SCIENTIFIC CRITIQUE OF **LEOPOLDINA AND EASAC STATEMENTS ON GENOME EDITED PLANTS IN THE EU**

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Executive Summary

The EASAC-endorsed Leopoldina Statement on the regulation of 'genome edited' plants is based on a limited number of selected publications. It fails to reflect the findings of at least 200 highly relevant published scientific studies.

These studies document adverse effects of existing genetically modified organisms (GMOs) on the environment and human health, and demonstrate the potential for negative outcomes of more recent genetic engineering tools.

They show that existing GMOs have failed to deliver on their claimed benefits, such as effective control of weeds and pests, resistance against diseases, drought tolerance, enhanced nutritious value and intrinsic yield gains. They also demonstrate the ecological and economic consequences of genetic contamination, as well as detrimental effects on smallholder farmers.

With regard to 'genome editing', the scientific evidence ignored by the authors of the Leopoldina Statement demonstrates that, contrary to their claims, the genetic alterations caused by these methods are fundamentally different from naturally occurring mutations.

The 'genome edited' crops listed in the Statement to illustrate the potential benefits of 'genome editing' are at preliminary exploratory research stages and most even miss functional proof of efficacy. They cannot be taken as evidence that expectations of beneficial traits are justified.

Similarly, the Statement's narrative equating *precision = control = safety* is not supported by the scientific evidence - not for older forms of genetic engineering and not for more recent forms of genetic engineering.

The Statement ignores the growing recognition among experts that the root causes of hunger are related to social and economic issues (conflict, poverty, exclusion, etc.) more than to crop yield. There is no record of GMO interventions increasing crop yields as such, or indeed reducing hunger. In contrast, a series of widely accepted expert reports have called for a rapid shift from input-intensive industrial agriculture to agroecological farming methods.

Based on a selective reading of the scientific evidence, the Leopoldina Statement recommends that the EU should exempt certain 'genome edited' organisms from the scope of its GMO legislation. It also calls for the longer-term loosening of GMO regulations applicable to existing transgenic organisms. Following that advice would move the EU away from the precautionary approach that is enshrined in the EU's founding treaties, and towards the US approach of ignoring potential risks and harm.

The body of evidence ignored by the Leopoldina Statement supports a conclusion contrary to Leopoldina's, namely that EU GMO regulations must be strengthened in order to take account of a new generation of GM organisms created with 'genome editing' tools.

Background and objectives

In July 2018, the European Court of Justice (ECJ) (Case C-528/16) ruled that organisms obtained by directed mutagenesis techniques (the Court's term for 'genome editing') are to be regarded as genetically modified organisms (GMOs) within the meaning of Directive 2001/18.

In response to the ECJ ruling, the German Academy of Sciences Leopoldina published a position statement in December 2019 urging European policy makers "*to exempt genome edited organisms from the scope of genetic engineering legislation if no foreign genetic information is inserted and/or if there is a combination of genetic material that could also result naturally or through traditional breeding methods.*" In March 2020, the European Academies Science Advisory Council (EASAC - formed by the national science academies of the EU Member States) endorsed the content and intention of this Statement with a 'Commentary on the statement by the German National Academy of Sciences Leopoldina'.

Our report (i) deconstructs the claims made in the EASAC-endorsed Leopoldina Statement, (ii) critically assesses the scientific foundations of both publications and (iii) provides some of the information, omitted by the Statements, that is publicly available as scientific evidence and research results. Assessing and fact-checking the claims made by both the Leopoldina Statement and the EASAC endorsement reveals a wealth of more than 200 highly relevant published scientific studies that they have ignored.

The 'collective voice of European science'?

The authors of the Leopoldina and EASAC Statements make it appear like they represent the scientific consensus in Europe. The Leopoldina describes itself as providing '*policymakers and society with independent, science-based guidance on issues of crucial importance for our future*[i].

EASAC states: "*EASAC – the European Academies' Science Advisory Council – is formed by the national science academies of the EU Member States, Norway and Switzerland to enable them to*

i E.g.Leopoldina. 2017. The German Academies of Sciences offer Recommendations for the Reform of Doctoral Practices, https://www.leopoldina.org/en/press-1/press-releases/press-release/press/2499/

collaborate with each other in providing independent science advice to European policy-makers. It thus provides a means for ***the collective voice of European science*** *to be heard*." EASAC also claims to '*provide independent, expert, evidence-based advice about the scientific aspects of public policy*' and deliver views that are '***vigorously independent of commercial or political bias***'[ii].

However, the EASAC-endorsed Leopoldina Statement relies on a limited selection of publications rather than the full body of scientific evidence. It ignores the more than 200 published scientific papers and documents cited in our report, which represent but a small part of the rich and diverse scientific literature that is pertinent to an inclusive, science- and evidence-based discussion about the potentials, risks and limitations of all genetic engineering techniques. This means the EASAC-endorsed Statement is at best representative of one view among a diversity of scientific opinions. It does not reflect a 'consensus' in science.

Making unfounded claims of GMOs' safety and efficacy

Both Statements claim that existing GMOs are safe and their intended traits are effectively achieved. They ignore the documented adverse effects of existing GMOs on the environment and human health, including the chemical pollution connected to the vast majority of current GMOs. They also ignore the fact that no intrinsic gains in yield have been proven, and fail to acknowledge the widespread evolution of resistance in plants and insects that the GMOs were meant to control, which has led to the loss of efficacy of the GM traits. The ecological and economic consequences of genetic contamination are also ignored. Also omitted are failures in India and Burkina Faso that illustrate the detrimental effects that these technologies have had on smallholder farmers' livelihoods. None of the documented cases of harm are mentioned by the EASAC- and Leopoldina authors.

The Statements' narrative equating *precision = control = safety* has been shown by empirical evidence to be false in relation to existing GMOs. It is increasingly shown to be untrue also for more recent forms of genetic engineering. A necessary prerequisite for exercising 'control' is precise knowledge not only about the targeted gene sequence to be altered or replaced, but also about the context within which the intervention is carried out. The lack of understanding of these complex networks of interactions, including networks of genes and their epigenetic regulation, is the reason why the 'precision' narrative has lost credibility as an indication of safety.

Unproven link between GMOs, crop yields and hunger

Another (old) narrative promoted by the Leopoldina Statement is the idea that reductions in hunger over the last century have been achieved due to 'science-based breeding'. While the yield increases of the Green Revolution are documented, no comparable recording has followed GMO interventions. More importantly, there is growing recognition among experts, ignored by the Statement, that the root causes of hunger are related to social and economic issues (conflict, poverty, exclusion, etc.) more than to crop yield.

ii EASAC. About EASAC. Accessed March 2021, https://easac.eu/about-easac/

Little evidence of efficacy of 'genome edited' crop plants

The Leopoldina Statement claims that 'genome editing' has already proved successful in generating a large number of 'market relevant' crops. However, only two 'new generation' GM crops are commercialised in the US, despite generous subsidies and a permissive regulatory environment. One of them is (yet another) herbicide-tolerant plant. Although 'genome editing' technologies have been deployed since the 1990s, the majority of 'genome edited' crops mentioned by the Statement are at exploratory stages without functional proof of efficacy.

False premise that 'genome editing' resembles traditional breeding

A growing body of evidence challenges the Leopoldina Statement's premise that 'genome editing' is akin to traditional breeding methods and therefore safe. It shows that the effects of 'genome editing' differ from those resulting from random mutagenesis. 'Genome editing' methods can result in the modification of many genes simultaneously, the alteration of all copies of a single gene, or the transformation of regions of the genome ordinarily protected from novel mutations. Further, repair mechanisms deployed by the cell following editing-induced mutations appear to differ from repair mechanisms used following random mutagenesis or naturally arising mutations. The error-prone repair mechanisms deployed to repair 'edited' DNA breaks lead to distinct changes in the genome.

There is nothing 'natural' in genetic engineering. All 'genome editing' methods aim to circumvent natural processes and turn them from 'repair' mechanisms into 'delete', 'insert' or 'replace' mechanisms. These natural repair processes are part of fine-tuned networks protecting some regions of the genome from mutations more than others. By contrast, so-called 'genome editing' procedures can indiscriminately access all genomic regions equally. Neither the epigenetic and genetic regulation of these cellular processes nor the consequences of these 'genome editing' interventions are well understood. Unintended effects have been documented in human and plant cells.

Promoting outdated models of 'regulation'

What the Statement proposes as an innovative and science-based model for European regulation actually predates any European or international GMO regulation. The model is founded in the US' decades-old policy that simply declares what is *not* being regulated, i.e. not evaluated at all. Such backward-looking policy releases developers from any responsibility to prove the efficacy and safety of their products. It cannot be called 'innovative'.

Overlooking recognised solutions

The Statement disregards a series of high-level expert reports that have called for a rapid shift away from input-intensive industrial agriculture, towards agroecological farming methods[iii]. These reports suggest that funding should be shifted towards solutions that work to address nutritional needs, food security, and environmental sustainability, as well as existing farmer knowledge and practices, leaving very little room for the patented interventions from genetic engineering with its questionable safety and success track record.

Conclusion

Our report provides some of the large body of information that the Statements have omitted, and that is publicly available as scientific evidence and research results. Had these publications, although not comprehensive, been included and evaluated in a balanced and transparent way, the Statements would have been unable to recommend the exclusion of certain forms of 'genome editing', or the wider relaxation of EU GMO regulations. In fact, the totality of the evidence available supports the contrary conclusion, namely that EU GMO regulations must be strengthened in response to the new generation of genetic engineering tools.

iii IPES-Food. 2016. From uniformity to diversity: a paradigm shift from industrial agriculture to diversified agroecological systems. International Panel of Experts on Sustainable Food systems, http://www.ipes-food.org/_img/upload/files/UniformityToDiversity_FULL.pdf; International assessment of agricultural knowledge, science and technology for development IAASTD 2009, https://www.weltagrarbericht.de/fileadmin/files/weltagrarbericht/IAASTDBerichte/GlobalReport.pdf and Transformation of our food system. The making of a paradigm shift. 2020, https://www.arc2020.eu/wp-content/uploads/2020/09/FullTextOfTransformationFoodSystems.pdf; Food and Agriculture Organisation FAO 2020. The state of food security and nutrition in the world, http://www.fao.org/3/ca9692en/online/ca9692en.html#chapter-executive_summary

Introduction

In July 2018, the European Court of Justice (ECJ) (Case C-528/16) ruled that organisms obtained by directed mutagenesis techniques, so-called 'genome editing' achieved through new genetic engineering techniques (NGET), are to be regarded as genetically modified organisms (GMOs) within the meaning of EU Directive 2001/18[iv] regulating the release of GMOs into the environment. The ruling marked the next round in the long dispute around genetic engineering in Europe and drew loud, and at times aggressive, protest from biotechnologists in industry and the public sector as well as likeminded colleagues and media[1]. This ECJ ruling triggered the German Academy of Sciences Leopoldina in December 2019 to publish a position statement written by 15 experts[2] from economics, law, theology and molecular biology urging European policy makers "*to* ***exempt genome edited organisms from the scope of genetic engineering legislation*** *if no foreign genetic information is inserted and/or if there is a combination of genetic material that could also result naturally or through traditional breeding methods.*" In March 2020, the European Academies Science Advisory Council (EASAC - formed by the national science academies of the EU Member States) doubled down on the Leopoldina Statement by producing a '*Commentary on the statement by the German National Academy of Sciences Leopoldina*'[3] which endorsed and echoed the content and intention of the Leopoldina Statement.

The Leopoldina describes itself as providing '*policymakers and society with independent, science-based advice on issues of crucial importance for our future*'. EASAC also claims to '*provide independent, expert, evidence-based advice about the scientific aspects of public policy*' and deliver views that are '*vigorously independent of commercial or political bias*'. These assurances notwithstanding, several among the authors of both statements had evident vested interests in the new genetic engineering techniques, in the form of their research funding, industry collaborations and patents[4]. Not surprisingly, the arguments made in both statements are clearly biased towards one side of the GMO dispute; their declarations are often based on opinion rather than evidence.

iv Directive 2001/18/EC of the European Parliament and of the Council (March 2001) on the deliberate release into the environment of genetically modified organisms; https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32001L0018

Where evidence is used, it can be shown to represent a biased selection of scientific evidence that fits the authors' world-view and commitments. Hence, at least the title of the Leopoldina Statement '*Towards a scientifically justified, differentiated regulation of genome edited plants in the EU*' is seriously misleading.

The EASAC-endorsed Leopoldina Statement (often also only called the 'Leopoldina Statement') recommends that EU legislation be revised to exclude so-called 'genome edited' organisms from current regulatory oversight as genetically modified organisms (GMO), claiming that there are no 'specific' risks associated with the technology. Instead, the authors promote the so-called 'product-based' 'deregulation' approach of the United States of America (US) developed in the 1980s, an outdated minority approach in the world (more details below) exempting in practice these GMO products from any regulatory oversight or responsibilities. While the statement refers to plants only, the requested changes to legislation would appear to apply also to 'genome edited' farm animals, wild species such as trees, insects, and birds, as well as fungi and other microorganisms, with the declaration: "*This statement focuses on the scientific, socio-economic and legal aspects of modern molecular plant breeding in the context of the European legal framework for GMOs. Of course, the underlying scientific advances and related legal issues also concern animals, fungi and other microorganisms*". Moreover, the statement calls not only for rapid deregulation of genome editing, but for the long-term substantial weakening of regulations applying to all genetically modified (GM) crops, going beyond the suggestion of the title in dealing with genome editing alone.

The analysis presented here aims to provide a detailed study of the Leopoldina Statement. It draws on scientific evidence to contest the claims of both safety and efficacy of 'genome editing' (and of first-generation GMOs in plants), and it questions the wider narrative framing the statement. While the discussions around new genetic engineering techniques apply to organisms beyond plants, this report focuses on 'genome editing' in plants, in response to the narrow scope set by the Leopoldina Statement. Instead of being captured by a single technological set, good policy-making should be based on an understanding of the whole range of technologies and strategies available to botanists, farmers and policy-makers.

False framing... again: Leopoldina revives the 'Feeding the world' narrative

From the Leopoldina Statement:

"Science-based plant breeding and other agricultural technologies, such as chemical fertilisation and chemical crop protection, have since contributed to continuously increasing agricultural yields, combating regularly occurring plant diseases and pests and thus decisively improving the supply of foodstuffs and thus food security. While at the beginning of the 20th century well over half of the world's population still suffered from insufficient food supplies, the proportion of starving people has now been reduced to around 10%, even though the global population has more than quadrupled in this period".

This introductory statement presents the old and simplistic claim that 'science-based' breeding is responsible for reductions in hunger over the 20th Century. Despite the average GM crop adoption rate increasing worldwide and reaching close to saturation for some crops in 2019;[5] the global prevalence of undernourishment (chronic food insecurity) and the total number of people going hungry has increased, not decreased, for several consecutive years. The global community's goals of September 2000 to halve the proportion of people who suffer from hunger between 1990 and 2015 has never been met[6]. Almost 690 million people were undernourished still in 2019[7].

The agricultural biotechnology business has long promoted the idea that it has a noble obligation of abolishing world hunger as a core value, despite increasing recognition that hunger is tied to poverty, social-exclusion and other factors related to economics and politics, not technological access[8,9,10,11]. Indeed, there is no clear evidence that productivity per se plays a pivotal role in global hunger[12,13,14]. While single-crop monoculture 'productivity' has increased in industrialised systems, this has not translated into enhanced global food security. Record levels of cereal grains were produced in 2016, but hunger and malnutrition persist because an increase in food supplies alone is not the solution to hunger or malnutrition[15]. This is exemplified by concerning figures of hunger even in countries with high agricultural 'productivity' such as the US, where some 37 million people were reportedly food insecure in 2019[16]. The US is one of the largest developers of GMO foods, cultivated within a heavily industrialised model, yet hunger persists. Industrialised agriculture is also a major driver of climate change due to the intensive use of fossil fuels, pesticides, fertilisers, mined water, and agricultural practices that degrade soils, pollute water and air, and result in biodiversity loss[17]. Indeed, a report by UNEP and Chatham House shows the global food system as the primary driver of biodiversity loss[18], in part caused by the continued focus on sheer productivity, rather than planetary and human health, through the destructive industrialised processes of chemical-dependent monocultures. Current GMOs are designed to work within, and thus promote, these industrialised models that are unsustainable and ill-suited to addressing the root causes of hunger.

Unreferenced claims in the Leopoldina Report that 'science-based' plant breeding and other agricultural technologies, such as chemical fertilisation and chemical crop protection are the prime reason for a reduction of global hunger from 50 to 10 % across the 20th century also fail to recognise its historical root causes, particularly in many currently low- to middle-income countries where major reductions have occurred (primarily China). It is a convenient misconception that hunger and food insecurity are the result of low productivity rates or insufficient 'scientific knowledge', instead of resting deeply in poverty due to the economics of inequality that derive from extractive colonial systems that broke down in the 20th century. It is well established that 20th century famines derive from the advent of export-driven monocropping, often at the expense of foods feeding local populations, and the rise in marketisation of foods for export, a new colonial-era practice[19,14,20]. The argument purportedly connecting hunger with a lack of technological access is perpetuated later in the Statement, which claims that low-income countries would particularly benefit from the technology were they not prevented from reaping the rewards of technological adoption because of the influence of EU laws as well as European GMO-opponents; Leopoldina states that "social and political opposition to GMOs in Europe has inhibiting effects on the use of this technology in developing countries". Beyond ignoring established evidence about the root causes of world hunger, such a narrative either forgets or chooses to ignore the historical role of many developing countries in leading the negotiations to institute precautionary regulations under the UN's Convention for Biological Diversity[21].

Indeed, the sole citation[22] to support a claim of benefit from GMO deployment was written by one of the authors of the Statement, and is not, as claimed, a conclusion that has attained broad scientific acceptance or consensus. The blanket claims of what the authors consider to be 'science-based' breeding successes for food production also completely fail to recognise that only in very few countries GMOs are consumed directly for food. These include, for example, South Africa where GM maize is a daily consumed staple food and, to a much more limited extent, the USA and perhaps a handful of other countries (e.g. Canada, China), where extracted GM crop ingredients (e.g. protein, oil) are commonly consumed within processed foods. In the US, also limited amounts of GM summer squash and GM papaya are consumed, neither one being a daily staple food nor do they have relevance for world hunger. Instead, the vast majority of GMOs are destined for animal feed for industrialised meat and dairy production for the eventual (over)consumption of factory-farmed meat predominantly in the industrialized, rich countries, to the detriment of the environment as well as human health predominantly in the GMO producing countries of South America as detailed below.

It is a convenient misconception that hunger and food insecurity are the result of low productivity rates or insufficient 'scientific knowledge', instead of resting deeply in poverty due to the economics of inequality that derive from extractive colonial systems that broke down in the 20th century

Current GMOs: Scientific bias and untruths

From the Leopoldina Statement:
"Until the 20th century, crops were improved with time consuming and protracted selection breeding……Science-based plant breeding and other agricultural technologies, such as chemical fertilisation and chemical crop protection, have since contributed to continuously increasing agricultural yields, combating regularly occurring plant diseases and pests and thus decisively improving the supply of foodstuffs and thus food security .

The EASAC statement endorsing the Leopoldina Statement even deems it unnecessary to further discuss "***the value of genome editing technologies, or GMOs, because this value is already demonstrable*** , albeit without offering any evidence in support of that claim. The authors of both statements nonetheless indirectly frame GMOs as having contributed to the purported benefits of 'science-based' breeding in reducing global hunger; but that has not happened.

The Leopoldina Statement calls for the long-term permissive US-style (de)regulation of all GM crops with a 'product-based' system, but it is noteworthy that it fails to give any examples of GM crop successes to date. Instead, they offer unsupported generalised claims, which constitute nothing more than a wish list such as the one above, that imply successes without evidence but just with self-referencing. Elsewhere, some of the authors have made claims of benefits such that there is "*robust evidence of GM crop benefits for farmers in developed and developing countries. Such evidence may help to gradually increase public trust in this technology*"[23]. But no such evidence has yet emerged.

The decades old, most common GM crop traits, both herbicide-tolerant and Bt varieties, were portrayed as traits that would improve food production by reducing overall pesticide usage, and to promote the use of smaller quantities of less dangerous herbicides while reducing yield losses. Herbicide tolerant GM crops are by far the largest part of the market today, with 88% of GM crops containing one or more herbicide tolerant traits[24]. These crops are genetically engineered to tolerate the associated broad-spectrum herbicide(s), allowing the blanket spraying of the crop, wiping out all other plants (except for herbicide-resistant super-weeds) but the GM crop, irrespective of whether it is a competing weed or a host of urgently needed biological diversity. Bt crops contain one or more insecticidal toxins (from the bacteria Bacillus thuringiensis Bt), intended to make them resistant to pests. These first (and, so far, also last) generation of GM crops were sold as tools for increasing agricultural sustainability. However, while there has been some evidence that herbicide-resistant GM varieties can provide some short-term cost-reductions, promised yield gains have failed to materialise. For example, cereal yield gains in Western Europe are accelerating and overtaking those of the USA's major cereal crops[25]. In Western Europe, maize crops are non-GM whereas in the US, GMO adoption is near ubiquitous certainly for maize the most common cereal commodity crop grown[26].

GMOs promote chemical use leading to environmental damage and ill health

In practice, the adoption of GM crops has resulted in a variety of problems. While the promised 'super plants' never materialized, the predicted 'superweeds' did. Over 40 most notorious weed plant species in the world have acquired one or more resistance traits to glyphosate-based herbicides alone and also insect resistance to Bt toxins is on the rise, resulting in increased pesticide use[27,28,29,30,31,32,33,34,35,36,37,38,39]. In the US, overall pesticide use has grown by 7% from 1996-2011[40]. Brazil and Argentina are the second and third largest producers of GM crops globally, with South America becoming one of the biggest markets for agrochemicals, including glyphosate[41]. In Argentina, government estimates show an increase of glyphosate use from 13.9 million litres in 1996, to 200 million litres in 2008[42]. GM crops have now been associated with a variety of detrimental environmental effects and biodiversity damage, such as contributing to the decline of monarch butterflies in the Americas due to blanket spraying of herbicide tolerant GM crops with glyphosate (often sold under the brand name RoundUp)[43,44,45,46,47], widespread contamination of air and water supplies with herbicides (including groundwater, rain, waterways and rivers, despite early claims that it was not expected to move to groundwater)[48,49,50,51,52,53,54,55,56,57], and toxic and chronic sub-lethal effects of glyphosate-based weedkillers on aquatic species including duckweed, tadpoles, frogs, snails, crayfish, crabs and fresh-water fleas,[58,59,60,61,62,63,64,65,66,67,68,69] and soil-living species such as earthworms[70,71,72,73,74]. This summary of a sample of scientific publications is by no means exhaustive, but it illustrates the scale and significance of the published scientific evidence that has been omitted and ignored by the EASAC-endorsed Leopoldina Statement when suggesting productivity gains with little or no references in support but remaining silent on productivity gains without GMOs and the price tag this packaged GM technology brought along.

While the promised 'super plants' never materialized, the predicted 'superweeds' did

Although epidemiological studies cannot, on their own, prove cause and effect, widespread chemical contamination, including aerial spraying of herbicide-tolerant GM crops, has also been linked to concerning rises in cancer and birth defect rates in Argentina[75,76,77]. These reports are consistent with the IARC's (2015)[78] designation of glyphosate as a probable human carcinogen, and reinforce concerns arising from other studies indicating that chronic exposure to glyphosate and other pesticides can cause a range of other effects on both occupational and public health. In response to escalating evidence of herbicide-resistance evolution against the first generation of Roundup/glyphosate resistant GM crops, a second generation of herbicide tolerant GM crops has been introduced, which are tolerant to additional herbicides such as glufosinate, 2,4-D, isoxaflutole and dicamba. Their introduction however, has also already led to concerns about the effects of the blanket spraying of these pesticides on human health and the environment. Adverse effects can include toxic pesticide residues on crops, increased weed resistance and the adverse effects of dicamba drift onto neighbouring crops[79,80,81]. For example, 2,4-D has also been linked to increased cancer rates in farm workers[82,83,84]. It is notable that, when the first generation of Roundup/glyphosate resistant GM crops were introduced in the mid 1990s, the widely promoted 'benefit' of those GM crops was that it would allow growers to stop using these other, supposedly more toxic compounds like 2,4 D, glufosinate, dicamba etc.[85]. Today, 25 years later, US industrial farmers have to use all of these toxic compounds to maintain the productivity of their industrial, high-input agricultural systems. Other detrimental farming practices have also been encouraged by GM crop cultivation, such as reduced application of integrated pest management, and reduced practice of sustainable techniques such as crop rotation, biological control, cover cropping and short-season crops[86].

The above-mentioned evidence of harm has been excluded from the Leopoldina Statement and the EASAC endorsement. Instead, the Leopoldina Statement makes vague claims that GMOs are a solution to destructive practices of monocultures and 'excessive use' of pesticides that they rightly acknowledge as posing challenges for climate change and environment (though what is deemed acceptable or 'excessive' chemical use by the authors remains unclear). However, the Statement fails completely on offering any analysis as to the reasons that led to the perceived 'excessive' use of chemicals in the first place which have all been part and parcel of what the authors have misleadingly called 'science-based' agriculture technologies. Of the three citations used to substantiate that claim, one is based on a meta-analysis co-authored by one of the authors of this Statement[23] that relies heavily on non-peer reviewed data from farmer surveys, field trials and meetings or conferences. The second two cited papers[87,88] refer solely to Bt crops and are either more than 15 years old or focus on a developing country. Such claims can at best be considered biased, and at worst, deliberately misleading as herbicide-tolerant crops were largely excluded from the analysis. It is also in direct contradiction to studies showing increased pesticide use (see below), and the very rationale that herbicide-tolerant crops require herbicide applications in order to unfold the 'benefit' of the GM trait.

Genetic contamination causes economic, societal and environmental harm

Gene flow, the introduction of genetic material from one population to another, results in genetic contamination of wild species and landraces with GM (transgenic) material. Other forms of contamination, either via contamination of seed stocks, or the spontaneous growth of volunteer plants from seed escape, may also occur. The risk of genetic contamination has often been dismissed as not being a risk in itself, being instead akin to gene flow between conventional crops and other species (including their wild relatives) that forms a part of natural evolutionary consequences. Establishment of GM crops has further been described as "*unrealistic*" due to the inability of domesticated crops to thrive[22]. However, genetic contamination has indeed occurred, with direct environmental, economic, and socio-cultural impacts.

Genetic contamination has been a serious problem resulting from both commercial cultivation and field trials of unapproved GM crops. Unintended contamination from field trials is a regular occurrence despite the use of containment practices, with 396 incidents being recorded across 63 countries from 1997-2013, and this is despite the lack of detection practices being widely deployed[89]. Thus, the real extent of contamination worldwide is unknown due to the lack of regulatory requirements to conduct sufficient sampling and surveillance.

Commercial cultivation has also led to significant adverse economic consequences for farmers and wider food markets from the efforts required to prevent contamination. Measures to prevent contamination have had a significant impact at different levels of non-GM supply chains, amounting to costs of up to 14 % of total product turnover at milling and processing stages[90]. In Switzerland, costs of co-existence measures have been estimated to be even higher, between 5-20 %[91], while in the US organic farmers have reportedly lost $6,532-8,500 per farmer in 2014[92]. For organic farming in the EU, the European Commission has noted that stricter segregation methods are needed to "*guarantee the associated price premium*"[93]. Feral plants have also been detected in Austria, where GM crops are not cultivated, encroaching on semi-natural environments under Central European climatic conditions[94]. Similarly, the sustained presence of unapproved GM rape seed along railroad tracks and in a port have been reported for Switzerland[95], and three feral species have established in Japan[96].

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Contamination of farmers' fields has also led to serious economic consequences. A 2015 USDA Organic Survey reveals that 92 U.S. organic farms suffered combined monetary losses of over $6 million between 2011 and 2014 due to GMO contamination[97]. Others have estimated that contamination of the total organic maize crop could cost U.S. organic farmers $90 million annually[98]. In Brazil, farmers lost higher premium prices for organic products because of GM contamination of organic soybeans[90]. Inadvertent contamination has also resulted in international bans on imports, as has been experienced with Japan banning Canadian wheat after contamination occurred from a field trial. The EU also banned Thai tinned papaya after it was contaminated from a research centre[99]. The EU has also banned Canadian flax following contamination events, while recalls of US corn following contamination were estimated to cost the company over $1 billion to compensate producers[100]. Honey shipments from Canada severely were impacted by GM canola contamination that cost $4.8 million due to the dropping of shipments[101]. Contamination events are also probably underestimated, with some only detected years after crops had been harvested. For example, herbicide-tolerant rice trials conducted in 1999-2001 in the US were only found to have contaminated rice shipments to the EU in 2006[100]. Contamination of wheat with unapproved varieties

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also led to class action lawsuits as a result of temporary bans by Japan and South Korea, forcing Monsanto to compensate farmers with a total of $350,000[102].

Contamination events also have had detectable adverse impacts on biodiversity. In Spain, contamination by GM events of organic maize led to the loss of farmers' varieties, which were particularly well-adapted to the local climate[103]. Such events threaten the availability of precious traits for breeding programmes of high-value germplasm[104], a risk that is extremely concerning, given the loss of crop biodiversity that has already occurred[105], threatening food security, particularly during ecological and climate crises. Maize landraces have also been contaminated in its centre of origin in Mexico, following years of controversial arguments over the issue[106].

Risk scenarios often fail to take into account the full range of potential consequences of contamination. For example, risk of transgene flow that confers herbicide tolerance has been assumed by regulatory institutions to "*not pose a problem for natural biodiversity because herbicides are not used in natural ecosystems*"[22]. The reductionist basis of such assumptions does not consider the potential wider, unintended effects that transgenes may exert on the rest of an organism's genome. A new 2021 study examining the effects of transgene flow from GM cotton to wild, indigenous cotton varieties in Mexico, highlights such risks and resultant adverse effects of genetic contamination on evolutionary and ecological processes, in wild, not experimental, conditions. Interplay between the herbicide-tolerance trait and other pathways involved in nectar production resulted in reduced nectar in wild plants, and its subsequent association with ant species that ordinarily protect the plant against herbivore damage. Increased herbivore damage resulted in raising serious concerns for the evolutionary processes of wild cotton species located in their centre of origin in Mexico[107].

Such experiences demonstrate some of the adverse economic consequences of GM crop cultivation, which has imposed significant opportunity costs on governments, that could otherwise have been invested into alternative opportunities. Such issues also threaten consumer choice at a time when European citizens are increasingly demanding what they deem to be ethically acceptable, nutritious foods, including organic products. The authors of the EASAC-endorsement and the Leopoldina Statement completely ignored the issue of transgene flow and GM contamination and its documented, massive ecological and economic consequences, while implying that the commercial costs of such accidents should rest with organic growers or conventional growers who choose to benefit from a GMO-free label. They will have to shoulder costs of labelling '*on a voluntary basis*' to provide consumer choice. Such a stance is a direct threat to such agricultural practice and its future sustainability, a problem that would only be worsened by the deregulation of 'genome edited' crops with no means to trace and document their products. It also reveals the authors' disregard for other agricultural production systems along with the social, ethical and cultural values apart from theirs.

Any proposal to exclude 'genome edited' crops from European GMO legislation will increase the probability of genetic contamination of wild species and crops that would go entirely unaccounted for

Any proposal to exclude 'genome edited' crops from European GMO legislation will increase the probability of genetic contamination of wild species and crops that would go entirely unaccounted for. However, the above experiences highlight the clear need for proper regulatory oversight to protect against environmental, socio-cultural and economic impacts.

GM traits have failed

Evidence for the unsustainability of these traits due to the evolution of resistance emerges from the introduction of increasing numbers of stacked GM varieties that are developed and marketed as counter measures. But the cultivation of those GM varieties that rely on multiple Bt transgenes, as well as on tolerance to several broad-spectrum herbicides that have troubling toxicity profiles, is even more problematic. Moreover, those varieties are also failing to resolve the challenges of emerging herbicide- and pest-resistance but rather continue to feed the pesticide-treadmill. Indeed, the US EPA has recently proposed the phase-out of all Bt maize and cotton crops that contain a single Bt toxin within three years, and all stacked (multi-toxin) hybrids that do not contain the Vip3a protein within five years[108]. The fall armyworm (*Spodoptera frugiperda*), another major crop pest that is now spreading from the Americas, now has proven resistance to all Bt toxins except for one[109]. Similar resistance has now been documented in newly invasive African populations of fall armyworms in Bt maize fields in South Africa[110], despite Bt crops being heralded by developers as a solution for small-holder farmers across Africa[111].

GMO failures have imposed detrimental impacts on farmers' livelihoods and food systems. GM cotton, widely adopted in India has resulted in stagnant yields after 20 years of cultivation, increased insecticide use, as a result of the failure of the Bt trait to offer long-term pest control, and increased farmer distress and indebtedness[112,113,114]. Indeed, increased yields are associated with increased pesticide use, which in turn have worsened the impact by pests not targeted by the Bt toxins. Although the farmer suicide epidemic has multiple causes, it has also been correlated to economic distress in rain-fed farms where Bt cotton is cultivated[105]. India's adoption of GM cotton, amidst long-standing, non-native hybrid cotton cultivation problems, garnered enormous interest from those wanting to assess if GMOs are indeed a useful tool for small-holder farmers in reversing the pest problems associated with the hybrid varieties. Despite the opportunity to improve the difficult circumstances for Indian farmers, Bt cotton has instead exacerbated their problems, and while direct links to suicides remain controversial, it is clear that Bt cotton has certainly not reversed the economic distress that farmers continue to face in the country. Researchers who have studied their long-term effects over 20 years also contest claims made by an author of the Leopoldina Statement as selective and biased, presenting an assertion of increased yields and pest protection by measuring only short term-impacts, prior to the emergence of pest resistance amongst other factors. Indeed, as noted by Kranthi and Stone (2020a)[115]:

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"*Qaim's data also cover only the first seven years of Bt cultivation. He saw "no indication that the benefits were fading" by 2008, after which he stopped collecting data and declared pesticide reductions to be "sustainable". Ironically, 2008 was the year that Bt resistance was first observed. If Qaim had examined long-term trends—whether statistically or graphically—he would have seen that by 2007 insecticide costs for managing non-target pests were rising ominously, that by 2012 insecticide costs for managing pink bollworm were rising, and that by 2018 cotton farmers were spending more than twice as much on insecticides as in 2005 when Bt seeds began to spread*".

In Burkina Faso, Bt cotton was adopted in 2008, but phased out in 2016 as a result of a drastic reduction in cotton quality that had negative impacts on their previously world-renowned cotton industry[116]. Despite the failures resting with the development process, the burden of economic costs was placed on small-holder farmers instead of the developers. South Africa, the only African country to widely adopt GMOs for food production, has also not seen a reduction in hunger. Indeed, some organisations report increases in hunger levels in the country despite the country's adoption of Bt crops[117,118].

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The selective analyses of GM crop performances to date by proponents of GMOs in general, make it even more vital that claims of the potential promises of such new GE techniques be scientifically scrutinised in order to develop sound agricultural policies, grounded in thorough evidence of efficacy and safety.

Complex traits, which are those mediated by a range of environmental and genetic factors, were promised to herald a new era of climate-resilient, or nutritionally-enhanced crops, but also these have failed to materialise. A case in point is the drought-tolerant maize developed by Bayer (formally Monsanto), already commercialised in the USA, and now targeted at Southern and Eastern Africa, but rejected by the South African authorities due to its failure to increase yield and lack of the claimed drought tolerance. For example, MON87460 was rejected by the South African authorities because it: "*…did not provide yield protection in water limited conditions*"[119]. Indeed, "*some trials even showed lower yields than conventional maize*" (ibid). The claim of drought tolerance has never been confirmed by independent scientific studies. The claim that the integration of the *cspB* transgene improves tolerance against drought rests entirely on claims by the producer. A study by Monsanto reported a (disappointing) expected 6 % reduction in yield loss from the 15 % loss observed under water-limited conditions over three seasons in the US, with one season observing a 0 % change in yield in comparison to conventional varieties[120]. Though this study purported to show a "yield increase", there was, in reality, still a 9 % yield loss under water-limited conditions. How *cspB* maize performs compared to known and well-documented maize varieties with tolerance to drought, in particular those that emerged from the Drought

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Tolerant Maize for Africa (DTMA) project, also remains to be determined.

GM Golden Rice has also been a failure to date after more than 25 years since its beginnings. Golden Rice variety GR2-R1 was hampered by low yields, dwarfism, bushy statue, pale leaves, late flowering and low fertility[121,122]. The later GR2E version has suffered degradation of beta-carotene during storage[123,124,125], with negligible evidence of health benefits[126]. A study of the seed selection practices of Philippine rice farmers has concluded that farmers are unlikely to plant Golden Rice rather than current varieties, unless induced to do so[127].

The dearth of complex traits on the market is in contradiction to the Statement's unreferenced assertion that genetic engineering tools have 'made breeding more targeted and efficient.' Indeed, developers and researchers have reported lengthier times for transgenic crop development over conventional methods[128]. Both agroecological and conventional methods have delivered the very same adapted varieties that genetic engineering has been promising us for decades but has yet to produce[129,130,131,132,133]. The huge scale of field trials is a testament to the lack of efficiency and efficacy of genetic engineering. In the US alone, APHIS permits issued for trial releases exceeded 22,000, which covered a variety of traits beyond herbicide tolerant and insect-resistant traits which make up nearly half of all trials, yet very little has materialised since they began in 1988. The lack of proven benefits was certainly not due to 'excessive' regulations, as the 'de-regulation' model promoted by the authors of the Leopoldina Statement is applied there – nor due to lack of funding. The scientific evidence points to the technology not being able to live up to its promises.

The failure of genetic engineering to deliver complex traits (e.g. drought tolerance, disease resistance, higher intrinsic yield) is not surprising. Complex traits by definition have the coordinated function of multiple gene families or even the entire genome of the organism at their basis (known as "omnigenics")[134]. As transgenic and 'gene editing' technologies can only handle or manipulate a few genes, it is beyond their capability to deliver complex multigenic or omnigenic characteristics into plants or animals. Furthermore, omnigenics also highlights that genes, and their products, work as an integrated network and not as isolated entities added up. Thus, while the addition of a new transgene or alteration in the function of just a single native gene by gene editing can have repercussions in the function of the entire network of host gene functions with far reaching consequences in terms of biochemistry and composition, it is unlikely, on the other hand, that such isolated interventions will be able to create the kinds of meaningful changes that are required for quantitative traits. This in turn can negatively impact crop and farm animal performance and could result in the production of novel toxins or allergens (see sections below: *Claims of safety of existing GM crops, Unfounded claims of safety and efficiency of 'genome editing'* and *Documented risks associated with genome editing*).

The scientific evidence from contemporary molecular genetics points to transgenic and genome editing technology as being conceptually flawed and not being able to live up to its promises

Thus, the scientific evidence from contemporary molecular genetics points to transgenic and genome editing technology as being conceptually flawed and not being able to live up to its promises.

Biased claims of safety of existing GM crops

From the Leopoldina Statement:
"*there is not a single documented case concerning the widespread use of permitted transgenic GMOs in which* ***unexpected*** *environmental or health* ***consequences*** *for humans or animals occurred.*"

"*… European projects on food safety and toxicology also failed to identify any* ***specific*** *and* ***systematic threats*** *posed by plants modified through 'genetic engineering'…*"

The Leopoldina Statement claims repeatedly that no adverse effects have resulted from transgenic GMOs, and that no risks related to the technology itself exist. However, the wording is, intentionally or not, quite ambiguous. It is unclear what the authors mean by 'specific' and 'systematic' threats and by 'unexpected' consequences and why should only these consequences and threats be deemed relevant? And by what scientific standards would 'unspecific' and 'unsystematic' threats be irrelevant? One of the very few (<5) references offered in support of such sweeping claims was a summary report of a European research program published over a decade ago (2010) covering research that started 20 years ago in 2001. Even a cursory glance at the content of the funded programs reveals that most of those claimed 300 million Euros research funds (actually summed up since the 'inception in 1982' of the 'Biomolecular Engineering programme' according to the report) went into technology promotion, development and communication projects that had little if anything to do with 'safety' or 'risk' or 'impact' issues. Under the so-called 'Environmental impacts of GMO' section, the featured studies are mainly classical research & development (R&D) programs for creating new GMOs or enabling/enhancing their introduction in agriculture and food systems, which had little if anything to do with risk or safety research that would allow to draw such sweeping safety conclusions. Research projects under this 'environmental impact' section included, for example, the development of GMOs with resistance against fungal diseases, resistance against nematode pests, with new GM traits with an 'appropriate poverty focus' for the Central Andes, 'selection system for transgenic crops based on modified plant-tubulin genes', developing GM 'wheat with enhanced nitrogen use efficiency', or demonstrating the 'appropriateness of Bt-transgenic cotton' and ensuring their sustainable GM crop production by developing target insect pest management programs.

Nevertheless, the authors of the Leopoldina Statement deplored that their safety claims are '*largely disregarded by the critics of genetic engineering*' citing also ENSSER. These 'safety claims' were not 'disregarded' but, on the contrary, they were carefully analysed and evaluated and, subsequently, disputed and refuted based on the scientific arguments and published evidence, again, compiled in this report. These safety claims are simply wrong and many risks became demonstrated harm that continue to be indeed systematic, even quite specific and some also expected (see below), and many had been postulated by critical scientists right from the start, which is a crucial fact

These safety claims are simply wrong and many risks became demonstrated harm

that remains unacknowledged by the authors of the EASAC-endorsed Leopoldina Statement. The authors of the EASAC-endorsed Leopoldina Statement later push for moving European regulations from what they call a 'process-based' to 'product-based' system with the "*requirement of an authorisation, application or notification solely to modified traits, since environmental and health risks can only arise from the modified traits of a plant and its use and not from the (novel) breeding technology underlying the modification*".

These assurances are patently misleading as scientific studies have revealed both expected and unexpected adverse consequences from 'process' and 'product' combined. Unexpected (or rather unpredictable) effects have been widely documented in a variety of crops as a result of the GE process, including differences in characteristics such as seed germination, weed suppression, pest resistance, (non-)drought-tolerance, height, yield and flowering time, as well as compositional differences. Several reviews have documented such unintended or unexpected or unpredictable effects[135,136,137]. A recent review by Wilson (2020)[126] records unintended effects that have occurred in widely commercialised varieties as well as those in crops having "complex" traits. For example, just for the Bt maize variety MON810, studies have revealed increased lignin content[138,139,140], altered kernel composition of sugar, osmolytes, branched amino acids, and proteins[141,142,143], decreased protozoan and nematode numbers, and drier rhizosphere soils[144,145], increased aphid susceptibility[146], delay in seed and plant maturation[147], and higher moisture content[148]. Adverse effects of herbicide-tolerant GM crops on biodiversity are well-documented, including contamination of water bodies and ground water, toxicity to a wide range of species from soil to aquatic organisms and insects (see above).

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Unintended, unpredictable and unexpected effects have been documented for other crops as summarised by Wilson (2020)[126] including in Bt11 maize, Event 176 Bt maize, 15560BG Roundup Ready maize varieties NK603, soybean event 40-30-2, MON89788-1, herbicide-tolerant winter rape, and Roundup ready oilseed rape. With regard to human health, no consensus on safety has been reached, with contradictory findings compounded by a lack of funding for independent studies (see Hilbeck et al., 2015and references therein).[149] Unintended effects on crops with "complex" traits include various potato varieties, cotton, buckwheat, rice and barley, and tomatoes [126].

Documented unintended effects are likely to be underestimated, considering the lack of publicly available data, due to limited independent research because of the proprietary nature of GM crop development

Documented unintended effects are likely to be underestimated, considering the lack of publicly available data, due to limited independent research because of the proprietary nature of GM crop development, the lack of assessments for numerous parameters during regulatory testing, or problems with standardisation of risk assessment protocols that would mask potential differences[126].

Lastly, it is important to recognise that unintended effects can arise from multiple parts of the GE technical process, which are also routinely deployed for genome editing techniques. To genetically engineer crops, genetic material has to be introduced or transferred into the plant cell and then integrated into its genome (its own DNA), which combines into the 'transformation' of the plant cell. The transformation process is stressful to the cells as well as to the genome, bombarding them with DNA-laden particles, subjecting them to electric fields to make their cell walls permeable, or using bacteria to infect the cells and deliver the genetic material, such as transgenes to cells. All of this requires many trials and errors until the genetic material will finally be integrated into the DNA of the receiving manipulated organism. These cells will then also have to recover and regenerate into a full plant. Such process-based genetic engineering supporting techniques have been shown to be associated with unintended effects such as small and large deletions and insertions as well as duplications of DNA segments and rearrangements like inversions and translocations[150,151,152,153,154]. Moreover, such process-based, unintended effects have been linked to increased levels of potentially toxic metabolites in commercialised varieties, with implications for human health[155]. Nonetheless, the authors of the Leopoldina Statement state that "*experiences show that possible risks may arise from the product or its modified traits and related agricultural practices (such as herbicide use), but not from the underlying breeding method*", misleadingly attempting to dissociate risks of old GMOs from the new versions.

Unfortunately, this widely documented scientific evidence of adverse and unexpected effects listed above at the level of safety, efficacy as well as economics, has been ignored in both the EASAC endorsement and the Leopoldina Statement.

New 'genome editing' methods: Unfounded claims of safety and efficiency

From the Leopoldina Statement:
"*there is scientific consensus that particularly plants genome edited with SDN-1 and SDN-2 can be equated with products of traditional random mutagenesis breeding in terms of their risk potential and continue to carry significantly fewer off-target mutations.*"

"*genome edited plants are equivalent to products of traditional breeding and even carry up to 100 to 1000 fewer unwanted (off-target) mutations than plants produced with traditional mutagenesis breeding*", offering "*high precision and efficiency using the cell's own repair systems*".

"*there is not a single documented case concerning the widespread use of permitted transgenic GMOs in which unexpected environmental or health consequences for humans or animals occurred*".

Extending from sweeping safety claims for current GMOs, the Statement continues to make contradictory claims about the increased precision and safety of so-called 'genome editing' techniques over existing GMOs (see above), whilst also arguing that existing GMOs are already safe. The thrust of the former argument is that where genome editing applications are used that can, *in theory*, generate final products without transgenic DNA (SDN-1 and SDN-2[v]), they are more akin to conventional breeding and random mutagenesis techniques than to GM organisms. Based on these claims, the authors advocate a quick regulatory change by simply excluding SDN-1 and SDN-

v Site-directed nuclease (SDN) -1, -2 and -3 are categories developed by the European Food Safety Authority (EFSA) to distinguish between different genome-editing outcomes. All three categories can use the same site directed nuclease to cause a DNA breakage at a specific site. The cell will now respond with one of its own repair mechanism, commonly either with the non-homologous end-joining mechanism (NHEJ), which sticks the loose ends back together in a random fashion (SDN-1) or the homology dependent repair (HDR), which requires a DNA template as instruction for the repair (SDN-2 and -3). In plants, the predominant repair mechanism is the error-prone non-homologous end-joining.
As defined by Agapito-Tenfen et al., (2018), SDN-1 generates random mutations at a targeted site within the genome. Site-Directed Nucleases-1 (SDN-1): The intended outcome is a site-specific small random mutation in form of an insertion or deletion (also called 'indels') generated by the cells non-homologous end-joining repair pathway. For

2 applications from GMO legislation by stating, *"the legal framework on GMOs should apply only to organisms in which the resulting genetic modification could not be achieved in a 'natural' way or by traditional breeding, or in which foreign or novel genetic information has been introduced into the genome, similar to Argentinian and US regulatory practice".*[2] The sole reference for claims of precision is a previous Leopoldina Statement, while claims of scientific consensus remain unsubstantiated and misleading.

Such unreferenced claims are repeated in the EASAC endorsement, which avoided outright claims of safety, but implicitly suggested it with the assertion that "*Unlike chemical- or radiation-induced mutagenesis, often traditionally used for crop improvement tools, the new breeding techniques do not create multiple, unknown, unintended mutations throughout the genome. Furthermore, the products of the new breeding techniques are also unlike genetically modified organisms (GMOs) used in agriculture, in being more precisely targeted and having no foreign DNA in the end product.*"

Claims of scientific consensus remain unsubstantiated and misleading

Despite those attempts to distinguish new GMOs ('genome edited' using SDNs) from older forms of genetic engineering (transgenesis, recombinant DNA technologies) on the basis of the former being more precise and, thus, even more safe than the latter, the Leopoldina Statement simultaneously argues that the older first generation transgenic technologies are also safe and, implicitly or explicitly, should eventually also be excluded from regulations. They conclude that it is "*not scientifically justifiable for the longterm regulatory approach to new breeding technologies to differentiate between benign genetic engineering without transgenes and **highrisk genetic engineering with transgenes**".* They advocate for trait-based (i.e. 'product'-based) (de)regulations "*since environmental and health risks can only arise from the modified traits of a plant and its use and not from the (novel) breeding technology underlying the modification".* [2] The reference to '***high-risk genetic engineering with transgenes***', however, remains at odds with the overall sweeping safety claims of GMOs (containing transgenes) with no further elaboration offered that would solve this puzzling statement.

SDN-1, only the SDN is provided to the cell, but no repair. Therefore, in the case of insertions, the inserted material is derived from the organism's own genome, i.e., it is not exogenous.

Site-Directed Nuclease-2 (SDN-2): The [result][intended outcome] is a site-specific pre-determined point mutation generated by the homology dependant repair pathway(specific nucleotide substitutions of a single or a few nucleotides or small insertions or deletions). For SDN-2, an exogenous DNA template is delivered to the cells simultaneously with the SDN for achieving desired nucleotide changes via homology dependent repair.

Site-Directed Nuclease-3 (SDN-3): The [result][intended outcome] is the insertion of a longer DNA sequence (e.g. a transgene) at a specific target site, by homologous recombination (HDR pathway). Exogenous DNA fragments or gene cassettes up to several kilo base pairs (kbp) in length can be inserted to a desired site in the genome or a gene (Agapito-Tenfen et al, 2018).

It is worth noting that such definitions have no legal basis, and are simplistic and roughly defined, with no clear distinction between categories SDN-2 and SDN-3. Further, which DNA repair pathway is deployed, and thus what outcome is achieved, is determined by the cell and not the developer or experimenter.

The report also suggests that "*there is currently no scientific evidence to associate directed genome editing methods with specific, novel risks*"[2]. Again, what exactly the authors mean by 'novel' and 'specific' remains unclear, but both are non-trivial and non-random qualifiers. The above-mentioned early identified risks of current genetic engineering technologies did materialize and have had harmful real-life consequences for the environment, human and animal health, farmer livelihoods and biodiversity. If risks are not novel but indeed parallel to first generation genetic engineering, we are faced with a repeated erosion of our biodiversity, human and environmental health. The term 'specific' remains entirely undefined.

Documented risks associated with genome editing

The generalised safety claims do not hold up even to basic scrutiny. Within the medical research community there is widespread recognition that unintended genomic effects such as on-target alterations, genetic deletions, and off-target activity are associated with these so-called 'genome editing' technologies[156,157]. As such, recent publications from prestigious medical institutions warned that such technologies could have unforeseen effects that may not only adversely impact the individual but that can also be passed to future generations[158]. Following the documentation of unwanted genetic changes in human cell experiments in three new 2020 publications, an author of one of the studies also warned of the serious consequences of unintended effects, explaining that some cells "*were so flummoxed by the alterations that they simply gave up on trying to fix them, jettisoning entire chromosomes, the units into which human DNA is packaged*"[159]. Concerns have been raised that such off-target genetic alterations and chromosomal rearrangements may trigger cancers[160].

The generalised safety claims do not hold up even to basic scrutiny

Such unintended effects can equally have implications for 'genome edited' plants or animals. Without adequate regulation for risk assessment, including testing and independent safety/risk assessment and research, such unintended genetic alterations, as detailed above, could be entirely missed, with the potential to adversely impact food and environmental safety, as well as agronomic performance. The Leopoldina Statement fails to provide scientifically robust arguments or, importantly, independent, published research data to prove that what has been observed and warned about for human cells would not also be the case for animal cells or for plant cells. For example, mutations or chromosomal damage may also trigger cancers in farm animals. In plants, such genetic effects may result in a variety of problems due to the loss of a gene's function, or alteration in its activity or function, with the potential to change allergenic or toxic products of the plant, or alter metabolic genes and thus agronomic performance, for example. Crucially, it is impossible to predict the implications of such genetic damage without systematic testing and assessment.

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Unintended effects have been widely documented and evidence has accumulated since the 2017 European Commission report, one of the only citations used by the statement to claim safety and efficiency. Unintended effects at the genomic level can be divided into those that occur at the target site (on-target effects), and those that occur elsewhere in the genome, called off-target effects, where unintended sites are also modified.

With regard to off-target effects, the authors of the Leopoldina Statement fail to acknowledge the array of studies showing off-target activity, a feature largely undisputed within the field.[161,162,163,164,165,166,167,168]. There is also failure to recognise the lack of studies that actually have performed thorough analyses such as whole-genome sequencing, as summarised by Modrzejewski et al., 2019[169]. Assessing unintended effects at off-target sites is much more difficult than detecting changes at target sites, because the number and positions of nucleotide changes are unknown, and current tools for their detection are not currently full-proof (see Agapito-Tenfen et al., 2018[170]), though additional tools such as long-range PCR and especially long-read DNA sequencing could aid in detection methods[171]. Such off-target changes could result in a variety of effects, including loss of gene function, or alteration of protein affinity or function. Non-coding effects on promoters, introns or terminators that can alter gene expression is also possible, with alterations in allergens in plants constituting a health risk for human and animal consumption[172]

Unintended effects have been widely documented and evidence has accumulated since the 2017 European Commission report, one of the only citations used by the statement to claim safety and efficiency

This sole reference used to make claims of precision, while supportive of 'genome editing' for plants, still acknowledges unintended effects including the *"presence of unintended exogenous DNA integrated into the genome"*[173]. Such unintended transgenic organisms resulting from 'genome editing' undermine attempts to make clear distinctions between 'genome editing' applications such as SDN-1 and SDN-2 from already established transgenesis techniques. Indeed, various studies have reported the accidental introduction of recombinant DNA since that report[174], including vector backbone and bacterial antibiotic resistance genes in genome edited cows[175], serum-derived goat and bovine genes in edited mouse cells, and bacterial DNA, at the target site in edited mouse cells[176]. With regard to plant editing, high frequency unintended transgene integration has been documented in *Arabidopsis* plants, as well as off-target effects that are aggravated in the next-generation[177]. The causes of next-generation effects were not investigated, but may suggest instability of the engineering process, and potentially unexpected outcomes. Unintended integration has also been documented in rice[178], and also when performing transient delivery of genome editing machinery[179]. Other on-target effects include large-scale deletions and rearrangements[171] exon skipping and recombination events[180,181], and high- frequency production of aberrant protein products[182,183]. A recent example was the use of SDN-1 'genome editing' to disrupt a gene in rice to make semi-dwarf varieties[184]. The authors reported a variety of mutations, insertions, deletions and rearrangements of DNA, which varied with different rice varieties. Unintended insertion of plasmid DNA used in the genetic engineering process was also detected. The rice also displayed reduced yield.

Crucially, on-target and off-target effects including unintended insertion of DNA are likely to be missed by current screening CRISPR analysis tools such as CRISPResso, CRISPR-RGEN, TIDE and ICE, which are designed to only sequence short- regions of DNA, and, thus, may miss unintended outcomes such as bigger changes like large deletions, rearrangements and unintended insertions. Indeed, reports that techniques such as PCR have failed to detect unintended effects such as integration events have already been reported[185,148,166]. Assessing sequences of longer fragments of DNA is required to detect unintended effects, such as long-read sequencing methods, but in plants, on-target effects are rarely checked. A recent study[186] has raised these concerns, stating that *"Such chromosomal rearrangements are not always easy to detect unless long-range PCR or long-read next generation sequencing (NGS), such as PacBio, are used. Therefore, quite possibly, in many plant studies where targeted mutagenesis was performed using CRISPR/Cas, such unintended genomic changes might have remained undetected since the above-mentioned techniques were rarely used for genotyping CRISPR/Cas-induced mutations in plants. Usually, it is short-range PCR and/or a short-read NGS technology, such as Illumina, which are used for genotyping of mutagenised plant lines."*

Proposals to move away from a 'process-based' regulatory system, where the risks of the genetic engineering process are included in the assessment, towards deregulation based on assumed, but increasingly questioned, 'precision' is a move towards reducing scientific inquiry and oversight

Off-target effects will be harder to detect, and would require unbiased sequencing protocols, which are rarely performed[169]. Such examples not only highlight the importance of screening, but also question the very notion that genome editing applications, particularly SDN-1 -2, do indeed produce non-transgenic crops in the conventional sense, which has been one of the main selling points for developers to date.

Proposals to move away from a 'process-based' regulatory system, where the risks of the genetic engineering process are included in the assessment, towards deregulation based on assumed, but increasingly questioned, 'precision' is a move towards reducing scientific inquiry and oversight. This comes at the very time that such technologies are rapidly evolving in the field of genetic engineering and synthetic biology, and locates responsibility for identifying unintended effects solely with the scientists who develop them. Such proposals are also problematic at a time when it is indeed the 'process' that takes centre stage in claiming property rights such as patent rights and license fee obligations with the use of these patented 'genome editing' tools. And it goes fundamentally against the above listed, emerging accumulating evidence that many unintended effects do indeed occur.

Such proposals are also problematic at a time when it is indeed the 'process' that takes centre stage in claiming property rights such as patent rights and license fee obligations with the use of these patented 'genome editing' tools

(Non)-Equivalence to conventional breeding and random mutagenesis techniques

'Genome editing' broadens the range of alterations that can be performed beyond those of traditional breeding or random mutagenesis, challenging the assumption that it is more akin to traditional breeding and random mutagenesis than first generation GMOs, made in the EASAC-endorsed Leopoldina Statement. Key differences between random mutagenesis and genome editing are summarised in Box 1.

'Genome editing' deepens the level of intervention beyond what can be achieved with existing techniques by the ability to create many simultaneous or successive alterations of genetic material. Indeed, EFSA has described the development of low gluten wheat by Sánchez-León et al., (2016)[187] and listed in Table 1, which had a total of 35 genes modified without the introduction of foreign DNA (SDN-1). While EFSA pointed out the complexities and depth of the interventions, they fell short of demanding a proper risk assessment of these complex genetic changes, taking into consideration issues such as molecular changes, gene expression and the potential impacts on heath and the environment (EFSA, 2021)[188]. The engineering of 35 genes is a clear example of what can now be achieved with genome editing but not traditional breeding, and increases the probability of interfering with metabolic pathways (far) beyond those being targeted.

'Genome editing' broadens the range of alterations that can be performed beyond those of traditional breeding or random mutagenesis, challenging the assumption that it is more akin to traditional breeding and random mutagenesis

Multiple copies and paralogues of genes can also be modified simultaneously and repeatedly, something that has not yet been achieved with conventional breeding, chemical mutagenesis or transgenic techniques, which is especially relevant to polyploid crops that have multiple copies of genes, including three of the crops listed in Table 1[189,190,187,191,192]. 'Genome editing' further allows for the generation of mutations in regions of the genome that are ordinarily protected by naturally existing DNA repair mechanisms[191]. 'Genome editing' further increases the mutation rate in genomic regions that normally correlate with the occurrence of fewer *de novo* mutations. Recent publications showed that the mutation rate across the genome is not random, but that the mutation rate depends of the DNA mismatch repair (MMR) and certain epigenetic modifications[193,194,195]. CRISPR/Cas systems have been used to modify conserved sequences, for example when applied in gene drive technologies[196]. TALENs, as well as ZFNs, have also been demonstrated to target conserved sequences[197,198]. Further, evidence suggests that mutations resulting from so-called 'genome editing' techniques are not repaired with the same processes as those that have occurred naturally, with high error rates in repairs of CRISPR-induced mutations[199,200,201]. This is a crucial aspect that differentiates 'genome editing' from traditional breeding and random mutagenesis, and reveals another unintended and unexpected by-product effect of 'genome editing'[202]. While there are distinctions between repair mechanisms in plants and mammals that must be considered when addressing such effects across organisms, it is also worth noting that current understandings of such mechanisms, whether it be plants or animals, are still in the phase of discovery and, thus, such uncertainties cannot justify deregulating such technologies. CRISPR/Cas has been used to overcome linkage drag effects where desirable genes are linked to undesirable genes[203,204]. Linkage drag, where a genetic trait of interest is inherited along with other genes that reduce the fitness of the plant, is a feature of traditional breeding.

Further, 'genome editing' usually involves identical supporting techniques to older transgenic techniques, including transformation and tissue culturing (see section: Claims of Safety of existing GM Crops). Thus, the narrative of safety and indistinguishability comes across as merely pushing for regulatory exemption to avoid costs and responsibility when the above literature is taken into consideration.

To push for deregulation of genome editing SDN-1 and -2 applications, the authors also state that "*established analytical methods often do not (or do not clearly) distinguish between genome edited organisms and naturally occurring or conventionally bred organisms*." And later, that "*The GMO authorisation procedure for placing on the market is also not practicable because and insofar as users of the new technologies are unable to provide specific detection methods*." The authors suggest as a solution rather to give up dealing with the challenges of detection that are essential to maintaining consumer choice. In contrast to this laisser-faire approach promoted by the Leopoldina Statement authors, independent experts in detection e.g. Bertheau (2019)[205] have contested claims of undetectability, and independent scientists have already published a protocol to detect CIBUS's commercialised canola variety.[206] Ironically, CIBUS, in response to that publication, is now claiming[207] that their canola's GM trait was actually an unintended mutation that accidentally arose as a result of the underlying GE process of tissue culturing. How that can be reconciled with the narrative of intentional, precise and control over so-called 'genome editing' is unclear. Moreover, simple methods used for current GMOs have recently been developed for use for genome edited crops[208]. It is, thus, evident that developers can certainly submit information on the alterations generated to assist in detection of the crop, if they want to or are required to. And if access to such data is ensured for public authorities, in the form of information-sharing databases, for example. So, event specific detection methods can be developed, based on current detection technology, if information about the intended alteration is available. Thus, developers can be requested to deliver this information as a prerequisite for approval.

Differences between genome editing and random mutagenesis

Genome editing can be used to modify multiple copies of a gene, increasing the depth of changes that can be made at any one time. This is highly relevant to plants, where many crop species are polyploid, with multiple copies of chromosomes. With random mutagenesis, this could not be achieved.

Genome editing can result in erroneous repair of DNA breaks caused by the techniques, such that both on- and off-target mutations may differ from those induced by random mutagenesis.

Genome editing can modify areas of the genome that are usually more protected from mutations induced by random mutagenesis, bypassing protected regions such as those protected by epigenetic processes.

Depth of intervention is increased with genome editing, which unlike random mutagenesis, involves directly intervening in an organism's DNA, with synthetic material from the laboratory directly inserted into cells.

Unsubstantiated promises of genome editing

The same overblown promises used to promote the existing generation of GMOs are now being recycled for the so-called new 'genome editing' technologies, despite the lack of rigorous science to substantiate them even for the existing first generation of GMOs. For example, the Leopoldina Statement says that "*Scientists largely agree that molecular breeding techniques will make an important contribution in the coming years to making agriculture more productive, less pesticide-intensive and more climateadapted through traits such as drought and heat tolerance*". The claim of speaking on behalf of the majority of scientists relies, again, on self-referencing: one paper by Qaim, and the other a 2013 EASAC report[209] that focuses largely on first generation GMOs, and a third paper[210], that rightly actually acknowledges the limitations of genome editing by stating that: "*It seems evident that complex traits such as stress tolerance or nutrient use efficiency will be more difficult to tackle than monogenic traits, which are frequent for disease resistance, herbicide-tolerance or quality traits*". However, all monogenic defence traits will suffer from the risks of resistance evolution, which is now resulting in the phase-out of near all insect resistant GM traits in the USA[108], regardless by which genetic engineering technique they were produced.

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EASAC also promotes such unsubstantiated promises, stating that: "*The scientific opportunities coming into range in plant breeding, for example, to develop more climate-resilient agriculture, resistant to the increasing abiotic and biotic stresses, have been examined previously by EASAC (for example EASAC 2017a, 2017b) and have been explored extensively in the scientific literature (for example, the recent comprehensive review by Bailey- Serres et al. (2019)).*"

The EASAC publications however, mention very few examples of crops in development, focusing on the deregulated US 'non-browning' mushroom for increased shelf-life, 'waxy corn' for industrial products, and 'cold-storage' potato crops, none of which address climate resilience or any other sustainability goal. The other crops mentioned are the preliminary research publications on fungus-resistant and drought tolerant maize traits[211,212], addressed in Table 1, that are yet to be demonstrated as efficacious or safe for health or the environment. They also conspicuously failed to mentioned the commercialised herbicide-tolerant canola by CIBUS (see below). The review by Bailey-Serres et al., (2019)[213] that is also referenced, primarily describes the needed advances yet to be made in order to achieve such beneficial traits, and cannot be used to serve as an example of concrete opportunities let alone documented successes.

The promises of benefits are not currently based on scientific reality

The promises of benefits are not currently based on scientific reality. 'Genome edited' crops were first demonstrated in the mid 1990s, as acknowledged in the Statement. In the USA, where they do not require market approval, just two varieties, a "high-oleic acid" soybean variety, and the herbicide-tolerant canola from CIBUS (noted above), have been commercialised. Such a dearth of commercialisations cannot be attributed to restrictive regulations. Similarly, 60 % of patents come from China[214] where field trials are permitted, yet commercial products remain lacking, notably a decade or more after the proclaimed 'discovery' of these tools. There is also no publication to substantiate the claim of health benefits from the soybean oil, which can also easily be substituted with other naturally oleic acid-rich oils, such as olive oil. A false sense of urgency to deregulate genome editing is evoked in the Statement that bears little relation to the actual R&D pipeline: "*There are several regulatory options for the amendment of EU genetic engineering legislation, which is urgently required*".

In reality, all developed 'genome edited' lines are far from anything marketable

Assessing more closely the claim of efficiency, the sole citation is again the 2017 high level EU advisory panel report. This report claims that the increased efficiency of 'genome editing' over other methods, such as random mutagenesis, is that these other techniques require backcrossing to remove the off-target mutations. However, as described above, 'genome editing' is also associated with off-target activity and other unintended effects. Further, such a promise also requires the ability to directly 'genome edit' all genotypes, i.e. varieties. In reality, all developed 'genome edited' lines are far from anything marketable and will mostly serve as basic exit material for conventional breeding, just as the material that is coming out of random mutagenesis techniques. Hence, all these lines still require backcrossing and breeding to finally become 'varieties' listed on the common catalogues from which farmers then finally can choose their cultivars. This may well be another explanation for the dearth of commercial products after a decade of promise and enormous amounts of funds going into this field.

With regard to the state of play of R&D, the authors write that there are 98 'market relevant' crop applications (and a total of 193 crops) in 28 crop species that have been demonstrated to have '*functional proof of the respective modification*'. They further state that which developments will reach the market '*depends largely on the economic and legal parameters*'. This fails to recognise the limited number of crop varieties and species that are amenable to the supportive techniques such as transformation and tissue culture, and the current lack of evidence that effective traits can be achieved in increased numbers, or indeed, any crop species. Over the past decade there have been literally thousands if not tens of thousands of such early experimental, proof-of-concept lines developed which have not subsequently yielded anything tangible. China, for example, has invested heavily in this research field, promoted by the government, with a

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growing number of studies being reported, yet there is no documented evidence that efficacious crops appear to be reaching the market[215].

To substantiate claims of advanced beneficial crop development, the Statement relies heavily on a review by Modrzejewski et al. (2019). However, the examples listed in this review reveal limited evidence of workable crop traits with promises of societal good (see Table 1).

The EASAC-endorsed Leopoldina Statement emphasises the development of beneficial traits such as abiotic and biotic stress tolerance. However, of the 24 references listed for biotic stress tolerance, only a single Chinese study presented trial data, comparing rice bacterial blight infection to parental varieties (Zhang et al., 2018). Of the eight references made for abiotic stress tolerance, a single publication presented trial data to validate efficacy of any traits, with data indicating that the crop is not drought-tolerant during the critical growth period (Table 1)[212]. The Modrzejewski et al. (2019)[169] publication also includes herbicide tolerant varieties as 16 out of 193 of the 'market relevant' crops that are listed in it. Herbicide tolerant GM crops are particularly controversial, as discussed above. However, there is no acknowledgement of the development of herbicide-tolerant genome edited crop varieties in the statement. In reality, one of the only two approved crops in the United States is CIBUS's herbicide tolerant canola. The largest number of crops referenced are those that aim to alter agronomic qualities, making up 47 of the 193 crop studies. Four of those are to alter fruit colour, hardly addressing world hunger or global ecological problems. Various crops are also being developed to serve industrialised agricultural systems including eight crops designed for developing hybrid varieties (e.g. male sterility and haploid induction), and another to prevent seed loss during mechanical harvest.

Rather than tackling the recognised problems of industrialised agriculture, the above-mentioned experiences serves to illustrate how GMOs can indeed be drivers of the very problems they purport to address. The current development of herbicide-tolerant and pest-resistant crops via 'genome editing' will likely only replicate these failures. The statement is careful to avoid any mention of 'genome edited' herbicide tolerant crop developments, giving an inaccurate picture of the current R&D state of play as if focusing on traits for 'societal good'. First generation herbicide tolerant crops effectively moved glyphosate from the margins to a new central role as a key agricultural input, with adverse effects now well established. The advent of herbicide-tolerant 'genome edited' crops will serve to prolong this chemical lock-in, by protecting demand for agrochemicals[216].

First generation herbicide tolerant crops effectively moved glyphosate from the margins to a new central role as a key agricultural input, with adverse effects now well established. The advent of herbicide -tolerant 'genome edited' crops will serve to prolong this chemical lock-in, by protecting demand for agrochemicals

The vast majority of R&D presented by Modrzejewski et al., (2019)[169] also pertains to commodity crops (or experimental model species) such as rice (the majority, reflecting the fact that China is the leading developer in this field), maize, (tomato), wheat, soybean and potato, going against the claim that 'genome editing' will promote, and is needed, for increasing biodiversity of agricultural systems, and address food security which rests on many local staple crops like cassava, yam, millets, tef and more.

Unlike the Statement, Modrzejewski et al., (2019)[169] acknowledges that "*as the genome-editing techniques, especially CRISPR/Cas, were just **recently** developed, the large majority of the existing applications represent basic research*." A decade is hardly 'recently' and certainly not when a technology is promoted on its 'speed'. In the Information Technology sector, the favourite field genetic engineers like to compare themselves to, one decade is an eternity during which uncountable novel products are reaching the markets on a yearly, if not monthly, basis. Further, the dubious claim of 'market relevance' or 'market orientated' is a vague term that obscures the reality that much of the research is still preliminary and not indicative of what will be submitted to market, if ever. They merely classified 'genome editing' applications as 'market-orientated' when studies met these basic criteria: (1) 'genome editing' was applied in any agricultural crop; (2) a trait was addressed that may perhaps be of interest for commercialisation, and (3) the targeted trait was expressed in the 'edited' plant material when grown typically in highly controlled, closed systems. Further, the description that those listed show "*functional proof of the respective modification*" avoids admitting that there is a lack of proof of efficacy of a given trait that is much more difficult, time consuming and costly to do. Even data showing proof of the genetic modification appears lacking for many of the crops, with the sole evidence being cited as applications to the US Department of Agriculture (USDA)'s APHIS, with no data provided (for 18 crops listed).

Looking more closely at the examples tabulated in the Statement on potential 'market relevant crops', taken largely from the Modrzejewski et al. (2019) paper, a second paper co-authored by one of the authors of this Statement (Zaidi et al., (2019); and a third paper (Eriksson et al., 2019), there appears to be negligible evidence of efficacy of any of the crops (summarised in Table 1). Further, even if they were proven to be efficacious in their intended design, it is questionable whether any of the traits listed are indeed needed (see table 1) with various crops designed for industrial purposes such as biofuels or as ingredients in processed foods. The overwhelming majority of crops have not been tested in field trials, with one wheat being one exception and one cassava variety another that, in fact, also is transgenic, carrying the plasmid DNA encoding for the genome editing machinery. Indeed, at least five of the 17 crops listed are still transgenic and, carrying vector sequences, with the banana variety having nothing to do with 'genome editing' at all. It remains another puzzle why it was included here in the first place.

TABLE 1. EXAMPLES OF 'MARKET RELEVANT' CROPS LISTED IN THE LEOPOLDINA STATEMENT[vi]

CROP SPECIES	TRAIT	TECHNIQUE	DEVELOPER/ REFERENCE	ENSSER COMMENTS:
ALFALFA	Reduced lignin content for 'nutritional improvement' of animal feed	TALEN	**Calyxt, Inc. & S&W Seed Company Collaboration** Commercial deal with S&W Seed company	No information available on what the target gene is in APHIS application. Claimed to be a KO (SDN-1), and null-segregant with "PCR analysis" performed to check the absence of transgenic DNA (no further details or data). Trials in development with S&W Seeds, with claims of market launch in 2021. As is common for GM trials produced by private companies, no field trials have been published. No data available at all, even on 'functional proof of modification' to show target change was achieved, nor efficacy data on reduced lignin, or 'improved rates of digestion, resulting in increased milk or beef production' as stated on CBI-deleted APHIS application. It can be assumed that studies have not been performed to assess trait improvement to substantiate this claim, based on information available. No biosafety assessment of any nature appears to have been performed, based on information available. **Complete absence of basic information on the performed genetic modification, trait efficacy, or biosafety risk.** **'Market relevance' cannot be concluded based on the absence of experimental data.**

vi APHIS is the US regulory body that oversees the importation, interstate movement, or environmental release of certain organisms developed using genetic engineering that may pose a plant pest risk.
(KO) = knock-out of a gene, to destroy gene function

CROP SPECIES	TRAIT	TECHNIQUE	DEVELOPER/ REFERENCE	ENSSER COMMENTS:
POTATO	Reduced acrylamide formation to increase storage life, and reduce levels of acrylamide which is a carcinogen	TALEN	Clasen et al. (2016)	Targeted the vacuolar invertase gene (VInv). Low acrylamide potatoes already exist but are unpopular for crisps as they lack flavour and good texture. No field trial data published though they were reportedly performed in 2015 Apparently plant material is being developed for commercial launch though no indication of commercial release date appears to have been given. Initial publication claims 73 % reduction in acrylamide in fried potatoes. However, levels are mediated by variety of environmental factors storage (temperature, use of sprout inhibitors, atmosphere), and growing conditions (rainfall, temperature and mineral content) (Kumar et al., 2004), but no details were given on where plants were grown, (e.g. indoor or outdoor) for analysis. (Publication has photo of potted plants). Reducing acrylamide is irrelevant to improving food production, and is instead designed for processed potato consumption. High acrylamide levels are chosen as better suited for chips and potatoes, so 'market relevance' also questionable regarding altered trait. Such a crop has no relevance for reducing hunger. No rationale for societal need for this crop trait, which serves to entrench unhealthy, processed food consumption instead of addressing nutritional needs, food security or environmental sustainability. Absence of basic information on the performed genetic modification, trait efficacy, or biosafety risk. 'Market relevance' cannot be concluded based on the absence of experimental data.

CROP SPECIES	TRAIT	TECHNIQUE	DEVELOPER/ REFERENCE	ENSSER COMMENTS:
CAMELINA	Improved fatty acid composition	CRISPR-Cas	**Developed by Montana State University, USA and Shanxi Agricultural University, China.** Ozseyhan et al. 2018.	Targeted all three copies of the fatty acid elongase 1 (FAE1) gene for SDN-1. **The crop is still transgenic, no removal of plasmid DNA.** Developed by researchers for apparent biofuels purposes due to rising US interest as biofuel species. Trait is the reduction of 'very long chain fatty acids' (VLCFAs) that are undesirable for industrial purposes. This resulted in concomitant increase in beneficial unsaturated fatty acids, but camelina oil is already very high in these fatty acids. This project thus suggests that a healthy source of nutritional fats is being investigated for converted into industrial purposes. Camelina cultivation for biofuel is also on the rise in the State of Montana, where this research was based.

CROP SPECIES	TRAIT	TECHNIQUE	DEVELOPER/ REFERENCE	ENSSER COMMENTS:
LETTUCE	Increased vitamin C content	CRISPR-Cas	**Chinese Academy of Sciences, Beijing, China** Zhang et al. 2018	Experimental crop developed to investigate engineering of genetic regulatory elements (upstream open reading frames (uORFs) for altering gene activity. Authors do not suggest marketisation of this crop, but instead discuss avenue of engineering uORFs in future to increase the gene expression. The editing of uORFs can increase mRNA translation, thereby increasing the amounts of protein synthesized. Also tested paraquat tolerance which is increased with increased vitamin C content. Analysis of unintended effects restricted to assessing 10 predicted off-target sites in each line. No field trial data. Comment from authors on potential unintended effects: "Vitamin C intertwined in such a large number of networks (photosynthesis, flowering, ROS signaling, cell growth/division, pathogen response) and elevation of AsA levels has been shown to alter the transcription of many genes, there could be unexpected, perhaps negative, consequences to significant elevation of AsA in plants beyond the normal physiological level. Additional research is needed in this regard." **This crop was not designed for commercialisation. It cannot be described as 'market relevant'.**

CROP SPECIES	TRAIT	TECHNIQUE	DEVELOPER/ REFERENCE	ENSSER COMMENTS:
SOY	Improved fatty acid composition	TALEN	**Calyxt, Inc.** APHIS database; Haun et al., (2014).	Commercialised crop but scientific demonstration of efficacy and safety is lacking. Trials remain unpublished. Claim to have made line in a single generation, due to lack of backcrossing, ignoring the potential for on- and off-target effects. No unintended effects assessed. Only checked for lack of transgenic material by short-read PCR analysis with 3 primer sets. This is insufficient to rule out transgenic DNA presence. The crop is suffering from lack of adoption by farmers, representing only 0.084 % of soybean cultivation in 2020 in the US. **Despite being commercialised and cultivated in the US, farmer adoption failure challenges the 'market relevance' of this crop.**
WHEAT	Improved fibre content	TALEN	**Calyxt, Inc.** APHIS database. Deregulated in 2018.	Cannot find any data to substantiate any claims of efficacy or safety. Rationale for increasing fibre in wheat extremely questionable. Diversification of diets and consumption of existing high fibre crops are existing solutions can be improved, mediated by de-industrialisation of food and farming methods. No clear societal benefit to this crop trait. Field trials were harvested in 2018. ISAAA reported an expected commercial launch in 2020, but the date was to have been revised back to 2022. **No evidence of 'market relevance' at this time due to complete lack of data, and delays in commercialisation timeline.**

CROP SPECIES	TRAIT	TECHNIQUE	DEVELOPER/ REFERENCE	ENSSER COMMENTS:
WHEAT	Low gluten content	CRISPR-Cas	Instituto de Agricultura Sostenible (IAS-CSIC), Córdoba, Spain; University of Minnesota, Minneapolis, US (author also Crop Pipeline Manager at **Calyxt Inc**); Universidad de Sevilla, Sevilla, Spain. Sánchez-León et al. 2018	Experimental crop with no field trial data to assess agronomic performance. Assessment of unintended effects limited to *in-silico* analyses and short PCR tests on less than 6 predicted off-target sites. Rationale to develop low-gluten wheat questionable. They appear unsuitable for the clinically defined subgroup, See[217]: "*Gene-editing can't do everything, cautioned Calyxt's Voytas. There are limitations to how much foods could be changed. Sure, scientists made wheat containing less gluten, but it's unlikely to ever be totally gluten-free for people who can't digest that protein, for example — or to make, say, allergy-free peanuts.* " A conventional variety was recently developed, challenging the need, and purported efficiency of genome editing in this case. [218]
MAIZE	Fungus resistance	CRISPR-Cas	**DuPont Pioneer** (CRISPR patent holder) APHIS database	Complete absence of basic information on the performed genetic modification, trait efficacy, or biosafety risk. 'Market relevance' cannot be concluded based on the absence of experimental data.
MAIZE	Drought tolerance	CRISPR-Cas	**DuPont Pioneer** (CRISPR patent holder) Shi et al. 2017	Field trials performed. They state their yield results are similar to previous results obtained from transgenic plants overexpressing the same gene, yet the transgenic variety has not appeared on the market. Increased yield compared to wild type plants was observed when the plants were stressed by drought at flowering time, but not when the drought stress occurred during the grain-fill period of growth. This suggests the maize was not drought-tolerant during the most critical period of growth and is therefore unlikely to make it to the market. **No safety data to substantiate any claim of safety.** **No evidence of commercialisation to claim 'market relevance' at this time.**

CROP SPECIES	TRAIT	TECHNIQUE	DEVELOPER/ REFERENCE	ENSSER COMMENTS:
COCOA	Fungus resistance	CRISPR-Cas	Fister et al. 2018	Experimental crop with no field trial data. Proof of principle with transient transfection. **Transgenic** knock outs were grown to full plants. Unintended effects detected. Metabolic drag detected with treated tissue growing very slowly, potentially resulting from constitutively activated defence system. *Arabidopsis* study on same target gene had lower seed weight and shorter root length.[219] **This crop is astandard transgenic GMO and thus cannot currently be described as 'market relevant GE-crop'.**
SOY	Drought tolerance	CRISPR-Cas	**USDA-ARS, USA** APHIS database	No data available to substantiate any claims of efficacy, safety or market relevance. No field trials published.
TOMATO	Bacterial resistance	CRISPR-Cas	**University of California, Berkeley, US.** Thomazella et al. 2016	Experimental crop with no safety or field trial data. Non-significant decrease in plant height. **There appears to be no peer-reviewed version of this publication. Claims of 'market relevance' premature.**
RICE	Fungus resistance	TALEN	**Iowa State University, USA** APHIS database	Complete absence of basic information on the performed genetic modification, trait efficacy, or biosafety risks. **'Market relevance' cannot be concluded based on the absence of experimental data.**
RICE	Salt tolerance	CRISPR-Cas	Duan et al. 2016	Experimental crop ONLY. Transgenic. Not a crop, but a basic research experiment where genetic elements were introduced into a plant as transgenes, to assess potentially their useful functions in salt adaptation. Transgenes were later modified with CRISPR to assess roles of genetic elements within the target gene. Claims of 'market relevance' are scientifically nonsensical.

CROP SPECIES	TRAIT	TECHNIQUE	DEVELOPER/ REFERENCE	ENSSER COMMENTS:
WHEAT	Fungus resistance	TALEN	Chinese Academy of Sciences, Beijing, China Wang et al. 2014	Experimental crop with no field trial data. Only tested infection with mildew in controlled environment. No assessment of unintended effects. Questionable rationale considering conventional variety already developed.[220] No data to substantiate any claim of safety or efficacy. No evidence of commercialisation to claim 'market relevance' at this time.
BANANA	Fungus resistance	Transgenic crop. No 'genome editing' technology used	Queensland University of Technology, Australia; Darwin Banana Farming Company, Australia; Wageningen University, The Netherlands Dale et al. 2017	Standard transgenic crop. Nothing to do with genome editing. The inclusion of this transgenic crop in the statement is an error and it should be removed.
CASSAVA	Virus resistance	CRISPR- Cas	University of California, Berkeley; Donald Danforth Plant Science Center, St. Louis, MO, USA Gomez et al. 2019	Transgenic crop. Field trials performed. Off-target effects detected in analysis of 5 off-target sites only. Difficult to remove transgene as cassava is propagated by cuttings.

Another major issue for 'genome editing' that negatively impacts efficiency is the serious major bottleneck created by the need to regenerate whole plants from a few transformed cells (Ahmed et al., 2018; Yin et al., 2017). Tissue culture simply does not work for many plant species (Gao, 2018). In addition, the success of targeted 'genome editing' relies on precise knowledge of a gene and its function and the type of DNA modifications required to produce the desired characteristics in the organism. This knowledge is often lacking, leading to a scarcity of validated targets (Ahmed et al., 2018). The claim that market or legal parameters are the cause of GMOs thus far being restricted to a few staple crops, ignores or diverts the attention from these technical reasons that only a few species are currently amenable to 'genome editing'.

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False arguments for changing EU legislation

Set out above is the evidence contesting claims of safety, efficiency, speed and indistinguishability of so-called 'genome editing'. The Leopoldina Statement makes additional arguments in calling for regulatory changes. One such additional argument is that regulations have held back innovation of existing GMOs and now 'genome editing', stating that "*further development of sustainable agriculture in Europe is considerably obstructed by the particularly restrictive, undifferentiated and time and cost-intensive approval processes for molecular breeding products. The absence of certain innovations also poses costs and risks for humans, nature and the environment*".

As detailed above, even countries with permissive regulations are not commercialising many crop products, if any, and none without which 'sustainable agriculture in Europe' (or elsewhere) would be 'obstructed'. Deregulation removes scientific practices from decision-making processes, leaving safety and efficacy of products to the markets, consumers and social policy. With genetic engineering and synthetic biology technologies evolving rapidly, it is the responsibility of scientists to advocate for oversight and resume responsibility for the safety of their products.

The authors also claim that conducting field trials is hindered by regulatory transparency that requires information to be shared on the location of trials, resulting in vandalism. Considering that it appears that there have been 80 documented instances of vandalism but over 3220 trials (around 2690 plant trials) conducted since 1991, fear of vandalism can hardly legitimate the authors' claim that trials are '*almost impossible*' (EC GMO register)[221].

Deregulation removes scientific practices from decision-making processes, leaving safety and efficacy of products to the markets, consumers and social policy

With regard to definitions, the Statement includes a tabulation of definitions from the EU as well as the international guidelines of the CBD's (UN Convention on Biological Diversity) Cartagena Protocol on Biosafety (CPB). This table claims that international guidelines likely place 'genome edited' crops outside of the definition of a GMO (called LMO, living modified organism, in CBD). However, this is inaccurate and goes against the legal and scientific understandings of the Protocol[222]. Thus, the Statement attempts to give a false impression of a lack of alignment of current EU regulations with the CPB, which is the gold standard of international guidelines of GMO regulations that have been ratified by over 170 countries[vii] worldwide.

The Leopoldina Statement also argues that smaller companies are forced out of the market by the EU's restrictive legislation. However, with the patenting of CRISPR methods, it is unclear how changing the EU legislation would increase market entry for smaller companies. Even though the CRISPR ingredients may be easily and cheaply available, it still requires a fully equipped molecular biology laboratory with all its expensive equipment (-80°C freezers, other storage facilities, equipment for DNA, RNA and protein analyses, tissue culture facilities, etc.), expensive infrastructure (such as fully controlled climate cabins, secure and fully climate controlled greenhouses) and, more importantly, highly skilled and educated expert scientists to explore, genetically engineer, reconstitute, test and multiply novel 'genome edited' organism. This will be hardly 'cheap' and 'easy' for small breeding companies and will almost always require bigger partners with bigger stakes in the business. Further, the authors speculate (naïvely) that because the patent holders are research institutions, they would be 'more generous' than private companies in licencing the technology to smaller companies. This assertion stands in contrast to the decade long, fierce and expensive patent battles that have taken place for the technology between the competing inventors[223]. They hardly fought these costly battles and (co-)founded highly valued start-up biotech companies to hand out their inventions and patented tools as charity gestures to small companies[viii]. As further evidenced in Table 1, crop development in the US, where the much applauded deregulation model is applied, are still dominated by corporations (including DuPont Pioneer, a leading CRISPR patent holder), and not research institutions.

Further, the authors speculate (naïvely) that because the patent holders are research institutions, they would be 'more generous' than private companies in licencing the technology to smaller companies. This assertion stands in contrast to the decade long, fierce and expensive patent battles that have taken place for the technology between the competing inventors. They hardly fought these costly battles and (co-)founded highly valued start-up biotech companies to hand out their inventions and patented tools as charity gestures to small companies

vii https://bch.cbd.int/protocol/parties/

viii https://www.forbes.com/sites/johncumbers/2020/10/06/jennifer-doudnas-new-gene-editing-company-launches-with-a-20-million-round-to-develop-genetic-medicines/; https://www.synthego.com/blog/crispr-startup-companies#caribou-biosciences-using-crispr-to-impact-several-industries

Failed reductionist GMO paradigm masks alternative solutions

The unreferenced and undefined claim of 'science-based breeding' being responsible for the 20th Century gains made in decreasing hunger reveals an ignorance, wilful or not, of food system advances that have taken place outside the paradigm of the 'science-based' breeding realm as imagined by the authors. Indeed, it is smallholder farmers that produce the vast majority of the world's food[224]. Agroecological production systems, based on a diversity of scientific and agricultural knowledge-systems and farmer practices, are advancing yields and biodiversity, outside of the realm of 'molecular-breeding' methods (see below). The value of crop breeding outside of the molecular science domain is indeed implicitly acknowledged by many GMO developers, who rely on existing elite germplasm for breeding, and the search for useful genetic traits that can be exploited by genetic engineers. One of the current bottlenecks in the generation of new traits, is the identification of genes that may confer traits of interest. Data mining of existing global seed biodiversity is occurring to search existing varieties for genes of interest, that have grown and evolved in the hands of farmers for hundreds and thousands of years[225], in what civil society organisations have referred to as epitomising the digital age of biopiracy[118].

The unreferenced and undefined claim of 'science-based breeding' being responsible for the 20th Century gains made in decreasing hunger reveals an ignorance, wilful or not, of food system advances that have taken place outside the paradigm of the 'science-based' breeding realm as imagined by the authors. Indeed, it is smallholder farmers that produce the vast majority of the world's food

Indeed, a series of expert consensus reports come to the same conclusions and have called for a rapid shift from input-intensive industrial agriculture, to agroecological farming methods[226,227,133]. A growing body of published science shows that farmers who rely on ecological methods for pest management instead of pesticides can meet or outperform their conventional counterparts in terms of yield and profits[228,229,230]. Agroecological outcomes in low-income countries have also documented 80% higher total (system) crop yields when systems are diversified, compared with conventional monoculture systems[133]. A 2007 study also reported 80 % increase in yield with organic over conventional agriculture[231], though more studies would be useful and

A growing body of published science shows that farmers who rely on ecological methods for pest management instead of pesticides can meet or outperform their conventional counterparts in terms of yield and profits

should be encouraged and publicly funded.

These successes have been obtained despite persistent underfunding or outright negligence of agroecological successes by government funding schemes[232]. Huge investments have gone and continue to go into GM research in the EU, far outstripping that for alternative pathways for food production, such as agroecology[233],[232]. A pitiful fig-leaf amount of funds goes into moving the science forward in organic production systems and agroecological approaches[234]. The asymmetrical funding situation cannot be overstated and could not be more extreme with single digit fractions of overall funding budgets flowing into organic and agroecological innovations. The current technology-focused research agenda is exaggerating the speculative delivery of effective 'genome editing' solutions, which can lead to opportunity costs for effective alternative solutions that are being neglected. Indeed, the experiences with first generation GMOs exemplify the limitations of the genetic reductionist paradigm in addressing complex issues such as drought-tolerance or pest resistance, which cannot be achieved by single or even multiple single-gene fixes. Indeed, at least 60 genes have been linked to drought tolerance, further mediated by environmental conditions[235], making any functioning and sustainable genetic engineering solution highly unlikely.

Huge investments have gone and continue to go into GM research in the EU, far outstripping that for alternative pathways for food production, such as agroecology

Citizens are increasingly concerned and vigilant about destructive food production systems. Wider scale adoption of transformative policies is required that harness the agroecological principles of ecology, as well as food and nutrition security, food sovereignty and justice by encouraging local production by small food producers through diversity of farmer knowledge and innovations.

The experiences with first generation GMOs exemplify the limitations of the genetic reductionist paradigm

The asymmetrical funding situation cannot be overstated and could not be more extreme with single digit fractions of overall funding budgets flowing into organic and agroecological innovations

The EASAC-endorsed Leopoldina Statement implicitly supports a business-as-usual approach as current farming systems are not questioned, but instead portrayed as a success. Portraying genetic engineering as a key solution to fixing what the authors refer to as the 'excessive use of pesticides' or climate change serves merely as attempts to deflect attention away from the fundamental flaws of industrialised agriculture and its role and responsibility as one of the most significant drivers behind the destructions the authors now claim to address with yet another techno-fix owned and promoted by the very same pesticide industries, paying lip service to public concerns with notions of 'climate-smart' agriculture, 'sustainable' or 'ecological- intensification', or indeed the industrialised production of organic agriculture. Fundamentally, the report's claim that "Scientists largely agree that molecular breeding techniques are needed" to deal with pesticide use and climate change, does not hold up under basic scrutiny and begs the question: What scientists working in which fields and for what purpose?

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Conclusions

The analysis of existing scientific literature clearly demonstrated the failures of existing GM crops to address chronic under-nutrition or environmental needs. GM crops have suffered from lack of trait development, declining efficacy and the manifestation of a variety of health, environment and socio-economic risks. Nonetheless, the Leopoldina Statement has entirely failed to recognise the wealth of evidence we have compiled above and, instead, proclaims their success and safety based on either no evidence or scant, mainly self-referential evidence. This has now been adopted as a founding argument for 'genome editing', which is asserted to be *even more safe*. While the authors like to present their recommendations as based solely on scientific rationale, their objectives simultaneously align with those of agrochemical corporations and other corporate players in the agro-food sector.

The evidence of risk associated with both existing and 'genome edited' GMOs serves to show the importance of EU legislation in protecting against their failures and harms. Nonetheless, the Leopoldina Statement proposes various (contradictory) forms of deregulation in order to usher 'genome edited' organisms into the EU. Short-term proposals are suggested to deregulate SDN-1 and -2 applications, in what is described as a US-style deregulation system, with the unsupported claim that such technologies are indistinguishable from conventional breeding. However, longer-term regulatory changes akin to the Canadian-style regulation system, where 'novelty' of a trait is the regulatory trigger, are proposed for all GMOs. This results in contradictory proposals of a trait-based Canadian system, but with process-based exceptions for 'genome editing' while denouncing the same process-based EU regulation system as unscientific. And it does not at all question the process-based patenting system centring on 'genome editing' methods.

An urgent shift away from a single-minded funding bias into genetic engineering is needed, towards solutions that work in unison to combat nutritional needs, food security, and environmental sustainability in a way that uplift the population of Europe, and appreciate and include farmer knowledge and practices that sustain us

EU governance has thus far insulated the region from such risks and some opportunity costs, and can instead focus on real holistic solutions for the real problems that the EU and wider world face. An urgent shift away from a single-minded funding bias into genetic engineering is needed, towards solutions that work in unison to combat nutritional needs, food security, and environmental sustainability in a way that uplift the population of Europe, and appreciate and include farmer knowledge and practices that sustain us. Balanced, nuanced and rigorous inquiry of claims and evidence is what is needed if Europe wants to stay at the forefront of innovation and progress.

ANNEX 1. A SUMMARY OF CLAIMS MADE IN THE EASAC ENDORSEMENT AND LEOPOLDINA STATEMENT.

UNSUBSTANTIATED CLAIMS IN LEOPOLDINA AND EASAC STATEMENTS	FACT CHECK OF CLAIMS:
"*Science-based plant breeding and other agricultural technologies, such as chemical fertilisation and chemical crop protection, have since contributed to continuously increasing agricultural yields, combating regularly occurring plant diseases and pests and thus decisively improving the supply of foodstuffs and thus food security. While at the beginning of the 20th century well over half of the world's population still suffered from insufficient food supplies, the proportion of starving people has now been reduced to around 10%, even though the global population has more than quadrupled in this period*".	Hunger is fundamentally an issue of economics and distribution, tied to poverty, social-exclusion and other (political) factors. While single-crop 'productivity' has increased in industrialised systems, this has not translated into food security. Record levels of cereal grains were produced in 2016, but hunger and malnutrition persist because an increased food supply alone is not the solution to hunger or malnutrition. In the US, where single-crop productivity is high, and GMOs are widely cultivated within an industrialised system, 37 million people were reportedly food insecure in 2019. Political changes including the collapse of colonial systems has also contributed to reductions in global hunger.
'*the value of genome editing technologies, or GMOs, because this value is already demonstrable*' "*there is not a single documented case concerning the widespread use of permitted transgenic GMOs in which unexpected environmental or health consequences for humans or animals occurred.*"	Existing GM crops do not display proven yield benefits. The vast majority of insect resistant crops have lost protection due to insect resistance, and were proposed for phase out in the US in 2020. Insect resistance has also exacerbated farmer indebtedness in India, who are now paying more for chemical protection. Burkina Faso phased out insect resistant cotton due to agronomic problems that reduced cotton quality and farmer incomes. Herbicide resistance is also reducing efficacy of herbicide-tolerant crops. While efficacy is not clearly demonstrable, unintended effects are widely established, including promotion of chemical use linked to environmental damage and ill health. Complex traits designed to combat societal problems such as drought and nutritional deficiencies have not materialised. Drought tolerant maize trials in South Africa showed no benefit over conventional varieties. Golden rice benefits remain questionable. Contamination of non-GM crops has had adverse biodiversity and economic consequences. Despite huge research and investments into GMOs, good quality traits are still lacking.

"there is scientific consensus that particularly plants genome edited with SDN-1 and SDN-2 can be equated with products of traditional random mutagenesis breeding in terms of their risk potential and continue to carry significantly fewer off-target mutations." "*genome edited plants are equivalent to products of traditional breeding and even carry up to 100 to 1000 fewer unwanted (off-target) mutations than plants produced with traditional mutagenesis breeding*", offering "*high precision and efficiency using the cell's own repair systems*". "*Unlike chemical- or radiation-induced mutagenesis, often traditionally used for crop improvement tools, the new breeding techniques do not create multiple, unknown, unintended mutations throughout the genome. Furthermore, the products of the new breeding techniques are also unlike genetically modified organisms (GMOs) used in agriculture, in being more precisely targeted and having no foreign DNA in the end product.*"	Current evidence suggests that genome editing can lead to various unintended effects, including off-target mutations and on-target unintended changes such as unintended insertion of DNA, and large-scale genetic deletions and rearrangements. The array of unintended effects challenges claims of precision. Unintended integration of genetic material also challenges the assumption that transgenic organisms are not generated with genome editing SDN-1 and -2 applications. Crucially, both intended and unintended changes can differ from those arising in conventional and random mutagenesis. Genome editing can perform deeper interventions than random mutagenesis. For example, it allows for the modification of many genes simultaneously, modifying all copies of a single gene, and modifying regions of the genome ordinarily protected from novel mutations. Further, repair mechanisms deployed by the cell differ following mutations arising from genome editing, with erroneous repair mechanisms deployed to repair DNA breaks induced by editing machinery, leaving behind distinct changes to the genome. Unintended effects of genome editing are undisputed in the medical research arena, acknowledging genetic damage and potential for illnesses such as cancers to arise. Such risks cannot be ruled out for genome edited plants and animals, where unintended effects may alter the composition of plants and thus safety and agronomic performance, or animals which may suffer unintended effects such as cancers. Such evidence challenges any claims of scientific consensus on safety, precision and equation to conventional breeding techniques.

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