Schouten replies:

Eriksson et al.¹ are eager to support transgenesis for plant breeding and regret that especially in the European Union (EU; Brussels) transgenic plants are negatively perceived by the general public². They admit that cisgenic products are better accepted, but warn against exempting cisgenic plants from the genetically modified organism (GMO) regulation. Their reasoning is that a favored position for cisgenesis would be detrimental for transgenesis. Transgenesis is in their view not "inherently unnatural and risky." They regard substitution of transgenesis by cisgenesis as a "giant leap backwards," as transgenesis opens a "virtually unlimited source of genetic variation: the entire clade of life"-whereas cisgenesis is limited to the gene pool of conventional breeding. Also, in their view, commercial release of cisgenic crops would further delay the public acceptance of transgenic applications in plant breeding.

I agree with Eriksson et al.¹ that transgenesis potentially provides numerous opportunities for sustainable food production. It opens unprecedented possibilities for improving biobased products and food with higher nutritional value. Eriksson et al.¹ mentioned the availability of the genes across the "entire clade of life." Actually, the possibilities of transgenesis are even wider, as also intelligently designed constructs can be synthesized, including RNA interference, and new combinations of protein domains, and all of these can be combined with smartly chosen promoters for targeted expression. However, cultivation of transgenic crops in the EU is very difficult, even after a painstakingly slow and cumbersome process of approval for commercial cultivation³. The current acceptance of transgenic crops in the production chain and among consumers is low in the EU and further declining^{3,4}. Only food products from animals that have been fed with imported, transgenic commodities are widely consumed because these animal products are not labeled as genetically modified (GM). Cisgenic food is substantially better accepted than transgenic food and this is borne out for public perception in the EU in particular². Even so, public acceptance is not the main reason for deregulating cisgenesis.

The European Food Safety Authority (EFSA; Rome) compared the biosafety of cisgenic plants with the biosafety of

transgenic plants and conventionally bred plants and concluded that cisgenic plants are as safe as (or as risky as) conventionally bred plants5. Transgenesis can introduce new traits to plants, and therewith possibly new risks compared with conventional breeding, according to EFSA. Very importantly, the implicit conclusion from this report is that GM technology itself is as safe as conventional breeding. Only foreign genes or synthetic constructs leading to novel traits may lead to risks that go beyond the risks of conventional breeding. The implicit conclusion of the EFSA report that GM technology itself is as safe as conventional breeding deserves a hearty welcome from people who are in favor of transgenesis.

Should cisgenic plants and their derived products be exempted from GMO regulation, this would be a principal and formal recognition of the low risk of GM technology for the environment and for feed and food. Eriksson *et al.*¹ should be enthusiastic about this, rather than worried.

Moreover, exemption of cisgenesis from the GMO regulation would be a breakthrough from a technology-based regulation toward a product-based regulation, a change that Eriksson *et al.*¹ probably welcome, too.

If consumers would buy cisgenic food products, this could lead to a wider acceptance of GM technology itself. This may lead in the long run also to a more balanced and less negative reaction of the general public toward transgenic applications.

When I initiated the concept of cisgenesis, I discussed this with the ethicist W. Kuhlmann (Philisophisches Institut, RWTH Aachen, Germany), who rejected transgenic crops and was partner in a European project on development of a cisgenic strawberry. At the end of the project, he rejected cisgenic crops, too, as he felt that acceptance of cisgenic crops might lead to a 'foot in the door' for transgenic crops, which he opposes. This is exactly the opposite concern expressed by Eriksson *et al.*¹.

The concept of cisgenesis was born in my mind after many discussions with social scientists, ethicists, consumers, biotechnologists and civil servants involved in biosafety evaluations of transgenic crops. We published it initially in 2000 in a book on ethical considerations of GMOs⁶. Cisgenesis is a result of taking the opinions and concerns of consumers seriously. Also it has taken into consideration that insertion of novel

genes and novel traits may trigger biosafety concerns, and thus lead to severe regulatory oversight. These biosafety issues can be evaded when using genes from the gene pool of the conventional breeder, which is not under this regulatory oversight. Personally, I am driven by feeling a responsibility for achieving proper valuation of the treasure chest of information about genes, genomes and alleles, in a way that is acceptable for the general public and that benefits the environment and food production. Also, it is important that the technology be accessible for small and medium-sized companies and for niche markets, without the burden of unbearable regulatory oversight. Sequence information of genes and whole genomes of plants is accumulating at an unprecedented speed. After the onset of whole genome sequencing we have entered the era of re-sequencing hundreds or even thousands of genomes of sexually compatible plants. This wealth of information of allelic variation can be exploited through marker-assisted breeding, but also by means of cisgenesis, if regulation does not needlessly block this cisgenic route.

Unfortunately, transgenic crops have failed to arrive in the EU, despite their potential for providing enhanced traits. This represents a missed opportunity, although in countries outside of the EU, commercial successes have been obtained for several transgenic commodity crops (http://www.isaaa.org/). I hope that cisgenesis will valorize the wealth of genomic information, which transgenesis could not redeem for the EU and other parts of the world, where antitransgenic crop attitudes and regulations prevail.

COMPETING FINANCIAL INTERESTS The author declares no competing financial interests.

Henk Schouten

Plant Breeding, Wageningen University and Research Centre, Wageningen, the Netherlands. e-mail: henk.schouten@wur.nl

- Eriksson, D., Stymne, S. & Schjoerring, J.K. Nat. Biotechnol. 32, 727 (2014).
- 2. Editorial. Nat. Biotechnol. 31, 767 (2013).
- 3. Laursen, L. Nat. Biotechnol. 30, 204–205 (2012).
- Gaskell, G. et al. Europeans and Biotechnology in 2010. Winds of change? (European Commission, October, 2010).
- 5. EFSA Panel on Genetically Modified Organisms. *EFSA Journal* **10**, 2561 (2012).
- Jochemsen, H. (ed.). Toetsen en begrenzen: een ethische en politieke beoordeling van de moderne biotechnologie (Buijten & Schipperheijn, 2000).