

Statement on the regulation of gene editing for crop breeding

The possibility to introduce targeted genomic changes through site-directed nucleases platforms or prime editors (i.e. gene editing) has revolutionized the research on the genetic basis of biological processes and has also opened the door to a wide range of applied uses. Among them the use of gene editing for plant breeding has been one of the fastest to be developed. This is in part because gene editing in plants does not raise the ethical questions that its use in animals, and in particular in humans, raises, but also because of the high potential these techniques have to improve, facilitate and accelerate plant breeding.

Humans have continuously selected those plants or combined different species to obtain plants better adapted to their needs since Neolithic times and plant breeding has allowed the successful improvement of crops that are the basis of world food production. The changes introduced in traits such as plant architecture, requirements for optimal growth, fruit size and composition and flowering time, are so important that cultivated plants could be considered as human inventions. Plant breeding relies on the use of available gene variants to introduce desired traits into cultivated varieties. Breeders have always used the best science to maximize the variability they can use, expanding the available gene pool to related species that are not spontaneously interfertile and, since the middle of the last century, inducing additional random mutations with physical or chemical agents. Random mutagenesis has been widely used and there are thousands of plant varieties derived from these techniques available in our markets (1). However, these techniques require the genetic screening of large mutagenized populations to search for the desired mutation, and a process of breeding out the undesired mutations that is long and tedious, and frequently incomplete. This is even more difficult for polyploid crops, where several gene copies have to be mutated to result in a new phenotypic trait. In addition, the randomness of these techniques makes it difficult to obtain new traits that require the introduction of precise genetic changes. Against this background, the possibility that gene editing technologies offer the selective introduction of precise nucleotides changes, constitutes a real advancement in the field. The genomic changes introduced are of the same nature than the ones resulting from spontaneous mutations or random mutagenesis and therefore, in general, no additional risks are foreseen linked to the process of gene-editing

The first products obtained from gene-edited crops reached the US market in 2019, and there are already an important number of crops approaching approval in different countries and that will reach the market soon. However, as it has already happened in the past with other biotechnology innovations in crop breeding, such as the use of transgenic plants, the development of gene-edited crops is not progressing at the same pace worldwide.

Although the commercialization of gene-edited crops requires a notification through a process that differs from country to country, and many of them decide on a case-

-by-case basis, most processes do not require an extensive safety analysis of plants containing only few nucleotide changes. This is the case of Canada and USA but also of Argentina, Brazil, Australia, Japan and India among others (2).

In the European Union (EU), discussions among Member States to decide on the legal status of gene-edited crops started as early as 2008, but no consensus on the regulation of gene-edited crops was reached. Following a request of different French organizations, the European Court of Justice (ECJ) issued a ruling on July 2018, which consider that the GMO Directive 2001/18/EC is also applicable to organisms obtained by mutagenesis techniques that have emerged since its adoption. As a consequence, and in contrast with the procedure for randomly mutagenized plants, gene-edited crops would have to follow the long and expensive GMO risk assessment process as a pre-requisite for commercial approval. This decision has generated an intense debate among scientists and stakeholders. First, there is the claim that these costs will seriously limit these techniques to high commercial value traits developed by big-enough companies that can afford the high costs associated with the approval process. Among the scientific community there is also the concern of the lack of scientific basis justifying regulating different mutations obtained by random mutagenesis or gene-editing that are similar or actually identical. Notably, the GMO EU Directive 2001/18/EC requires the development of a specific detection method for each GMO as a pre-requisite for approval, which, as mutations introduced through gene-editing are indistinguishable from spontaneous mutations, renders the GMO EU Directive 2001/18/EC impossible to apply, as such, to gene-edited crops.

For these reasons, the Group of Chief Scientific Advisors of the Scientific Advice Mechanism of the European Commission recommended revising the existing GMO EU Directive 2001/18/EC to reflect current knowledge and scientific evidence, in particular on gene editing and established techniques of genetic modification (3). There is ample consensus in the scientific community that the GMO legislation is not fit-for-purpose. For example, ALLEA, the European Federation of Academies of Sciences and Humanities, which represents more than 50 academies from over 40 EU and non-EU countries-, considers that continued policy restrictions may hamper the selection of more productive, diverse, and climate-resilient crops with a reduced environmental footprint, and urges for a revision of the legal framework that considers both potential benefits and risks (4).

As a first step to redefine the legal status of gene-edited crops in the EU, the Council of the European Union requested on October 2019 the European Commission to submit a study to clarify the situation and propose a possible way out by April 30 2021.

European scientists and stakeholders are waiting for this study to be published and the EU-SAGE network, representing researchers from 133 leading European plant science institutes and learned societies have recently sent a letter to the President of the European Commission and to several Commissioners that points to the need that the study will promote a proportionate, non-discriminatory regulatory status of genome-edited crops under Union law and to the requirement of an internationally

harmonized approach to the regulation of gene-edited crops (5).

ARRIGE is an international non-governmental organization that promotes the development of genome editing technologies within a safe and ethical framework for individuals and for our societies. ARRIGE agrees with the content of the EU-SAGE letter and advocates for a proportionate and science-evidence based regulation, which focuses more on the characteristics of the final product and less on the technique used to develop it. This decision does not only affect the EU, but it may also have impacts on international trade and cooperation with developing countries, and very likely, also on the EU research and innovation landscape. This regulation should ensure the safety of the products while facilitating the use of gene-editing to help breeding the best possible crop varieties needed for a sustainable and equitable food production in the context of global population growth and climate change.

Statement promoted by the ARRIGE Scientific Committee and endorsed by ARRIGE

8 April 2021

References

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2. Menz J, Modrzejewski D, Hartung F, Wilhelm R, Sprink T. Genome Edited Crops Touch the Market: [A View on the Global Development and Regulatory Environment](#). Front Plant Sci. 2020 Oct 9; 11:586027
3. Statement by the Group of Chief Scientific Advisors. [A Scientific Perspective on the Regulatory Status of Products Derived from Gene Editing and the Implications for the GMO Directive](#), 13 november 2018
4. [Academies' report reviews debate on genome editing for crop improvement](#). 29 October 2020
5. [EU-SAGE letter to the President of the European Commission and to several Commissioners](#), February 2021