is screened and analysed to check where the introduced genes have been incorporated and to see how the insertions have affected the expression of genetic traits. Only the transformations that look promising are kept for further development and eventual commercialisation.

Genome editing has been described as a more precise and controllable method of genetic engineering, because tools such as CRISPR can be programmed to target a specific site in the genome, cut a chosen link in the DNA chain, and reconnect the cut pieces – removing, inserting or rearranging genes in the process – in quite precise and predictable ways. Again, things are slightly more complicated in practice. Research has found that CRISPR can produce unintended effects, both at the target site and in other places along the genome. Scientists argue that these issues can be managed by carefully programming the CRISPR-Cas tools, and by screening the transformed organisms to ensure that the alterations are as desired and intended.

A transformed political economy?

In the West, many of the first generation of commercial GM crops were developed mainly by, or with the backing of, large agribusiness-and-biotechnology companies.[1] These companies' ability to dominate the new market for genetically modified (GM) crops was enabled and assisted by several factors that had to do with the contemporary political economy of modern biotechnology. Key among these were the ability to obtain patents on GM products, which allowed them to control access to commercially valuable transgenic material. Developing and applying the novel technology required some big investments in scientific laboratories and greenhouses, which were beyond the reach of small players. The big firms also used their spending power to purchase small biotechnology startups in order to gain control of their transgenic technologies, and to purchase big seed companies in order to have access to their stocks of valuable germplasm and to use their sales and distribution networks to reach farmers with the new seeds.

Equipped with these advantages, a handful of large transnational companies has dominated the market for transgenic crops and traits, driving a rapid and significant concentration of the seed industry. In this context, an ongoing source of concern has been the difficulty faced by smaller firms and public-sector plant breeders seeking access to transgenic breeding material on favourable terms. Another concern in some markets is that commercial farmers may have fewer choices in the seeds they can plant, and the associated technologies, such as herbicides, which they are permitted or obliged to use alongside proprietary GM cultivars.

There is much excitement around the potential for genome editing to improve the speed, precision and effectiveness of crop breeding programmes, compared to the first generation of genetic engineering techniques. The procedures involved are also expected by some stakeholders to be significantly less expensive than classical genetic engineering, making them more affordable for use by small and medium enterprises and by public sector organisations. If these predictions are correct, genome editing could make improved cultivars easier and cheaper to develop, which could undermine the dominance of the big biotechnology companies and improve the supply of varieties intended for poorer and economically marginalised farmers. However, these expectations that the technology will be more accessible have been questioned by some commentators, analysts and campaigners.

In particular, concerns have been voiced that intellectual property rights over key aspects of CRISPR technology could impede scientific research and technological innovation. A related question is whether genome-edited organisms could be amenable to patenting in the same way as classical GMOs. There has been some debate about this issue, but the likely implications are

[1] In China, public sector researchers and state-controlled companies played the leading roles.

unclear. Some commentators have suggested that the techniques involved in genome editing make the transformed organisms intrinsically harder to identify as products of genetic engineering. Unless a plant contains genetic sequences that have been patented or perhaps lodged with an agency that regulates seed or plant breeders rights – processes which require the developers to describe the genetic identity of the cultivar in a public register – it may be practically impossible to identify that the genetic sequences found in the plant have been modified with genome editing tools. In principle, the novel sequences might have arisen from a natural mutation or conventional selective breeding. This could make it harder for breeders or seed companies to claim or enforce proprietary rights over some kinds of cultivars (e.g. intragenic varieties). If so, some applications of genome editing technology might be more readily accessible than classical GMOs to small firms and public breeders. The actual implications may depend on how intellectual property rules are framed and enforced in each jurisdiction.

Similar issues might arise with regard to the responsible stewardship of genome-edited organisms. A lively and contentious debate has surrounded the possibility that GMOs released into farming and food systems could cause harm to the environment or to consumers, and some stakeholders have similar concerns about genome edited organisms. If such organisms are difficult to identify and trace in the market or the environment, it could make regulatory oversight difficult or impossible. Would it then be practical or appropriate for governments to seek to make seed companies or merchants responsible or legally liable for harm that might be caused by genome edited varieties that they have released?

The resolution of these questions could have substantial implications for the shape and organisation of an emerging market for genome-edited plant varieties. Besides ensuring that genome-edited organisms can be released into the environment and food chains safely and in the public interest, policy frameworks and regulatory regimes will in part determine whether, and on what terms, it may be practical, affordable and profitable for various public and private stakeholders to develop and release genome-edited crop varieties. It remains to be seen what kinds of business models might emerge for a commercial trade in genome-edited crop varieties, or whether they will be the same as those for earlier types of GM cultivar, which typically rely on controlling access to proprietary genes via patents and contracts. Might they follow novel competitive strategies that deliver value to seed companies, as well as farmers and consumers, in other ways?

A transformed geopolitical context

The classical techniques of genetic engineering were developed during the 1980s and the first GM crop varieties were commercialised in the 1990s. The GM crop economy emerged in the aftermath of the Cold War and the inauguration of the World Trade Organisation (WTO). This was the era of economic globalisation, guided along neoliberal lines. Countries around the world opened their markets to international trade and foreign investment, including populous nations such as India and China. The North American Free Trade Agreement (NAFTA) was implemented, the European Union's (EU) single market was established, and various other regional trade agreements were concluded. Commercial agribusinesses were able to enter new markets and expand transnationally. The international trade in agricultural products was never wholly liberalised, but flows of agricultural products increased markedly, including horticultural exports from sub-Saharan Africa into Europe.

Against this background of market opening and globalisation, the trade in GMOs proved to be controversial and the world market became segmented into countries that embraced the new technology enthusiastically and those that proceeded much more cautiously. In particular, the EU market remained largely resistant to the wide commercialisation of GM crops and foods. This created tension between the EU and the USA and affected flows of commodity exports, such as soybeans grown in South America that were routed towards North American and other markets instead of European destinations.

Meanwhile, transgenic soybeans, maize, cotton and canola began to be planted widely in North and South America and Australia. Transgenic cotton was commercialised in China, South Asia and a handful of African countries. GM varieties of maize were planted in South Africa. Elsewhere, transgenic varieties of a few minor crops, such as papaya, were cultivated on small areas. However, the slow expansion of the global market for GM crops undoubtedly disappointed the early expectations of corporate managers and investors. Transgenic cultivars of wheat and rice have not yet been cultivated anywhere on a significant scale. Bt cotton has been planted on large areas in China, India, Pakistan and South Africa, but commercialisations of transgenic cotton and maize among small-scale farmers in South Africa and Bt cotton in Burkina Faso fell short of the developers' expectations.

Meanwhile, farmers in countries that embraced GMOs in agriculture, such as the USA and Canada, have grappled with accumulating challenges in their farming systems, such as the emergence of herbicide-tolerant weeds, and insects that have developed resistance to Bt crops. Newer transgenic crop varieties have been introduced to help manage these issues, but some farmers are finding that the costs and complexity of cultivation in GMO-centred production systems are increasing. For some farmers and investors in GM crop technologies, not to mention many environmentalists and some consumers, the early promises of GM crop technology were overstated.

Today's geopolitical context is substantially different from the situation that surrounded the commercial release of GMOs during the 1990s and 2000s. It is an open question whether this significantly altered geopolitical landscape has implications for the potential commercialisation of genome-edited crops and foods in different jurisdictions around the world. However, the global context is different enough to assume that it could make a substantial difference to the prospects for developing and releasing new genetically engineered organisms.

Since the global financial crisis of 2008, and especially in the last half decade, the rules-based international trade regime shepherded by the WTO is being undermined by countries that have started to adopt more nationalist and mercantilist policies on trade, notably the United States. In the global South, rising powers such as China, Brazil and India – all of which have significant domestic capacity in biotechnology – have become increasingly important as trading partners, investors and aid donors to poorer countries, particularly in sub-Saharan Africa.

Meanwhile, even as the scientific evidence and consensus on the causes of global climate change and its potential impacts on agriculture and food security have strengthened and deepened, multilateral action to reduce greenhouse gas emissions and implement adaptation measures has been faltering and is being undermined. The Covid-19 pandemic has led food system experts and policy analysts to highlight the fragility and vulnerability of global food production systems and food security.

Emerging questions for Europe and the UK

The European Court of Justice (ECJ) ruled in July 2018 that genome-edited crops should be regulated under the same rules as genetically modified organisms (GMOs) within the EU single market (see Briefing 2). The United Kingdom has left the EU, and the British government intends to adopt a permissive approach to genome edited crops and foods. If it does so, the UK will align itself with the USA instead of the EU, and its domestic agriculture and its trade relations will be significantly affected (see Briefing 3). Whether the EU's internal policies on agriculture and food will be affected by Brexit remains to be seen.

The ECJ ruling has been criticised by some stakeholders and praised by others. It is contentious because it has implications for the development and application of genome editing techniques and products within the EU (and possibly the UK), and because European rules will have knock-on effects for the trade in agricultural products across the Atlantic and the Mediterranean. The EU policies and regulations governing genome editing in agriculture may also influence African nations that export agricultural products to European countries, as well as those which receive aid and technical support from Europe.

Societal debates and conflicts about genome editing, like previous struggles over GMOs, are about much more than the technical characteristics of specific products or processes. The debates raise large questions about the democratic governance of emerging technologies, ethical dimensions of human–nature relations, policy questions about land use, consumption and food security, and questions of social justice relating to the distribution of socio-ecological and economic costs and benefits. More broadly they concern the shaping and direction of alternative future pathways for agriculture and food.

The GEAP3 Project Policy Hub

The Genome Editing and Agriculture: Policy, Practices and Public Perceptions (GEAP3) network is an international research consortium that brings together social scientists, policy experts and bio-scientists to explore the domestic and international ramifications of the EU's policy and regulatory approach to genome editing in agriculture. The network is exploring and analysing key developments in genome editing and their implications for agriculture through three hubs: policy, practice, and public perceptions.

The GEAP3 Policy hub is exploring systematically the implications of the EU's regulatory approach to genome editing. The hub is examining how competing visions for the governance of genome editing conflict or may be reconciled. For further information on the GEAP3 network and the Policy hub, please visit the project website at https://www.geap3.com

Other GEAP3 briefings in this series

Briefing 2: Genome Editing in Agriculture: The Politics of Regulation in the European Union

Briefing 3: Genome Editing in Agriculture: Regulation in the United Kingdom after Brexit

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Further reading

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