Submission

by Poppy Growers Tasmania Inc

In response to
Invitation to Comment in respect of Regulations to Control SDN-1 Modified Organisms in Tasmania

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3rd February 2021

The Hon Guy Barnett
Minister for Primary Industries and Water
Minister for Energy
Minister for Resources
Minister for Veterans' Affairs
SDN-1 Regulations
Agriculture and Water Division
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3 February 2021

Dear Minister Barnett

Response to the Invitation to Comment on the Draft *Biosecurity (SDN-1 Modified Organism) Regulations 2020*

Thank you for the opportunity to provide comments on the draft *Biosecurity (SDN-1 Modified Organism) Regulations 2020.* Poppy Growers Tasmania Inc (PGT) has collaborated extensively with Tasmanian Alkaloids Pty Ltd trading as Extractas Bioscience (Extractas) and Sun Pharmaceutical Industries Australia Pty Ltd (Sun Pharma) to provide this submission.

About Poppy Growers Tasmania

PGT was established on an informal basis in 1964 to assist growers as the poppy industry was in early establishment phase in Tasmania.

It was formally established in 1971 along with the poppy industry's first commercial production in Australia, at that time based solely in Tasmania.

Poppy growing remained solely in Tasmania until approximately 2015 when some production was undertaken on mainland Australia.

Today Australia produces approximately 50% of the global demand for opiate based pain management medicines for the world pharmaceutical industry. Tasmania produces approximately 95% of that demand.

PGT is a voluntary, not-for-profit grower association with a Committee of Management consisting of 14 poppy growers drawn from each growing area of the State. Approximately 93% of poppy growers are members of PGT.

There are approximately 400 poppy growers spread across the entire growing area on the North West Coast, North East Coast, Northern Midlands, Midlands, Southern Midlands, Central Highlands and Derwent Valley.

In fact Poppies are grown in all of Tasmania's nationally acclaimed irrigation areas.

PGT is the peak industry organisation charged with representing the interests of Tasmanian poppy growers in respect of security, governance and commercial matters at all levels of Government, State,

National and International, including ongoing liaison and negotiation with the three licensed and approved Australian poppy companies.

Crops genetically modified for pharmaceutical purposes and not intended for use as food or feed may be authorised for release to the Tasmanian environment for limited and controlled release or commercial purposes under the *Genetically Modified Organisms Control Act 2004.* On the surface, this would appear to exempt pharmaceutical poppies from the current Moratorium on commercial GMO production in Tasmania, however we are aware that this authorisation is subject to:

- Prior approval by the national OGTR as required;
- Assessment by DPIPWE of the likelihood of GMO entry into the broader environment, other than plants, or human and animal food supplies;
- Conditions as required.

Thus we feel that "real" exemption for non-food pharmaceutical crops from the *Genetically Modified Organisms Control Act 2004* and the proposed *Biosecurity (SDN-1 Modified Organism) Regulations 2020* is less certain than has been widely proposed. We are therefore of the view that we have a potential stake in the proposed changes to this legislation.

Further,

(i) A significant quantity of poppy seed is sold for culinary purposes on both the domestic and international markets. The sale of seed for culinary purposes would constitute use for food, which comes under the control of the proposed new regulations.

(ii) Extractas and Sun Pharma are constantly looking for new production, processing, and extraction opportunities as part of their ongoing strategies of innovation, diversification and utilisation of core capacity and capabilities. Future opportunities may very well include food crops and products, and it is important that both companies have freedom to operate in the research and development space and maximum operational and development flexibility.

(iii) Extractas, Sun Pharma and PGT represent and collaborate with rural producers who are diversified in terms of crop production, including food production enterprises. We feel the need to take a wider view of our responsibility to our grower base including providing technical comments on changes to legislation and regulation that could potentially affect their livelihoods.

Extractas, Sun Pharma and the PGT have three broad concerns regarding the proposed new biosecurity regulations:

1. Freedom to Operate and Ability to Access and Utilise and Important Research and Development Technology

Site-Directed Nuclease-1 (SDN-1) is one of a suite of new breeding technologies which are being considered for use by innovation-based companies such as Extractas and Sun Pharma. Essentially SDN-1 is a mutation breeding technique. Mutation breeding seeks to develop new traits and breeding lines through the alteration of the nucleotide sequence of the genome of an organism. In conventional mutation breeding (CMB), propagules and parts of the organism (in our case generally seeds) are exposed to mutagenic chemicals (e.g. ethyl methanesulfonate or EMS) or radiation (generally x-rays, gamma rays or fast neutrons) which induce deletions in the nucleotide sequences of the target organism. Mutations occur naturally in organisms at about 10^{-4} to 10^{-6} per generation but with CMB this can be increased to 0.14-0.6%. CMB is a useful plant improvement tool and companies such as Extractas and Sun Pharma

have used it very effectively to produce pharmaceutical poppies with distinct chemotypes and desirable traits such as significantly increased yield. That said, CMB does have a number of drawbacks. Large numbers of propagules need to be treated with mutagens to produce an effective population from which to select potentially useful breeding lines that occur with relatively low frequency. Mutagenesis with chemicals and radiation is generally not targeted and can result in undesirable traits, changes to multiple traits and physiological damage. Several generations of breeding may be required to stabilise useful mutations and remove deleterious ones and it may take many years to introgress these useful characteristics into commercial cultivars.

SDN-1, on the other hand, is a targeted technology which uses nuclease enzymes to cleave phosphodiester bonds between nucleotides of targeted nucleic acid sequences. This technique causes small deletions which then repair through natural cell processes. It is relatively quick and simple to use and free from many of the drawbacks associated with CMB. SDN-1 offers the prospects of a targeted plant breeding technology with a significant reduction in time to commercialisation for new cultivars. This technology does not use recombinant DNA and does not lead to the insertion of foreign DNA. As a result, SDN-1 has the potential to transform commercial plant breeding programmes and is of intense interest to Extractas, Sun Pharma and most other plant-based industries. In poppies, it may have potential to induce resistance to diseases such as systemic downy mildew, induce differential herbicide resistance to aid in the management of wild poppies and to develop novel commercially exploitable traits. Extractas is also interested in the potential of this technology for plant improvement in medicinal cannabis.

We understand that the current GMO legislation and proposed Biosecurity Regulation allow for the licensing of companies and organisations to use SDN-1 for research and development purposes. However, commercialisation of new varieties developed using SDN-1 will fall under the moratorium on GMOs for food crops in Tasmania and be subject to an approval process for non-food pharmaceutical crops. This approval process will presumably involve wider industry and/or community consultation with the very real chance that these varieties will not receive adequate support for approval for formal commercialisation. In such an uncertain regulatory and approval environment, companies such as Extractas and Sun Pharma may be unwilling to invest significant amounts of funding in R&D using this technology in Tasmania and may be forced to commercialise new varieties arising from the use of SDN-1 in mainland Australian states where the legislative environment is not as restrictive. Thus, in reality this technology will not be available for use by industry in Tasmania, and the Tasmanian economy will not benefit from the large potential gains available using this technology if this draft Biosecurity regulation is adopted by the Tasmanian Government.

2. The Basis for the Proposal to Regulate SDN-1 in Tasmania and Potential Flow-on Effects

In 2018, the European Court of Justice (ECJ) ruled that mutation breeding was a form of gene editing and was therefore regulated under the *2001 GMO Directive*. They further ruled that CMB (using chemicals and radiation) would be exempt from regulation on account of their history of safe use, but that new gene-editing technologies such as SDN-1 should remain regulated under the GMO Directive. Individual EU member countries are free to adopt these rulings, and 19 member states have currently adopted these restrictions. It should be noted that these rulings have attracted wide international criticism from the international scientific community. Australia and the USA have officially decided not to regulate SDN-1 as a GMO technology. It is difficult to separate “artificial” SDN-1 technology from natural cell processes and even more difficult to conceive of a credible safety risk from the use of this tool in plants. In reality, the European decision to regulate SDN-1 bears all of the functional attributes of a non-tariff trade barrier and it appears that it is being used in this regard in some European country markets. Extractas, Sun Pharma and PGT have additional concerns in addition to the lack of a robust scientific or safety rationale for regulating SDN-1 under GMO legislation.

For example, there are those politically active international groups including Greenpeace, Friends of the Earth Europe, BUND, GeneWatch, the Association of Food Without Genetic Engineering (VLOG) and the Corporate Europe Observatory who are seeking to ban or regulate all forms of mutation breeding. The ECJ has already ruled that mutation breeding is a form of gene editing and thus varieties produced in this way are subject to regulation as GMOs in this jurisdiction. These organisations are very influential in Europe and it is easy to envisage a situation in which some European countries move to ban products derived from all forms of mutation breeding, including CMB. This may prove problematic for the Tasmanian Government. Having made the decision to regulate SDN-1 organisms in Tasmania in an attempt to counter the decision of some EU countries to use the regulation of SDN-1 for restrictive trade practices, will the Tasmanian Government extend this to CMB should this too become regulated by European countries?

The Tasmanian poppy industry relies very heavily on poppy varieties that have been developed through CMB. Alkaloid poppies have a farm gate value of $60 million with a total annual value to the state of around $240 million and directly employing 250 FTEs with a further 250 FTEs indirectly benefiting. Should CMB crops become regulated in Tasmania, then the major commercial poppy companies may have no other option than to commercialise varieties produced though mutation breeding in mainland jurisdictions which are unencumbered by such restrictive regulation. This would have a significant negative effect on the Tasmanian economy.

3. Compliance, Regulation and Enforcement of SDN-1 in Tasmania

The 'Fact Sheet' on the proposed *Biosecurity Regulations 2020* states that the regulation will be administered and enforced through a registration system. Under this registration system persons or organisations intending to import, use, or create SDN-1 modified organisms in any commercial, scientific research or other activity will need to be registered with Biosecurity Tasmania. It further suggests that the regulation will be enforced through traceability. The scientific literature is quite clear that SDN-1 modified organisms are indistinguishable from natural mutations or CMB produced varieties. In the case of GMOs produced using recombinant DNA technology, modified varieties can be identified through laboratory analysis "exotic" genetic material such as promoters and terminators from *Agrobacterium tumefasciens*, cauliflower mosaic virus and nopaline synthase terminator (NOS), or the kanamycin resistance market gene, using PCR of LAMP analysis. No such tests exist for SDN-1 modified organisms as the technology does not insert foreign DNA or promoters and terminators. Thus, the proposed Tasmanian approach is a registration and traceability scheme but is not underpinned by any tangible means of enforcement. It is, in fact, an "honesty scheme" relying on the ethics and integrity of industries, organisations and individuals. This raises a number of issues for Extractas, Sun Pharma and the PGT:

(i) We are of the view that the burden of compliance will largely be borne by Industry and organisations such as Extractas and Sun Pharma. In a situation where the regulator cannot effectively enforce the regulation or indeed differentiate the 'regulated' material from natural or CMB produced material, then our concern is that the onus will fall on us to prove the unprovable. That is, that the material has or has not been produced by SDN-1. We are curious to know how the Tasmanian Government will deal with this when inevitably these cases proceed to legal determination.

(ii) We have concerns regarding the potential for non-compliance with this regulation. Within Tasmania, ethical organisations such as Extractas, Sun Pharma and the PGT will clearly agree to follow the regulations including registration and enforceability. However, SDN-1 technology offers significant opportunities for innovative R&D and large potential economic returns. Thus, it is conceivable that registered and unregistered facilities within Tasmania could decide not to declare SDN-1 derived varieties or report on SDN-1 R&D and it would be

very difficult for Tasmanian government agencies to ensure compliance. The proposed legislation may in fact cause the use of this technology to go "underground" in some circumstances disadvantaging those companies which operate ethically, and which operate within the spirit of the legislation.

(iii) We have concerns regarding the importation of SDN-1 modified organisms from interstate and overseas. Biosecurity will be relying on importers to declare SDN-1 modified organisms which are indistinguishable from natural mutations and CMB-induced organisms. There may be organisations and individuals that are tempted to import SDN-1 modified varieties as natural or CMB-induced varieties. The experience with PBR natural mutations such as those which occurred with the hundreds of bud sports in Red Delicious apples highlights the difficulties in determining provenance in this type of material and thus legal enforcement. Biosecurity Tasmania may try to enforce this by requiring importers to prove the provenance of imported varieties, but will this survive legal challenge in an environment where there is no definitive scientifically accepted test of origin?

(iv) Extractas and Sun Pharma import significant quantities of germplasm from overseas. This is currently particularly so in the case of medicinal cannabis varieties which are being sourced to establish a wide genetic base for varietal development in Australia. Extractas obtains material from reliable and well-established sources, however they rely on the integrity of the supplier for the provenance of this material, and they have no way of checking to ensure that material has not been developed using SDN-1 technology. The proposed legislation will place the onus for certification and compliance on Extractas and they will not be able to provide the required certifications for imported plant material with any certainty. In such an uncertain operating environment Extractas management may decide not to invest further in importing additional commercially important germplasm into Tasmania. This may have adverse commercial impacts for Extractas and the Tasmanian economy and ultimately reduce their ability to compete with mainland medicinal cannabis producers who are not encumbered by such legislation.

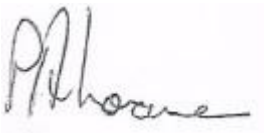
(v) The fact that SDN-1 induced organisms are indistinguishable from natural or CMB-induced material is widely known. Given that the proposed *Biosecurity Regulations 2020* may very well be unenforceable logistically or legally, that unregistered laboratories may be able to operate within the state, and that SDN-1 varieties may be able to be introduced from mainland Australia and overseas, will the Tasmanian scheme be acceptable to overseas countries who prohibit imports products produced from SDN-1 varieties? How will the Tasmanian Government defend the integrity of the Tasmanian scheme and will it help Tasmanian producers to overcome a potentially serious non-tariff barrier in some markets as proposed?

Extractas, Sun Pharma and PGT understand that some Tasmanian producers and companies are adversely affected by the bans on products from SDN-1 varieties imposed by some European countries. That said, we are of the view that the Tasmanian Government has a responsibility to consider the implications of the proposed Biosecurity Legislation for the wider agricultural production and value adding in Tasmania. We note that policy and economic analyses of the proposed changes did not accompany the documentation regarding the Biosecurity regulations, and we would be very interested in receiving copies of these when they become available.

We therefore urge the Tasmanian Government to seriously reconsider the regulation of SDN-1 technologies in Tasmania and the effects that the *Biosecurity Regulations 2020* may have on Tasmanian industries and the government's target for the value of agricultural production reaching $10 billion by

2050. We would welcome the opportunity to meet with you to further discuss PGT, Extractas, and Sun Pharma's concerns regarding the proposed regulation of SDN-1 in Tasmania or to provide additional information to support our concerns.

Yours sincerely



Philip Loane
President
Poppy Growers Tasmania Inc

SDN: Site-Directed Nuclease technology

For many years, plant breeding has been a trial and error exercise, whereby new varieties are produced from a cross between parental plants or through self-pollination. The process is based on identifying a desired characteristic in one plant - for instance higher resistance to a specific disease - and crossing it with another plant which allows the desired trait to appear in the offspring. However, a series of unwanted characteristics is transferred as well, which requires several more breeding cycles in order to be replaced by desired traits. This form of breeding takes many years to accomplish, which represents a very long time span given the need to rapidly address issues linked to climate change and food security. In order to speed up the process and allow for more precision and efficiency, new methods are needed. Several New Breeding Techniques (NBTs) have already been developed, including Site-Directed Nuclease (SDN) technology.

Obtaining desired characteristics through targeted adaptations

Three main SDN technologies currently in use include: Meganucleases, Zinc-Finger Nucleases (ZFNs) and Transcription Activator Like Effector Nucleases (TALENs). These technologies rely on biological molecules that have both a DNA-binding domain that recognizes a specific DNA sequence (the site-direction) and a DNA cleavage activity (the nuclease), which, when added to a plant cell, result in a specific, predetermined break in the plant's DNA. The plant's natural DNA repair mechanism recognises this break and repairs the break using enzymes naturally present in the cell.

The goal of SDN technology is to take advantage of the targeted DNA break and the host's natural repair mechanisms to introduce specific small changes at the site of the DNA break. The change can either be a small deletion, a substitution or the addition of a number of nucleotides. Such targeted edits result in a new and desired characteristic, such as enhanced nutrient uptake or decreased production of allergens.

SDN applications are divided into three techniques: SDN-1, SDN-2 and SDN-3 (see Figure 1, opposite):

SDN-1 produces a double-stranded break in the genome of a plant without the addition of foreign DNA. The spontaneous repair of this break can lead to a mutation or deletion, causing gene silencing, gene knock-out or a change in the activity of a gene.

SDN-2 produces a double-stranded break, and while the break is repaired by the cell, a small nucleotide template is supplied that is complementary to the area of the break, which in turn, is used by the cell to repair the break. The template contains one or several small sequence changes in the genomic code, which the repair mechanism copies into the plant's genetic material resulting in a mutation of the target gene.

SDN-3 also induces a double-stranded break in the DNA, but is accompanied by a template containing a gene or other sequence of genetic material. The cell's natural repair process then utilizes this template to repair the break; resulting in the introduction of the genetic material.

SDN-1 and SDN-2 do not use recombinant DNA, do not lead to the insertion of foreign DNA. As such, they do not produce new plant varieties that fall under the scope of the GMO legislation. In the case of SDN-3, the newly developed plant should fall under GMO legislation only if foreign DNA exceeding 20 bp is inserted.

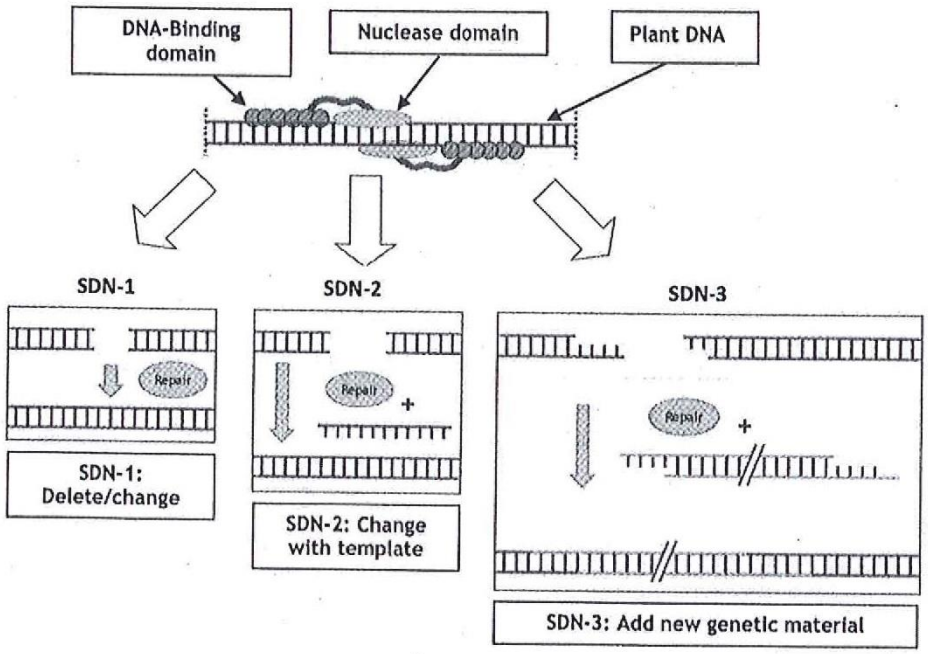


Figure 1. Simplified overview of the main SDN techniques. In all three techniques, the nuclease domain of the SDN-complex causes a double strand break in the DNA, after which one of the three techniques applies. Nucleotide colour-coding: green equals endogenous, occurring in the plant before the technique is applied; red equals a change in the genetic code. 'Repair' indicates the natural repair mechanism present in the plant.

Where can Site-Directed Nuclease technologies be applied?

SDN technologies can create specific and targeted mutations in the genome of a plant, in order to obtain plants with improved characteristics. Random mutations - induced with the help of chemical agents or radiation - have traditionally been used by plant breeders. However these random mutation methods also produce a series of undesired traits which must be eliminated through a series of lengthy breeding cycles. SDN technology allows for specific and targeted mutations, thus enabling

new plant varieties to be developed significantly faster than with traditional methods as no further breeding has to be undertaken to eliminate unwanted characteristics.

Benefits

Site-Directed Nuclease technology can be used to precisely remove undesirable traits in plants such as anti-nutrients or allergens, in order to reduce environmental pollution or to enhance the nutritional value of a crop, for instance in maize. It can also modify certain existing characteristics in a plant to respond to consumer needs such as enhanced shelf-life and improved taste or texture, for instance in tomatoes.

SDN technology: a strong driver for Europe's economy and innovative potential

Small and Medium Enterprises (SMEs) represent a large part of the EU's innovative plant breeding sector. These companies could especially benefit from SDN technology to answer market demands and develop new varieties that are more sustainable, respond to environmental and consumer demands and produce higher yields in a whole range of plants, including fruit and vegetable crops. Before this can happen however, EU Member States must align their position toward Site Directed Nuclease technologies. If they can build on the notion that it allows for new plant varieties to be developed in much the same way as conventional breeding or biological reproduction methods (e.g. asexual reproduction), then the European plant breeding sector can free itself from expensive regulatory burden and enhance its competitiveness. Indeed, companies, and SMEs in particular, will be able to focus their resources on research and valorisation of innovation within Europe rather than having to do so in non-EU countries - an added value for the European agricultural sector and economy as a whole. It will also level the playing field and allow the EU to effectively compete with other markets where the technique could be applied.

About the NBT Platform

The NBT Platform is a coalition of SMEs, large industry and prominent academic research institutes, which strives to bring clarity to the European debate on NBTs. Its aim is to provide policy makers and stakeholders with clear and precise information on NBTs and to generate awareness about their potential benefits for the European economy and society as a whole.

Contact us via info@nbtplatform.org

Analysis Gene editing

UK may allow gene editing in crops

If a consultation leads to the use of tiny DNA changes to improve the nutrition of food, it could be a potential benefit of Brexit, finds **Michael Marshall**

THE UK government is exploring the possibility of using gene editing to modify livestock and food crops, for instance to make crop plants resistant to disease. Gene editing is strictly regulated in the European Union, in what virtually amounts to a ban, but now the UK has left the EU it has some freedom to set its own rules.

The consultation was announced by environment secretary George Eustice at the Oxford Farming Conference last week.

"Gene editing is a mechanism to precisely edit the genome of an organism," says Lesley Torrance at the James Hutton Institute in Dundee, UK. Instead of inserting entire genes, or changing DNA at random, gene editing allows for highly specific changes, even altering a single "letter" of an organism's DNA sequence.

This is made possible using a technology called CRISPR-Cas9, which in 2020 won two of its pioneers the Nobel prize in chemistry.

One potential use of gene editing is to improve the iron content of white flour, says Janneke Balk at the John Innes Centre in Norwich, UK. In the UK, the law requires that white flour must contain a minimum amount of iron, so the iron is added artificially. Balk's lab is exploring ways to create high-iron wheat by gene editing.

However, before Brexit, such crops had little chance of reaching supermarkets, because the EU has a fraught history with genetic modification. It has strictly regulated "transgenic" crops, which carry genes transplanted from other species. Genetically modified crops like these prompted the 1990s scare around "Frankenfoods" and were opposed by environmental groups like Greenpeace. This opposition was primarily cultural, because the health and environmental risks from these crops were minimal.

Gene editing causes much smaller changes than wholesale gene transplants – no more significant than those associated with a technique used by plant breeders for decades. Since the 20th century, breeders have often created mutations at random by exposing seeds to chemicals or radiation. Plenty of foods were made this way.

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Gene editing is so precise it can change one "letter" in a genome

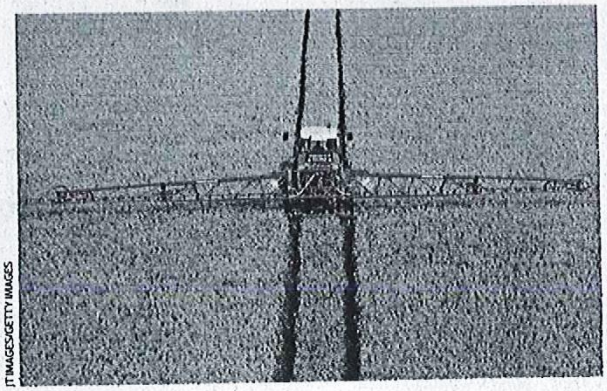
For this reason, many researchers had hoped that gene editing would escape the stringent regulation that has stymied transgenic crops in the EU, and instead be governed by the more permissive regulations used for conventional breeding and radiation mutagenesis. However, in 2018, the European Court of Justice ruled that gene-edited crops should be treated as equivalent to transgenic crops, and subjected to the same lengthy approval process.

"Before the ruling from the European Court of Justice, it was eaten in the EU in a limited way, because various countries had independently made a decision that actually, if it is just this small mutation that isn't different from something you can do naturally, it shouldn't be treated as GM," says Wendy Harwood, also at the John Innes Centre.

For many crop biologists, the situation is bizarre. "Radiation mutagenesis creates massive random mutations across the entire genome, yet plants produced by this process do not undergo the same regulatory regime [as gene editing]," says Torrance.

Leaving the EU's gridlocked approval system for gene editing is a potential benefit to the UK from Brexit, although it isn't yet clear how much the UK government plans to change the rules.

For Balk, every new crop should be judged on its own merits. "What gene is it, what have you changed, have you checked everything, yes or no?" she says. Whether the genetic change was achieved by CRISPR, radiation or something else is secondary to its actual effect, she argues. ■



Rapeseed can be modified with gene editing

JT IMAGES/GETTY IMAGES

Environment

2020 was the joint hottest year on record

Adam Vaughan

LAST year was the joint hottest globally and by far the warmest year recorded in Europe, making the years from 2015 onwards the warmest six worldwide on record.

Global average temperatures in 2020 tied with 2016 at 0.6°C above the long-term average – despite the absence of an El Niño event, a climate phenomenon that has a warming effect. There was an El Niño in 2016.

Europe, by contrast, demolished records by a wide margin in 2020, at 1.6°C above the long-term average. The previous record was 2019, which was 1.2°C above the average.

The figures were released by European Earth observation programme Copernicus. Aggregated figures due shortly from other major data sets, including those of the UK Met Office and US agencies NASA and the National Oceanic and Atmospheric Administration, may yet relegate 2020 to the second or third warmest year on record.

Copernicus's 2020 figures show a clear north-south split, with below-average temperatures in the southern hemisphere and above-average ones in the northern hemisphere. Siberia and other parts of the Arctic reached 3 to 6°C above average in some regions.

Figures published last week by Mark Parrington at Copernicus also show that, while media attention focused on exceptional blazes in the US and Australia, global carbon emissions from wildfires were at one of their lowest levels in two decades in 2020 due to below-average fire activity in Africa.

Separately, the UK Met Office said it expects carbon dioxide levels in the atmosphere this year to pass the milestone of being 50 per cent higher than before the industrial revolution, reaching 417 parts per million between April and June, when seasonal CO_2 levels peak. ■