Response by Claire Robinson of GMWatch and Dr Michael Antoniou to the UK government's Genetic Technologies (Precision Breeding) Bill and accompanying Impact Assessment

On 25 May the UK government introduced into Parliament the first draft of the "Genetic Technologies (Precision Breeding) Bill",[1] which aims to remove almost all regulatory controls, including in-depth risk assessment and labelling, of most types of genetically modified (GM) crops, farm animals, and foods.

The criteria for these exempted genetically modified organisms (GMOs) are that every feature of its genetic makeup (genome) could have resulted from "traditional processes"[2] or "natural transformation". It calls these exempted GMOs "precision bred organisms".

The Bill is accompanied by an Impact Assessment.[3]

The Bill and Impact Assessment are deeply problematic, as they cast aside the interests of public health and the environment and raise animal welfare concerns, in the rush to smooth the path to market for new experimental GM crops and animals.

From the standpoint of science, the Bill is a fabrication based on dishonesty and a determination recklessly to dismiss years of peer-reviewed findings on the effects of gene editing and other new GM technologies.

The people who are most culpable in the production of this Bill are the scientific advisors to the government. They are entrusted by the public to act in an objective and impartial manner and stay true to the science. Yet they appear to have acted in complete contradiction to established scientific understanding. The only possible motivation seems to be economic interests and a political wish to align the food and farming sectors of England with those of the USA and other GMO-producing countries, such as Canada, Brazil, Australia and Japan.

Our specific concerns are listed below, with our proposed Amendments to the Bill.

1. For most GMOs, the Bill doesn't require an in-depth risk assessment for health and environment and removes existing protections for both.

The Bill claims that it "will not have the effect of reducing the level of environmental protection provided for by any existing environmental law".[4] But this is false. The Bill both weakens and contravenes existing law.

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[1] https://publications.parliament.uk/pa/bills/cbill/58-03/0011/220011.pdf

[2] Examples given are breeding, grafting, or "induced mutagenesis". The latter technique, in which mutations are induced by exposure to chemicals or radiation, is currently viewed as a GM technique by EU law but is exempted from the requirements of the GMO regulations due to its long history of assumed safe use.

[3] https://publications.parliament.uk/pa/bills/cbill/58-03/0011/ImpactAssessmentGeneticTechnology(PrecisionBreeding)Bill.pdf

[4] The Explanatory Note (b).

In existing law before Brexit, the release of GMOs in the UK was governed by the EU Directive 2001/18[5] and the UK's Environmental Protection Act (EPA) 1990.[6]

The EU Directive requires a mandatory risk assessment for human and animal health and the environment for each GMO released. It also requires that Member States take "all appropriate measures… to *avoid adverse effects* on human health and the environment which might arise from the deliberate release or the placing on the market of GMOs"[7] (our emphasis). The criteria for placing a GMO on the market must ensure "a high level of safety to human health and the environment and be based on the scientific evidence available on such safety", as well as on the experience gained from the release of comparable GMOs.[8]

It is important that the risk assessment is conducted by genuinely independent people. Currently the Advisory Committee on Releases to the Environment (ACRE), which has issued guidance on what constitutes a GMO that "could have been produced by traditional breeding techniques or could have arisen through natural processes",[9] does not meet this standard, as 100% of the members have actual or potential conflicts of interest with the industry they are supposed to regulate.[10]

The precautionary principle – the principle that an authority can take action "in the face of a possible danger to human, animal or plant health, or to protect the environment", even in a situation of scientific uncertainty[11] – must be taken into account when implementing the Directive.[12]

The UK EPA requires that the person who releases the GMO take measures "to *avoid damage* to the environment" which may result (our emphasis).[13] The "environment" is defined in the EPA as including any living organisms supported by the environment.

In contrast, the new Bill fails to provide for a mandatory risk assessment of each GMO for health and environment. The provisions of the Bill only "*may" or may not* ensure that "the production of any such food or feed will not have adverse effects on the environment", and only "*may" or may not* ensure that "consuming any such food or feed in place of other food or feed that it might reasonably be expected to replace will not be nutritionally disadvantageous to humans or animals" [14] (our emphasis).

The Impact Assessment published by DEFRA and dated March 2022 is clearer in intention. It confirms that "The Bill will repeal the need for consent and risk assessment for qualifying PBOs [precision bred organisms] and replace it with a framework for a transparent notification system for developers who wish to understand the regulatory status of their products early in product development (pre-R&D)."[15]

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[5] http://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX%3A32001L0018
[6] https://www.legislation.gov.uk/ukpga/1990/43/part/VI
[7] Article 4.1.
[8] Article 16.2.
[9] https://www.gov.uk/government/publications/acre-guidance-on-genetic-technologies-that-result-in-qualifying-higher-plants/technical-guidance-on-using-genetic-technologies-such-as-gene-editing-for-making-qualifying-higher-plants-for-research-trials
[10] https://www.gmwatch.org/en/106-news/latest-news/19999
[11] https://eur-lex.europa.eu/EN/legal-content/summary/the-precautionary-principle.html
[12] Preamble (8).
[13] EPA 1990, Part VI, Preliminary, 106(1). https://www.legislation.gov.uk/ukpga/1990/43/part/VI
[14] Part 3, 26(3)(b).
[15] Impact Assessment, 3.2.1.3, 18. https://publications.parliament.uk/pa/bills/cbill/58-03/0011/ImpactAssessmentGeneticTechnology(PrecisionBreeding)Bill.pdf

The Impact Assessment also says, "A new scheme … capturing PBOs, as described by the Bill, will be introduced by the FSA [Food Standards Agency] under secondary legislation. This will involve a lighter-touch risk assessment of food and feed products (the full details of this new food and feed regulation/framework and information requirements are under discussion)."[16]

The section of the Bill on risk assessment states that the legislation dealing with them will be subject to the negative procedure.[17] **Secondary legislation that is subject to the negative procedure means that there will be no debate in Parliament about these crucial aspects. Therefore proposals to weaken the risk assessment must be strongly opposed while the Bill is still in draft form.**

Section 4.1 of the Impact Assessment describes several options that are under discussion for the new regulatory framework.[18] The government's "preferred option" is Option 3A: "Introduce a new category of organisms, the PBO, which have been developed using modern biotechnology but could otherwise have arisen through traditional breeding methods. Remove current GMO regulations for qualifying organisms and replace with an independently verified, light-touch, notification and certification system for marketing use. Revoke 'The Genetically Modified Organisms (Deliberate Release) (Amendment) (England) Regulations 2022' and reinstate provisions into the Bill, to maintain self-certification for non-marketing uses."[19]

The Bill fails to make explicit any aim of ensuring a high level of safety to human and animal health and the environment. It also fails to mention the precautionary principle.

The exemptions from existing regulatory controls will apply to most GMOs – not just when gene editing is used to disrupt a gene (SDN-1) or modify a gene (SDN-2), but also when whole new genes are inserted (SDN-3), as specified by the ACRE guidance on gene-edited plants that accompanies the new legislation.[20] In respect of the gene insertion procedure, SDN-3 gene editing is comparable to old-style transgenesis.

However, it is important to note that biosafety concerns around GMOs are not confined to the introduction of foreign DNA or foreign genes. As a review pointed out, the occurrence of hazards from gene editing cannot be correlated in all cases with an exogenous (foreign) origin of the introduced DNA sequences.[21] All types of gene editing – including SDN-1 and -2 – are prone to unintended effects that could change patterns of gene function and thus the biochemistry of gene-edited plants, which in addition to negatively impacting crop performance can make them toxic or allergenic, able to adversely affect wildlife, or able to impact the health of gene-edited animals.[22]

The "notification only" system for GMOs favoured by the government appears to be not based on the existing science, but a political move designed to bring the UK into line with the US, which has a similar system of deregulating these organisms.

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[16] Impact Assessment, 3.2.2.2, 24.
[17] Part 2, 17(6).
[18] Impact Assessment, 4.1.
[19] Impact Assessment, 3.2.2.2 (24).
[20] https://www.gov.uk/government/publications/acre-guidance-on-genetic-technologies-that-result-in-qualifying-higher-plants/technical-guidance-on-using-genetic-technologies-such-as-gene-editing-for-making-qualifying-higher-plants-for-research-trials ; https://www.gmwatch.org/en/106-news/latest-news/20023
[21] https://www.mdpi.com/2673-6284/10/3/10
[22] https://gmwatch.org/en/news/archive/2019/19223 ; https://www.mdpi.com/2223-7747/10/11/2259/htm

Amendments required: A mandatory risk assessment for human and animal health and the environment must be conducted by genuinely independent people for all types of GMOs released (including GMOs produced by gene editing and other new GM techniques), without exception. A high level of protection for human and animal health and the environment must be specified as an aim of the Bill. The precautionary principle must be taken into account in the implementation of the Bill.

2. The Bill does not require exempted GMOs to be labelled.

The Bill contains provisions that "may" or may not impose requirements for traceability of exempted GMOs.[23] Labelling is not mentioned at all. In the Impact Assessment, only two options (1 and 4) of six allow for mandatory labelling of all GMOs and neither is the government's preferred option (3a), which does not mention labelling.

This is in contrast to the EU Directive, which requires traceability and clear labelling for all products consisting of or containing GMOs, and products derived from GMOs, at all stages of their placing on the market.[24]

As stated by GeneWatch UK:

- Traceability and labelling are essential to allow GM-free products (including organic products) to continue to be sold, and to allow UK food and feed products to be traded with countries where GMOs that are exempt under the Bill continue to be regulated. Failure to ensure traceability could lead to massive costs to farmers, food manufacturers and retailers if products are rejected by consumers, manufacturers, traders, importers, or retailers when the presence of unauthorised GMOs cannot be guaranteed.
- Traceability and labelling are also essential for imported products, which could contain exempt GMOs and end up in untraceable or unlabelled products that might also be exported on to other countries.
- Traceability and labelling are essential to allow consumer choice and maintain consumer trust in the food chain.
- Traceability and labelling are essential to allow products to be withdrawn if anything goes wrong.
- Health and environmental risk assessments are also essential to protect human health and the environment.[25]

Amendment required: The Bill must make a provision that all GMOs, including those covered in the new Bill, must be fully traceable and clearly labelled as GMOs.

3. The Bill ignores the process by which the GMO was developed, even though knowledge of the process used gives crucial information about the risks posed by the GMO.

By ignoring the process by which the GMO was developed, the Bill allows almost every type of GMO, including older-style transgenic GMOs, to be included in the definition of a

[23] Part 3, 26(2)(b).
[24] Preamble (40) and (42).
[25] http://www.genewatch.org/uploads/f03c6d66a9b354535738483c1c3d49e4/genewatch-fsaletter-may22-web.pdf

"precision-bred organism", on the supposed grounds that the GMO "could have resulted"[26] from traditional processes, such as breeding.

Knowledge of the process by which a GMO is developed is crucial as it informs regulators about where things can go wrong and what to look for, and thus put in place appropriate regulations to protect health and the environment from unintended outcomes.

For example, gene-edited cattle, engineered to be hornless, were claimed by Recombinetics, the developer company, to be free from any unexpected alterations[27] and thus an example of "precision breeding".[28] In arguments that have become all too familiar, these cattle were used to put forward the idea that because "The effects of genome editing are largely identical to those of… natural processes", gene-edited organisms should not be regulated.[29]

However, the cattle were found by scientists at the US Food and Drug Administration (FDA) to unexpectedly contain rogue genetic material, including genes encoding antibiotic resistance. The scientists had decided to run their own thorough analysis of the publicly available whole genome sequencing data on the gene-edited cattle's genomes[30] – an analysis that the developer clearly failed to do, or to do properly. The genes encoding antibiotic resistance could have escaped into the environment, be taken up by bacteria, and spread to humans or other animals, further compromising the effectiveness of antibiotics against diseases. Once these risks were uncovered, Recombinetics' plans to commercialise the cattle were scrapped, at least for now.[31]

As well as bringing about the intended change(s), gene editing processes also induce many unintended changes, as explained below (in the section, "The Bill calls the exempted GM technologies 'precision breeding', misleading the public). It is not scientifically valid in the absence of supportive empirical evidence to assume that the GMOs produced by gene editing are safe, that they are the same as can occur naturally, and that they will not result in any special risks to human and animal health or the environment. Proper testing must be carried out in each case and independent risk assessments performed.

Amendments required: Full details of the process used to generate each GMO, including those covered by the Bill, and the precise nature of the genetic modification in a given GMO, must be placed in the public domain. The Bill must recognize the unintended effects of the GM processes, including gene editing, as well as the intended effects. It is broadly accepted that unintended genetic alterations are an innate property of GM processes, including gene editing procedures. Crucially, as GM processes radically differ from natural reproduction, the quality as well as the quantity, of unintended genetic variation arising from them markedly differs from what may occur naturally. Long-read whole genome sequencing must be performed to identify the full range of genetic effects, both intended and unintended. Each stage of the GM process must be considered in the risk assessments for health and environment.

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[26] Part 1, 1(2).
[27] https://www.nature.com/articles/nbt.3560#article-info ; https://www.independentsciencenews.org/news/fda-finds-unexpected-antibiotic-resistance-genes-in-gene-edited-dehorned-cattle/
[28] https://www.technologyreview.com/2019/08/29/65364/recombinetics-gene-edited-hornless-cattle-major-dna-screwup/
[29] https://www.nature.com/articles/nbt.3566
[30] https://www.nature.com/articles/s41587-019-0394-6
[31] https://www.wired.com/story/brazils-plans-for-gene-edited-cows-got-scrappedheres-why/

4. The Bill unscientifically dismisses crucial genetic elements that could make the difference between safety or serious risk from the GMO.

In determining whether a feature of an organism's genome could have resulted from traditional processes, the Bill states that the following will not be considered:

- The gene copy number of the feature
- Its epigenetic status, or
- Its location in the genome[32]
- Genetic material that does not result in the production of a functional protein.[33]

Contemporary understanding of gene function, especially across an organism's whole genome, as well as experience of outcomes from GM processes stretching back decades, shows that there is no scientific justification for dismissing these elements. All these elements will not only impact the function of the newly introduced genetic feature, but also the modified organism's host genes. Thus, ignoring or dismissing these effects of the elements puts public health and the environment at risk.

Copy number of genes: In the field of human medical genetics, which appears to be far more safety-conscious than the field of agricultural genetic engineering, the copy number of genes is acknowledged to be "pivotal in biological pathways" and to play an important role in susceptibility to major common diseases.[34]

In livestock animals, the copy number of genes is known to "alter the gene expression and change the phenotype of an individual"[35] – factors that could make the difference between health and severe disease, abnormalities, or premature death.

In plants, the copy number of specific genes has been linked to important traits such as flowering time, plant height and resistance to environmental stressors.[36] The copy number of genes has also been found to be linked to evolutionary adaptation in plants and to affect defences against diseases.[37]

In transgenic plants, the copy number of the transgene(s) can affect the stability of the desired GM trait.[38] Stability of the GM trait is one of the criteria named in the Bill for determining whether a GMO is a "precision bred organism".[39]

While the Bill may assume that GMO developers will ensure the stability and phenotypic normality of their product, this is likely to be restricted to aspects such as whether the plant or animal looks normal and grows acceptably. Less obvious aspects at the level of the organism's biochemistry, including unexpected toxicity or allergenicity, or altered nutritional value, will easily pass unidentified into our fields and onto our dinner plates, without strict regulatory requirements for testing and independent assessment.

Given all the above, it seems extraordinary, as well as determinedly at odds with the science underpinning gene editing, that the Bill would dismiss taking account of gene copy

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[32] Part 1, 1(5).
[33] Part 1, 1(6).
[34] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2920180/
[35] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5960796/
[36] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4544587/
[37] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5259951/
[38] https://pubmed.ncbi.nlm.nih.gov/26670088/
[39] Part 1(2)(b).

number in the consideration of whether a GMO could have arisen from “traditional processes” or “natural transformation” and therefore be exempted from in-depth risk assessments.

Epigenetic status: Epigenetics means “above genetics” and refers to molecular structures that are associated with DNA and which regulate the function (expression) of genes in the organism. Therefore epigenetic status in any given part of an organism is crucial in controlling overall global patterns of gene function and thus health or disease status. Importantly, epigenetic status is dynamic and can change not only in response to internal cues within the organism, but just as crucially, to changes in the environmental (weather, soil condition, application of agrochemicals), leading to dramatic alterations in global patterns of gene function and the performance and composition of the organism.

Under current UK and EU law, differences in gene regulation in a GMO compared with the non-GMO parent are not taken into account in GMO risk assessments. However, such differences can become a risk if, for example, environmental conditions change (such as climate changes, pest attacks, or pesticide applications). Such environmental stresses can alter the functioning of the genetically manipulated genes. This could trigger adverse effects on the biochemistry of the plant, affecting its performance in the field or its safety for consumption or the environment, even if no such effects were observed in the laboratory or in field trials. For example, altered plant biochemistry can include the production of novel toxins or allergens, or altered levels of existing toxins or allergens.

While the new Bill requires that the GM traits in “precision bred organisms” are stable, it does not specify that their stability must be tested under different environmental conditions.

The influence of the environment on epigenetic status and thus gene regulation will be markedly amplified if the genes whose products (DNA methyltransferases, histone protein modifiers, miRNAs) are at the basis of building the layers of epigenetic control are either intentionally or unintentionally altered by GM, including gene-editing, procedures.

The importance of epigenetic status of gene-edited plants is illustrated by the findings of an experiment with Arabidopsis plants. The researchers used CRISPR/Cas gene-editing tool to try to remove a section of DNA important for cold tolerance from the plants’ genome. The Crispr/Cas9 tool was used to simultaneously target and silence three genes in the genome. The three genes are similar in their structure and located close together in the genome. Three 'lines' of the same species were used; all had different origins. All three lines had the same gene sequences with regard to cold tolerance. However, the success rate of the intended gene manipulation in one line of Arabidopsis was 33%, whereas in another line it was only 3.7% – about a tenth of the former. According to the authors, epigenetic effects were likely to be responsible for the differences between the different lines.[40]

These results show that gene editing outcomes do not solely depend on DNA sequence. Epigenetic status controlling global patterns of gene expression can also be a decisive factor and can therefore play a large role in determining the risk or safety of the GMO in question.

Location in the genome: Position effects, or location of the genetic feature, are crucial to the safety of the GMO for health and environment. A position effect is defined as a

[40] https://www.frontiersin.org/articles/10.3389/fpls.2017.01910/full

deleterious change in the level of gene expression brought about by a change in the position of the gene relative to its normal chromosomal environment, but not associated with a mutation or deletion of the gene.

Gene expression can be greatly influenced by its position in the genome, to the extent that in human genetics, gene position can make the difference between health and serious disease.[41]

In mammalian cells, transgene expression was found to vary more than 1,000-fold based on genomic location.[42] In transgenic animals, position effects can strongly influence the transcription of foreign genes, leading to complications such as low frequencies and levels of gene expression and abnormal patterns of expression. The seriousness of these effects has prompted scientists to spend years looking for ways to overcome them.[43]

Major problems caused by position effects negatively impacting gene function is one of the main reasons why GM crop developers must screen hundreds, if not thousands, of individually created transgenic plants to find a few suitable candidates to take forward. This is because each individually created transgenic plant contains the transgene inserted at different locations in the plant genome and thus is subject to different position effects. Only a few transgenic plants will harbour transgene integrations at locations that fortuitously permit a suitable level and stability of expression.

While gene editing aims to create targeted mutations and thus to overcome position effects, this has not been achieved. As a scientific review has pointed out, whilst the actual gene editing allows modifying the DNA at a target site, the claimed precision may not hold true for the delivery and integration of its tools. The common use of older-style first-generation genetic engineering techniques to integrate DNA encoding the CRISPR/Cas components results in insertion at a random location in the genome, often with multiple and flawed (e.g. partial) copies. Random integration of the transfer DNA (T-DNA) from Agrobacterium-mediated plant transformations (and fragments thereof) could have unwanted consequences for the resulting GMO, such as the disruption of genes important for plant growth or development.[44]

In addition, in gene editing, off-target cuts, deletions, insertions and rearrangements of DNA, including insertions of foreign DNA and foreign genes, are common and a major concern.[45]

In one study, the DNA template encoding CRISPR/Cas9 was not only detected at the target location in soybeans as intended, but also at other multiple, apparently random, genomic locations.[46] In another study, CRISPR/Cas sequences were found at multiple

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[41] https://academic.oup.com/hmg/article/7/10/1611/635945
[42] https://www.sciencedirect.com/science/article/pii/S0092867413008891
[43] https://pubmed.ncbi.nlm.nih.gov/7569038/
[44] https://doi.org/10.1146/annurev-genet-120215-035320 ; https://doi.org/10.1023/a:1023929630687 ; https://doi.org/10.1186/s12302-020-00361-2
[45] https://www.sciencedirect.com/science/article/pii/S216225311630049X ; https://www.nature.com/articles/nbt.4192 ; https://www.nature.com/articles/s42003-019-0705-y ; https://www.jbc.org/content/early/2020/03/11/jbc.RA120.012933 ; https://www.ncbi.nlm.nih.gov/pubmed/27902801 ; https://www.sciencedirect.com/science/article/pii/S1673852720300916 ; https://www.nature.com/articles/s42003-019-0300-2.pdf?origin=ppub
[46] https://doi.org/10.1104/pp.15.00783

genomic sites that were similar to the transgene integration sites, indicating that the integration of CRISPR/Cas sequences might not be completely random.[47]

A 2019 study on CRISPR/Cas-mediated gene editing of rice plants begins by noting that "gene targeting in plants is still very inefficient" and that variability in position of the guide RNAs used to target the editing tool to a specific site in the genome can result in "dramatic developmental phenotypes" (abnormal characteristics) when the target genes overexpress. The researchers achieved a partial success by designing guide RNAs specifically for the rice plants studied, in that they no longer observed "strong detrimental effects", but they concluded that the topic requires further study to refine approaches.[48]

Given the generally acknowledged importance of position effects and the difficulties that scientists experience in overcoming them, it is not comprehensible that the Bill allows them to be ignored in determining whether or not a GMO is a "precision bred organism" that can be subjected to a weaker form of regulation than other GMOs.

Genetic material that does not result in a functional protein: [UPDATE 15 JUNE 2022: There are two ways of interpreting this clause. First, the inserted genetic material could encode, either intentionally or unintentionally, for a protein that is not known to have any function. However, proteins that are assumed to be non-functional, in the absence of experimental evidence to support such an assumption, can still interact with other proteins (either enzymes, structural proteins, or signalling proteins) to change their form or otherwise modify their behaviour, which can have a significant impact on the affected plant or animal.

Second, genetic material introduced into an organism could be intentionally designed not to code for any protein. Examples of such genetic elements are those that innately possess gene regulatory properties (e.g. enhancers) and encode for RNA molecules involved in the process of RNA interference regulation of gene expression.

Both these types of non-protein coding genetic elements can have wide-reaching unintended effects on multiple gene functions, which can lead to alterations in the organism's biochemistry and composition, with unknown consequences to human and animal health and the environment.
END OF UPDATE 15 JUNE 2022]

In addition, some GMOs are engineered not to produce a functional protein but to change their RNA content in order to produce dsRNA (double-stranded RNA) molecules that alter (usually decrease) gene expression. These GMOs are described as RNAi (RNA interference) type organisms.

dsRNA molecules are stable in the environment and in digestion. Once taken up, the dsRNA can circulate throughout the body and alter gene expression in the consumer animal. In some cases, the dsRNA taken up is further amplified or causes a secondary reaction that leads to more and different dsRNAs ("secondary" dsRNAs), with unpredictable targets. They also readily transfer to mammals through food where they can circulate in blood and alter gene expression in organs.[49]

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[47] https://doi.org/10.1186/s12896-020-00604-3
[48] https://doi.org/10.1007/s42994-019-00007-9
[49] http://www.sciencedirect.com/science/article/pii/S0160412013000494#

Risks include unintended gene silencing in the organism itself or in organisms that consume or are otherwise exposed to the dsRNA, as well as toxic effects, for which evidence already exists. Some dsRNA molecules can have profound physiological effects on the organism that makes them. Physiological effects are the intended outcomes of exposure to dsRNA incorporated into food sources for invertebrates and biopesticides, and could cause off-target effects and adverse effects in nontarget organisms. [50] As one researcher stated, “A daunting outcome is raised, that each [dsRNA] formulation might have its own risks”.[51]

Other types of GMO may be engineered with DNA sequences that do not code for a protein but act as powerful genetic regulatory elements designed to affect the function of host genes around their site of integration in the genome.

An example is the gene-edited hornless cattle discussed above, which were engineered with the POLLED genetic sequence variant (for hornlessness) with no known or predicted protein-coding genes.[52] Even though the POLLED allele does not code for proteins, it influences the function of multiple genes, which lead to hornlessness. This illustrates the fact that even non-coding DNA elements, when engineered into plants or animals, could have major downstream phenotypic consequences. Therefore it is absurd to suggest that the insertion of non-coding genetic elements with major genetic ramifications qualifies as “precision breeding” and thus does not require as much regulatory scrutiny as other types of GMO.

Amendments required: The four genetic elements listed in the Bill as not to be considered in determining if an organism is “precision bred” and so can be subjected to weaker regulation than other GMOs, should be deleted. Contemporary principles of molecular genetics and genomics, as well as empirical experimental observations, demonstrate on the basis of the strongest scientific evidence that the Bill is wrong in its reasoning to ignore the four genetic elements listed as being irrelevant in determining precision bred organism status of a plant or animal. There is no scientific justification for assuming that these elements can be ignored in determining “naturalness” or degree of safety for health and the environment. The Bill should state that all types of GMO pose their own risks and that risks must be individually assessed on a case-by-case basis.

5. The Bill includes animals and fails to protect their health and welfare.

GM gene-edited animals are included in the Bill’s deregulation plans. This has shocked some observers, as the government’s response to the public consultation of 2021 suggested that the deregulation of gene-edited animals would be sidelined for a time and that the plans would initially focus only on plants.[53] This temporarily reassured Compassion in World Farming, which said in September 2021, "Compassion is pleased that DEFRA recognises the need to give consideration to the animal welfare and ethical

[50] http://www.sciencedirect.com/science/article/pii/S0160412013000494#
[51] https://pubmed.ncbi.nlm.nih.gov/16520821/
[52] https://www.nature.com/articles/nbt.3560
[53] UK Government (2021). Consultation outcome: Genetic technologies regulation: government response. 29 Sept. https://www.gov.uk/government/consultations/genetic-technologies-regulation/outcome/genetic-technologies-regulation-government-response. "We will start by looking to ease some of the burdens which currently apply to research and development for gene edited plants, while maintaining the present regulatory system for animals and other organisms."

concerns raised during its consultation. As a result, any changes to legislation to permit the gene editing of animals will come later."[54]

But the government has rushed ahead with including gene-edited animals in the deregulation proposals of the Bill, even though the Impact Assessment specifies that the deregulation proposals "would apply to plants initially, with powers to apply this change [to] animals under secondary legislation", thus "accounting for consumer concerns by allowing more time for due consideration to be given to remaining areas of uncertainty around the role of labelling and ethical questions".[55]

The government's intention raises serious questions about animal welfare. Attempts to produce GM gene-edited animals have failed in their objectives, involved animal suffering and exploitation, and presented new risks to health and environment. [56] The government's intention to use secondary legislation to expand deregulation from plants to GM animals suggests an agenda to avoid the type of scrutiny entailed in primary legislation.

Also, most gene editing of animals currently involves cloning as a necessary step, with its accompanying risks of inefficiency, non-viable fetuses, stillbirths, and high frequency of birth defects.[57]

Promoted "benefits" of gene-edited animals include producing pigs resistant to respiratory diseases.[58] But the technology, if it works as intended, will likely be used to increase animals' tolerance to inhumane, overcrowded conditions, as Compassion in World Farming has warned.[59]

Regarding the marketing of GM animals covered by the Bill, the notifier only has to self-declare that they do "not expect the health or welfare of the relevant animal or its qualifying progeny to be adversely affected… by any precision bred trait".[60] If harm does occur, the notifier only has to state that they did not "expect" it, in order to escape sanction by the law.

The notifier does have to provide their own "assessment" of the risks to the health or welfare of the animal "which could reasonably be expected to result" from the GM trait and explain the steps that they have taken to avoid such harm.[61] But nowhere in the Bill is there a requirement that they are legally bound to prevent such harm and nowhere are steps to achieve this end laid down by the law. And contrary to existing law, no requirement for a mandatory risk assessment is specified for the marketing of GM animals

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[54] https://www.ciwf.org.uk/media/press-releases-statements/2021/09/defra-must-not-permit-the-gene-editing-of-farm-animals

[55] Impact assessment, 4.1, 31.

[56] Examples include a gene-edited super-muscly pig. https://www.scientificamerican.com/article/super-muscular-pigs-created-by-small-genetic-tweak/ . Conventionally bred super-muscled animals are known to have serious health problems: http://www.grandin.com/welfare/genetics.animal.welfare.html and https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=&ved=2ahUKEwjHr_6DxYn4AhWUiFwKHS3FBvsQFnoECAgQAQ&url=https%3A%2F%2Fwww.ciwf.org.uk%2Fmedia%2F3816969%2Fmodern-breeding-technologies-and-farm-animal-welfare.pdf&usg=AOvVaw0WwyeafdEvYr5KqOlZFTQd . There is no reason to assume that gene-edited super-muscled animals will not suffer from the same problems.

[57] https://www.gmwatch.org/en/106-news/latest-news/19315 ; https://pubmed.ncbi.nlm.nih.gov/16110893/ ; https://pubmed.ncbi.nlm.nih.gov/11841470/

[58] https://www.ed.ac.uk/research/animal-research/news/agreement-targets-disease-resistant-gene-edited-pi

[59] https://www.ciwf.org.uk/media/press-releases-statements/2021/09/defra-must-not-permit-the-gene-editing-of-farm-animals

[60] 11(3).

[61] 11(4)(a) and (b).

or their food products. GM animals intended for marketing “may” or may not be subject to regulations concerning the effects of the intended GM trait on their health or welfare;[62] the production and marketing of food products derived from GM animals “may” or may not entail a risk assessment for health and environment.[63]

Amendments needed: The government must remove animals from the Bill as their health and welfare would be unacceptably put at risk under the Bill’s weak provisions. Laws must be passed to ban the inhumane and unhealthy conditions for livestock animals that currently serve as the pretext for introducing disease-resistant gene-edited animals.

6. The Bill calls the exempted GM technologies “precision breeding”, misleading the public and Parliament.

The UK government claims, “gene editing is different from genetic modification, because it does not result in the introduction of DNA from other species and creates new varieties similar to those that could be produced more slowly by natural breeding processes”.[64]

But gene editing *is* genetic engineering or genetic modification, as confirmed by authorities from the EU Court of Justice,[65] to the US National Institutes of Health,[66] to the US Food and Drug Administration.[67]

Also, the definition of a GMO is not an organism that contains foreign DNA from other species, contrary to the semantics of the UK government:

- The Cartagena Protocol on Biosafety, an agreement signed by nearly 200 nations, including the UK,[68] defines a living modified organism (its term for genetically modified organism) as “any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology”.[69]
- The EU Directive 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”.[70]
- The US Food and Drug Administration defines a GMO as “a plant, animal, or microorganism that has had its genetic material (DNA) changed using technology that generally involves the specific modification of DNA, including the transfer of specific DNA from one organism to another”.[71]

None of these authorities define a GMO as an organism that contains DNA from another species. The UK government is attempting to redefine a GMO against all rules of science and logic, and contrary to definitions accepted by other authorities, apparently in order to pursue Boris Johnson’s economic agenda to “liberate the UK’s extraordinary bioscience sector from anti genetic modification rules”.[72]

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[62] Part 2, 25(1).
[63] Part 3, 26(3)(b).
[64] https://www.gov.uk/government/news/plans-to-unlock-power-of-gene-editing-unveiled
[65] http://curia.europa.eu/juris/documents.jsf?num=C-528/16 ; https://curia.europa.eu/jcms/upload/docs/application/pdf/2018-07/cp180111en.pdf
[66] https://www.nih.gov/news-events/gene-editing-digital-press-kit
[67] https://www.fda.gov/food/agricultural-biotechnology/types-genetic-modification-methods-crops
[68] https://bch.cbd.int/protocol/parties/
[69] https://bch.cbd.int/protocol/cpb_faq.shtml#faq3
[70] Article 2(2).
[71] https://www.fda.gov/food/consumers/agricultural-biotechnology
[72] https://www.gmwatch.org/en/106-news/latest-news/19059

In addition, the words “precision breeding” are a misnomer and mislead the public, as a large number of scientific studies show that gene editing is not precise. The only aspect that is precise is that the initial double-strand cut in the DNA can be targeted to a specific site in the DNA. But unintended changes can also occur, both at the on-target site (the intended gene editing site) and off-target (elsewhere in the genome).[73]

The effects of these unintended changes, in terms of food and environmental safety, are unknown but are likely to vary from case to case. Their implications, including any resulting risks, must be individually assessed by an independent authority, based on testing data that must be required to be supplied by the notifier. Such data should include long-read whole genome sequencing and “omics” molecular analyses (transcriptomics, metabolomics, and proteomics) to identify changes that could affect food or environmental safety.

Amendments required: The Bill should be rewritten to abandon the misleading term “precision breeding” and to bring the definition of GMOs, including those produced by gene editing procedures, into line with the scientific facts and the definitions used by other widely accepted competent authorities, including the Cartagena Protocol, to which the UK is a signatory. These changes would avoid misleading the public.

7. Anyone – however inexperienced, irresponsible, or even malicious – who wishes to experiment with planting GMOs can do so without permission from the authorities or meaningful regulatory oversight.

Under the previous law, anyone wishing to release experimental GM crops or animals for non-marketing purposes had to seek permission from the relevant authorities. The new Bill has no such requirement. Instead the person who wishes to release such GMOs only needs to “notify” the Secretary of State of their intention.[74] He or she is defined as the “notifier”.

No distinction is made between bona fide researchers, who might reasonably be expected to understand what measures to take to protect public health and the environment from contact with the GMO, and persons who wish to release such organisms for trivial or even malicious reasons, and without due care for health and the environment.

Amendments required: The Bill should be rewritten to require that the permission of the regulatory authorities be sought by anyone who wishes to release a GMO. The regulator must retain the authority to refuse an application if biosafety measures are inadequate.

Conclusion

The Bill is scientifically untruthful and irresponsible. It chooses to ignore contemporary understanding of molecular genetics, which has revealed the complexities and intricacies of how the genome of an organism, either plant or animal, works as a finely balanced interdependent network of genes. In addition, the Bill dismisses years of peer-reviewed findings on the effects of gene editing and other new GM technologies.

The scientific advisors to the government are entrusted by the public to act in an objective and impartial manner and stay true to the science. Yet they appear to have acted in complete contradiction to established scientific understanding. The only possible

[73] https://gmwatch.org/en/news/archive/2019/19223
[74] Part 2, 3(1)(a) and 4.

explanation seems to be economic interests and a political determination to align the food and farming sectors of England with those of the USA.

The Bill drastically weakens existing protections for health and environment. For most GMOs, the Bill does not require an in-depth risk assessment for health and environment and removes existing protections for both. The Bill does not require exempted GMOs to be labelled, thus removing choice from consumers, farmers and growers alike.

The Bill ignores the process by which the GMO was developed, even though knowledge of the process used gives crucial information about the risks posed by the GMO.

The Bill makes the arbitrary decision that a GMO qualifies as "precision bred" and therefore does not need to be subjected to in-depth risk assessment or labelling if its developer self-declares that it could have arisen by natural processes.

In order to decide whether or not an organism is "precision bred" and could have arisen naturally, the developer is explicitly given permission by the Bill to dismiss elements of the GM-induced genetic "feature" as unimportant – namely:

- the copy number of genes of the feature
- its epigenetic status, and
- its location in the genome

– even though the type and quantity of these GM-induced "features" could make the difference between safety or serious risk for any given GMO.

The Bill also allows GM material that does not produce a functional protein to be dismissed in the consideration of whether the GMO is classed as “precision bred”. However, classes of GMOs engineered not to produce a functional protein can nevertheless contain introduced genetic elements that can markedly alter multiple gene functions, with dramatic changes in the characteristics of the organism. This includes the production of RNA molecules that alter gene expression, which has been flagged by scientists as posing a risk of silencing the genes of animal or human consumers of the GMO or of unintendedly silencing genes in the organism itself.

Dismissing these elements from consideration runs counter to prevailing scientific knowledge of molecular genetics and the technological principles underpinning genetic engineering and thus is irresponsible in the extreme. Given that there is no scientific justification for dismissing the importance of these elements, it appears that the motivation is economic expediency. Both GMO developers and regulators know that these aspects of any given GMO are in practice unpredictable, uncontrollable, and potentially risky, and they wish to "bake in" permission for developers to dismiss them from consideration.

The Bill includes animals in its deregulation plans and fails to protect their health and well-being – raising serious questions about animal welfare. Attempts to produce GM gene-edited animals have failed in their objectives, involved animal suffering and exploitation, and presented new risks to health and environment. The Bill allows a free-for-all in the development of these engineered animals.

The Bill calls the exempted GM technologies “precision breeding”, misleading the public and Parliament and effectively trying to hide experimental GMOs in our fields and on our plates.

Finally, the Bill allows anyone – however inexperienced, irresponsible, or even malicious – who wishes to experiment with planting GMOs to do so without permission from the authorities or meaningful regulatory oversight.

In short, the Bill is a fabrication based on dishonesty, with its seemingly sole objective being political and potential commercial expediency.

As a minimum, we propose the following Amendments to the Bill:

1. A mandatory risk assessment for human and animal health and the environment must be conducted by genuinely independent people for all GMOs released, without exception. A high level of protection for human and animal health and the environment must be specified as an aim of the Bill. The precautionary principle must be taken into account in the implementation of the Bill.

2. The Bill must make a provision that all GMOs, including those covered in the new Bill, must be fully traceable and clearly labelled as GMOs.

3. Full details of the processes used to generate each GMO, including those GMOs covered by the Bill, must be placed in the public domain and considered in the risk assessments for health and environment. The Bill must recognize the unintended effects of GM processes, including gene editing, as well as the intended effects. Long-read whole genome sequencing must be performed to identify the full range of effects, both intended and unintended.

4. The four genetic elements listed in the Bill as not to be considered in determining if an organism is “precision bred” and thus if it can be subjected to weaker regulation than other GMOs, should be deleted, as it is completely contrary to the science that underpins GM processes. The Bill should state that all types of GMO pose different risks and that the risks of each one must be individually assessed on a case-by-case basis, taking into account the processes used to create the GMO.

5. The government must remove animals from the Bill as their health and welfare would be unacceptably put at risk under the Bill’s weak provisions. Laws must be passed to ban the inhumane and unhealthy conditions for livestock animals that currently serve as the pretext for introducing disease-resistant gene-edited animals.

6. The Bill should be rewritten to exclude the misleading term “precision breeding” and to bring the definition of GMOs into line with the scientific facts and the definitions used by other widely accepted authorities, including the Cartagena Protocol, to which the UK is a signatory. These changes would avoid misleading the public and Parliament.

7. The Bill should be rewritten to require that the permission of the regulatory authorities be sought by anyone who wishes to release a GMO. The regulator must retain the authority to refuse an application if biosafety measures are inadequate.