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EU rethinks genome editing

The proposal by the European Commission for new rules on gene-edited plants aims to align legislation with new developments in biotechnology. Yet concerns remain that have to do not only with biology.

While mutation breeding has been in use since the 1930s, and the risks of recombinant DNA technology were scientifically discussed during the Asilomar Conference in 1975, the public GMO debate started in the late 1970s over philosophical rather than biological questions. In their 1977 book *Who Should Play God?*, Jeremy Rifkin and Ted Howard[1] asked whether gene modification is a line that humans should not cross. To suggest that modifying wood for the purpose of ship or house building crosses such a line would seem too much of a challenge to human nature, although the effects of deforestation and historic fires clearly associate risks with such traditional technologies. However, while the modification of materials such as wood generates little contention, there seems to be a culturally inherent sanctity around information, including genetic information, such that anything that attempts to change it appears heretical. Yet the very nature of information is adaptability; in the wrong context in an ever-changing world, it would quickly lose its function.

EU regulation 1829/2003 on genetically modified food and feed[2], which is still in place twenty years after it was introduced, is based on the assumption that genetic modifications can be identified and traced to their sources. Today, the toolkit that allows us to modify genomes has dramatically expanded, and it has become evident that the legal framework from 2003 is no longer appropriate to classify modifications that are not easily traceable. Numerous countries, including the UK, have already adapted legislation to take account of such new developments; and recently, the European Commission proposed changes to the rules regarding genetically modified plants[3]. According to this proposition, genetically modified plants that were created with new genomic techniques (NGTs) should be divided into two categories. While category 2 plants should remain under current GMO legislation, category 1 plants should be exempted from GMO legislation because the modifications could, in principle, originate from natural mutation or conventional breeding, making unambiguous traceability impossible. The definition of category 1 plants is specified in Annex I of the proposal[3]. It shall contain plants with deletions or inversions of any number of nucleotides, as well as any insertions as long as no endogenous gene is disrupted and the inserted DNA already exists in the breeder's gene pool. Any other insertions should not be longer than 20 nucleotides, as longer sequences are statistically unlikely to occur randomly in large genomes. A random sequence of 20 nucleotides should statistically occur once in a genome of 10^{12} nucleotides, and large crop genomes come too close to this range to unequivocally determine a foreign origin of any sequence of this length or shorter.

For broad public acceptance of this proposal, it is critical to reflect on the definition of the term GMO. It can be defined either on the level of the production process (for example "A genetically modified organism (GMO) is an animal, plant, or microbe whose DNA has been altered using genetic engineering techniques"[4]) or on the level of the resulting product ("Genetically modified organism (GMO) means an organism […] in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination"[5]). Category 1 plants are still GMOs according to the first definition but not according to the second definition, which forms the basis of EU law. If a GMO is defined on the level of the production process, then category 1 plants pose a threat to markets that have developed around a 'GMO-free' label, as possible contamination is not sufficiently traceable to the production process.

In fact, very similar problems exist in completely different markets. For example, the jewellery market is based on the assumption that jewels are rare and hence valuable. When technology allows the production of cheap synthetic jewels that cannot be distinguished on the level of the product from the natural ones, then the risk of 'contamination' of high-priced natural jewels poses a threat for the market if the synthetic ones cannot be traced to their artificial origins. Here, just as in the GMO debate, the differences that are relevant for the market lie in the production process and not the final product.

The term GMO is prone to give the erroneous impression that organisms contain a stable and well-defined genetic code relative to which a GMO is genetically modified. This is of course not the case, as all genomes are modified relative to each other. The fear that a targeted genetic edit could be less safe than the same one gained in a random process, such as mutation as a result of radiation or chemical treatment of germline cells followed by selective breeding, is difficult to justify scientifically. The idea behind breeding is to optimize traits, and this is always based on genetic modification, be it naturally over a very long period, artificially via mutation breeding followed by selection of the desired modifications, or by direct introduction of these desired modifications by genome editing. If the resulting products are principally the same, then there should be no difference on the level of product safety.

Generally, risk assessment should be complemented by an opportunity assessment, as in many cases the opportunity to obtain climate-resilient crop varieties in a timeframe that keeps pace with climate change greatly outweighs the risks. Genome editing may also result in crops with traits that reduce dependency on large quantities of fertilizer and pesticides, thereby supporting efforts to reduce eutrophication and environmental pollution. Such beneficial traits that have been achieved through genome editing are collected and made publicly available by the European Sustainable Agriculture through Genome Editing (EU-SAGE) organization, which represents scientists from numerous plant science centres in Europe.

Finally, there is a justifiable fear that multinational companies could be implementing genome editing with the aim of patenting plant products rather than the applied techniques. According to current EU legislation it is possible in principle to patent genome-edited plants, but the procedure for a potential patent infringement would require traceability[6]. If an edited plant is indistinguishable from one that could have originated naturally or by conventional methods, the idea of a patent

on the product rather than the production process is counter-intuitive. This is even more the case if edited plants can outcross, making it very difficult to trace back any potentially patented origins.

The EU should be commended for attempting to tackle the question of genetic modification and editing in a more scientific way. However, fears that persist in wide sections of the population are not necessarily restricted to this scientific basis. As long as the broad public does not agree on the definition of a GMO, markets based on a GMO-free label will try to defend their grounds against any technology. And farmers will fear the effects of patent restrictions as long as patent law is not incorporated in an adequate way.

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