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Genome-Edited Food Crops

Overview

- The Government is proposing that genome-edited crop plants are exempted from Genetically Modified Organisms (GMOs) regulations, provided the genetic changes could occur naturally or via existing conventional breeding techniques.
- Genome editing can manipulate DNA at specific positions in the genome to shorten timeframes for plant breeding of useful traits. This process can lead to unintended alterations of the genome, but these may be fewer than for conventional breeding.
- Some stakeholders believe this regulation change for genome-edited food crops could provide health and environmental benefits and make use of UK-funded research.
- Key issues for public acceptance and trust of genome-edited crops are tightly bound to transparency and how the public view potential risks and benefits.

Genome editing creates the possibility of making more precise alterations in the DNA of food crop plants than existing approaches. This POSTnote: describes genome editing technology; identifies which food crops are currently undergoing editing and why; describes the regulation and registration of genome-edited food crops; discusses issues around trade; and describes stakeholder views about the technology.

Background

Genome editing encompasses a variety of techniques that add, remove, or replace DNA at targeted locations within the genetic code of living cells (the genome).[1] The techniques can alter individual DNA bases (A,T,C and G) within the genome to modify the regulation or function of an existing gene,[2] or with lower efficiency, insert a new gene to provide novel traits (PN 541 and 548).[3,4] Because of the mechanism involved, the European Court of Justice (ECJ) ruling in 2018 implied that genome editing techniques alter the genome in such a way that would not occur naturally/by mating and should not be exempt from regulation because they do not have a long safety record.[5,6] Following this ruling,[5] the UK regulates all genome-edited organisms as Genetically Modified Organisms (GMOs): "An organism…in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination".[7] GMO regulations cover organisms in which DNA has been inserted into their genomes, regardless of whether the DNA is from a species that can interbreed, or cannot interbreed ('foreign DNA', PN 548).[8] Regulations only allow GMO foods to enter the market, if it has been demonstrated that: they are not nutritionally disadvantageous; they do not have adverse effects on health or the environment.[9,10] Any GMO approved for market placement must also be accompanied by an analytical method that provides unequivocal identification of that GMO.[9,10]

Genome-edited crops must currently follow GMO regulations for field trials and for placing on the market.[5,7] Field trials are experiments that evaluate the consequences of changes to crops in agriculturally relevant conditions,[11] which are typically repeated over different years, seasons and environmental locations.[12,13] To conduct field trials involving GMOs, researchers must obtain consent from the Secretary of State under the Environmental Protection Act 1990[14] and the GMO (Deliberate Release) Regulations 2002.[15] Application fees and measures to ensure compliance with current regulations can amount to regulatory costs of approximately £10,000 per field trial.[16] The UK Government, following their recent consultation on the regulation of genetic technologies in 2021,[17] has outlined a plan to change regulation for certain genome-edited plants in two stages:[18] first to exempt them from GMO field trial regulation in England,[19] and then from the regulatory definition of a GMO. In April 2021, the European Commission also questioned whether the EU's regulatory framework for GMOs was 'fit for purpose' in the face of new technologies.[8] This was based on genome editing (and other genetic technologies) producing plants whose final genome does not contain foreign DNA[20] and are indistinguishable from plants that could be developed by conventional breeding or could occur by nature.[21]

Genome editing is a tool that may make food crop breeding more efficient,[1] and are the focus of this POSTnote, but plants are also bred for other purposes such as trees for bioenergy.[22,23] Experts across government,[18] academia and industry largely agree that genome editing could help breeders to enhance crops (PN 589, Box 1).[24–27] However, other commentators do not agree that the possible benefits will be realised.[28,29] The UK Innovation Strategy 2021 proposes the use of genetic engineering tools such as genome editing to support the 'bioeconomy' (PN 589), with biological applications estimated to 'unlock' £1.5-3 trillion by 2030–2040.[30] The National Food Strategy 2021 led by Henry Dimbleby has considered how genetic technologies can benefit future food production.[31] Of the new genetic technologies to develop new plant varieties, genome editing of food crops has undergone significant research and development (R&D),[32] with one genome-edited crop product currently on the market in the US,[33] and another in Japan.[34] Some stakeholders raise issues with deregulation, such as over-promising on societal benefits,[35,36] unforeseen risks,[37] and repeating GM debates on the biodiversity impacts of herbicide-tolerant crops.[38]

Genome editing technology

Genome editing, involving techniques such as the widely used method called CRISPR/Cas,[39,40] can be achieved in several ways. One method uses a soil bacterium (Agrobacterium) to deliver Transfer-DNA (T-DNA) carrying genes to achieve the editing.[1] This T-DNA inserts into the plant genome to create the molecular tools to 'search' for and 'add/remove/replace' DNA in a different area of the plant genome that is pre-defined by the operator.[41] Breeding the next generation of plants will produce some plants free of the 'foreign' T-DNA (PN 541).[42] In other methods no foreign DNA is integrated into the genome; either the instructions to build the molecular tools[43] or the protein tools themselves[44] are delivered into plant cells.[45] The EU Food Safety Authority proposes that risk assessments should take into account whether, in the final genome-edited plant product, only existing DNA is altered or if external DNA is inserted.[46–48] Some techniques allow faster, more precise 'upgrades' to conventional breeding,[1] but others are compared to a more targeted version of genetic modification (GM).[49–51] Regulation for such a fast-developing technology area may require legislation that is not linked to a particular technology because that technology could be rapidly superseded.[50,52]

Genome editing and genetic modification

Genome editing can more accurately introduce small changes in the DNA sequences of specific genes known to affect plant traits than conventional plant breeding.[1,53] Some forms of genome editing can be used to insert genes of interest (foreign or non-foreign DNA) at target sites of the genome that are pre-defined, so as to reduce the likelihood of altering or interrupting other genes.[48,54,55] However, genome editing that inserts genes creates plants that are still classified as GMOs.[56] Such methods are not yet well-developed,[3,4] but are evolving rapidly.[54] By contrast, inserting genes with GM (at random locations of the genome) is well-developed.[57–60] At present, genome editing is likely to be used to seek genetic outcomes that are argued to be more akin to those of conventional breeding.[61,62]

Genome editing and conventional breeding

Traditional breeding uses the DNA changes (mutations) that spontaneously occur every time DNA replicates in nature (e.g. 120 per seed of wheat[63]). Plant varieties with mutations that are induced by chemical and irradiation techniques are already exempted from UK (retained EU) GMO regulation (Case C-528/16)[5] due to their long history of use since the 1950s.[64] Over 3000 crop varieties have been developed by the latter techniques, which generate thousands of mutations at a time.[64–67] By contrast, genome editing enables the creation of targeted mutations (e.g. a single, or a few DNA base changes) that mimic the changes that occur in nature.[68] Traditional breeding to transfer a desirable trait into a cultivated crop variety from a non-cultivated crop relative requires a long breeding process.[69,70] Typically this requires at least six subsequent generations of breeding back to the cultivated variety to 'reconstruct' previous desirable trait combinations that were present in the cultivated variety.[65,71,72] Genome editing increases the efficiency of introducing single and multiple plant traits,[62,65,73] and can remove undesirable genes without removing nearby (genetically linked) desirable genes.[74] Proponents argue that genome editing may shorten the 8–20 year development of conventional crop breeding to 3-4,[75–78] bringing new varieties to market more efficiently.[27]

Unintended sequence alterations

Computational tools that analyse the genome sequence enable the design of genome editing methods that are highly targeted to a specific genetic location.[79,80] However, genome editing can still lead to unintended sequence changes.[80] For public trust and acceptability on safety, the consequences and risks of these relative to other breeding techniques need to be assessed and understood.[39] Undesired DNA changes may be detected by sequencing whole genomes of plant lines and comparing with validated reference sequences.[81–83] If they result in a safety concern, these lines will not be commercialised.[84] Researchers indicate[83,85,86] that unintended sequence alterations caused by genome editing[87] are minimal compared to natural breeding[88,89] or use of chemicals and irradiation.[90] However, genome editing processes involving plant tissue culture are much more likely to generate unintended changes to the genome.[83,87,91] and even small genetic changes can, in theory, have effects.

Mutations are more likely to occur in nature and through conventional breeding,[83] but off-target mutations might occur during genome editing.[20,92] These are unintended DNA changes that are typically seen at locations in the genome with DNA sequences that closely resemble that of the intended target,[83] and that might result in undesirable changes in plant traits.[63,81] DNA repair mechanisms are involved in off-target, and natural mutations.[63] Careful design of sequence targets can minimise off-target mutations.[83,93–95] For crops such as banana and potato that are grown asexually,[96] breeding to remove off-target mutations is impracticable[97] and a higher standard of design may be needed.[98] A systematic review of 555 articles looking at the effects of genome editing on changes showed that 3% of potential locations contained off-target mutations, but none of these could be correlated to the process of genome editing.[99] The Advisory Committee on Releases to the

Environment (ACRE, a non-departmental public body) found no evidence to suggest that off-target sequence alterations produced by genome editing pose a greater risk than those induced via chemicals or irradiation.[88,100] Small DNA fragments from genome editing methods can remain in the following generation of plants, even after removal attempts.[23,101,102] It is uncertain whether this represents any risk in terms of off-target mutations,[103] but has been identified as a concern for regulatory systems in the EU, USA, South America and Japan.[104]

Changes to regulation

Following a recent consultation on the regulation of genetic technologies,[17] the UK Government is introducing two legislative changes for genome-edited crop plants:[18]

- a statutory instrument has been laid[19] under existing powers in the Environmental Protection Act 1990,[14] to exempt genome-edited crops with changes that could have been achieved via conventional breeding, or which could occur naturally, from the GMO regulation for field trials in England.
- new primary legislation is planned to amend the regulatory definition of a GMO to exclude these crops, and to consider regulatory measures to allow commercialisation.[18]

Field trials

Field trials are required to see how crop traits that are developed and tested in a laboratory setting work in an agricultural setting.[105,106] Few field trials on genome-edited crops have been carried out in England.[12,107,108] Prior to the ECJ ruling,[5] the UK Government exempted genome-edited crops from GMO field trials.[109] The legislative changes proposed should make it easier to conduct field trials, which is likely to boost R&D capacity.[110,111]

Clarifying which genetic changes will be regulated

Commentators have called for clarity on which genetic changes will be regulated.[112] The UK Government has stated that guidance will be published.[18] Genetic changes occur randomly in nature and in a hectare of wheat every single DNA base is estimated to be naturally mutated in at least one individual seed.[35] However, some genetic changes occur extremely rarely,[50,113,114] such as the transfer of 'foreign DNA' from a bacterium into sweet potato thousands of years ago.[115,116]

Regulatory landscape

Regulatory approaches to genome-edited crops differ internationally.[32,117] In 2018, 13 nations supported an international statement to the World Trade Organisation in favour of science-based and internationally-harmonised regulation of genome editing in agriculture.[118] These nations treat certain types of genome-edited crops as non-GMOs, typically if the products only contain DNA from species that can interbreed (such as in Argentina,[119,120] Brazil and the USA),[32] or do not have novel characteristics (Canada).[121,122] The USA regulates products with multiple, but not single, gene edits.[123] Genome-edited products are currently regulated as GMOs in the EU and New Zealand.[32] The European Commission is planning a public consultation on GMO legislation in 2022.[124] The way in which genome-edited crops are regulated has an impact on R&D, and a route to market.[119] Genome-edited crops under development could have benefits for consumers and producers (Box 1).[125,126] Between 1996–2020, 232 studies on crops of commercial interest listed 140 different genome editing applications across 41 different crops.[32] Most of these applications are led by researchers located in China (101), followed by in the USA (78), Japan (17), Germany (7) and France (7)[32] and 3 applications by UK researchers.[12,127,128]

Registering new plant varieties

Plant breeders have established systems for registration of new plant varieties to assess safety, novelty and usefulness.[129] Some commentators have raised transparency concerns over whether genome-edited crops can be registered as conventionally bred varieties.[52] The Royal Society of Biology proposes a 'genome-edited' category to address this.[52,129] The Food Standards Agency (FSA) holds legal responsibility to assess whether genome-edited foods pose human health and nutrition risks.[130,131] GMO regulations require crops to be tested for food safety, including the effects of interactions with the environment.[7] The UK regulates new varieties that are bred conventionally if they present a risk to health and life (of humans, animals, or plants), cultivation (of other plant varieties or species), or the environment.[129]

Route to market and licencing

UK academics and investors mostly collaborate on early stage testing of biotechnology crops,[132] and have called for a clear route to market for genome editing.[112,133,134] International scientists, some governments and agribusiness professionals argue that developing a genome-edited crop (from idea to market) is more expensive when regulated as a GMO (US$ 24.5 million) than as a non-GMO (US$ 10.5 million).[135] The European Federation of Biotechnology has moved research, development and production to outside the EU to avoid these regulatory burdens.[136,137] Route to market could also be impeded by intellectual property and patents, which are given to products that are novel, inventive and useful,[138] and are intended to drive innovation.[138–140] EU biotech patent issues have been debated since the 1990s, but this is exacerbated by the speed at which genome editing can alter multiple,

Box 1: Genome-edited crop products

Genome-edited products are under various stages of development: commercialisation (CM), field trials (FT), glasshouse trials (GT) or discovery (DC). Products include:

- Two genome-edited crops are currently on the market,[33,34] both of which have intended **benefits for consumer health**. These are soybean oil (in the USA only) with reduced saturated fat[141] (CM, 2019)[33] and tomato (in Japan only) that accumulates a chemical that lowers blood pressure[142] (CM, 2021).[34] Products in development with other potential health benefits include: wheat with reduced carcinogens upon baking[143] (FT);[107] wheat with higher dietary fibre (FT);[144] chickpea with higher protein (DC);[145] peanuts that are allergen-free (DC)[146] and wheat that is gluten-free (DC).[147] Products aimed at **consumer convenience** include fruits that are seedless (DC),[148] coffee with reduced caffeine (DC)[149] and corn that is higher in thickening starch (DC).[150]
- Products aimed at **benefits for crop productivity** by means of **crop protection** include rice (FT)[151] and canola (GT)[151] that are tolerant to herbicides. Such applications are controversial due to the blanket spraying of the crop with the associated herbicide.[152] **Lower chemical inputs** might be achieved in: canola (FT),[151] banana (DC),[153] wheat (DC),[151] and rice (DC),[151] that are resistant to diseases; and rice (DC) and canola (DC)[151] that use nitrogen fertilizer more efficiently.[151] **Improved harvest yields** via canola whose pods resist shattering (FT).[151]

patentable traits[154] in a single generation,[78] with thousands of patent applications filed for genome-edited crop traits.[155] However, breeders who struggle to remove multiple patented plant traits from crop varieties may need complex licence negotiations to further develop and market these.[78,156] Traditionally bred crops cannot be patented[157] and are granted Plant Variety Protection (PVP) as intellectual property rights (PN 517).[129,158] PVP allows breeders to harness variation created by others, avoiding the obstructions caused by patents.[159–161] It is not clear which intellectual property approaches UK breeders will choose to adopt for genome-edited crops.[162]

Key issues

Proponents of genome editing view it as just another tool for crop improvement.[21,163] Others have highlighted concerns about over-hyping the technology,[36,164] and have questioned whether the proposed timelines for benefits will be delivered.[35] Public acceptance, in terms of potential risks and benefits, emphasise the importance of traceability, transparency and public engagement, impacts on farming and trade.

Public acceptance

Public acceptance of genome-edited food depends on perceptions of risks and benefits.[165] Public perception of risk is often said to be lower for genome editing than genetic modification,[166,167] and more positive to genome editing of plants than of animals.[168,169] Consumers are more likely to be in favour if they can see direct, personal and tangible benefits,[170] which is conditional on no health risks.[166,171] Similar to other studies,[172] an FSA survey found greatest willingness (48% yes, 34% no, 19% unsure) to eat genome-edited food if it was better for the environment.[166] Other commentators have also suggested assessing these crops for potential societal and environmental benefits.[50,129] Risk acceptability is not only determined by quantifying unintended consequences.[51,84] It also depends on equitable and proportional distribution of their tangible and potential benefits,[173,174] and the wider social and economic benefits.[126,175–177] All European Academies support assessing the risks and benefits of both adopting[178,179] and not adopting[180] genome-edited crops.[51] Trust in institutions using biotechnology affects perceptions of risks and benefits.[181,182] Trust may be built collaboratively by understanding the diversity of perspectives, motives and values surrounding genome editing.[183–190] Polarised debates on genome-edited foods may increase public disquiet.[191] Regulators framing genome editing as similar to natural processes[185] may increase perceptions of disingenuity.[192,193] Consumer choice,[166] trust[161,186] and trade[194] rely on traceability and transparency of genome-edited food crops.

Detection and traceability

Commentators believe that consumers have the right to make choices based on transparent, publicly available food supply chain information.[166,195,196] However, it is not yet possible to unequivocally[197] determine if mutations have occurred by genome editing, as it does not leave any marker in the genome (PN 517).[21,53,198] This raises questions about the extent to which genetic detection might benefit traceability.[199,200] Even a single DNA base change can be detected with existing technology,[201] and whole target genomes could be compared to a reference genome to screen for mutations in products not known to have genome edits.[202–204] However, these do not provide evidence of genome editing.[21,202,205] UK seed market testing regulations for commercialisation requires traceability (provenance).[206] An international public registry of all commercial agricultural biotechnology products, including genome editing, may inform targeted testing and transparency.[161,207–209] However, some types of genome-edited plants are already de-regulated as conventional varieties in countries such as Australia.[194,210]

Transparency and labelling

The European Group on Ethics in Science and New Technologies recommends that traceability and labelling should only be mandatory for mutations that could not have occurred naturally.[200] In Japan, a genome-edited tomato is voluntarily labelled;[211,212] a sentiment analysis of Japanese Twitter posts showed 62.8% of tweets negative about the lack of mandatory labelling policy.[213] Responses to an FSA 2021 survey of 2066 adults aged 16–75 in England, Wales and Northern Ireland showed 63% and 21% rated labelling of possible genome-edited food products for sale in the UK as "Very important" and "Fairly important", respectively.[166] At workshops, 73% supported a product link for further information,[166] which could include provenance, nutrition and sustainability metrics.[35,200]

Public communication and engagement

Surveys and textual analyses have found that consumers have a low level of knowledge of genome editing.[166,170,214] This may affect public engagement in ethical debates,[215] and delivering accurate and meaningful information on the genome-edited product without creating misunderstanding.[166,216] Explaining genome editing at an FSA workshop helped participants to form opinions, increasing both non-concern (28% to 57%) and concern (33% to 42%).[166] Engaging the public may guide decisions about deploying genome editing,[185,190] which may require engaging a diversity of cultures and regions[161] through approaches such as a Stakeholder Advisory Panel.[50]

Impacts on farming

Use of GM and genome-edited products are prohibited in organic farming,[217] with financial losses due to GM contamination incurred (448 across 64 countries 1997-2016) [218,219] and the risk of withdrawal of organic certification and product recalls.[220,221] Particular concern has been raised for crops genome-edited to be herbicide-tolerant,[38,50,215,222,223] which could cause unintended declines in biodiversity and genetic diversity in crop varieties.[184,224–226] Others suggest use of genome editing will reduce chemical inputs by breeding for traits such as disease resistance.[227,228]

Domestic and international trade

Trade of genome-edited food crops is a complex issue.[32,194,229] Planned changes to field trial regulation will only apply to England.[18] Scotland has committed to seek alignment with current EU regulations on GMOs,[230,231] and Wales are against deregulating genome editing from GMO regulation.[232,233] Of the 27 EU countries, 16 prohibit use of GMOs,[234] and products from genome editing may still be licenced as GMOs if there are no changes in EU policies.[124,224] There is no international organisation that oversees regulatory alignment of genome-edited food products,[117,207,235–237] and agreeing international definitions will be a key step for harmonising regulation.[238] The International Seed Federation guidelines propose exempting products that contain only stable insertions of genetic material from plant species that can interbreed naturally.[239–242]

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