GENE EDITING
MYTHS AND REALITY

A guide through the smokescreen

THE GREENS/EFA in the European Parliament

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INTRODUCTION

An unprecedented drive is under way to promote new genetic modification techniques that are collectively termed gene editing – most notably CRISPR/Cas. The agricultural biotech industry claims that these techniques can provide solutions to our food and farming problems, including the challenges posed by climate change, pests, and diseases.

This guide looks at the claims and shows them to be at best misleading and at worst deceptive. Each of the eight chapters focuses on one claim about gene editing and presents the evidence proving it to be false.

In the EU, all of the claims are brought with the intention of questioning the existing GMO regulations and getting GMOs engineered with gene editing excluded from them. These regulations exist in order to protect public health and the environment and to give consumers and farmers the right to know what they are eating and planting in their fields.

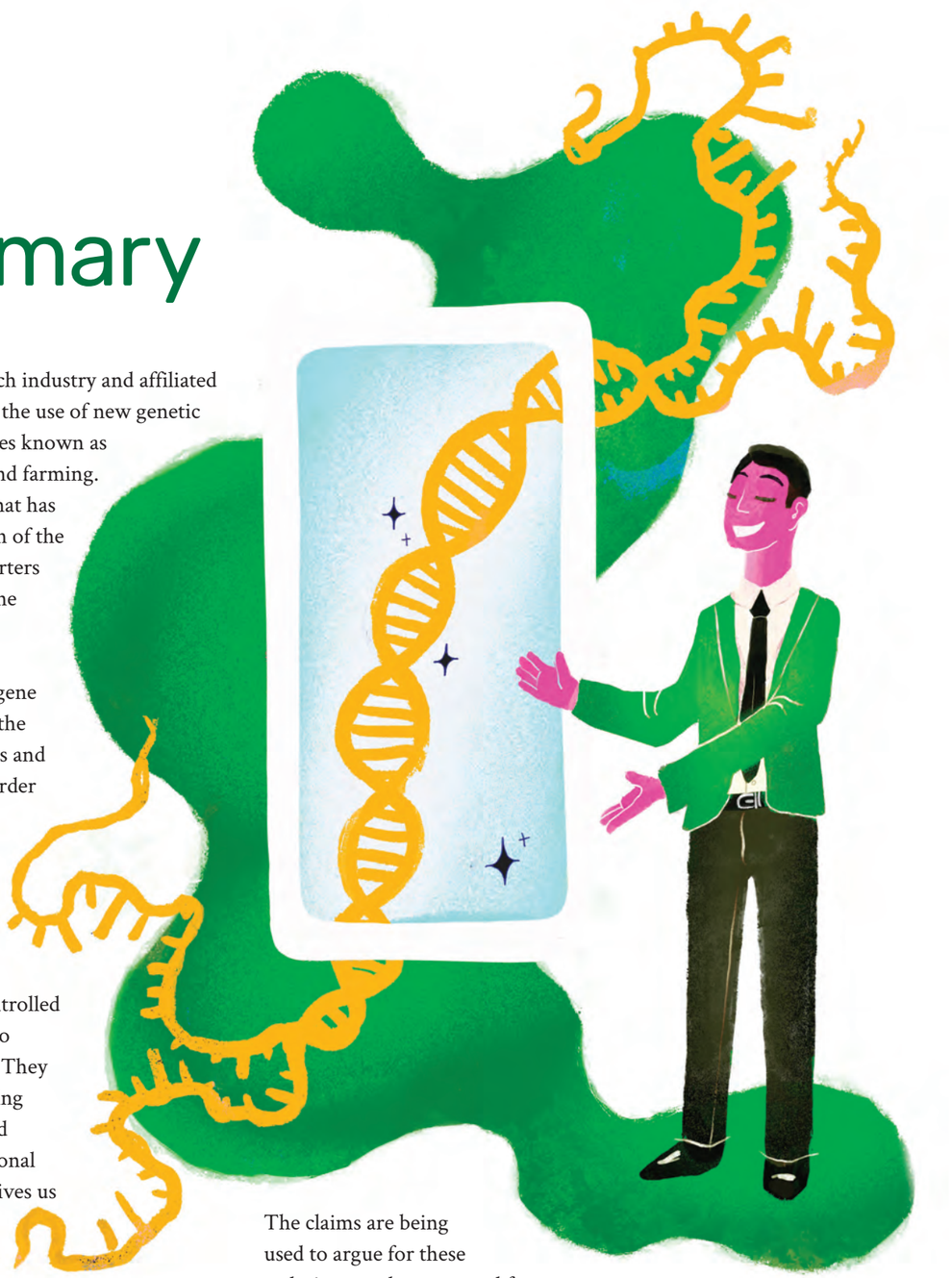
It is worth noting that those who want to exclude gene editing from the GMO regulations also question those regulations as they apply to older-style GMOs. They say GMOs are beneficial and safe, and cast doubt on the need for safety assessments and labelling.

However, to exempt gene editing from the GMO regulations – or to dismantle the regulations for all GMOs – would be a step backwards and a dangerous weakening of EU health and environmental standards. This is because many of the risks attached to older-style GMOs still apply to gene-edited GMOs, and they also present new and special risks.

This guide focuses mainly on gene editing in plants because this is the area that has caught the imagination of GMO developers, researchers, and the media worldwide, though some information on livestock gene editing is also included.

It shows that gene editing is a costly and potentially dangerous distraction from the real solutions to the challenges faced by our food and farming sectors. These are mentioned throughout and form a major focus of the final chapter.

Summary



The agricultural biotech industry and affiliated groups are promoting the use of new genetic modification techniques known as gene editing in food and farming. The main technique that has caught the imagination of the industry and its supporters is the CRISPR/Cas gene editing technique.

The industry is using gene editing to manipulate the genomes of crop plants and livestock animals, in order to confer new traits. They make a range of claims for these techniques – for example, that gene editing is precise, safe, and so highly controlled that it only gives rise to predictable outcomes. They also say that gene editing is widely accessible and quicker than conventional breeding, and that it gives us the tools to enable us to meet the challenges of environmental degradation and climate change.

However, none of these claims stand up to scrutiny, as shown by the evidence presented in this guide. All are exposed as false or misleading.

The claims are being used to argue for these techniques to be exempted from the EU's GMO regulations. This would mean that products of these techniques would not be subjected to safety testing, traceability, or GMO labeling, and EU countries could not ban their cultivation. As a result, these GMOs would end up on our fields and plates untested and unlabelled, and farmers and food producers – including those operating under organic systems – would have no way of avoiding them.

The misrepresentation begins with the terminology used to describe them. Contrary to industry claims, gene-editing techniques are not breeding techniques, but are genetic modification techniques that share some of the same methods as old-style genetic modification.

Gene editing causes many unintended changes and genetic errors

Also contrary to the claims made, these techniques are not precise or controlled, nor do they have predictable outcomes.
In addition to the intended genetic change, gene editing causes many unintended changes and genetic errors. This can include the inadvertent addition of foreign DNA from other species, or even entire foreign genes, into the genome of gene-edited organisms, even when the intention is specifically to avoid this.

The effects of these changes on the composition of gene-edited crops, foods, and animals, as well as the consequences to health and the environment, have not been investigated and remain unknown. In food crops, they could include the production of unexpected toxins and allergens, or altered levels of existing toxins and allergens.
The industry says that the changes made by gene editing in crops and livestock animals are small and the same as could happen in nature. But this claim is proven false by the worrying surprises that have already come to light. For example, the company that developed gene-edited hornless cattle claimed they were free from unintended effects of the gene editing. But the cattle were revealed by US regulators to contain bacterial DNA and foreign genes that confer resistance to antibiotics.

Also, CRISPR gene editing of rice plants was shown to cause a wide range of unintended mutations, both at the intended editing site and at other locations in the genome.

The researchers who made this discovery warned that CRISPR gene editing "may be not as precise as expected in rice". They added, "early and accurate molecular characterization and screening must be carried out for generations before transitioning of CRISPR/Cas9 system from lab to field" – something that is not generally done by developers.

Given the inherent inaccuracy of gene-editing techniques and the challenges of producing gene-edited plants or animals that perform as expected, claims that gene editing can produce useful traits far more quickly than conventional breeding are highly questionable. Even if the time taken to gain regulatory approval is excluded, it is unlikely that the time needed to commercialize gene-edited crops will be significantly shorter than with conventional breeding. Moreover, achieving useful traits in crops or animals is not just a matter of speed – it is a question of using the best tools for the job, and GM approaches are not an efficient route.

Despite years of research and permissive regulatory regimes in some countries, only two gene-edited products have successfully made it to market and neither was produced with the much-hyped CRISPR/Cas tool.

The claim that gene editing, in particular through CRISPR/Cas, will make agricultural innovation accessible to publicly funded breeding programmes is disproven by the fact that the technology is already owned and controlled by a very few large corporations, led by Corteva and Monsanto/Bayer. While evaluation and research licences can be obtained cheaply or free of charge, commercial licences and associated royalty payments on product sales will remain too expensive for anyone apart from large multinationals. Gene-edited products are also patented: in crop plants, patents cover seeds, plants, and often the harvest, raising issues of consolidated control of the food supply, farmers' autonomy, and loss of food sovereignty.

A form of emotional blackmail is being used to convince policymakers of the moral imperative to embrace new GM technologies. The promise is that these technologies will enable the development of crops that require less pesticide and are adapted to climate change.

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However, the same promises were also made for first-generation GM crops and proved false. New GM techniques are unlikely to succeed where "old GM" failed, because desirable traits such as pest and disease resistance and adaptation to climatic changes are genetically complex traits that cannot be achieved by manipulating one or a few genes.

Conventional breeding, in contrast, continues to be highly successful in achieving such traits and far outstrips GM approaches.

It is not enough to focus on genetics as the solution to agricultural problems – whole systems approaches are needed. This would entail a large-scale shift to proven-successful agroecological systems of farming, which include low-input, genuinely sustainable, and regenerative methods. These methods are already available and only need to be properly supported to enable broader rollout

Gene editing is a costly distraction from real, systems-based solutions

Gene editing is a costly distraction from these systems-based solutions. Its exclusion from EU GMO regulations would serve to boost a questionable experiment with unknown consequences for people, animals and the environment. It would also deprive European consumers, farmers and breeders of the right to know where these GMOs are and impede advances in non-GM approaches, including organic and agroecological systems. It would represent a significant weakening of EU health and environmental protections and undermine the rollout of proven effective and sustainable solutions to our food and farming challenges.

1. Gene editing is genetic engineering, not breeding

MYTH

Gene-editing techniques are “new breeding techniques”, “precision breeding” or “breeding innovation”.

REALITY

Technically and legally, gene-editing techniques are genetic modification techniques, not breeding methods.

The agricultural biotechnology industry and its lobbyists often refer to new genetic modification (GM) techniques, especially gene editing, as “breeding innovation”, “precision breeding techniques” and “new breeding techniques”.[1,2,3,4] They strenuously try to avoid the terms “genetic modification” and “genetic engineering”. Corteva, the company that controls the use of CRISPR gene editing in crop plants, even argues that “CRISPR-produced plants are not GMOs”.[5]

European institutions also avoid the terms “genetic modification” and “GMO”. The Council of Ministers introduced the term “novel genomic techniques”,[6] which the Commission adapted to “new genomic techniques”.[7] The Commission also talks about “new techniques in biotechnology”.[8]

The use of the term “breeding” appears to be an attempt to give an air of naturalness to the new genetic engineering techniques and thus convince the public to accept them. It may also be an attempt to make the application of GMO regulations appear counterintuitive and illogical: If gene-edited products are not GMOs, why should they be regulated as GMOs?

However, gene-editing techniques are not breeding techniques. They are technically and legally GM techniques, give rise to genetically modified organisms (GMOs), and fall within the scope of EU GMO laws, as confirmed by the European Court of Justice ruling of 2018.[9,10]

EU law defines a GMO as an organism in which “the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination”.[11] This wording accurately describes the way in which older-style transgenic and new GMOs, such as gene-edited plants, are produced. Genetic modification employs artificial techniques that require direct human intervention in the genome. In contrast, the terms “mating and/or natural recombination” describe natural processes used in conventional plant and animal breeding.

EU law defines a GMO as an organism in which “the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination”

EU GMO law exempts some GMOs, such as those produced using a decades-old technique called mutation breeding (also called random mutagenesis), from its requirements for authorisation, traceability and labelling. But this is only possible if they were produced using techniques that have a “long safety record”.[9] This is clearly not the case with gene editing.

HOW DOES GENE EDITING WORK?

Old and new GMOs have more in common than proponents would have us believe. Of three steps involved in genome editing – gene delivery, gene editing, and whole plant regeneration in tissue culture – the first and last essentially remain the same. The first step, delivery of foreign genetic material into the plant cells (also called GM transformation) is usually done with the help of small circular DNA molecules (plasmids) that are introduced into the cells using a soil bacterium called Agrobacterium tumefaciens or a method called particle bombardment. The plasmid then inserts itself into the plant cell's DNA.

Regarding the "editing step", the majority of gene-editing applications involve first cutting the DNA with enzymes, called nucleases, which are supposed to act only at chosen sites in the genome of a living cell.

These gene-editing applications are called "site-directed nuclease" or "SDN" procedures. The SDN creates a double-strand break in the DNA. The enzymes most commonly used for this cutting are the Cas family of proteins (for CRISPR) and FokI (for TALENs and Zinc Finger Nucleases).[12]

The cutting event triggers alarm signals in the cell, as broken DNA is dangerous to the organism. So the cell initiates a DNA repair process to mend the double-strand DNA cut. While the initial break in the DNA can be targeted to a specific site in the genome, the subsequent "repair" is carried out by the cell's innate repair mechanisms and cannot be controlled by the genetic engineer.'

While the initial break in the DNA can be targeted to a specific site in the genome, the subsequent "repair" cannot be controlled by the genetic engineer

The repair is often not clean or precise, but can result in "chromosomal mayhem" in the genome, to cite the title of a commentary on studies on CRISPR/Cas gene editing in human embryos.[13]

The result of the repair is called the "edit". Researchers must select from many edited organisms to obtain the one they desire.[12]

Some divide SDN procedures into SDN-1, SDN-2, and SDN-3.[14] They can be defined as follows:

• SDN-1 refers to disruption of the function of a gene (also known as gene knockout). The repair of the double-strand break in the DNA results in either a deletion (removal) of part of the gene or the insertion of additional DNA base units, which are taken from the genome of the organism that is being edited. This disrupts the sequence of the gene and thus knocks out its normal function.

• SDN-2 refers to gene alteration. While the break is repaired by the cell, a repair template is supplied that is complementary to the area of the break, which the cell uses to repair the break. The template contains one or several DNA base unit sequence changes in the genetic code, which the repair mechanism exchanges into the plant's genetic material, resulting in a mutation of the target gene. The mutated gene will then produce an altered protein product with an altered function.

• SDN-3 refers to gene insertion. The DNA break is accompanied by a template containing a gene or other sequence of genetic material. The cell's natural repair process uses this template to repair the break, resulting in the insertion of new genetic material (foreign DNA, which can include a whole new gene). The aim is to confer novel functions and characteristics on the organism.

Another gene-editing technique is oligonucleotide-directed mutagenesis (ODM). ODM does not cause a double-strand break in the DNA. Instead it involves the introduction of short sequences of synthetic DNA and RNA – called oligonucleotides – into the cells. The oligonucleotide interacts with the cell's DNA, tricking the cell's repair mechanisms into altering the cell's own DNA to match that of the oligonucleotide.

All these techniques will change the biochemistry of the plant – this is the aim of gene editing – so that a new trait can result.

GENE EDITING IS GENETIC MODIFICATION

Although GM and conventional breeding will result in the creation of new varieties, the two are distinct methods and are not interchangeable. Gene editing is clearly a GM technique but conventional breeding is not, however hard the agricultural biotech industry tries to blur the boundaries.

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2. Gene editing is not precise and causes unpredictable genetic errors

MYTH

Gene-editing tools such as CRISPR/Cas bring about changes in the genome in a precise and controlled way, with predictable outcomes.

REALITY

Gene editing is not precise, but causes many genetic errors, with unpredictable results, in addition to any intended genetic change.

The agricultural biotech industry and its allies claim that gene-editing tools such as CRISPR/Cas bring about changes in the genome in a precise and controlled way.[1,2,3] Some even claim that they bring about only the specific intended changes and nothing else.[4,5] They argue that gene-edited products should therefore be excluded from the regulatory oversight applied to older-style transgenic GMOs,[3,5] where (in most cases) DNA is introduced from another species into a part of the genome that cannot be determined beforehand.

However, these claims do not survive scrutiny.A large and ever-growing number of scientific studies in human, animal and plant cells show that gene editing is not precise but gives rise to numerous genetic errors, also known as unintended mutations (DNA damage). These occur at both off-target sites in the genome (locations other than that targeted for the edit) and on-target (at the desired editing site). The types of mutation include large deletions, insertions, and rearrangements of DNA.[6,7,8]

These mutations occur at various stages of the process, including stages that gene editing has in common with old-style transgenic GM methods, such as tissue culture and GM transformation by Agrobacterium tumefaciens infection (in which this soil bacterium is used to insert the foreign genetic material into the DNA of plant cells).[9]

Even the intended changes can cause unintended effects ("pleiotropic effects") in the edited organism,[10] since genes and their protein or RNA products act in networks and not in isolation.

GENE EDITING PRODUCES A RANGE OF UNINTENDED MUTATIONS

Even the simplest application of gene editing (so-called SDN-1), which is intended to destroy a gene function, can lead to unwanted mutations.[11,12,13] These mutations can lead to the creation of new gene sequences producing new mutant proteins, with unknown consequences to the health of consumers of the gene-edited organism. In addition, alterations in the pattern of gene function can take place within the organism whose genome has been modified.

> Unwanted mutations can lead to the creation of new gene sequences producing new mutant proteins, with unknown consequences to the health of consumers of the gene-edited organism

In plants, these alterations can lead to compositional changes, which, scientists warn, could prove to be toxic and/or allergenic to human or animal consumers.[6,8,14]

Unintended mutations and their effects are under-researched in plants compared with human and animal cells. But since the mechanisms of gene editing and subsequent DNA repair are the same between animals and plants, there is every reason to believe that the types of unintended mutations seen in human and animal cells will also be found in plants. Recent research in rice plants attests to this fact.[15]

A study on rice varieties found that CRISPR gene editing caused a wide range of undesirable and unintended on-target and off-target mutations. The researchers were aiming to improve the yield of already high-performing varieties of rice by disrupting the function of a specific gene, in an SDN-1 (gene disruption) procedure.[15] They were trying to produce small insertions and deletions of DNA base units in the genome. However, what they got was quite different. In many cases they found large insertions, deletions, and rearrangements of DNA, raising the possibility that the function of genes other than the one targeted could have been altered.[15]

> In plants, alterations in the pattern of gene function can lead to compositional changes, which could prove to be toxic and/or allergenic to human or animal consumers

As for the hoped-for increased yield, the opposite was found – yield was reduced.[15] This should not come as a surprise, as yield is a genetically complex trait that involves the functioning of many, if not all, gene families of the plant. Thus altering the function of one gene to improve yield could be viewed as a futile exercise.

The researchers warned that CRISPR gene editing "may be not as precise as expected in rice". They added, "early and accurate molecular characterization and screening must be carried out for generations before transitioning of CRISPR/Cas9 system from lab to field".[15] Developers do not generally do this, or if they do, the results are not published.

The researchers concluded, "Understanding of uncertainties and risks regarding genome editing is necessary and critical before a new global policy for the new biotechnology is established".[15]

INADEQUATE SCREENING FOR UNINTENDED MUTATIONS

Most studies that look for unintended mutations in gene-edited plants grossly underestimate the number of mutations resulting from gene editing and associated processes such as tissue culture (growth of plant tissues or cells in a growth medium). This is true both for studies that conclude that gene editing causes many such mutations and those that conclude that it causes few or none. The reason is that the authors of these studies use inadequate detection methods – short-range PCR and short-read DNA sequencing – to look for mutations. They only look at short stretches of the DNA around the targeted editing site and computer programme-predicted off-target sites.

As Kosicki and colleagues found in a study on human cells, short-range PCR and short-read DNA sequencing can miss major genetic errors, such as large deletions and insertions

and complex rearrangements of DNA.[16,17] The researchers concluded that a combination of long-range PCR and long-read DNA sequencing is needed to spot the full range of unintended mutational effects.[16] FDA scientists have made the same recommendation, with regard to gene-edited animals.[18]

This principle applies to plants just as much as animals, since the mechanisms of gene editing and the subsequent repair that forms the "edit" are the same.

In a scientific review, Kawall and colleagues confirmed that the "vast majority" of studies on gene-edited plants used biased detection methods to screen for genetic errors, meaning that they will miss many such errors. Among studies on gene-edited animals, none included a thorough analysis of genetic errors.[6]

CIBUS'S CANOLA: "PRECISION" GENE EDITING OR ACCIDENT IN A PETRI DISH?

In September 2020, the biotech company Cibus claimed that its herbicide-tolerant SU Canola (oilseed rape) was not gene-edited but was the result of random mutation caused by tissue culture – effectively, an accident in a laboratory Petri dish. This claim came after the company had for many years said (including to regulators) that SU Canola was made with its "precision gene editing" technique, called oligo-directed mutagenesis (ODM).[19,20,21] In fact, ODM constitutes the very foundation of its business model.[22]

> The vast majority of studies on gene-edited plants used biased detection methods to screen for genetic errors

Indeed, numerous public records point to the fact that Cibus used gene editing in the process of engineering SU Canola.[19,20,23] But it turned out that the oligonucleotide used was designed to produce a different genetic change from the one that was found to confer herbicide tolerance in SU Canola and that Cibus described in its patent application.[21] So the "precision" tool did not work as intended, leading Cibus to announce that the crop was not gene-edited after all.

It would appear that Cibus made that claim only to evade EU GMO regulations. The timing is remarkable: Shortly before Cibus made its statement,[20] a scientific paper had been published, reporting the development of the first publicly available detection method for SU Canola.[24] However, under EU law, even if the specific mutation that confers the herbicide tolerance was not the intended result of the ODM editing process, the fact that the ODM tool was used to develop the SU Canola means that it is a GMO. Since it has no EU authorisation, its presence in EU imports would be illegal.[23]

This episode raises questions about Cibus's honesty and transparency. But more importantly, it shows that the precision and control claimed for the ODM gene-editing technique was false.

"OLD" MUTAGENIC GM TECHNIQUES ARE USED IN GENE EDITING

First-generation genetic engineering techniques are still often used to introduce CRISPR editing tools into plant cells. Plasmids containing genes encoding the CRISPR/Cas editing tool are introduced into the cells using either Agrobacterium tumefaciens infection or particle bombardment.[6] In addition, tissue culture is used to grow the plant cells. All three processes are highly mutagenic.[25] The mutations caused by these processes will be in addition to the unwanted mutations caused by the gene repair process (the actual "edit").

> A study on CRISPR gene-edited rice has found that many off-target mutations resulted from tissue culture, and yet more resulted from Agrobacterium infection

A study by Tang and colleagues on CRISPR gene-edited rice illustrates the mutagenic nature of these processes. The study found that many off-target mutations resulted from the tissue culture, and yet more resulted from Agrobacterium infection (around 200 per plant). In contrast, seed saved from non-GM rice plants had only 30–50 spontaneous mutations per plant.[9] Thus the study found that the CRISPR process, taken as a whole, caused large numbers of off-target mutations and far more than conventional breeding.

Ironically, this study is often cited as an example of the precision of this gene-editing tool. This is because it found that the CRISPR editing tools themselves did not introduce many off-target mutations into the plants' DNA.[9] However, this finding is likely not accurate, due to the researchers' use of inadequate screening methods (see "Inadequate screening for unintended mutations", above) – they did not use long-read DNA sequencing. Also, the findings must be viewed in the context of the above-mentioned separate study on rice that found that CRISPR gene editing caused a wide range of unintended on-target and off-target mutations.[15]

THREAT TO HEALTH AND ENVIRONMENT

Based on the above evidence, gene editing is neither precise nor controllable, but could inadvertently produce traits that threaten public health and the environment.

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3. Gene editing causes genetic changes that are different from those that happen in nature

MYTH

Changes brought about by gene editing are the same as could happen in nature or mutation breeding.

REALITY

Gene editing causes genetic changes that are different from those that happen in nature or mutation breeding and their consequences are poorly understood.

Lobbyists claim that gene editing techniques "generally create plant products that may also be obtained using earlier breeding methods"[1] such as mutation breeding, or that could result "from spontaneous processes in nature".[2]

Mutation breeding (also called random mutagenesis) is a decades-old technique in which seeds are exposed to chemicals or radiation to induce mutations in the hope that one or more may result in a useful trait. The lobbyists say that gene editing is more precise than muta

tion breeding, yet mutation bred plants are exempted from the requirements of the GMO regulations, so gene-edited plants should also be exempted.[3]

However, claims that gene editing can produce organisms that could arise in nature or through mutation breeding are entirely theoretical.

No one has proven that any given gene-edited organism is the same as a naturally occurring vor mutation bred organism, either at the level of the genome or in terms of its molecular composition (the proteins and natural chemicals that make up the structure and function of the organism).

Indeed, if someone were to produce a gene-edited organism that was the same as a naturally bred one, this would call into question any patent on the gene-edited organism, as patents require an “inventive step”.

NO EVIDENCE THAT CHANGES FROM GENE EDITING ARE FEWER THAN FROM CONVENTIONAL OR MUTATION BREEDING

Dr Michael Antoniou, a molecular geneticist based at a leading London university, said that claims that the mutations induced by gene editing are the same as could happen in nature or mutation breeding are scientifically unfounded. Moreover, he said there is no evidence demonstrating that gene editing is more precise, in the sense of causing fewer mutations, than conventional breeding or mutation breeding.

He said “Gene editing can cause large deletions, insertions, and rearrangements in DNA, which can affect the function of multiple genes at off-target and on-target sites.” I am not aware of any studies using reliable screening methods that compare the frequency of these types of large-scale DNA damage in conventionally bred, mutation bred, and gene-edited plants. What we do know is that there is clear experimental evidence showing that assumptions that gene editing only causes small insertions and deletions at off-target and on-target sites are false.”[4]

> “Gene editing can cause large deletions, insertions, and rearrangements in DNA, which can affect the function of multiple genes at off-target and on-target sites”
> - Dr Michael Antoniou

MUTATIONS FROM GENE EDITING ARE DIFFERENT IN TYPE FROM THOSE FROM CONVENTIONAL OR MUTATION BREEDING

Evidence shows that mutations induced by gene editing are not the same as those induced by chemicals or radiation in mutation breeding. For example, a scientific review shows that gene editing can produce changes in areas of the genome that are otherwise protected from mutations.
In other words, gene editing makes the whole genome accessible for changes.[5]

Dr Michael Antoniou says that mutations induced by mutation breeding will more often than not occur in areas of the genome that are non-coding and non-regulatory and therefore are unlikely to affect gene function.

With gene editing, in contrast, mutations are more likely to happen at locations in the genome that directly affect the function of one or more genes. First, there is intentional targeting of a gene’s coding region or its regulatory elements to alter its function. Gene editors will preferentially target sites that are relevant for protein production and gene regulation for alterations, since the objective is to change a trait. Second, much of the off-target mutation-causing activity of the gene-editing tool will occur at locations within the genome with a similar DNA sequence to the intended target site. This means that if the intended gene editing target site is a gene’s coding region or its regulatory elements, off-target mutations will occur in other genes with a similar DNA sequence.

As a result, off-target and unintended on-target mutations are likely to affect important protein-coding gene regions and gene regulatory activity.

A separate scientific review shows that gene-editing techniques enable complex alterations of genomes that would be extremely difficult or impossible to achieve with conventional breeding or mutation breeding. In gene editing, so-called multiplexing approaches allow the targeting and alteration of multiple gene variants, which can be members of the same or different gene families.[6]

In summary, gene editing can cause specific unintended effects and can be used to generate novel genetic combinations that cannot readily be achieved using conventional breeding or mutagenesis techniques. It can overcome genetic limitations that exist in conventional breeding.[6]

These unique attributes of gene-editing applications show that they pose unique risks, justifying strict regulation.

REDESIGNING NATURE

CRISPR inventor Jennifer Doudna has made clear that the aim of CRISPR gene editing is not to replicate or enhance nature but to redesign and replace it. She wrote:
"Gone are the days when life was shaped exclusively by the plodding forces of evolution. We're standing on the cusp of a new era, one in which we will have primary authority over life's genetic makeup and all its vibrant and varied outputs. Indeed, we are already supplanting the deaf, dumb, and blind system that has shaped genetic material on our planet for eons and replacing it with a conscious, intentional system of human-directed evolution."[7]

However, given that scientists do not fully understand the function of the vast complex networks of genes and their products that constitute a healthy functioning organism, they are not remotely close to being able to predict the outcome even of a single gene manipulation. Thus it is difficult to see how a new era in human-led predictable, directed evolution has dawned. From this perspective, when it comes to evolutionary processes, it is arguably genetic engineering that is a "deaf, dumb, and blind system", rather than nature.

> The limitations imposed by natural processes may help, rather than impede, evolution

The limitations imposed by natural processes may help, rather than impede, evolution.

NOT NATURE-IDENTICAL

The evidence shows that the genetic changes brought about by gene editing are different from those that would happen in nature or mutation breeding and their outcomes and the risks attached to them are poorly understood.

With this in mind, gene editing must remain under the EU's GMO regulations and the risk assessment should be broadened to take account of the special risks attached to the technology.

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4. Gene editing is risky and its products can be unsafe

MYTH

The precision and control of gene editing mean that it is safe-by-design.

REALITY

The unintended outcomes of gene editing lead to risks, which are poorly understood.

Claims that gene editing is "breeding", that it is "precise", and that outcomes are "nature-identical" are often made to imply that gene-edited organisms will be safe-by-design.

Some GMO developers have gone further, explicitly claiming that gene-edited plants are just as safe as conventionally bred ones.
Bayer claims that compared with conventional breeding, CRISPR/Cas gene editing is "simpler, faster and more precise, with no impact on the safety of the final crop compared to traditional plant breeding".[1]
And Corteva says that CRISPR-edited plants are "as safe as plants found in nature or produced through conventional breeding".[2]

> Some GMO developers claim that gene-edited plants are just as safe as conventionally bred ones

The agbiotech industry argues that it would therefore be "disproportionate" to subject these products to GMO regulatory requirements aimed at ensuring their safety.[3] Corteva sees no need to conduct safety testin on its gene-edited crops

and says it tests CRISPR-produced plants in "the same way" as it tests conventionally bred plants.[4]

However, as we have seen in previous chapters, gene editing is not precise, nor are the outcomes identical to those of conventional breeding. While the initial cut in the DNA can be targeted to a specific region of the genome, the subsequent DNA repair process causes unwanted mutations both at on-target and off-target sites in the genome.[5,6,7]

Techniques common to both gene editing and older transgenic GM methods, such as tissue culture and GM transformation, will lead to additional mutations (see chapter 2).

> Unintended genetic changes will alter the pattern of gene function within the organism

These unintended genetic changes will alter the pattern of gene function within the organism. In plants, this can alter biochemical pathways and lead to compositional changes, which, scientists warn, could include the production of novel toxins and allergens or altered levels of existing toxins and allergens.[8,9,10]

GENE EDITING CAN UNINTENTIONALLY ADD FOREIGN DNA IN THE GENOME

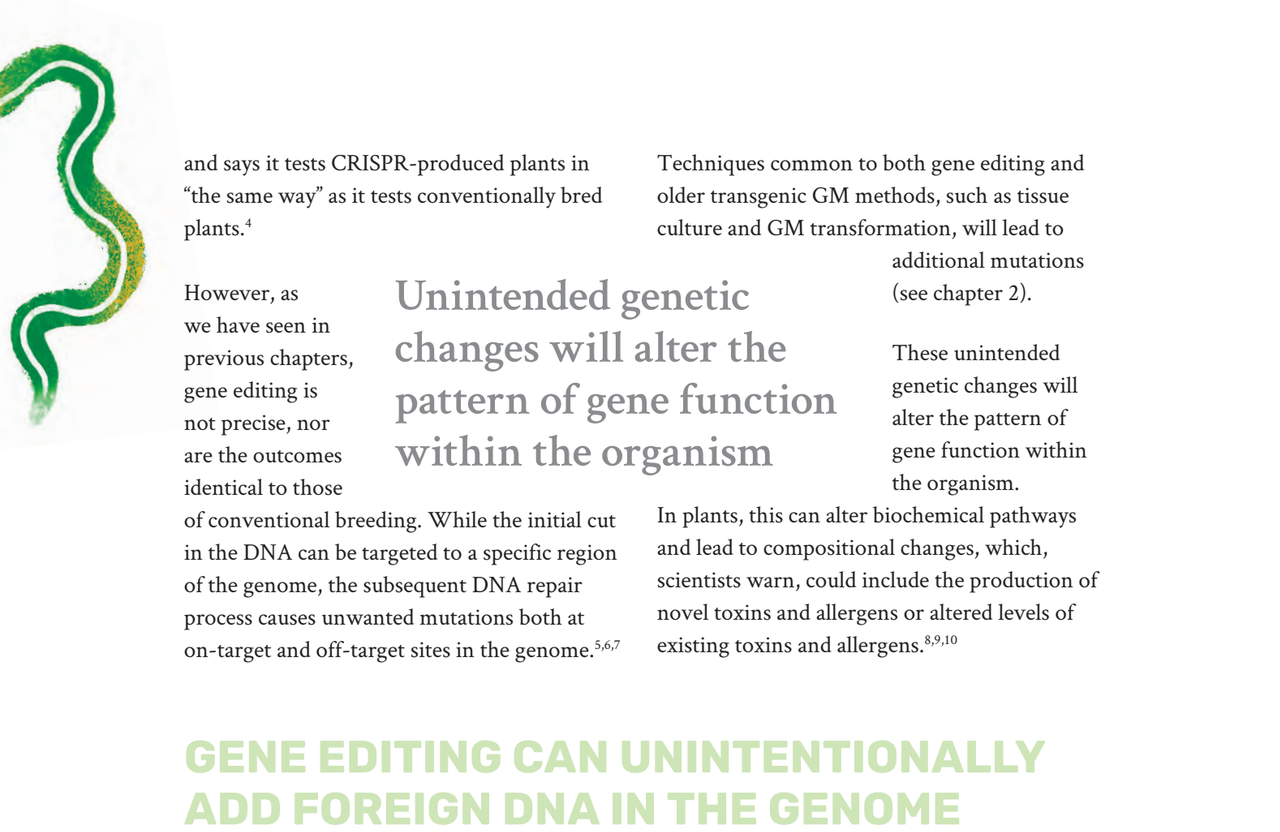
The presence of unintended mutations has been well documented in human and animal cells and has begun to gain more attention in plants.[11] However, another unwanted outcome of gene editing has received little attention and it is unclear to what extent it occurs in animal and plant cells and what the effects might be.

> Edited mouse genomes unintentionally acquired bovine or goat DNA

This outcome was highlighted in a study by Japanese researchers. The study found that even SDN-2 (gene alteration) applications of CRISPR/Cas gene editing, which aim not to introduce foreign DNA, resulted in the unintended incorporation of foreign and contaminating DNA into the genome of gene-edited organisms.[12] This unwanted result is not restricted to CRISPR but has been found with other types of gene editing, too.[13]

Specifically, the researchers looked at the effects of CRISPR/Cas gene editing in mouse cells and embryos and found that edited mouse genomes unintentionally acquired bovine or goat DNA. This was traced to the use, in standard culture medium for mouse cells, of foetal calf serum and goat serum extracted from cows or goats.[12]

Even more worrisome, amongst the DNA sequences inserted into the mouse genome were bovine and goat retrotransposons (jumping genes) and mouse retrovirus DNA12



(retroviruses include cancer-causing "onco-retroviruses" and human immunodeficiency virus, HIV, which can lead to AIDS). Thus gene editing is a potential mechanism for horizontal gene transfer (the transfer of genetic material by any method other than "vertical" transmission of DNA from parent to offspring) of disease-causing organisms, including, but not limited to, viruses.[14]

The study also found that DNA from the genome of E. coli bacteria can inadvertently integrate into the target organism's genome. The source of the E. coli DNA was traced to the E. coli bacterial cells used to produce the vector plasmid. The plasmid is a small circular DNA molecule that carries the genes giving instructions for the manufacture of the CRISPR/Cas components (and in SDN-2 applications, the DNA repair template) into the cells. Importantly, the researchers used standard methods of vector plasmid preparation, so this type of contamination could happen routinely.[12]

> Gene editing is a potential mechanism for horizontal gene transfer of disease-causing organisms, including, but not limited to, viruses

These findings are clearly relevant to gene-edited animals, but how do they relate to plant gene editing? Tissue culture medium containing components from animals is not used in making gene-edited plants, so the presence of animal DNA is not a concern.

However, in cases where genetic engineers deliver the gene-editing tool into plant cells encoded by a plasmid, there are two ways in which foreign DNA can become inadvertently integrated into the genome of the plant being edited. First, the plasmid encoding the gene-editing tool, either as a whole, or fragments thereof, can become integrated. Second, DNA from the genome of the E. coli bacteria used to propagate the plasmid can often contaminate the final plasmid preparation used in the gene-editing process, and thus could end up being integrated into the gene-edited plant's genome.

Foreign plasmid or bacterial genomic DNA could be inadvertently incorporated during plant gene editing. Therefore regulators must legally oblige developers to conduct appropriate in-depth molecular genetic characterisation of their products to ascertain if such an outcome has taken place or not.

SDN DISTINCTIONS NOT USEFUL FOR JUDGING RISK

The distinction between SDN-1, -2, and -3 is not useful for differentiating levels of risk for each type of gene-edited organism. This is because SDN-1, -2, and -3 refer to the intention of the gene editing and not the actual outcome, whereas the outcome of a gene-editing event can be very different from the intention.

Also, even small changes in the genome can cause large effects.[15,16] The London-based molecular geneticist Dr Michael Antoniou said, "The size of genetic changes does not determine risk, since small genetic changes may result in dramatic and novel effects. For example, a small deletion or insertion following a gene-editing event could result in creating a new gene sequence, which can give rise to a novel mutant protein with unknown functional consequences. This is why all of the mutations caused by gene editing must be assessed on the basis of what they do, as well as what type and how numerous they are."

The size of genetic changes does not determine risk, since small genetic changes may result in dramatic and novel effects

SDN-1 and -2 applications are often assumed to be less disruptive than SDN-3 because there is no intention to permanently integrate foreign DNA into the genome. However, there is no evidence that the mutations caused are fewer, smaller, or less risky in type. In fact, major mutations, including large deletions, insertions, and rearrangements of DNA, have been found to be generated even by SDN-1 procedures.[17,18]

Indeed, all types of gene editing – SDN-1, -2, and -3 – can be carried out at multiple locations of the genome using multiplex approaches, which target several genes at once, or in repeated, sequential applications.[19,20,21] Thus claims that the changes made are "small" and "similar to what might happen in nature" are misleading, as several individually small changes can combine to produce an organism that is very different from the parent organism. While even small changes can produce large effects, a number of small changes made via gene editing can result in even greater changes, which increases the possibility of unintended alterations in the edited plant's biochemistry and overall composition, with unknown consequences for both crop performance and the health of the consumer.

Thus the risks of both small and large changes must be carefully assessed. Although unwanted genetic changes have been studied in gene-edited organisms to some extent, no safety studies have been carried out with gene-edited products. Such studies are compulsory under EU laws before a GMO product can be placed on the market.

GENE-EDITED CATTLE CONTAINED ANTIBIOTIC RESISTANCE GENES

Claims of nature-identical or safe-by-design gene-edited products should be viewed with scepticism, as demonstrated by the case of the gene-edited hornless cattle.

In 2019 researchers at the US Food and Drug Administration (FDA) analysed the genomes of two calves13 that had been gene edited by the biotech company Recombinetics using the TALEN tool in an SDN-3 (gene insertion) procedure. The aim of the genetic manipulation was to prevent the animals from growing horns by inserting into their genome the POLLED gene, taken from conventionally bred hornless cattle.

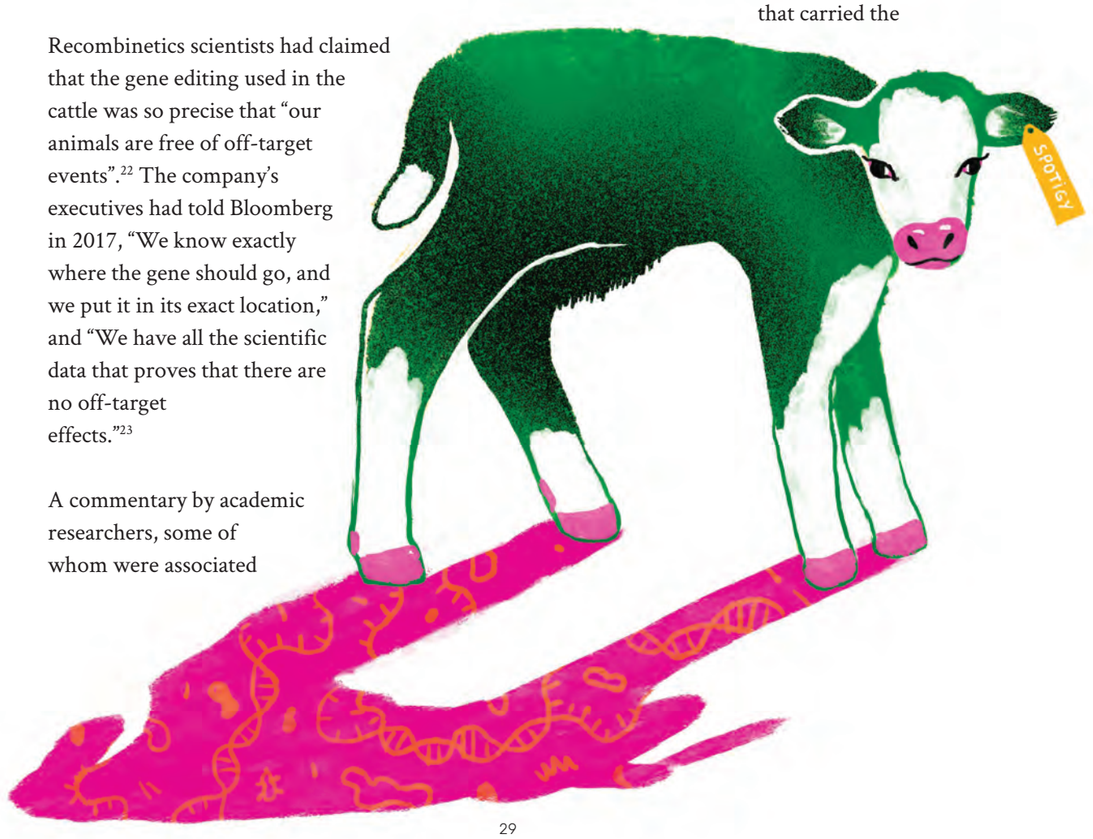
These claims were proven false by what the FDA scientists found

Recombinetics scientists had claimed that the gene editing used in the cattle was so precise that "our animals are free of off-target events".[22] The company's executives had told Bloomberg in 2017, "We know exactly where the gene should go, and we put it in its exact location," and "We have all the scientific data that proves that there are no off-target effects."[23]

A commentary by academic researchers, some of whom were associated with Recombinetics, claimed that the gene editing used in the cattle was precise, that the changes brought about are largely identical to what could have arisen naturally, and that any animals with unwanted traits would be excluded from breeding programmes.[24]

However, all these claims were proven false by what the FDA scientists found.

At one of the target sites of the gene-editing procedure within the calves' genome, the POLLED gene had inserted as planned. However, at the other intended gene editing site, two copies of the entire circular plasmid DNA construction that carried the



POLLED sequence, which acted as the repair template DNA in the SDN-3 procedure, had been unintentionally integrated. These unintentionally integrated plasmids contained complete gene sequences that confer resistance to three antibiotics (neomycin, kanamycin, and ampicillin).[13]

It is not known if the presence of these antibiotic resistance genes could affect the health of the animal or of people who consume its products. However, one risk that merits investigation is that these genes could transfer to disease-causing bacteria, which would then become resistant to antibiotics, threatening human and animal health.[25]

The Recombinetics scientists had missed these unintended effects because they used inadequate analytical methods.[22] Tad Sontesgard, CEO of Acceligen, a subsidiary of Recombinetics that owned the animals, said, "It was not something expected, and we didn't look for it". He admitted that a more complete check "should have been done".[23]

As a result of the FDA scientists' discovery, Brazil cancelled its plans to create a herd of the gene-edited hornless cattle.[26]

> Developers cannot be trusted to self-regulate and determine for themselves whether the changes induced by gene editing are safe

Developers cannot be trusted to self-regulate and determine for themselves whether the changes induced by gene editing are safe or the same as could happen in nature. Strict regulation must be in place to ensure thorough screening for unintended effects. As commonly used screening methods will miss many mutations, a combination of long-range PCR and long-read DNA sequencing must be used, as noted in chapter 2. In addition, safety studies must be conducted to better understand the risks to public health and the environment posed by the gene-edited organism.

WHY GENE EDITING RATHER THAN BREEDING?

The failure of the gene-edited hornless cattle venture raises an obvious question: Why didn't the developers simply cross the gene into the elite Holstein breed through breeding, instead of gene editing the Holstein?

The team of academic scientists cited above, some of whom were associated with Recombinetics, wrote that in principle, conventional breeding could achieve this end, but in practice the cost would be prohibitive: "No breeder can afford to undertake this approach."[24] In a separate paper, Recombinetics scientists cited a shortage of breeding sires producing commercially available POLLED semen and the poor "genetic merit" of polled Holstein sires – they said breeding for the POLLED trait brings along other undesirable traits such as poor milk yield.[22]

The supposedly slow speed of conventional breeding programmes relative to gene editing was cited by both sets of authors.[22,24]

However, this does not seem to be true for Europe.[27] According to a breeder of polled Holsteins in Pennsylvania, USA, Europeans "aggressively selected for the trait, and now they are years ahead of us as far as polled genetics. Animal welfare legislation in Europe based on consumer pressure will drive even further use of polled."[27]

Hendrik Albada, co-owner of the Hul-Stein Holstein herd in the Netherlands, said polled sires are popular in Europe based on genetic merit alone – almost 10% of the cows in Germany in 2015 were bred to a polled bull.[27]

It seems that conventional breeding has already achieved what GMO advocates claimed could only be done quickly through gene-editing technology. The cost and time involved are not prohibitive; polled cattle are produced with high genetic merit; and good progress has been made in availability of polled sires.

This example shows that society needs to critically evaluate claims that gene editing is the only or best solution to a given problem.

ORGANISMS WITH UNWANTED MUTATIONS MAY NOT BE REMOVED FROM BREEDING PROGRAMMES

GMO developers often claim that gene-edited organisms with genetic errors and unwanted traits will be eliminated from breeding programmes,[24] or that the errors can be removed by subsequent backcrossing; thus they are nothing to worry about.

> Experience with first-generation GM crops shows that backcrossing as conducted by GMO developers does not reliably remove unwanted traits

However, the case of the gene-edited cattle that turned out to unexpectedly contain antibiotic resistance genes (see above) shows that GMO developers cannot be relied upon to identify genetic errors and unwanted traits13 and that strict regulation must be in place to enforce thorough screening.[28]

Experience with first-generation GM crops shows that backcrossing as conducted by GMO developers does not reliably remove unwanted traits and that crops with such traits have reached the market.

For example, in the case of glyphosate-tolerant NK603 maize, an increase in certain compounds was found in the GM crop compared with the non-GM parent, which could prove either protective or toxic, depending on context. In addition, metabolic imbalances were found in the GM maize, which could affect nutritional quality.[29] These unwanted changes may explain adverse health impacts observed from consumption of the maize.[30] In the case of GM MON810 Bt insecticidal maize, it contained an allergen, zein, that was not present in the parent crop.[31] It is possible that the developer did not notice these changes, or if they did, deemed them unimportant.

With GM vegetatively propagated crops, such as potatoes, bananas, and fruit trees, the presence of large numbers of unwanted mutations is inevitable. This is because propagation takes place not by seeds produced by sexual reproduction (pollination), but by various asexual methods, including growing from tubers (e.g. potatoes), cuttings (e.g. bananas), and grafting (e.g. fruit trees such as apples) – generating a new plant from a part of the parent plant. This means that mutations caused by genetic engineering processes (including gene editing) cannot be bred out by backcrossing and will persist into the final marketed product.

GENE-EDITED ORGANISMS NOT SAFER THAN OLDER-STYLE GMOS

It is a common misconception that gene-edited organisms are safer than older-style GMOs. But there is no scientific basis to this notion, as confirmed by Bayer scientist Dr Larry Gilbertson, who said that the risks of new techniques like gene editing and older techniques of genetic modification are the same: "I don't think there's a fundamental difference in the risk between these two technologies since they're both fundamentally just changes in DNA."[32]

> "The risks linked to the use of those new techniques/ methods of mutagenesis might prove to be similar to those which result from the production and release of a GMO through transgenesis"
> - European Court of Justice

In 2018 this scientific reality was reflected in the European Court of Justice ruling that gene-edited organisms (called in the case "new techniques/ methods of mutagenesis") must be regulated in the same way as older-style GMOs. The court explained:

"The risks linked to the use of those new techniques/ methods of mutagenesis might prove to be similar to those which result from the production and release of a GMO through transgenesis, since the direct modification of the genetic material of an organism through mutagenesis makes it possible to obtain the same effects as the introduction of a foreign gene into the organism (transgenesis) and those new techniques make it possible to produce genetically modified varieties at a rate out of all proportion to those resulting from the application of conventional methods of mutagenesis."[33]

Gene-editing techniques pose new and different risks compared with older-style transgenic GM techniques. Some scientists therefore argue that the EU's risk assessment guidelines should be expanded to take these risks into account.[8,15,16] Interestingly, neither the Bayer scientist, nor the European Court of Justice, nor the scientists who warn of the special risks of gene editing support the notion that gene-edited organisms are safer than older-style transgenic GMOs. These claims are based on marketing concerns, not science.

COMPARING GENE EDITING WITH MUTATION BREEDING IS MISLEADING

Advocates of gene editing claim that it is more precise and thus safer than mutation breeding.[34] But this claim is misleading because it is the wrong comparison. Although mutation breeding is used alongside conventional breeding, it is a minority method that cannot be equated to conventional breeding. The standard method of conventional breeding is cross-breeding and selection of desired traits. The process can be made quicker and more efficient by using the biotechnologies known as marker assisted selection and genomic selection[35,36] (use of these technologies does not in itself result in a GMO). Standard conventional breeding has an undeniable history of safe use and is the technique that should be used as the comparator to gene-edited crops.

> Just how risky mutation breeding is for health and environment remains unknown because controlled studies have not been done

As we have seen in chapter 3, gene editing is different from mutation breeding and would lead to different risks. Just how risky mutation breeding is for health and environment remains unknown because controlled studies have not been done, though there is suggestive evidence that it may be less risky than gene editing.[8]

Nevertheless, for the plant itself, mutation breeding is widely recognized as risky, unpredictable, and inefficient at producing beneficial mutations. Plant cells can be killed by exposure to the chemical or radiation, while many of the resulting plants are deformed, non-viable, and/ or infertile.[37,38,39]

Mutation breeding is recognised under EU law as genetic modification. It is exempted from the requirements of the regulations because (despite the absence of research on risk) it is deemed to have a history of safe use.[40] But this clearly does not apply to gene editing, which has no history of use, let alone safe use.[8]

REGULATORY OVERSIGHT CRUCIAL

Gene editing technology produces unintended outcomes, which can pose risks to human and animal health and the environment. Even if developers are optimistic that unwanted outcomes can be eliminated, they do not:
• properly screen for them – arguably because that would defeat the purpose of using gene editing to gain time
• reliably remove them
• always have the ability to remove them (with vegetatively propagated crops).

For these reasons, stringent regulatory oversight is crucial, as FDA scientist Steven M. Solomon recommended for gene-edited animals in the US,[28] and as the European Court of Justice has ruled with regard to all gene-edited organisms in the EU.[33]

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5. Gene-edited products are detectable

MYTH

Gene-edited products cannot be distinguished from products developed through conventional breeding.

REALITY

Methods can be developed to detect all products of gene editing, provided information on the genetic change is available.

Industry associations have claimed that many gene-edited products cannot be distinguished from products developed with conventional breeding.[1] And according to Bayer, a change made through gene editing is "indistinguishable from a conventional breeding breakthrough or a natural mutation".[2]

The objective of these claims seems to be to persuade the EU authorities not to even try to apply the EU's GMO regulations to gene editing.

However, already-available, standard GMO detection techniques allow unambiguous detection and identification of a wide range of genetic modifications, from the smallest – e.g. a point mutation of a single nucleotide (DNA base unit) – to the largest, e.g. insertion of large genetic sequences, provided information on the genetic change is available. Also, any patented seed product can be distinguished from other products. Otherwise it would be impossible to enforce patent rights.

> Any patented seed product can be distinguished from other products

In fact, patents generally encompass specific genomic sequences independently of how they are derived. For example, crops developed through mutation breeding can be identified on the basis of the specific sequences that characterise them and that are described in the patent.

When these specific sequences are known, not only the developer but also others can develop specific detection methods for these crops. This has been done for Cibus' SU Canola. Cibus has developed its own detection method to identify its product, and submitted it to Canadian authorities,[3] but the authorities refused to make it available to Canadian NGOs on grounds that it was confidential business information. However, a team of scientists has developed an open-source detection method for this GM crop based on publicly available information.[4]

> When the specific sequences that characterise a crop are known, not only the developer but also others can develop specific detection methods

SU Canola represented a particularly challenging case, since the alteration in its genetic blueprint consists of only a "single base pair" (DNA base unit) change within a specific gene. The researchers confirmed that a single base pair change can be detected with standard GMO detection technology based on polymerase chain reaction (PCR) methodology. Thus it is likely that detection methods can be developed for most, if not all, gene-edited organisms, according to the researchers, provided enough information on the nature of the edit is available.[4]

They stated: "Our work demonstrates that it may be possible to develop event-specific, GMO regulation compliant detection methods for virtually any gene-edited organism based on information disclosed by the developer or gathered from the public domain."[4]

UNKNOWN GENE-EDITED CROPS

Critics of the open-source SU Canola test have focused on the fact that it does not detect the GM method used. Some – like the European Plant Science Organisation (EPSO) – also said that it does not solve the problem of unknown genetic modifications.[5]

However, EU law does not require that detection tests are able to specify the GM method used to develop the crop. A scientific review by researchers from Germany's Federal Office of Consumer Protection and Food Safety (BVL) and Julius Kühn Institute recognised that GMO detection methods generally do not allow any conclusions on the process used, whether they be gene-editing techniques or older-style transgenic genetic modification techniques. However, the researchers commented that "bioinformatics and statistical considerations might help to evaluate whether a detected sequence was potentially introduced by genome modification".[6]

The detection of unknown GMOs has never been solely reliant on the detection methods used in the laboratory

The detection of unknown GMOs has never been solely reliant on the detection methods used in the laboratory. The EU's Joint Research Centre said in 2017 that the most efficient way to test imports for unknown GMOs was to check authorisations in other countries, patent applications, scientific publications, and other information to apply a targeted approach. The laboratory detection test can then be used to provide confirmation of information gathered through other means.[7]
In addition, it is unlikely that a large number of unknown gene-edited crops will be in circulation. Seed companies talk about gene editing when they use it because they want to be able to profit in the marketplace from the use of these new GM techniques.

So far, only two gene-edited crops have been commercialised : Cibus's SU Canola and Calyxt's "high oleic" asoybean with an altered oil profile. Thus far it has proved possible to track a significant number of gene-edited products developed worldwide for commercial markets, as the Julius Kühn Institute in Germany has done for a peer-reviewed publication.[8]

Also, the potential for unknown GMOs to slip through official controls is not new. The same is true for the GM crops that have been successfully regulated in Europe and other countries for the last two and a half decades.

Today's strategies for screening for unknown GMOs do not capture all of them. They only identify those that carry certain common genetic sequences that are used as "screening targets". But the number of GM crops lacking common sequences has been increasing in recent years. It is possible that currently there are unauthorised GMOs in the marketplace that have not been detected because they do not carry any common sequences. No one claims that for this reason, the EU GMO legislation is impossible to enforce and thus useless.
By analogy, no one would suggest legalising burglary because criminal laws do not prevent all burglaries.

Unknown gene-edited crops are just another category of GM products that GMO screening methods can miss and that must be detected by event-specific methods such as the one developed for SU Canola. The presence of gene-edited products in the commercial food system does not create a new set of circumstances that demands fundamental changes in the regulatory regime for GMOs.

The researchers who developed the test for SU Canola believe it may be possible in the future to develop screening methods for various classes of gene-edited crops.[4]

TRANSPARENCY REQUIRED

In the meantime, transparency must be demanded from developers of gene-edited organisms. Under the EU's GMO regulations, agricultural biotech companies are required to provide a detection method and "reference" sample material for each GMO that is authorised, though the sector has not yet submitted any gene-edited GMOs to be marketed in the EU.

It cannot be the job of governments, civil society, or academia to fill knowledge gaps created by industry secrecy

Meanwhile researchers at North Carolina State University are calling for a coalition of biotech industry, government and non-government organizations, trade organizations, and academic experts to work together to provide basic information about gene-edited crops to lift the veil on how plants are modified and provide greater transparency on the presence and use of gene editing in food supplies. They believe that such transparency is crucial to building public trust and confidence in gene-edited products.[9]

However, the primary responsibility for transparency over gene-edited products lies with their developers. It cannot be the job of governments, civil society, or academia to fill knowledge gaps created by industry secrecy.

Once information has been disclosed by the developer, it should be organised in a publicly accessible resource. We can use what is already there – the Biosafety Clearing-House of the Cartagena Protocol on Biosafety,[10] the EUginius GMO database of the Federal Office of Consumer Protection and Food Safety (BVL) in Germany and Wageningen Food Safety Research in The Netherlands,[11] and the register set up by the European Commission for EU-authorised and withdrawn GMOs.[12] The EU must ensure that countries wishing to export to the bloc participate in these registers.

The European Commission's register of EU-authorised GMOs is required by EU law to also "contain, where available, relevant information concerning GMO which are not authorised in the European Union".[13] The Commission and/or member states should work with international partners to meet this requirement.

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6. Gene-editing technology is owned and controlled by big corporations

MYTH

Gene editing, and the CRISPR tool in particular, puts the power of genetic engineering into the hands of hundreds of thousands of scientists, including those working in publicly funded institutes and small companies.

REALITY

Gene editing technology for agricultural use is already firmly under the control of the multinationals that dominate the seed and agrochemicals markets. Corteva has become the main gatekeeper of CRISPR patents in the agricultural arena.

Advocates claim that gene-editing techniques, especially those using the CRISPR/Cas system, can democratise genetic engineering because they are cheaper and easier to apply than older genetic modification techniques. Jennifer Doudna, one of CRISPR's inventors, said the technology "became a democratising tool that allowed labs to do experiments that in the past had been prohibitive for various reasons, whether due to expense or just technical difficulty".[1] Bayer calls CRISPR the "most 'democratic'" gene-editing tool, which is so "cheap and simple" that it can be used by "universities and institutes that do not have major research budgets".[2]

It is further argued that if gene editing were exempted from the EU's burdensome and expensive-to-comply-with GMO regulations, it would be removed from the control of the big agbiotech multinationals and be made available to public research institutes and universities, non-profit organisations, and small and medium-sized enterprises (SMEs).[3,4] The seed industry claims that GMO regulations "prevent most of Europe's plant breeding companies from developing and using these methods".[5]

TECHNOLOGY PATENTS

Claims of democratisation through new GM techniques must be viewed in the light of the fact that these techniques are patented, as are their products – the plants and animals developed using them. Patents are monopoly rights. Patent holders have the right for up to 20 years to prohibit others from exploiting the patented invention or to charge royalties for its use. This is not just about limiting commercial exploitation, but also further innovation. Exclusive patent rights prohibit others from building on the protected invention, as research exceptions to patent rights are usually very strictly formulated.

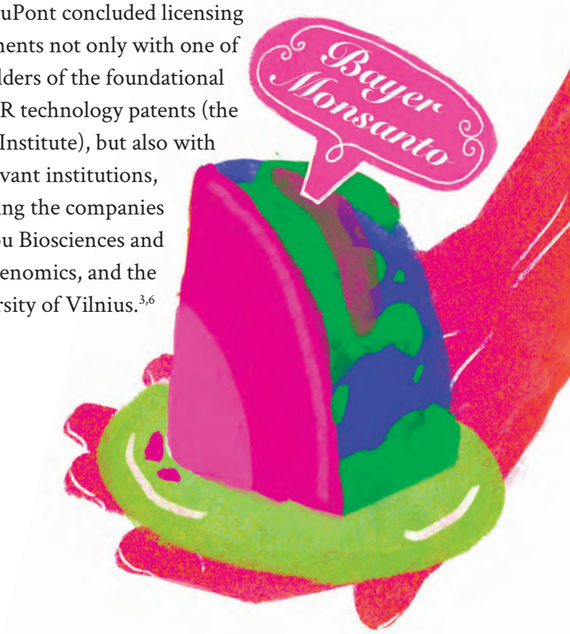
> Patent holders have the right for up to 20 years to prohibit others from exploiting the patented invention or to charge royalties for its use

The Broad Institute of MIT and Harvard, the University of California, the University of Vilnius in Lithuania, and the University of Vienna are the main institutional "inventors" of CRISPR technology.[6,7,8,9] Between them they have filed (and fought each other over[9]) hundreds of foundational patents, some of which have already been granted in Europe.[6]

LICENSING AGREEMENTS

Once technology patents are granted, patent owners can conclude licensing agreements with companies allowing them to use the technology in certain areas or in a specific application. These agreements can be exclusive or non-exclusive. Other companies can obtain licensing agreements only if the rights to use the patents are granted non-exclusively to a licensee. An overview of CRISPR-based gene-editing technology licensing agreements was published in Science in 2017.[8]

In the areas of CRISPR gene-edited plants and livestock, licensing agreements reached by patent owners, the Broad Institute and the University of California (or its spinoff company Caribou Biosciences), with licensees DowDuPont (now Corteva) and Bayer/Monsanto, are particularly important.[6,8] DowDuPont concluded licensing agreements not only with one of the holders of the foundational CRISPR technology patents (the Broad Institute), but also with all relevant institutions, including the companies Caribou Biosciences and ERS Genomics, and the University of Vilnius.[3,6]



CARIBOU BIOSCIENCES AND ERS GENOMICS

Corteva (the agricultural division spun off from DowDuPont) is the main gatekeeper for CRISPR patents in the agricultural arena[10] and has gained unprecedented market power due to its ability to grant access to this patent pool.[6] To understand why, we need to learn the history of the CRISPR licensing agreements.

> The story begins with two biotech startups co-founded by the inventors of CRISPR technology

The story begins with two biotech startups co-founded by the inventors of CRISPR technology. The first, Caribou Biosciences, was co-founded in 2011 by one of the inventors of CRISPR-based gene-editing technology, Jennifer Doudna from the University of California. The second, ERS Genomics, was co-founded in 2013 by another CRISPR technology inventor and patent owner, Emmanuelle Charpentier, as a "licensing engine" that "exists to make the [CRISPR] technology more broadly available under appropriate commercial licences". ERS Genomics has signed non-exclusive and exclusive licensing agreements with companies operating in different fields.[8]

DuPont (later DowDuPont and now Corteva) concluded its licensing agreement with Caribou Biosciences in 2015. In the deal, DuPont received exclusive rights for CRISPR technology applications in major row crops and non-exclusive rights in other agricultural

applications.[11] In 2016 Caribou reached a deal with the company Genus in which the latter received an exclusive licence to use CRISPR technology in certain livestock species.[12]

DuPont also reached an exclusive licensing agreement in 2018 with ERS Genomics. The agreement gave DuPont exclusive rights to use CRISPR technology in the agricultural area. ERS Genomics also granted sub-licensing rights to DuPont. DuPont's agricultural division was spun off in 2019 as an independent entity named Corteva. Thus Corteva achieved its dominance of the CRISPR technology in the agricultural field.

DEMOCRATISATION OR PATENT CARTEL ?

Jean Donnenwirth of DowDuPont (now Corteva) presented the company's agreements on 5 November 2018 at a meeting between the EU Commission and various interest groups, according to Dr Christoph Then of Testbiotech, who was present. According to Donnenwirth, DowDuPont succeeded in combining 48 basic patents into a common patent pool (35 patents from the Broad Institute, 4 from the University of California, 2 from the University of Vilnius, and 7 from DowDuPont).[6]

Donnenwirth said that access to this number of patents is necessary for full use of the technology in plant breeding. DowDuPont can offer bundled, non-exclusive licenses giving access to this patent pool. The conditions include appropriate fees, reporting obligations, compliance with guidelines, and confidentiality.[6] The first company to licence CRISPR technology under these conditions in 2018 was the US company Simplot, which develops GM potatoes.[13] In 2019, a French company, Vilmorin & Cie, followed.[14]

Christoph Then commented, "DowDuPont has unprecedented market power thanks to the possibility of granting access to this patent pool: What is on the one hand touted as a 'democratisation' of patent law turns out, on closer examination, to be a means of controlling competitors and protecting a dominant position. DowDuPont becomes, so to speak, the gatekeeper of an international patent cartel."[6]

PATENTS ON "NEW GM" CROPS DOMINATED BY DOWDUPONT, BAYER/MONSANTO

The 'democratic' credentials of gene editing are determined not only by access to the technologies but also by access to their products – gene-edited crops and seeds. But just like the technologies, the products are circumscribed by intellectual property rights.

According to Christoph Then, patent applications involving new and old genetic engineering relate to plants with modified growth and yield, composition, or resistance to disease, as well as technical modifications of the nucleases. As a rule, the patents cover methods, seeds, plants and often also the harvest.[6]

Both Bayer/Monsanto and DowDuPont have applied for patents on glyphosate-tolerant plants produced with the CRISPR-mediated gene-editing process. This means that the core agricultural GMO business – the marketing of herbicide-tolerant plants such as soy, corn, oilseed rape/canola and cotton – can continue to be protected by new patent applications in the future.[6]

Both Bayer/Monsanto and DowDuPont have applied for patents on glyphosate-tolerant plants produced with the CRISPR-mediated gene-editing process

The owners of the patents are largely the same multinationals that dominate the GMOs and agrochemicals markets. Christoph Then wrote in 2019 : "DowDuPont leads the field in the new genetic engineering methods for crops, with around 60 international patent applications, while Bayer/Monsanto follows in second place with more than 30. Calyxt… comes in at more than 20. Syngenta and BASF are also involved, and a few patents have also been applied for by traditional breeding companies such as Rijk Zwaan and KWS."[6]

A 2016 review of the intellectual property rights landscape by Egelie and colleagues found that "larger industry players, with Dow and DuPont at the forefront, already appear to be more in control of the technology's agricultural and food applications."[15]

LOST ACCESS TO TRADITIONAL CULTIVARS

In a discussion dominated by concerns about gaining access to CRISPR technology, it is easy, as pointed out by Maywa Montenegro de Wit of the University of California, to forget the crucial issue of farmers "losing access to traditional cultivars that might be displaced with expanded markets in new biotech crops, or mined as genetic resources for breeding gene-edited varieties".[1] There is a danger that farmers will be forced to pay for access to gene-edited seeds and breeds, but lose access to non-GM seeds and breeds in the process.

ACCESS TO THE TECHNOLOGY FOR SMES ACTING ALONE IS ILLUSORY

Could the de-regulation of gene editing help empower small and medium size enterprises (SMEs) to develop the gene-edited crops and foods that will enable us to meet the challenges of climate change?[4,16]

This prospect is highly unlikely, according to molecular geneticist Dr Michael Antoniou, who has many years' experience of developing patented biotech products for medical research with SMEs and larger companies.[4]

He explained that different types of licences exist for technologies like CRISPR gene editing, which industry-based researchers (including those working in SMEs) must take out at different stages of product development. These include evaluation, research, and commercial licences. Evaluation licenses are granted to researchers by the patent owners or their sub-licensing affiliate companies to allow the researchers to do preliminary work to see if the technology could be useful. If the researchers want to pursue a particular application, they can apply to the patent owners for research licenses.[4]

Evaluation and research licences are often granted quite cheaply, and fees can even be waived altogether, since the technology owners want it to be used to develop a product that can be commercialised.
Even when evaluation and research licence fees are charged, a typical SME could afford them.[4] But at the commercialisation stage, things can quickly get very expensive, with technology patent holders demanding high payments for use of the technology, in the form of commercial licence fees and royalty payments on product sales.

As an example, Corteva has made a commitment to allow free access to the CRISPR technology for "universities and nonprofit organizations for academic research". The company has claimed that this will put the CRISPR technology "in the hands of many", resulting in "a wide array of benefits for the global food supply".[3] But scientists will only be able to use CRISPR for basic non-commercial research, not for developing commercial products. Maywa Montenegro de Wit concluded: "Despite the opening up of CRISPR IP [intellectual property] for non-commercial research, CRISPR's commercial development remains tightly bound up in patents and licensing agreements – a landscape already showing strong signs of agroindustry dominance."[1]

> "Despite the opening up of CRISPR IP for non-commercial research, CRISPR's commercial development remains tightly bound up in patents and licensing agreements"
> - Maywa Montenegro de Wit

Plant breeders using conventional breeding to develop a new plant variety can protect it through plant breeders' rights. But if they decide to use CRISPR (whether or not the technology is regulated as GM), they will need to learn to navigate a far more complex and expensive process. They will have to compensate the CRISPR patent holder(s) both at the research and development stage and also at the commercialisation stage.
Patent and licensing fees will raise the cost of variety development considerably.

Patenting fees can easily accumulate to six-figure sums, since patents must be applied for – and patent lawyers engaged – in each territory where intellectual property rights are sought. The patenting process can drag on for years, with lawyers' fees rising all the while.[4]

GAME FOR BIG PLAYERS

Due to the expense involved, SMEs on their own will never be able to afford the patents and commercial licensing agreements that govern gene editing.
So the system in the agricultural biotech market is, and will remain, that researchers based in small companies or universities, often with industry funding, "invent" a GMO and partner with investors and/or a large company to patent the product, obtain regulatory approval, and bring it to market. The inventors and their institutions enjoy a profit-sharing arrangement with the investors or large partner company. Often in this process, the SME is bought up by larger companies.[4]

> At the end of the day, gene editing is a game for big players and will remain so

This business model is not considered a cause for lamentation. On the contrary, it is celebrated as a path to success for all involved, including the individuals and SME that invented the product.[4]

However, at the end of the day, gene editing is a game for big players and will remain so. The notion that CRISPR will grant small players access to the technology is a myth.

PATENTS THE DRIVING FORCE OF OLD AND NEW GENETIC ENGINEERING

Experience with genetic engineering to date shows that patent law has been the driving force behind development. The advent of genetic engineering marked the first time that patent law was systematically applied to plant breeding. Large agrochemical companies, which had previously protected their pesticides with patents, now also applied for patents on GM seeds and at the same time bought up many plant breeding companies.[17]
With new genetic engineering techniques, this strategy has continued and been expanded. Already, corporations such as Corteva and Bayer/Monsanto control large parts of the seed market.[17] Patented genetic engineering techniques such as CRISPR gene-editing technology help them extend and deepen this control.[6]

> The advent of genetic engineering marked the first time that patent law was systematically applied to plant breeding

Therefore gene-editing technology will not make genetic engineering accessible to publicly funded breeding programmes, but will further consolidate power within the big multinationals.

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7. Gene editing is not a fast or reliable route to desired outcomes

MYTH

Gene editing achieves desired traits more quickly than conventional breeding.

REALITY

There are many lengthy steps in bringing a gene-edited product to market, even without considering regulation, and conventional breeding is more successful in achieving desired traits.

Gene editing is promoted as the fastest and most efficient way to achieve plant breeding goals.[1,2] According to Corteva, "CRISPR-produced plants can be developed in just a few years versus what often takes decades",[3] and Bayer insists that useful crops can be developed "in a fraction of the time compared to older methods".[4]

The companies often suggest it is onerous regulations that hold back what would otherwise be rapidly introduced gene-edited products. Corteva argues that "treating CRISPR-produced crops as GMOs would substantially slow down their path to market and adoption of CRISPR innovation in agriculture."[3]

However, while breeding a new plant variety is generally a lengthy process, there is no evidence that producing a viable gene-edited variety will be any quicker. Even in countries with light-touch regulations like the US and Canada, only very few gene-edited products have made it to market. A gene-edited tomato approved by the Japanese government in 2020, which was engineered to contain a compound said to lower blood pressure, took 15 years to develop.[5] That is the same time period that experts estimate is needed to develop a sexually propagated non-GM crop – or an older-style transgenic GM crop.[6,7,8]

PROCESS FOLLOWING THE "EDIT" TAKES TIME

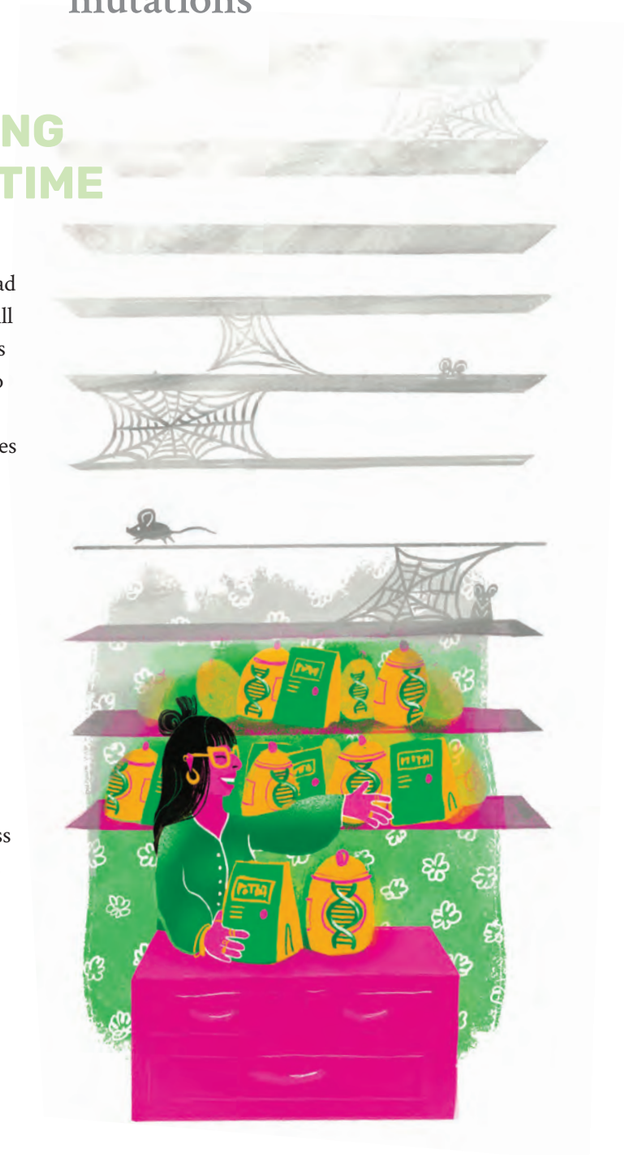
As shown in chapter 2, gene editing and its associated processes (such as tissue culture) lead to many unintended effects, some of which will affect plant performance and growth as well as the desired trait. So gene-edited plants need to go through a laborious process of screening, selection and backcrossing with the parent lines to remove any obvious undesired mutations.

In addition, several years of greenhouse and field trials must be done to ensure that the desired trait expresses in a stable way through the generations and that the plant copes with environmental stresses, such as bad weather conditions and pest attacks.

Moreover, genetically modified products are normally only placed on the market once patents are granted – and the patenting process can take years. This means the overall process before products can be commercialised can be lengthy.

All this is without the time needed to put the plant through regulatory processes.

Gene-edited plants need to go through a laborious process of screening, selection and backcrossing with the parent lines to remove any obvious undesired mutations



UNIMPRESSIVE RECORD

While gene editing is presented as a cutting-edge new technology, it has actually been around for some years. In 2012, Jennifer Doudna and Emmanuelle Charpentier proposed that CRISPR could be used for programmable editing of genomes[9] and it was first shown to work in plants in 2013.[10] The editing tool later named TALENs was described in 2009–2010.[11,12] Regarding crops engineered with the editing tool called oligonucleotide-directed mutagenesis (ODM), maize was described in 2000[13] and rice in 2004.[14]

Yet to date, despite the permissive egulatory systems in place in North and South America,[15] only two gene-edited plants have made it to market – neither of which were engineered using the much-touted CRISPR technology. These are Calyxt's altered-fat-profile soybean, engineered with TALENs,[16] and Cibus' herbicide-tolerant canola/oilseed rape, engineered with ODM. The ODM maize[13] and rice[14] do not appear to have been commercialised anywhere in the years since they were announced in 2000 and 2004. The same is true of a non-browning mushroom, engineered with CRISPR/Cas,[17] as well numerous other products. According to Testbiotech, "around 80 plants developed with new GE techniques have been deregulated by the US FDA".[18]

To date, only two gene-edited plants have made it to market – neither of which were engineered using the much-touted CRISPR technology

Consumer and food industry mistrust of gene-edited foods is also a delaying factor in commercialisation. The gene-edited tomato approved by the Japanese government has not yet been commercialised, reportedly due to food producers shying away from the technology in the face of consumer rejection. A survey of about 10,000 people by the University of Tokyo found that 40% to 50% did not want to eat gene-edited crops or animal products, with just 10% showing interest in trying them.[5]

This record suggests that gene editing is not the efficient and speedy route to obtaining successful agricultural traits that is

claimed. The unimpressive record of products brought to market in countries like the US and Canada shows that it is not regulations that slow market access, but factors inherent in the development of GM products, as well as market rejection.

During the 20 years that gene editing has existed, there has been much research activity – often generously funded with taxpayer money – but very few marketable products. In the meantime solutions have already been found to problems such as extreme weather conditions linked to climate change. These solutions rely on already proven and available approaches.

In the meantime solutions have already been found to problems such as extreme weather conditions linked to climate change

For example, while research on gene-edited saline-tolerant crops struggles to progress beyond the early stages,[19] farmers in India have rapidly and successfully remediated soil that was made saline by a devastating tsunami. The key was found in organic soil regeneration methods and local seeds adapted to the conditions.[20]

Also, conventional breeding has consistently outstripped genetic engineering techniques (old and new) in producing crops tolerant to stresses such as drought,[21] floods,[22] pests,[23] and diseases.[24] For more examples of successful alternatives to GM approaches, see chapter 8.

IS SPEED DESIRABLE?

Speed in bringing new products to market and fast replacement of products is a business model that is interesting for some seed/agrochemical companies and livestock breeders, but less relevant for farmers, who may be better served with robust, locally adapted varieties and breeds that they can use over a long timespan. In addition, it does not serve consumers, whose primary concern is a safe, wholesome, and accessible food supply.

In cases where speed is important, gene editing is not the quickest or most reliable way to produce crops with desired traits. In contrast, conventional breeding has proven highly efficient and successful in producing such crops.

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8. Gene editing is a risky and expensive distraction from proven successful solutions to food and farming problems

MYTH

Gene editing is necessary to grow food that is better for people and the environment, so not applying it would be morally reprehensible.

REALITY

We need to scale up proven successful solutions – conventional breeding and agroecology – from which genetic engineering is an expensive distraction.

Industry lobbyists claim that the use of gene editing is of "unprecedented importance" to deal with climate change and scarcity of natural resources such as arable land and water. They say it is necessary to develop crops that are pest- and disease-resistant and can adapt to difficult climatic conditions such as drought, heat, and salinity.[1,2]

According to Bayer, gene editing is "fundamental in achieving the goals of the EU Green Deal"[3] that aims to tackle both climate change and environmental degradation and make the EU economy sustainable. The company says that if the EU fails to "reverse legislation" that blocks gene editing, it could: "miss out on one of the most promising innovations of our lifetime to enable more sustainable resilient food systems".[4]

Bayer says the EU could "miss out on one of the most promising innovations of our lifetime to enable more sustainable resilient food systems".

The EU seed industry association, which Bayer is part of, says it is the EU's "prohibitive" GMO laws that prevent innovation "for a more sustainable agri-food system at the pace that is urgently needed".[1]

Such arguments create a context in which genetic engineering is viewed as the moral imperative – and rejection, or even just regulation, as morally reprehensible.

NEW TECHNIQUES, OLD CLAIMS

Claims that genetic engineering can help farmers to deal with adverse conditions and protect the environment are not new. First-generation transgenic GM crops were promoted on the basis of claims that they would be adapted to difficult climatic conditions, such as drought, and reduce pesticide use.[5]

These promises proved false. Regarding drought, a transgenic GM drought-tolerant maize from Monsanto was released in 2011, but the US Department of Agriculture (USDA) said it was no more effective than conventionally bred varieties.[6] Farmer adoption of varieties in which the drought tolerance was achieved via GM has "lagged behind" varieties in which it was achieved by conventional breeding.[7]

The claim of reduced pesticide use also proved to be false Herbicide-tolerant GM crops are sold by agrichemical companies in tandem with their proprietary herbicides. They have increased the use of chemical weedkillers, including products containing the "probable carcinogen" glyphosate.[8,9]

> Herbicide-tolerant GM crops are sold by agrichemical companies in tandem with their proprietary herbicides

Insecticide-producing GM crops (so-called Bt crops) rapidly lost effectiveness against targeted pests, fell victim to Bt toxin-resistant and secondary pests, and are now used in combination with chemical insecticides.[10,11,12,13,14,15,16,17,18] These include highly toxic neonicotinoid insecticidal seed treatments, the use of which has risen in parallel with Bt crops in the USA.[16]

GENE EDITING APPROACHES TO PEST CONTROL SET TO FAIL

Agricultural biotech companies are promoting the newer techniques of gene editing as a way to manage insect pests that would reduce the need for chemical insecticides. Proposed approaches include altering plant composition in order to repel pests.[19]

However, these approaches may meet the same fate as older-style GM crops – as pests can rapidly evolve resistance to environmental stresses, whether they consist of sprayed-on chemical pesticides, built-in pesticides like Bt toxins, or plants genetically engineered to repel pests.

In the UK, Rothamsted Research's so-called "whiffy wheat" trial, in which wheat was genetically engineered to release an aphid-repelling chemical found in mint, failed after £2.6 million of public money was spent on the project. The aphids rapidly got used to the smell.[20]

Ironically, previous government-funded research undertaken by Rothamsted and others demonstrated that aphid levels can be kept below economically significant levels by maintaining diverse field margins and hedgerows.[21] This innovative research was based on an understanding of agroecology. But seemingly, it has been ignored by GM researchers and their institutions.

CONVENTIONAL BREEDING AND GOOD FARMING PRACTICES WORK BETTER TO FIGHT PLANT DISEASES

Seed industry associations say that gene editing is a way to fight plant diseases while reducing pesticide use. One promotional video claims that wheat can be gene edited to make it resistant to rust and powdery mildew diseases.[22]

However, powdery mildew-resistant wheat has already been developed through conventional breeding, helped by marker assisted selection.[23] Progress has been made in gene mapping for powdery mildew resistance in wheat, to help breeders who want to use these techniques.[24]

Rust-resistant wheat varieties have also been developed via conventional breeding.[25,26,27] According to the International Maize and Wheat Improvement Center (CIMMYT), its "rust-resistant varieties now cover more than 90% of the wheat farming area in Kenya and Ethiopia".[28]

> The key to controlling both crop diseases and insect pests lies in prevention through good farming practices

Attempts to achieve disease resistance through gene editing are unlikely to match these conventional breeding successes. Disease-causing microorganisms, like insect pests, have great genetic diversity and thus adaptability, so they can easily "break" a resistance based on changes in one or a few genes.

Moreover, the key to controlling both crop diseases and insect pests lies in prevention through good farming practices such as crop rotation,[29] which is often ignored in monocrop, industrialised agriculture.

GENE EDITING CANNOT CONFER DESIRABLE COMPLEX TRAITS

Conventional breeding continues to outstrip GM in developing crops with durable resistance to pests and diseases, drought tolerance, enhanced nutritional quality, and tolerance to salinity.[30,31,32,33] This is because these are genetically complex traits, meaning that they are the product of many genes working together in a precisely regulated way. Such traits will be extremely difficult or impossible to achieve by manipulating one or a few genes, which is all that gene editing and genetic modification in general can achieve, even using multiplex approaches.

> Genetically complex traits will be extremely difficult or impossible to achieve by manipulating one or a few genes

GM has largely succeeded only in producing crops with genetically simple traits such as herbicide tolerance or the ability to express an insecticide. Gene editing is set to continue on the same path. The gene-edited crops commercialisation pipeline is mainly characterised by genetically simple traits, such as or herbicide tolerance, or modified composition to increase product shelf life or provide raw materials for processing industries.[34] These traits do not improve the sustainability or climate resilience of agriculture, but allow developers to continue to sell GM seeds with agrochemicals and help industry to optimize its manufacturing processes.

It is not surprising, then, that thus far the only gene-edited crops that have made it to market are Calyxt's soybean and Cibus' SU Canola. The soybean has an altered fat profile to avoid creating unhealthy trans fats when cooking food at high temperatures.[35] The canola has been engineered to enable increased herbicide use without killing the crop – the opposite to the claimed reductions in pesticide use from gene-editing technology.

GENE EDITING CAN BRING ADDITIONAL RISKS

Gene editing plants for disease resistance brings other risks, too, some of which have already come to light. Attempts to use CRISPR gene editing to produce virus-resistant cassava plants failed, and in the process broke their already-existing natural resistance to a different, more widespread virus.

The experiment also resulted in the propagation of mutated viruses that, if they had escaped the laboratory, could have led to "the development of a truly pathogenic novel virus", according to the researchers.[36] The lead researcher questioned on Twitter whether this was a "risk" worth taking in fields. Meanwhile, non-GM programmes for breeding and supplying virus-resistant cassava have proven successful over many years, but struggle for funding.[33]

Currently, so-called gene drives, a particular application of gene-editing technology, are being promoted as a way to eradicate insect pests.[19] But the risks posed by gene drives are unpredictable and the impacts potentially severe.[37]

SYSTEMS, NOT JUST GENES

When it comes to solving challenges of pests, diseases, or climate change, it is crucial to look at whole farming systems rather than employing a reductionist approach that only looks at genes, especially genetic engineering approaches that only manipulate one or a few genes. As well as robust crops providing stable yields under adverse conditions, we need resilient farming systems that cope with a variety of environmental stresses. Such systems include soil building with organic matter to retain moisture and planting a diversity of crops to prevent pest and disease problems.

> Agroecology projects in the Global South and other developing regions have produced dramatic increases in yields and food security

Successful systems approaches include :

• The organic system. In the longest-running trial comparing organic and conventional grain cropping systems (including GM crops), the Rodale Institute Farming Systems Trial, researchers found that organic systems produce yields that are competitive with conventional systems after a 5-year transition period. Yields in the organic systems were up to 40% higher in times of drought. The trial also found that organic systems use 45% less energy and release 40% fewer carbon emissions. Crop rotations were used instead of pesticides to control pests.[38]

• The System of Rice Intensification (SRI). SRI is an agroecological method of increasing the productivity of rice by changing the management of plants, soil, water, and nutrients. The benefits of SRI include yield increases of 20–100%, up to a 90% reduction in the amount of seed required, and water savings of up to 50%.[39]

• Agroecology projects in the Global South and other developing regions. These projects have produced dramatic increases in yields and food security.[40,41,42,43,44,45]

OVER 400 INTERNATIONAL SCIENTISTS SAY AGROECOLOGY IS THE WAY FORWARD

In 2008 a ground-breaking study on the future of farming was published. Sponsored by the World Bank and the United Nations and conducted by over 400 international scientists, the International Assessment of Agricultural Knowledge, Science and Technology for Development (IAASTD) did not endorse GM crops as a solution to world hunger.

The report noted that yields of GM crops were "highly variable".
It added that safety questions remained over GM crops and that the patents attached to them could undermine seed saving and food security in developing countries. The report concluded that the key to food security lies in agroecology.[46]

EXPENSIVE DISTRACTION

GM approaches have been shown to be an expensive distraction from already-available approaches to solving challenges of climate change, pests, and diseases. These approaches, based on the science of agroecology, are also the most sustainable way to end our dependency on chemical pesticides.

The need to reduce pesticide use is pressing, but this goal will not be achieved by looking to companies that sell these products

The need to reduce pesticide use is pressing, but this goal will not be achieved by looking to companies that sell these products. In fact, the agricultural biotech companies promoting gene editing (for example, Corteva, Bayer, Syngenta, and BASF) are also agrochemical companies and their business model is built on selling seeds in a package with pesticides and other chemical inputs.

Resources should instead be directed towards making proven-successful agroecological methods more widely available to farmers.

In a time of climate and ecological breakdown, this – not risky genetic engineering technologies owned and promoted by agrichemical companies – is the moral imperative.

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CONCLUSION

The evidence presented in this report shows that gene editing is imprecise and that its outcomes are uncontrollable. Numerous types of unintended mutations have been shown to arise from gene editing, including large deletions, rearrangements and insertions at on-target and off-target sites of the genome. These will cause altered gene function, leading to compositional changes in plants that could result in toxicity or allergenicity. Gene editing in animals has also been shown to have unpredictable and potentially dangerous outcomes.

In gene editing, unlike with transgenic technology, traditional mutagenesis or conventional breeding, any region of the genome can be targeted. In addition, given that gene editing will be used simultaneously or sequentially to target one or more genes, the risks will be compounded with each step.

Inadequate screening by developers could result in harmful traits persisting in products reaching the marketplace. In order to protect health and environment, all types of unintended effects of gene-editing techniques should be taken into account in a detailed process- and product-based risk assessment, as some scientists recommend.

Given the uncertainties and risks attached to gene editing, it is unacceptable to weaken the regulations governing these genetic manipulation techniques. Rather, the existing protocols for GMO risk assessment should be extended and strengthened to take account of gene editing’s particular risks.

In particular, broadening the risk assessment to include new molecular analysis tools (“omics”) would help to identify important unintended changes in transgenic and gene-edited GM crops.

Given that gene editing can only manipulate a limited number of genes, it will fail to deliver on desirable complex genetic traits such as drought tolerance, pest resistance and disease resistance, which involve multiple gene families working together.

Furthermore, ownership and control of gene-editing technology is in the hands of a very few large corporations, which means that it will not democratize agriculture but will instead lead to further consolidation of the seed industry and threaten food and seed sovereignty.

In the interests of public health, the environment, and a resilient food system, gene editing must remain under the current EU GMO regulations. Furthermore, risk assessment guidance should be tightened to take into account the particular risks posed by this technology.

The climate and sustainability crises demand that we implement proven-successful agroecological solutions to the problems in our food and farming systems, rather than pursuing risky and expensive gene editing approaches.

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