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A new chance for genome editing in Europe

European universities and research institutions helped to pioneer the development of key technologies for the genetic engineering of crops[1]. Despite its early leading role, Europe has largely resisted the use of modern genetic technologies in agriculture. The combined implementation of an unofficial moratorium on the cultivation and import of transgenic genetically modified organisms (GMOs) (1998–2004) and a strict approval process for transgenic GMOs established by a 2001 European Union (EU) directive[2] has severely constrained innovation by both the public and private sectors in the past decades. The hurdle of restrictive GMO regulation created a situation in which many larger corporations and enterprises have relocated their R&D efforts to places and markets more open to technological innovations. At the same time, small and medium-sized enterprises (SMEs) and public research institutions had little prospect of seeing their GMO research reach the field. This discouraged translational and applied research in this area and also prevented the rigorous testing of scientific hypotheses with field experiments.

The opposition to crop genetic engineering has been mostly fueled by misguided fears of potential toxicity to humans and animals, as well as environmental risks caused by the integration of DNA from other species into crop genomes. Therefore, the emergence of technologies for genome editing[3] without the use of exogenous DNA has opened new discussions about crop genetic engineering. Notably, such improved genome-edited crop varieties are often indistinguishable from varieties obtained by classical breeding. The adoption of these editing methods led scientists in Europe to speculate that they might be freed from the strict regulatory framework that transgenic plants were subjected to under Directive 2001/18/EC on the release of GMO plants[4]. However, the 2018 judgment[5] of the European Court of Justice dashed these hopes with a very narrow interpretation of the 2001 Directive, concluding that genome-edited plants, even if they had no exogenous DNA in their genomes, must be subject to the same restrictions as transgenic GMOs. As existing regulations for transgenic GMOs are accompanied by extremely high compliance costs, a similar scenario was feared for new genome-edited plants[6–8].

Fortunately, the European Commission (EC) has recently proposed a new, more liberal law to govern the cultivation of plants created using new genomic techniques (NGT), most prominently, genome editing[9]. Compared to current rules, the new law relies more on published scientific evidence, opening the possibility to register genome-edited plants as varieties that would be exempt from the regulations for transgenic GMOs through the introduction of two plant categories. Category 2 includes plants with more extensive genetic modifications and is subject to similar rules to current transgenic GMOs, while Category 1 crops, classified as plants with genomic modifications that closely resemble conventionally bred varieties, would have a lower regulatory threshold. The technical specifications for Category 1 largely align with those already used by other countries, such as Argentina and Australia, and this would promote more consistent regulation internationally. This hope is supported by recent reports from Argentina, where a case-by-case approach to determining whether or not a plant product derived from genome editing should be considered a transgenic GMO has indeed led to a surge in genome-edited products developed and registered by local SMEs and public research institutions[7].

However, as with any legislation, the devil lies in the details. Unlike other countries that have adopted rules for genome-edited plants, the EC proposes an exception for organic agriculture. The EC seeks to define organically produced genome-edited plants differently, categorizing all organic genome-edited plants without exogenous DNA (Categories 1 and 2) as regulated GMOs. This is in line with the "principle of coexistence" previously implemented by the EU to prevent the presence of transgenic plants in organic fields[10]. We are concerned about this aspect of the EC's proposal because it is both confusing and not based on scientific fact. Suggesting that some genome-edited plants are non-regulated GMOs for conventional producers but regulated GMOs for organic farmers creates regulatory uncertainty. For example, there is no clear mechanism or framework for dispute resolution in cases where an organic producer finds their systems 'contaminated' with seeds or plants that are defined as GMO for them, but classified as Category 1 non-regulated plants for non-organic producers and seed companies. Furthermore, defining genome-edited plants as regulated GMOs for organic farmers and consumers discriminates against members of the organic and agroecology movement who embrace the use of genome editing for sustainable agriculture.

Another seemingly arbitrary clause in the proposed legislation relates to the engineering of herbicide tolerance. We welcome the fact that this is, in principle, a step in the right direction, moving from process-based to trait- or product-based regulation. However, herbicide tolerance can be valuable when used judiciously by farmers because it may help to improve soil health and reduce carbon emissions through no-till farming[11,12]. This trait can be engineered not only by conventional transgenesis and genome editing, but also through spontaneous or induced mutations. Not only are plants arising from the latter already being deployed in the EU – for example, for sugar beet[13] – but the EU has also funded research projects for the generation of non-GMO herbicide-resistant varieties for other crops[14]. The EC proposal excludes herbicide-tolerant plants from reduced regulatory hurdles, even if these plants resemble conventionally bred ones. In other words, gene-edited herbicide-tolerant plants have increased regulatory burden compared to gene-edited plants with other traits, although they have a comparable scale of genomic edits. Presumably, this exclusion is based on the intense political opposition to the use of certain herbicide-tolerant plants, especially glyphosate-resistant ones[11,12]. It is illogical to penalize herbicide-tolerant plants generated by genome editing while permitting their conventionally bred counterparts. In some species, herbicide tolerance is also used as a tool to successfully select gene-edited plants during the development process. The EC fails to acknowledge these alternative applications of herbicide tolerance, and we fear that an overly rigid approach in this regard might restrict the use of genome editing techniques. The threshold of 20 nucleotides that can be replaced or added appears seemingly arbitrary as it is apparently based

on observations made in natural populations of the model species *Arabidopsis thaliana* that revealed only limited sequence variation because of technical constraints with early sequencing technology[15]. The use of genome editing in other plant species that might differ in their genomic variation and the combination of several editing events will probably require further clarification and possible expansion of the 20-nucleotide threshold. It is also unclear whether this refers to separate instances of genome modification – for example, 20 single-base-pair changes – or whether changes of up to 20 consecutive nucleotides are included.

Lastly, the proposal mandates the notification and labeling of NGT plants or the reproductive materials used to produce them. However, it remains unclear how such labeling rules can be effectively enforced, as Category 1 plants can have edited genomes that are not easily distinguishable from genomes of conventionally bred plants. While the desire to promote transparency through labeling is understandable, the legislation does not ensure that labeling or mislabeling can be adequately verified, thereby imposing undue risks on breeders and seed producers.

We welcome that the EC has made efforts to facilitate the rapid adoption of gene editing by SMEs with the new proposal because it is expected that the Category 1 plants will be released with a significant reduction of the compliance costs as compared to GMOs under the 2001 Directive. The new NGT Regulation also recommends that member states offer incentives such as fee waivers to help them to gain authorization for their varieties. This focus deserves recognition, as adapting European agriculture to climate change will increasingly necessitate technological solutions tailored to local and regional challenges. A robust network of technologically advanced SMEs is more likely to drive investment, development and distribution of crop traits, promoting sustainability in locally adapted, consumer-preferred varieties. However, arbitrary rules such as conflicting definitions of Category 1 genome-edited plants for conventional and organic agriculture pose a threat to the development of such an SME network and could again favor large multinational corporations. During preliminary discussions at the European Council[16], some member states have asked for the ability to ban the cultivation of specific NGT plants in their territories. Such country-specific bans will not be easily enforceable for many Category 1 plants. Moreover, this may lead to further inequities in productivity within European agriculture and disincentivize research and innovation.

An important concern is that the new legislation will have impacts beyond European borders, namely for all who are involved in agricultural trading with the EU. For instance, the export of fresh fruits, vegetables, tobacco, cocoa, coffee, tea, processed agricultural goods and flowers to the EU from Africa has risen rapidly in the past two decades[17], with a concomitant increase in the participation of small-scale African farmers in horticulture for export[18]. African governments have a vested interest in maintaining this source of much-needed foreign currency, and therefore they tailor their own biosafety and export legislation, if any, to avoid conflict with EU requirements. At first glance, the EC proposal is a welcome development for governments such as those of South Africa, Kenya, Nigeria and Egypt, who have already legislated in favor of the commercialization of crops created with modern genetic technologies. In fact, if the proposed legislation becomes law, these countries can easily pivot to using genome editing for the mutual benefit of their European trade partners. More importantly, countries that have so far been reticent to adopt or have outright banned genome-edited crops now have an incentive to change course for their own economic benefit. However, for the small-scale farmers exporting their organically grown produce to Europe, such as Zimbabwean blueberry farmers, the new proposal, if it becomes law, means that they will have to forgo the benefits of genome editing as they need to maintain their EU market. One likely scenario is that African governments may seek to maintain their foreign currency income from agricultural produce by enacting blanket legislation against genome-edited crops, as they have done in the past against transgenic GMOs[19], thereby affecting the adoption of improved varieties of important local staples such as maize, cassava and rice.

In conclusion, we find much to appreciate in what will hopefully be only the beginning of a more scientifically sound approach to genetic technologies in EU agriculture. By embracing genome editing, European breeders and seed producers be in a better position to develop not only more sustainable and resilient crops, but also crops, especially vegetables, with immediate consumer benefits, such as improved nutritional value[20]. Given its global economic importance, the policies of the EU may have long-term impacts on other countries trading with the EU. Therefore, we must caution against using unscientific criteria to impede the technology's progress in organic production and creating barriers for specific applications of genome editing. By doing so, the EU risks getting caught up in the unproductive scientific debates that have characterized the discussions around GMOs for 30 years. We appeal to EU legislators: prioritize scientifically informed decision-making over arbitrary rules that hinder innovation.

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D.W. holds equity in Computomics, which advises plant breeders. D.W. also consults for KWS SE, a plant breeder and seed producer with activities throughout the world. All other authors declare no competing interests.