

EASAC Statement on New Breeding Techniques

Summary

New Breeding Techniques are emerging rapidly from advances in genomic research, for application in crop improvement. They enable precise, targeted, reliable changes in the genome (and, thus, are different from Genetically Modified Organisms, GMOs, produced previously) and have significant potential for the sustainable intensification of agriculture and food security, when used as part of the deployment of all available approaches and building on existing good agronomic practice. Unlike chemical or radiation induced mutagenesis, often traditionally used as a basis for crop improvement, the New Breeding Techniques do not create multiple, unknown, unintended mutations throughout the genome.

For several of the techniques, the resultant plant product is free from genes foreign to the species and would not be distinguishable from the product generated by conventional breeding techniques. This calls into question what is meant by genetic modification and raises issues for the modernisation of regulatory frameworks.

EASAC recommends that:

- EU policy development for agricultural innovation should be transparent, proportionate and fully informed by the advancing scientific evidence and experience worldwide.
- It is timely to resolve current legislative uncertainties. We ask that EU regulators confirm that the products of New Breeding Techniques, when they do not contain foreign DNA, do not fall within the scope of GMO legislation.
- The aim in the EU should be to regulate the specific agricultural trait and/or product, not the technology.
- The European Commission and Member States should do more to support fundamental research in plant sciences and protect the testing in field trials of novel crop variants.
- Modernising EU regulatory frameworks would help to address the implications of current policy disconnects in support of science and innovation at regional and global levels. At the same time, there is also continuing need for wide-ranging engagement on critical issues and this should include re-examination of the appropriate use of the precautionary principle.

Introduction

Agriculture continues to face major challenges to deliver food and nutrition security at a time of increasing pressures from social and economic inequity and instability, population growth, climate change and the need to avoid further loss in ecosystem biodiversity. The production of more food, more sustainably, requires the development of crops that can make better use of limited resources.

As described in detail in previous EASAC work (2004, 2011, 2013, 2014), agricultural innovation can capitalise on the rapid pace of advance in functional genomics research. Genetic crop improvement has potential to enhance agricultural resource use and efficiency (supporting sustainable farming methods that prevent, for example, soil erosion, water shortages and water pollution), yields and disease resistance and to improve characteristics of the harvested product such as nutritional content, storage performance or processing properties. Therefore, harnessing crop genetic improvement technologies for the sustainable intensification of agriculture, should form part of the deployment of all available approaches, traditional or novel, building on existing achievements for good agronomic practice.

Previous EASAC work (2013) has discussed the present and future value of genetically modified (GM) crops (in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination) and the issues to be resolved in making best use of the research taking place worldwide. In addition, we highlighted the great importance of other, more newly established, molecular breeding techniques now emerging from advances in biotechnology for application in programmes of crop improvement. This mix of New Breeding Techniques is maturing rapidly and, for several of the techniques, the resultant product is free from genes foreign to the species. This raises issues for the modernisation of regulatory frameworks because, in some cases, the product would not be distinguishable from one generated by conventional breeding techniques, and calls into question the definition of what is meant by genetic modification.

Since the publication of our EASAC report in 2013, outputs have appeared from various other bodies about the New Breeding Techniques. These include:

- (i) A Statement in Germany by the Leopoldina German National Academy of Sciences together with acatech, the German Academy of Science and Engineering and the Union of the German Academies of Sciences and Humanities (Leopoldina et al. 2015).
- (ii) A Statement in the UK by the Biotechnology and Biological Sciences Research Council (BBSRC 2014), with further discussion of issues in a report by the Parliamentary House of Commons Science and Technology Committee (House of Commons 2015).
- (iii) A letter from the Dutch government to the European Commission in late 2013 recommending exemption for cisgenesis from the EU GMO regulations.
- (iv) At the EU level, by the European Plant Science Organisation (EPSO 2015).
- (v) By the OECD, in their work on environmental risk assessment (OECD 2014).

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- (vi) In other regions worldwide, for example the scientific panel convened by Food Standards Australia New Zealand to provide an opinion on which food products derived from New Breeding Techniques should be regarded as GM food (FSANZ 2014).

Taken together, these recent outputs indicate the potential value of New Breeding Techniques and the lack of any new safety issues emerging. However, for the EU, the concerns for innovation expressed by EASAC in 2013 have been reinforced by these more recent publications: there is lack of certainty in the legal situation, and the possibility of over-regulation may result in the EU failing to make the most of the New Breeding Techniques' potential for agriculture. At the same time, some environmental NGOs have lobbied (Panella et al. 2015) for stringent EU regulation to be applied to the New Breeding Techniques, regarding them as if they were all tantamount to transgenesis (GM) in their genetic engineering interventions.

The purpose of the present Statement by EASAC is to take account of the recent published evidence and advice appertaining to New Breeding Techniques in order to review and extend our input to policy makers in the EU Institutions and Member States. We do not directly discuss GM crops further in our recommendations here, although there may be some issues common for all the crop genetic improvement technologies as described in the following sections and Appendix 1, and the conclusions we reached in our previous work relating to GM crops (2013) have not changed.

What are New Breeding Techniques and what can they do?

As discussed in our previous work (EASAC 2013), New Breeding Techniques can be used to generate new plant varieties specifically and effectively. Examples of initial impact are described in Box 1.

Box 1: Examples of applications of New Breeding Techniques

Herbicide-tolerant oilseed rape

The company Cibus has used gene editing technology for a product that does not integrate foreign genetic material (Anon 2015). This commercial crop is generated using genome editing, the variant has been planted in the USA in spring 2015 and has authorisation to cultivate in Canada. German authorities have said that they would not consider products created by gene editing as GM but rather as products of conventional breeding, but that this judgement would change if the European Commission decides otherwise.

Potato with reduced bruising, browning and reduced propensity to generate acrylamide

The USDA and FDA¹ have approved a potato variant developed by the company Simplot that contains no foreign DNA (elements were transferred from sexually compatible wild potato) and uses RNA interference to reduce the level of several enzymes including polyphenol oxidase responsible for bruising and browning. This variant, by lowering the level of the

¹ <http://www.fda.gov/NewsEvents/Newsroom/Press/Announcements/ucm439121.htm>.

amino acid asparagine and of reducing sugars, also has reduced ability to generate the potentially carcinogenic metabolite acrylamide at high temperatures (Waltz 2015).

Applications of genome editing

A recent literature survey (Araki & Ishii, 2015) reviews research in major crops (including barley, maize, rice, soybean, sweet orange, tomato, wheat) and notes whether the assessment of side-effects (induced off-target mutations) was attempted. Among the recent advances in genome editing is the development of mildew-resistant bread wheat and a maize line containing lower levels of phytate (Jones, 2015).

The New Breeding Techniques described in previous EASAC work include:

- Cisgenesis – transfer of gene(s) from same or closely related species.
- Intragenesis – insertion of reorganised coding region of gene derived from the same species.
- Targeted mutagenesis – mediated, for example by zinc-finger nuclease or TALEN (Transcription Activator-Like Effector Nuclease) technology.
- Other transient introduction of recombinant DNA, for example oligonucleotide-directed mutagenesis and agro-infiltration.
- Other new techniques – for example, RNA-induced DNA methylation gene silencing), reverse breeding, grafting non-GM scion onto GM rootstock.

In addition, more recently it has become clear (for example, Jones 2015), that other genome editing techniques, perhaps particularly CRISPR/Cas (Clustered Regularly Interspersed Short Palindromic Repeats), for targeted insertion or deletion will make an increasing, well-controlled, contribution.

We do not further discuss the technical detail of these methodologies, which can be found for example in the publications by Podevin et al (2012), the UK Advisory Committee on Releases to the Environment (ACRE 2013), BBSRC (2014), and Leopoldina et al (2015), but interpret and summarise some of the key implications as follows:

- As a result of the rapid pace of advance in sequencing and characterising plant gene functions, the New Breeding Techniques enable targeted, more precise and reliable, changes to be made to genomes in adding, removing or replacing DNA at specified locations.
- The risks and benefits of the new plant variant are determined by the changes introduced, not by the method used to introduce them.
- Unlike chemical or radiation induced mutagenesis, often traditionally used as a basis for crop improvement, the New Breeding Techniques are less prone to create multiple, unknown, unintended mutations throughout a genome. Unlike GM, many of the New Breeding Techniques will result in no foreign DNA in the product.
- In some categories, therefore, the products of the New Breeding Techniques cannot be distinguished from those same DNA changes produced by conventional breeding

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techniques, whose products can be placed on the market without prior authorisation. If epigenetic approaches are adopted (altering gene expression), there will be no DNA sequence changes made. Thus, in some cases, it will not be possible to discern the method used to produce the new crop variety.

Regulation and EU innovation

The EU Member State “New Techniques” expert working group (Podevin et al 2012) clarified and documented where New Breeding Techniques fall outside the scope of the current GMO legislation, concluding that the legal definition of a Genetically Modified Organism did not apply to most of the New Breeding Techniques. This assessment is consistent with other analysis (for example ACRE 2013). Thus, these techniques either fall within the exceptions already established by legislation or should be made an exception because the resulting products do not differ from plants obtained by conventional breeding (EPSO 2015). However, currently in the EU there is confusion and controversy as to how the new approaches should be regulated and until clarity is reached, research and its applications are hampered. The US authorities have already indicated that crop varieties generated through genome editing do not constitute GMOs (Jones, 2015)².

The EU registration costs, in terms of money and time, for a new crop variant are likely to be low if classified as a non-GMO but high if classified as a GMO. This distinction is particularly important for smaller and medium-sized enterprises and public sector researchers with limited resources: classification as a GMO would constrain applications to traits for high-value crops. It would be unfortunate if the “cost of entry” for New Breeding Techniques could only be afforded by large multinational companies interested in markets for globally traded crops.

Generally, EU legislation has not kept pace with the progress made in crop genetic science nor with the accumulating evidence base for safety and positive socio-economic impacts worldwide. Specifically for the New Breeding Techniques, we re-affirm and extend the conclusions drawn in the earlier EASAC work:

- Evidence-based policy It is vital that the EU legislative position is fully informed by the advancing scientific evidence and experience worldwide and that the processes for deciding on regulatory oversight are transparent.
- Legal certainty It would now be timely to resolve the issues that are creating uncertainties for researchers, plant breeders and farmers. We ask that EU regulators confirm that the products of New Breeding Techniques, when they do not contain foreign DNA, do not fall within the scope of GMO legislation, consistent with the advice of the “New Techniques” expert working group (Podevin et al 2012) and other expert groups (for example ACRE 2013).
- Regulating trait/product The agricultural regulatory framework must be proportionate and EASAC recommends that the aim should be to regulate the trait

² A detailed review of the current regulatory frameworks of the US Department of Agriculture (USDA) and the Animal and Plant Health Inspection Service (APHIS), with assessment of newer breeding tools including site-directed nucleases, cisgenesis and transgenesis, is provided by Camacho et al, 2014.

and/or product and not the technology. That is, risk assessment should be based primarily on the specific, science-based characterisation of new plant cultivars, by whatever method generated, not on the processes by which they are generated. Trait/product based approaches are already in place in various forms, for example in Canada, Argentina and the USA (Araki & Ishii, 2015). A trait-based regulatory system would have a further advantage in focusing discussion on agricultural priority traits (BBSRC 2014).

- Supporting fundamental research Reforming the EU regulatory framework requires clarity and consistency in definition as to what constitutes a novel plant trait (EPSO 2015). It is also of continuing great importance to pursue fundamental research to identify additional tools for New Breeding Techniques and to ensure their thorough characterisation in terms of all effects on the plant cell.
- Supporting testing The assessment of risks and benefits of novel crop variants by laboratory experiment and field tests should be supported by Member States, that is protected from vandalism and damage (Leopoldina et al 2015).
- Implications of re-nationalisation (devolution) of approval mechanisms EASAC recognises that the recent decisions by the European Commission, Parliament and Council of Ministers³ to allow Member States to authorise banning or restricting cultivation on their territory of European Commission-approved agricultural biotechnology products for non-scientific reasons has introduced new flexibility in some respects. This does not mean, however that Member States should make their own decisions about what constitutes New Breeding Techniques. It is now important to modernise the European Commission regulatory approval system so that the Member States can make their political decisions on products characterised and assessed by the EU regulatory authorities in terms of the best scientific evidence.
- Impacts of EU policy decisions Unless these reforms are introduced, it is possible that the EU will fall further behind other regions in terms of developing and using New Breeding Techniques. In this eventuality, the EU will struggle to fulfil its potential in contributing to global research and innovation for food and nutrition security. This has various other negative implications: for the vigour of the EU science base (responsible for much of the earlier research on New Breeding Techniques); for researcher and plant breeder careers; for competitiveness and the Knowledge-Based BioEconomy; for international trade; and for EU participation in international research programmes (Leopoldina et al 2015). There may also be additional negative impact on innovation in developing countries (EASAC 2013) who have concerns about their export markets or who are inclined to look to the EU to express R&D leadership.
- Need for continuing engagement on critical issues The criteria and standards for assessment of innovative agricultural products need to be sufficiently robust to accommodate future scientific advances and socio-economic changes, and the increasing regulatory experience (Araki & Ishii, 2015). There is some evidence that

³Directive 2015/412, new rules formally approved 2 March 2015, <http://www.consilium.europa.eu/en/press/press-releases/2015/03/150302-new-gmo-rules-get-approved>.

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consumers in the EU would accept cisgenic products in preference to transgenic products (Delwaide et al. 2015) but there is continuing need for pro-active engagement by policy-makers to understand and discuss the perspectives of interested parties, including researchers, farmers, consumers and industry, addressing key questions, among them those associated with social, economic and ethical aspects (Palmgren et al 2015). This discussion must include re-examination of the appropriate use of the precautionary principle (Appendix 1) and of how to bring agriculture in alignment with other sectors in regulating the trait/product rather than the technology used.

EASAC stands ready to help mobilise the scientific community and utilise our existing networks worldwide in order to contribute to the continuing debate and impel action.

Appendix 1: The use of the precautionary principle in evaluating crop genetic improvement technologies

In their letter to the Commissioner for Health and Food Safety (Panella et al 2015), a group of NGOs asked that EU laws on genetic engineering should be applied to the New Breeding Techniques and should continue to be based on the precautionary principle, transparency and traceability. However, the recent UK House of Commons Science and Technology Committee report (House of Commons 2015) provides detailed analysis of the application of the precautionary principle to genetic technologies for crop improvement and questions its continuing use in this area.

This UK parliamentary committee quotes from the Communication from the European Commission (European Commission 2000), stipulating the relevance of the precautionary principle to *“those specific circumstances where scientific evidence is insufficient, inconclusive or uncertain and there are indications through preliminary objective scientific evaluation that there are reasonable grounds for concern that potentially dangerous effects on the environment, human, animal or plant health may be inconsistent with the chosen level of protection”*.

The UK parliamentary report (2015) agrees that the precautionary approach is appropriate if these circumstances pertain but for genetic modification concludes that:

- The scientific evidence is not insufficient, inconclusive nor uncertain.
- The objective scientific evidence indicates that any risk from GM crops derives from the trait displayed rather than any inherent risks posed by the technology. There is no indication that there are reasonable grounds for concern that these products might lead to potentially dangerous effects on the environment, human, animal or plant health.
- Any legislation embodying the precautionary principle must allow for an exit from precautionary measures once there is strong scientific consensus that any risks are low.

Furthermore, as emphasised in the UK parliamentary report (2015), the European Commission’s Communication also states that reliance on the precautionary principle is no excuse for derogating from the general principles of risk management. These include:

- Proportionality – that is, the regulatory measure taken is not disproportionate to the desired level of protection and does not aim at zero risk. Proportionality as a moral principle, as a guide to decision making, and in relation to the precautionary principle is discussed in detail by Hermeren (2012).
- Non-discrimination – comparable situations should not be treated differently and different situations should not be treated in the same way.
- Consistency – new measures should be consistent with measures already adopted in similar circumstances.
- Taking account of scientific developments – to re-examine precautionary measures as appropriate.

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- Examining benefits and costs – of action or inaction, from both economic and wider societal perspectives.

The UK parliamentary report (2015) concludes that these principles of risk management are not being met in the case of EU GM crop regulation. EASAC is concerned that an inappropriate application of the precautionary principle, inconsistent with the general requirements of risk management, will also hinder innovation associated with the New Breeding Techniques.

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