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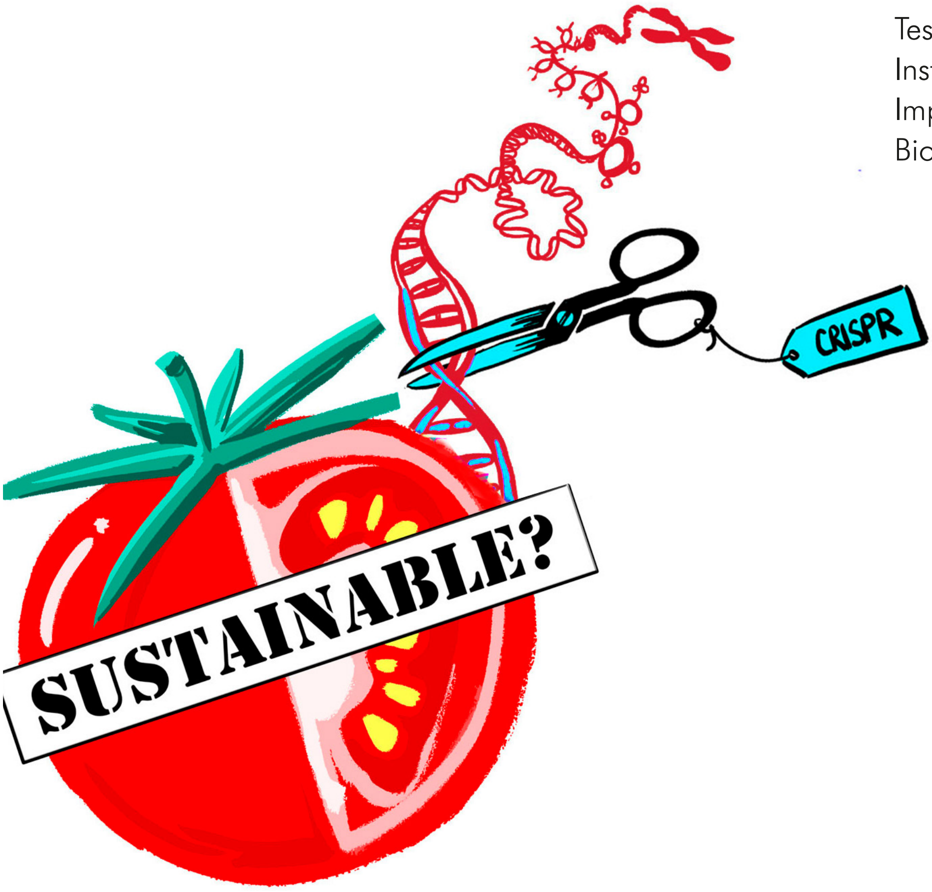

Genetic engineering in agriculture: between high flying expectations and complex risks

The use of genetic engineering in agriculture requires a comprehensive technology assessment

Matthias Juhas, Andreas Bauer-Panskus, Christoph Then

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Testbiotech is an independent institute for impact assessment in the field of genetic engineering. Our work is strictly based on scientific principles and evaluates the available information from the perspective of protecting health, the environment and nature. Testbiotech is free of any interests in the development, application and marketing of genetically engineered products. We are funded by private donations, public project and foundation funds.

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Summary

The introduction of transgenic plants into agriculture around 30 years ago was accompanied by many promises of benefits and high expectations, most of which have either not or only partially been realised. At the same time, there have been hardly any systematic or independent studies to objectively assess the actual impact of the transgenic plants on agriculture.

So far, most of the cultivated transgenic plants have almost exclusively just two traits: herbicide resistance and insecticidal toxins. Nevertheless, it was found that their long-term and large-scale cultivation has tended towards destabilisation of agro-ecosystems in areas where the plants are grown. Although in the short-term some regions saw a decrease in the use of pesticides, this was often followed by a substantial increase. Two of the main reasons for this were the emergence of 'pest' resistance and 'weeds' adapting to the herbicides; one further reason was the increased occurrence of insect species that had previously played only a minor role. Inevitably, this has led to a veritable 'arms race' in the fields, with companies developing transgenic plants that besides being made resistant to more and more herbicides also produce more and more insecticidal toxins.

As far as risks are concerned, various authorities have carried out risk assessments of individual genetically engineered plants ('events'). They have, however, so far failed to make detailed assessments of the combinatorial and cumulative effects, or assess any interactions between the genetically engineered (GE) plants. Current risk assessment does not therefore adequately cover either systemic environmental effects or food safety. At the same time, multiple studies have shown that interactions between the GE plants (events) or between their traits, can cause further destabilisation in agro-ecosystems, e.g. through the accelerated spread of certain 'pests'.

Several growing regions are already seeing an uncontrolled spread of transgenic plants, including in wild populations. This is already affecting some countries where the GE plants are not grown and also, in some cases, centres of biological diversity. Given this situation, there is a higher likelihood that spontaneous crosses with transgenic plants will lead to 'next generation effects', i. e. characteristics will be seen in the offspring of transgenic plants that were unknown at the time of the original risk assessment.

There are further problematic impacts on agriculture that are often discussed but have not yet been resolved at the policy level. These include patents on GE seeds, which have led to a strong corporate concentration in the field of plant breeding, and thus enabled a handful of large globally-active corporations to expand their dominant market position. As a result, these corporations are now able to influence cultivation practices in many regions throughout the world. In this respect, they appear to be paying very little attention to the actual problems in agriculture, and seem to be far more interested in making a profit. A further, as yet unsolved problem, is the coexistence of GE crops alongside traditional or organic production systems that want to avoid the use of any GE organisms.

In order to deal with the negative impacts that could be caused by the possible introduction of plants derived from new genomic techniques (NGTs) (or New GE, new genetic engineering), the existing approval procedures should be updated and supplemented by a comprehensive technology assessment (TA). The aim of a TA would be a full and comprehensive investigation of the potential advantages and disadvantages of NGT applications, including the ecological and socio-economic impacts. Besides allowing excessive expectations to be critically reviewed, it would help to prevent potentially negative impacts on ecosystems, safeguard the natural balance and limit, as far as possible, environmental interventions.

NGTs can be used to make much more profound genetic changes than was ever possible with conventional breeding (including random mutagenesis). Even if no additional genes are introduced, the genetic changes often go far beyond what is known from previous breeding methods. As a result, it is also possible to achieve

extreme expressions of certain traits, with considerable side effects and risks for the plants, animals and the environment. Such side effects ('trade-offs') can, for example, disrupt interactions with the environment, result in animal welfare issues or endanger food safety. They can also make crops more susceptible to climate stress and disease. Whether plants that are more resistant to negative environmental influences, such as climate change and plant diseases, can ever actually be produced in this way does, however, remain to be seen. While NGTs have great potential for genetic changes, it is not easy to translate this potential into actual benefits.

NGTs also target natural (non-domesticated) populations, such as wild herbs, trees, bees, other insects and soil organisms. The resulting genetically engineered organisms have not evolved naturally, and can therefore negatively impact ecosystems on several levels. Releases of these genetically engineered organisms could even have the potential to alter the further trajectory of evolution and disrupt future adaptation processes. There is a risk that a combination of these organisms could negatively impact the respective species, populations and ecosystems, and thus extend the risks beyond those identified for the individual NGT organisms prior to approval. Similar to the pollution of the environment with plastics and chemicals, it does not have to be a specific NGT organism that causes the problems. Rather, it is the totality of the effects of different GE organisms and their interactions that can be decisive. In this context, any problems in the environment or in the organisms themselves could persist for a very long time and burden many future generations. The introduction of GE organisms into the environment should therefore be limited as much as possible.

The use of NGTs are often justified by the assertion that new solutions are needed to secure world food security, especially against the backdrop of climate change. However, new solutions cannot be considered to be sustainable if their use can result in ecosystems being overburdened by mass releases of non-adapted organisms, or if risks accumulate and go unnoticed in food production, or if breeding is hindered by patents and the interests of consumers are disregarded.

The concepts of nature conservation and environmental protection are largely based on the principle of avoiding interventions. These concepts must also be applied in the field of genetic engineering. From this perspective, the introduction of a technology assessment into genetic engineering regulation can help to effectively control and limit the type and number of potential releases of genetically engineered organisms.

Appropriate criteria would be needed to make fact-based decisions on sustainability and any potential benefits of NGTs in agriculture. These would enable a technology assessment to identify negative effects at an early stage in breeding, agriculture and food production and, above all, prevent alleged NGT solutions from creating new problems for the environment, ecosystems and future generations.

1. Introduction

The Brundtland Commission on Environment and Development (WCED, 1987) at the United Nations introduced the concept of sustainability into the debate on the environment in its 1987 report. It defined sustainability, which originated in forestry, as a "development that meets the present needs without compromising the ability of future generations to meet their own needs". Since then, the concept, which is primarily based on criteria related to economic considerations, has been very successful and is also reflected, for example, in the United Nations' 'Sustainable Development Goals' (SDGs).

However, its broad definition, its frequent and now interdisciplinary use often lead to questionable applications. In many cases, the term sustainability refers primarily to the fact that certain technologies or individual products will perform better than previous products or technologies in terms of specific criteria, e. g. reduction of CO2 emissions, reduction of pesticides or efficient use of resources. As a result, sustainability goals are increasingly limited to introducing new products or technological innovations into existing systems without further developing these systems as a whole, and only focussing on 'improving' certain characteristics of the products. These expected 'benefits' are then equated to sustainability. The new, 'better' products are subsequently replaced by 'even better' or 'even more efficient' products or processes. This approach follows the growth-based market logic in keeping with innovation and marketing cycles integral to the system.

Against that backdrop, the term 'sustainability' in connection with genetic engineering appears to have considerable ambiguity. One example of a fundamental question that needs to be asked in this context is: To what extent can genetically engineered plants and animals actually replace traditional breeding and food production methods without endangering food security and the basic characteristics of life? A further question concerns the actual suitability of genetic engineering for solving problems, e. g. adaptation to climate change and reducing pesticide use. Is it primarily about profits or about 'real progress'? And what new problems and dangers can arise when genetically engineered organisms are introduced into ecosystems?

If questions like these are not answered well in advance, there is a danger that any negative ecological and economic consequences will be shifted to future generations. This would essentially contradict both the idea of future-oriented agriculture and the original concept of sustainability as defined by the Brundtland Commission.

In the EU, sustainability is a particularly important argument in the discussion on the future regulation of 'new genomic techniques' (NGTs). However, the debate on the use of NGT crops and their potential benefits often treat a number of aspects as if they have already been proven, e. g. the possible elimination of synthetic-chemical pesticides, the drastic reduction of CO2 emissions or higher efficiency.

For example, the EU Commission gave the impression in a public consultation that the claimed benefits of NGT crops are already a given fact (EU Commission, 2022):

> *"...that plants obtained by NGTs have the potential to contribute to the objectives of the European Green Deal and in particular to the Farm to Fork and Biodiversity Strategies and the United Nations' SDGs for a more resilient and sustainable agri-food system. Examples of potential benefits include plants more resistant to pests, diseases and the effects of climate change (e.g. notably increasing severity and frequency of extreme heatwaves, droughts and rainstorms) or environmental conditions in general, or requiring less natural resources and fertilisers. NGTs could also improve the nutrient content of plants for healthier diets, or reduce the content of harmful substances such as toxins and allergens."*

Furthermore, in the same public consultation, the EU Commission suggested that labelling could be used in future to provide consumers with information on the sustainability contribution of the respective NGT plants or products. To be effective, the labelling would need to adhere to sufficiently clear, transparent standards and criteria to enable reliable assessments of sustainability and potential benefits. So far, however, as was the case for the introduction of transgenic crops, there is no established framework with clear, transparent standards and criteria to make evidence-based decisions about the sustainability and potential benefits of these products. Unless such standards are introduced, there is a high risk of spreading misinformation and distortion of competition.

In order to achieve real sustainability or actual progress, it is therefore important to distinguish between empty promises or expectations that are too high and real possible benefits. The technical potential of NGTs and their scope make it necessary to define appropriate criteria at this stage in order to identify solutions that are as suitable as possible, and to evaluate them according to their actual necessity.

Even in future it will not be feasible to assess all possible effects of the various genetically engineered organisms on the environment. Introducing such organisms into the environment must, therefore, be strictly limited if this is to be handled responsibly. Otherwise, as with other problematic substances (e. g. plastics, pesticides and other chemicals), the number of genetically engineered organisms that are released may unbalance the stability of ecosystems. In order to avoid such tipping points, any releases must be limited to what is actually necessary - whereby lower-risk alternatives, e. g. those derived from conventional breeding, agroecology or other sectors within food production systems, must always be included in these considerations.

In the past, technologies that were used to solve problems (in the fields of energy, agriculture and transport, amongst others) frequently caused new problems, such as climate change, nuclear waste, environmental pollution or species extinction (EEA, 2001). It is, therefore, essential that such negative effects on the environment, and also potentially negative socio-economic consequences, must be prevented as far as possible with the help of a prospective technology assessment for applications of new genomic techniques.

2. Experience with transgenic plants so far

The introduction of transgenic plants about 30 years ago was originally justified by, amongst others, potential benefits in plant breeding, agriculture and food security. Specifically, it was about achieving goals, such as saving on the use of pesticides, increasing yields, resistance to environmental influences or even food, all of which would have advantages for consumers. However, developments fell far short of what was published and forecast in, for example, an Organisation for Economic Co-operation and Development (OECD) report, which was based on industry surveys (Table 1).

Table 1: "Expected development of agrobiotechnology", OECD 1992

1990-1993	Tolerance to herbicides and pesticides
1993-1996	Improvements in processing
1996-1999	Industrial production of pharmaceutical products
1999-2003	Environmental Tolerance
2003-2006	Direct increases in yield

So far, only very few genetically engineered traits have been brought to market. These are almost exclusively herbicide resistances (especially to the total herbicide, glyphosate) and the production of insecticides (especially Bt toxins from the soil bacterium *Bacillus thuringiensis*). This is also reflected in the characteristics of plants approved for import into the EU (Fig. 1).

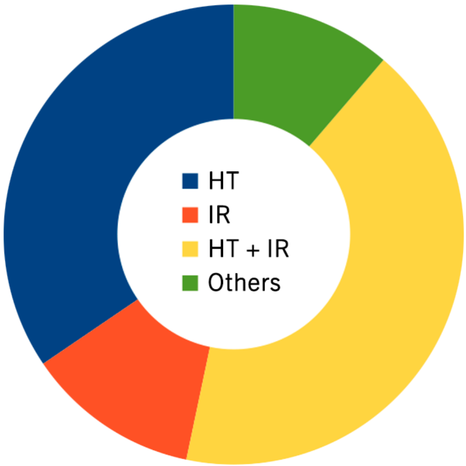

**Figure 1: Approvals of genetically engineered plants in the EU (PlantGeneRisk database, as of January 2023).[1]
HT: Herbicide tolerant Plants (37); IR: insecticide producing plants (13); HT+IR: combinations of both traits (45); Other (12): 6x altered oil-content (soybean), 2x pollen sterility (canola), 2x improved ethanol processing (maize), 1x increased biomass content (maize) and 1x drought tolerance (maize).**

The following section examines from a critical perspective some of the experience gained in the agricultural cultivation of transgenic crops in regard to sustainability and economic efficiency (2.1), the effects on food production and plant breeding (2.2), the effects on biodiversity and the stability of ecosystems (2.3) and also the issue of benefits for consumers (2.4). It is becoming increasingly clear that many of the expectations associated with the use of genetic engineering in agriculture have failed to materialize.

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[1] https://www.testbiotech.org/en/database

There is, furthermore, often a lack of independent, i.e. not industry-led, data and assessments of the effects of genetic engineering in agriculture, food production and seed production. Findings include a number of contradictory statements, which can, amongst others, be traced back to different methods of data collection. Clearly, in some cases the expectations that were originally raised differ significantly from reality.

Besides focussing on the systemic effects, the following section also includes a discussion of what prospective technology assessment (TA) should do in order to prevent similar misjudgements or misguided developments in the future. It is important to have this debate now as the EU is currently holding intensive discussions on the future regulation of new genomic techniques.

2.1 Sustainability and economic efficiency

Numerous experts, often closely affiliated to the industry, have published studies stating that the cultivation of transgenic plants is, at least to a certain extent, associated with considerable benefits for the environment (Brookes & Baarfoot; 2014; Brookes & Baarfoot, 2020; Brookes, 2022b/c), health (Smyth, 2019), economic efficiency (Gianessi & Carpenter, 2000; Kaphengst et al., 2010; Klümper & Qaim, 2014; Brookes, 2019; Brookes, 2022a) or large-scale adoption (e.g. Kovak et al., 2022). Beneficial factors cited include higher yields, lower greenhouse gas emissions, improved soil quality, less use of pesticides and increased profit margins (especially in developing countries).

In contrast, other publications have shown that, contrary to expectations, the amount of herbicide used in growing genetically engineered crops has not decreased, but has actually increased over time (see 2.1.1). There are studies examining social, economic and ecological sustainability aspects, which fundamentally question the sustainability of transgenic plant cultivation (Fischer et al., 2015; Binimelis & Myhr, 2016; Phélinas et al., 2017; Catacora-Vargas et al., 2018). These studies come to very different conclusions than the previously mentioned studies.

Experience gained from the cultivation of genetically engineered plants is thus assessed very differently, and is contingent upon the context, questions posed, methodology and economic expectations. The following section summarises and evaluates from a critical perspective some of the experience gained from the cultivation of transgenic plants.

2.1.1 Herbicide resistance and pesticide use

Many studies conclude that herbicide use - particularly the amount of glyphosate, but also glufosinate, 2,4-D or dicamba - in maize, soybean and cotton fields has not decreased but, in fact, significantly increased, especially in the main growing regions in North and South America (Benbrook, 2012; Coupe & Capel, 2015; Schütte et al., 2017; Miyazaki et al., 2019; Schulz et al., 2021). A major cause of this increase is the spread of herbicide-resistant weeds, particularly weeds that are resistant to glyphosate. When Monsanto applied for the commercial cultivation of the glyphosate-resistant genetically engineered maize NK603 in the USA in 2000, some experts warned that the weeds could quickly become resistant to the herbicide. Monsanto, however, put forward counter-arguments that convinced the authorities. The application for approval from 2000 states:[2]

> *"Although it cannot be stated that evolution of resistance to glyphosate will not occur, the development of weed resistance to glyphosate is expected to be a very rare event because:*

- *weeds and crops are inherently not tolerant to glyphosate, and the long history of extensive use of glyphosate has resulted in few instances of resistant weeds;*

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[2] http://www.aphis.usda.gov/brs/aphisdocs/00_01101p.pdf, quoted after Then (2015)

- *glyphosate has many unique properties, such as its mode of action, chemical structure, limited metabolism in plants, and lack of residual activity in soil, which make the development of resistance unlikely;*
- *selection for glyphosate resistance using whole plant and cell/tissue culture techniques was unsuccessful, and would, therefore, be expected to occur rarely in nature under normal field conditions."*

This forecast was obviously wrong. The "WeedScience" database (www.weedscience.org) has for several years continued to monitor the evolution of glyphosate-resistant weeds, amongst others, in various US states. These weeds can either no longer be controlled with glyphosate or only with very high doses. In the USA, according to the database, 17 weed species resistant to glyphosate are currently registered in over 40 states[3] and approximately 60-80 per cent of the areas cultivated with maize, soybean or cotton are now affected by glyphosate-resistant weeds (Brookes, 2022c). The economic damage is considerable.

2.1.2 Cost development and profit expectations

According to Benbrook (2012), figures provided by Dow AgroSciences show that, even before 2012, the spread of glyphosate-resistant weeds has increased costs for US farmers by 50-100 per cent. According to the studies cited in the report, the cost of growing soybeans in Arkansas increased from $16 to $44 per acre (≈0,4 ha), soybeans in Illinois from $19 to $31, and corn in Iowa from $19 to $32.

According to Science (Service, 2013), the cost per hectare of cotton cultivation in the southern US increased dramatically in just a few years - from 50-75 to 370 US dollars; for growing soybeans in Illinois from 25 to 160 US dollars per hectare. As a result of these cost trends, cotton production declined by 70 per cent in Arkansas and 60 per cent in Tennessee. Cotton production in the USA recovered slightly from 2015 onwards when seed and fertiliser prices fell, but this temporary development did not last, and production costs started to rise again in 2019 (Figs. 2 and 3).[4]

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[3] https://weedscience.org/Pages/filter.aspx

[4] https://www.ers.usda.gov/webdocs/DataFiles/47913/CottonCostReturn.xlsx?v=6554.7

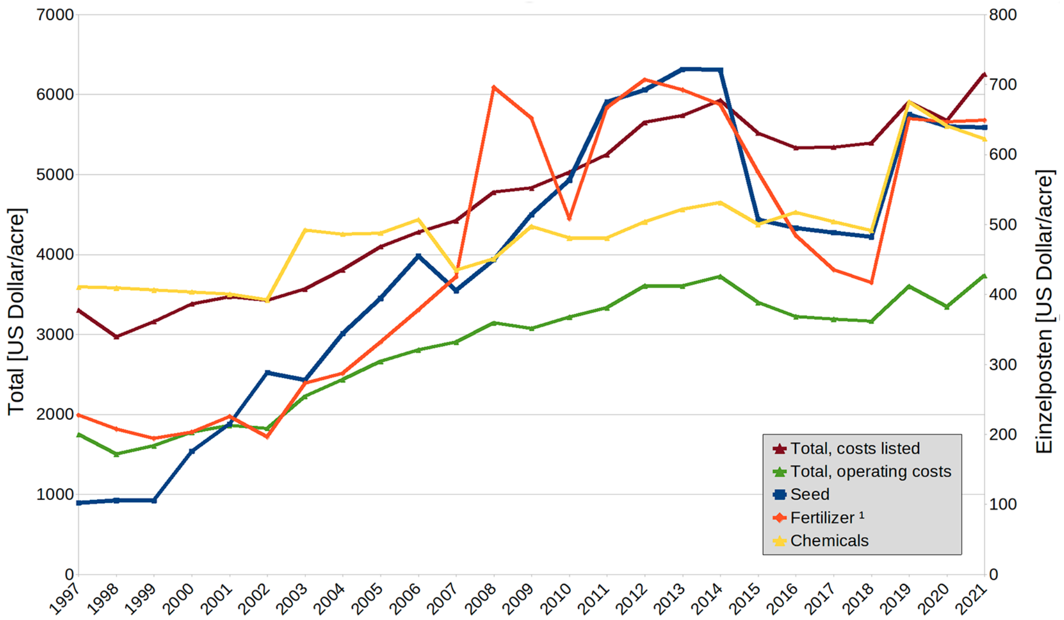

Figure 2: Development of operating costs for cotton cultivation in the USA.[5]

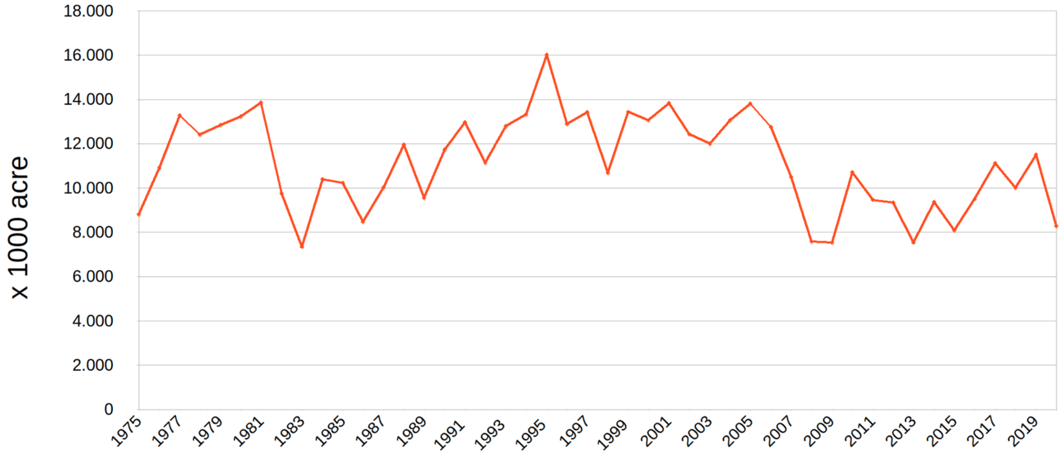

Figure 3: Cotton harvest quantities in the USA between 1975 and 2020.[6]

Similarly differentiated reports on lower yields, rising costs and lower returns are also available, e. g. for the cultivation of genetically engineered cotton in the so-called 'Cotton Belt' of the USA (Jost et al., 2008), Bt cotton in China, India and South Africa (Glover, 2010; Gutierrez et al., 2020; Kranthi & Stone, 2020; Najork et al., 2022) as well as on a global level (Finger et al., 2011; Catacora-Vargas et al., 2018).

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[5] https://www.ers.usda.gov/webdocs/DataFiles/47913/CottonCostReturn.xlsx?v=6554.7

[6] https://www.ers.usda.gov/webdocs/DataFiles/48516/U.S.CottonSupplyandDemand.xlsx?v=5046.1

According to the database, there are worldwide currently 56 weed species resistant to glyphosate,[7] most of which are associated with the cultivation of genetically engineered plants (Heap & Duke, 2018). The top countries in this context are the USA and Argentina with 17 resistant species each, followed by Brazil (11) and Canada (8). Further resistance has now also been documented for almost ten years in Australia and South Africa, but also in Europe and Asia, i. e. countries in a total of six continents (Heap, 2014; Sammons & Gaines, 2014). In terms of the number of species resistant to individual active ingredients in herbicides, glyphosate already ranks second in the top ten, after atrazine, which has now been banned in the EU for about 20 years.[8]

2.1.3 Resistance and secondary infestation with insect pests

At the same time, the cultivation of plants producing their own pesticides (mainly Bt toxins) led to both the development of insect resistance and secondary pest infestations caused by the exchange of insects in different regions (Zhao et al., 2011; Tabashnik et al., 2013; Cheke, 2018; Gassmann, 2021; Xiao et al., 2021).

The first resistances in the cultivation of genetically engineered Bt plants emerged about 20 years ago. Since then, the development of resistance to the Bt toxins - and consequently crop damage - has increased significantly and spread worldwide (Fig. 4). In addition, there is growing evidence that other insect pests throughout the world have a reduced sensitivity to Bt toxins (Tabashnik et al., 2023). The period for the development of such resistance in insect pests has halved from eight to four years on average (Tabashnik & Carrière, 2017, Tabashnik et al., 2023). Causes for this acceleration include the parallel development of resistance to multiple Bt toxins with similar mechanisms of action as well as the large-scale and repeated cultivation of Bt crops (Bernardi et al., 2015; Zukoff et al., 2016; Jakka et al., 2016; Ludwick et al., 2017; Machado et al., 2020; Gassmann, 2021). These multiple resistances are now causing major problems in the USA. The US Environmental Protection Agency therefore recommends phasing out Bt plants.[9],[10] Transgenic plants that produce the only currently still effective Bt toxin, Vip3Aa, are the sole exception. In the south eastern USA, for example, the corn earworm (*Helicoverpa zea*) showed an up to 150-fold higher resistance to the commonly used transgenic Bt toxin Cry1Ab in more than 80 per cent of field populations, although it has remained susceptible to the Vip3Aa20 toxin in the same region (Niu et al., 2021). In the meantime, however, there have been some reports of first resistances to Vip3Aa in this area (Yang et al., 2021). Another example is the Western corn rootworm (*Diabrotica virgifera virgifera*) which has developed resistance to the corresponding Bt toxins, partly due to the dominant inheritance of Bt resistance and possibly even positive effects of the Bt toxins on the fitness of the surviving larvae (Oswald et al., 2012; Gassmann, 2021). In response to this increasing Bt resistance, genetically engineered maize was subsequently equipped with additional transgenes that activate the RNA interference mechanism (RNAi). The RNAi mechanism switches off the metabolic genes of the larvae, thus ultimately causing the insects to die (Darlington et al., 2022). However, various resistance mechanisms to the RNAi method may also become established, thus making it questionable whether this strategy will provide permanent and sufficient protection against the rootworm (Khajuria et al., 2018).

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[7] https://www.weedscience.org/Pages/filter.aspx

[8] https://www.weedscience.org/Pages/Graphs/activebyspecies.aspx

[9] https://www.dtnpf.com/agriculture/web/ag/crops/article/2020/09/29/epa-proposes-phasing-dozens-bt-corn

[10] https://www.regulations.gov/document/EPA-HQ-OPP-2019-0682-0052

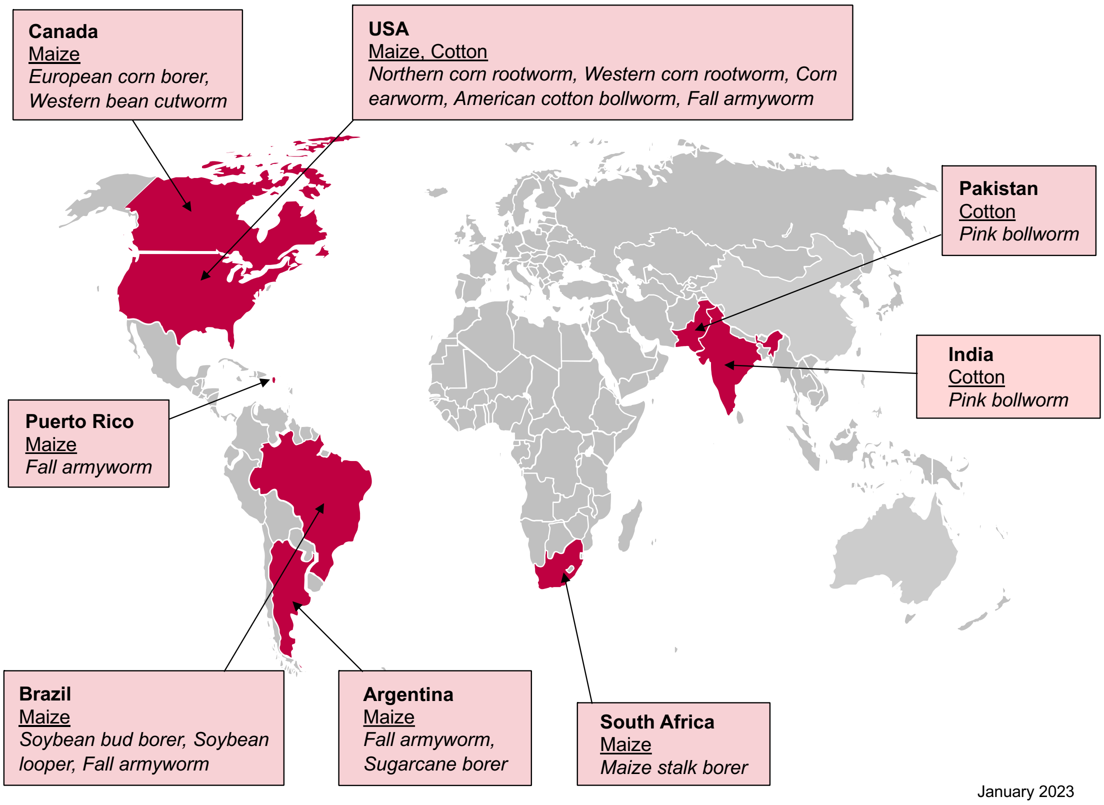

Figure 4: Important pests around the world have meanwhile developed resistance to Bt toxins (according to Tabashnik et al., 2023)

Secondary pest infestation is a further problem. The Bt toxins in genetically engineered plants are only effective against a limited number of pests and thus the plants are still susceptible to many other pests. The control of primary plant pests has meanwhile caused the emergence of secondary pest infestations (Fig. 5) - this is also an indirect effect of the cultivation of Bt plants. In addition to the increase in resistance, these secondary pests are now a further major problem associated with the cultivation of Bt crops, again requiring the use of synthetic pesticides, and thus again increasing costs for farmers (Men et al., 2005; Zhao et al., 2011). In North and South America as well as in China and India, the increasing occurrence of such secondary pests has been reported for over ten years (especially in the cultivation of Bt maize and cotton) (Naranjo, 2011; Zhao et al., 2011; Smith et al., 2018). In addition, new species were recorded that have not previously been observed in these regions before (Nagrare et al., 2009; Tay et al., 2013; Horikoshi et al., 2021).

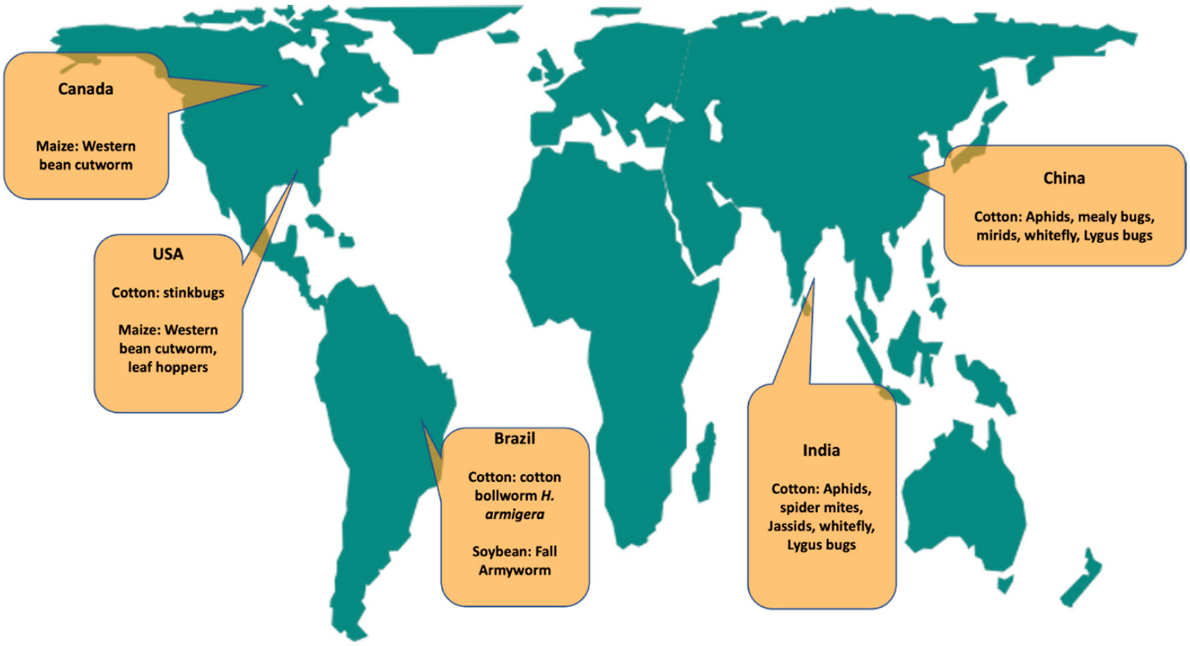

Figure 5: When Bt crops are grown, secondary pest infestations occur as a result of pest replacement (Third World Network, 2022). Some other secondary pests that have meanwhile appeared in soybean fields in Brazil (soybean looper) are now also resistant to Bt toxins (Horikoshi et al., 2021).

The answer of the genetic engineering industry to these problems is to bring plants to the field that produce several insecticides themselves, so-called 'stacked events'. These stacked events are created by crossing genetically engineered plants to combine multiple traits. The resulting genetically engineered plants often have multiple resistances to herbicides and currently produce up to half a dozen insecticides, whereby the insecticides are mostly synthesized on the basis of synthetic DNA and are, in some cases, very different to variants that occur in nature (Fig. 6). Stacking the intended traits combines and magnifies both risks and uncertainties associated with the parental plants.

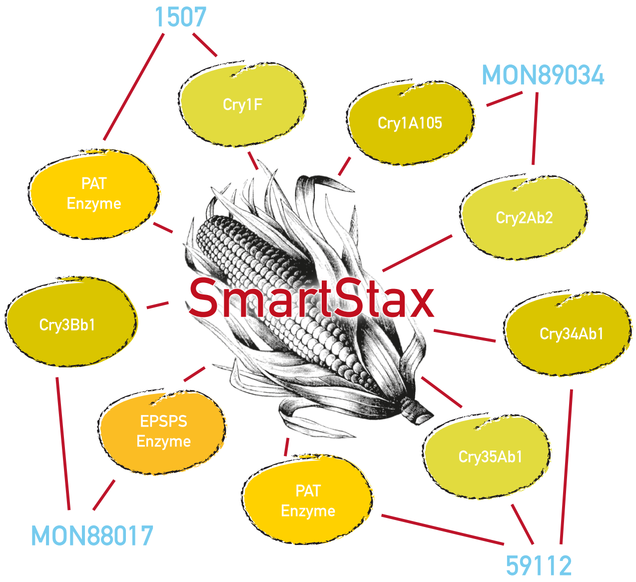

Figure 6: 'SmartStax' corn (originally Monsanto and Dow AgroSciences). The corn is a combination of four genetically engineered events (MON88017, MON89034, DP59122, DP1507): it produces six Bt insecticides (Cry toxins from different *Bacillus thuringiensis* strains, one of which, Cry1A105, is synthetically produced) and is tolerant to two herbicides (glufosinate through the PAT enzyme and glyphosate through the EPSPS enzyme)

However, this increases the environmental load, the probability of unwanted interactions in the field and in the harvest and, last but not least, also increases seed costs. In addition, satisfactory efficacy has in many cases not been achieved (see, e. g. Schulz et al., 2021).

As a result, in some regions of the USA the cost of growing transgenic cotton has increased so much that it has been discontinued (Benbrook, 2012; Service, 2013). Several factors play a role in this respect, including the expense of chemical crop protection (see Fig. 2). It has also been shown that smallholders in South Africa are facing rising production costs for Bt cotton (Pschorn-Strauss, 2005; Fok et al., 2007; Schnurr, 2012).

Strong increases in operating costs have also been documented for the production of soybean and maize,[11],[12] but these markets have benefited from a growing global demand: there has often been a high demand for these crops in recent years, not only as food and feed, but also as a resource for use in agrofuels. It can be assumed that increasing prices for these commodities are one reason why the cultivation of these crops is more profitable than that of transgenic cotton.

2.2 Systemic effects on food production and plant breeding

After the introduction of genetic engineering into agriculture, there were fundamental changes in market strategies and corporate structures in the agricultural sector, especially among large corporations, which ultimately led to a concentration in the seed sector. The cultivation of transgenic plants has also had various undesirable consequences for farmers and consumers.

2.2.1 Corporate concentration

Possible markets and sales channels for genetically engineered products were systematically analysed very early on in order to safeguard the profit strategies of the corporations. In 1992, the OECD published a survey of companies active in the field of agrogenetic engineering (OECD, 1992). The result:

> *"Three different strategies were mentioned by companies active in the field of plant biotechnology: the first is to act as a supplier of specific technologies (gene packages); the second is based on using biotechnology to gain control of strategic seed markets; the third strategy is to gain a foothold in downstream markets in order to take advantage for themselves of the industrial value added that cannot be recovered through revenue from seed sales alone."*

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[11] https://www.ers.usda.gov/webdocs/DataFiles/47913/SoybeansCostReturn.xlsx?v=9414.4

[12] https://www.ers.usda.gov/webdocs/DataFiles/47913/CornCostReturn.xlsx?v=9414.4

In retrospect, it is clear that this corporate strategy was far more successful than any of their announcements about products that were supposed to provide real benefits for consumers. Agrochemical companies began systematically buying up seed companies and applying for patents as early as the 1980s and 1990s, in parallel with the development of the first genetically engineered crops (see also Then, 2015).

Patents on transgenic plants have, in particular, led to a strong corporate concenvtration in the seed sector in recent years (Howard, 2009; Howard, 2015; Bonny, 2017, Clapp, 2021). Corporations that are actually primarily active in the agrochemicals business have gained a dominant market position by patenting seeds and buying up breeding companies. This includes four large corporations: Bayer (formerly Monsanto), Corteva (formerly DowDuPont), SinoChem (ChemChina/Syngenta) and BASF, which control about 50 per cent of the commercially traded seed market - and over 60 per cent of the agrochemicals market (Fig. 7; Clapp, 2021; ETC Group, 2022).

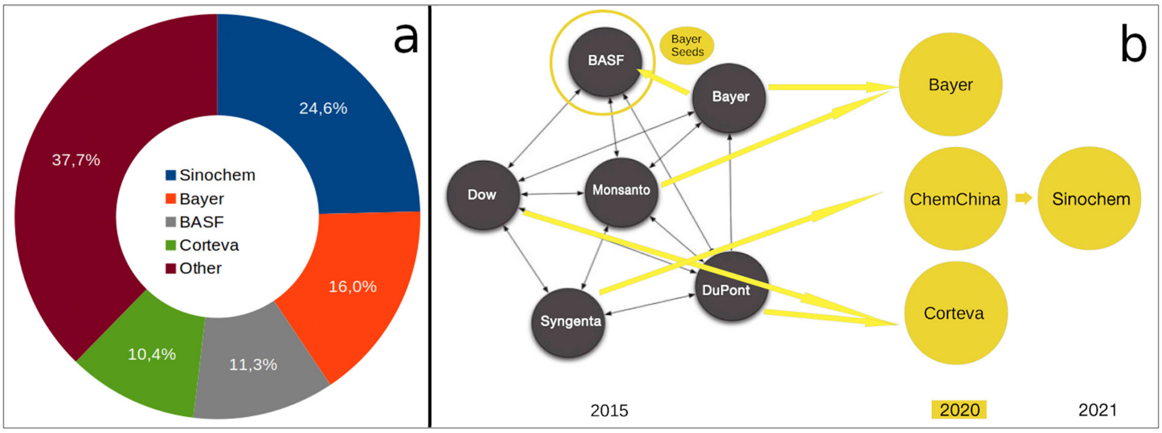

Figure 7: (a) Percentage share of the world's top-4 agrochemical companies in global agrochemical sales in 2020. Sinochem (China): $30.6 billion; Bayer (Germany): $9.9 billion; BASF (Germany): $7 billion; Corteva (USA): $6.4 billion; Others: $23.5 billion (modified according to ETC Group, 2022). (b) Corporate concentration in the seed market between 2015 and 2020: Monsanto was acquired by Bayer (which in return had to sell its seed sector to BASF), ChemChina acquired Syngenta, Dow and DuPont joined forces to form Corteva for their seed business. Finally, in 2021, the mega-merger of two Chinese state-owned companies, Sinochem and ChemChina, which is currently not only the world's largest chemical conglomerate, but also the leading company for industrial agricultural inputs (modified according to Testbiotech, 2021b).

Over the last twenty years these large companies have established herbicide-tolerant genetically engineered crops to create a so-called 'technological lock-in', hedging dependency on their pesticides (which are now relatively cheap due to, for example, the expiry of glyphosate's patent protection in 2000), and thus not only consolidating but further expanding their market power. The new business models of these companies are no longer based on the sale of efficient (expensive) herbicides adapted to (single) resistances of genetically engineered plants, but on the marketing of transgenic plants with multiple resistances ('stacked events', which became necessary mainly due to the increase in herbicide-resistant weeds) against three or more different herbicides.[13]

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[13] Gil Gullickson, New tech coming in seed traits, Successful Farming, 30 November 2020: https://www.agriculture.com/crops/corn/new-tech-coming-in-seed-traits

2.2.2 Contaminations

Seeds are often contaminated with transgenic material during transport, processing or directly in the fields, which is very problematic for food production. This has created major problems for freedom of choice within the different farming systems, particularly for farmers in North and South America. In Canada, for example, it is now almost impossible to cultivate transgene-free canola, as surrounding fields are regularly contaminated by pollen. In addition, genetically engineered seeds can survive in the soil and remain ready to germinate for over ten years. This leads to the unintended growth of transgenic plants and even more seeds that can survive in the soil (see, amongst others, Bauer-Panskus et al., 2013). The continuous cross-breeding of transgenic traits into new, conventionally-bred rape varieties over the years is also forcing farmers to buy genetically engineered seeds in order to gain access to modern, high-yielding varieties, as most transgene-free varieties have been withdrawn from the market (CBAN, 2019).

In Brazil, there has apparently been large scale contamination of maize seeds, also affecting regional varieties (Fernandes et al., 2022). Similar reports are also available from South Africa (Iversen et al., 2014) and Mexico (Quist & Chapela, 2001; Dyer et al., 2009; Agapito-Tenfen et al., 2017; Agapito-Tenfen & Wickson, 2018). These contamination incidents are particularly serious because they also affect varieties that are propagated by farmers themselves, and can thus unintentionally spread further.

Over the years, contamination with genetically engineered rice, linseed and wheat has also repeatedly led to considerable costs for seed producers and food manufacturers (Price & Cotter, 2014).

2.2.3 Food safety

In the EU, only one authorisation has so far been issued for the cultivation of a genetically engineered plant (maize MON810), although more than 90 authorisations have been granted for the import of different genetically engineered plants (events) or their harvest. The imports are mainly used as animal feed. All the approvals for the marketing of transgenic plants for use in food and feed are based on EU Regulation (EC) 1829/2003 and Implementing Regulation 503/2013. Risk assessment carried out by the European Food Safety Authority (EFSA) is also based on these provisions. It covers the potential effects of genetically engineered organisms on human and animal health as well as on the environment. Molecular characterisation and comparative analysis of the new traits assesses intended and unintended genetic changes, gene expression (of the newly inserted genes) and changes in phenotype (such as composition of ingredients) compared to conventionally-bred plants. In addition, toxicity and allergenicity as well as any potential environmental effects are assessed within this framework. Decisions on authorisations are made by the 27 member states and the EU Commission. Furthermore, environmental monitoring (post-market environmental monitoring (PMEM)) is mandatory after products are brought to market - this is also assessed by EFSA. However, the current PMEM standards do not allow for the collection of sufficiently reliable information on the effects of genetically engineered food or feed, which is why it has so far largely been a process without any substantial scientific content (Testbiotech, 2021a).

Current authorisation practice is not sufficient to meet the actual complexity of the risks. The reasons for this include the increase in herbicide-resistant weeds and the adaptation of pests (see 2.1.2 and 2.1.3), which have led to a veritable 'arms race' in the fields of various growing regions: up to six insecticides are currently combined with several resistances to herbicides in individual varieties of the above-mentioned 'stacked events' (maize, soybean, cotton) - see PlantGeneRisk database[14] and Fig. 6. The 'stacked events' achieved through (multiple) crosses of transgenic plants now account for the majority of approvals (e. g. in the EU: 26 'single events' vs. 70 'stacked events', see Fig. 8).

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[14] https://www.testbiotech.org/en/gendatenbank

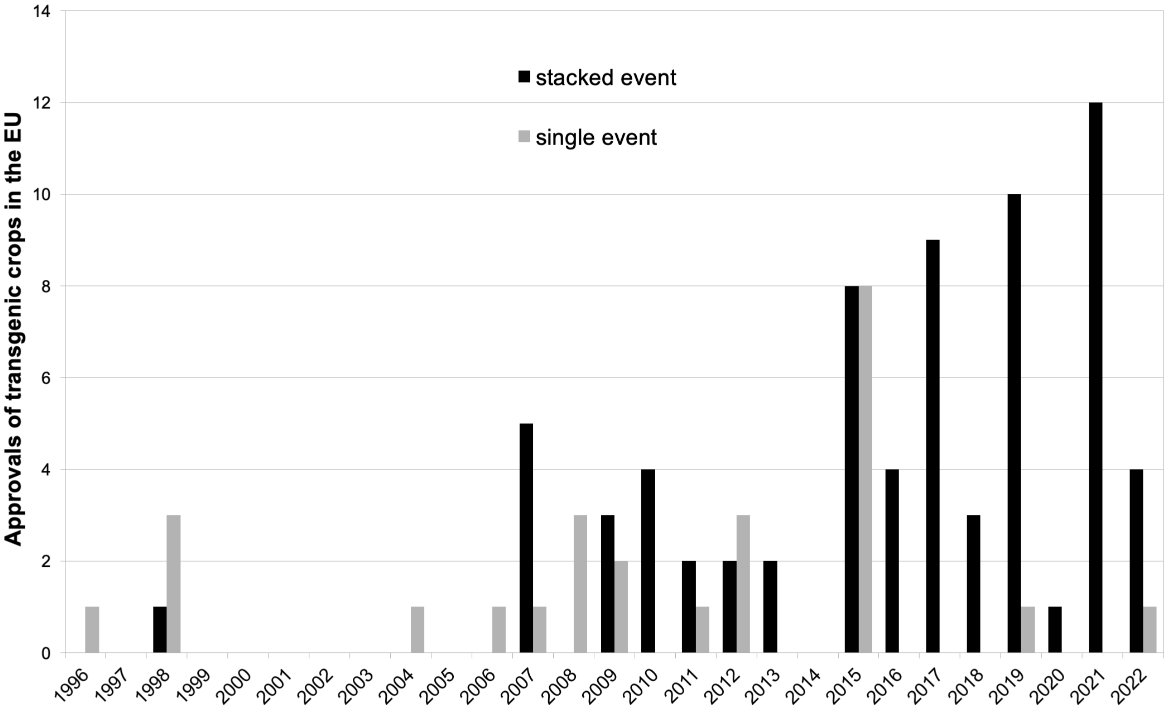

Figure 8: Genetically engineered plants approved in the EU (almost exclusively for import) that contain only one transgene ('single event') or several transgenes ('stacked event').[15]

Since the total amount of insecticides produced in 'stacked events' can vastly exceed that of the plants producing only individual insecticides, the exposure of the environment and the harvest to these toxins is also increased. At the same time, the list of herbicides to which the plants are made resistant continues to increase, which means that the harvest is regularly contaminated with a cocktail of residues from the complementary herbicides. This clearly poses new challenges for risk assessment, as interactions are much more difficult to assess than the risks of individual active substances (overview and further sources: Testbiotech 2021a). The combinatorial effect of the individual insecticides and herbicides can also be synergistic under certain circumstances, which means that the possible health effects can subsequently exceed the sum of the individual substances. Similar issues arise when crops from different plants are mixed into food or feed. The effects can also be triggered indirectly, for example, if consumption of the products changes the composition of the microorganisms in the gut (microbiome); this has been described in several publications on the herbicide, glyphosate (overview and further sources: Testbiotech 2021a). Amongst other things, this could promote chronic inflammatory processes, e. g. in the gastrointestinal tract (for the possible mechanisms, see overview in Parenti et al., 2019). So far, such effects have almost never been taken into account in risk assessment.

These problems affect all Bt plants currently grown or imported, as well as all mixtures of these plants into food and feed. However, neither EFSA nor the industry have carried out any detailed investigations. For example, the EU does not request any empirical studies on the overall toxicity of 'stacked events' in which the residues of the complementary herbicides (to which the transgenic plants have been made resistant) are regularly combined

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[15] https://www.testbiotech.org/en/gendatenbank

with the plant-derived insecticides (overview and further sources: Testbiotech 2021a). The authorities have also failed to apply modern methods with which the changes in plant metabolism and gene expression could be studied in more detail. For example, the so-called 'omics' methods could be used to investigate changes in genes (e. g. by examining the entire genome using 'whole genome sequencing'), cells (total RNA or proteins produced) or organisms (characterisation of all metabolic properties). It is, however, clear from its review of procedures up until 2030 that EFSA has no intention of requiring 'omics' data.[16]

These gaps in risk assessment have in recent years increased uncertainties about the safety of the imported crops. Besides an increasing number of registrations, more new mixtures of herbicide residues and insecticidal proteins are now being imported.

Imports of genetically engineered plants into the EU are, therefore, insufficiently investigated in regard to the systemic, combinatorial and chronic effects of food and feed consumption. The approval- and risk assessment of genetically engineered imports into the EU do not cover the specific residues of complementary herbicides, their mixtures or possible interactions with insecticides (Commission Implementing Regulation (EU) No 503/2013; Testbiotech, 2021a). One reason: the EU carries out separate risk assessments for herbicides and genetically engineered plants. Moreover, the current methodology to assess combined, accumulated and chronic health effects is insufficient for reliable assessment. As a result, risks can accumulate unnoticed in the food chain.

2.3 Effects of transgenic plants on ecosystems

A systematic approach to assessing environmental and biodiversity impacts is often lacking. This also applies to the import of transgenic plants into the EU, as environmental impacts in the countries where the transgenic plants are cultivated are often ignored, e. g. combinatorial effects of the various herbicides and insecticides, the use of active substances that are now banned in the EU, and last but not least the loss of the rainforest. As a result, there is an evidential need for a comprehensive and independent technology assessment that goes beyond the risk assessment of individual genetic engineering events. Some of these environmental impacts may be linked to the cultivation of transgenic crops, but are not necessarily caused by the use of genetic engineering methods. In addition, damage and/or interactions within the ecosystems and in biodiversity caused by the genetic modifications have also been observed, as the following examples show.

2.3.1 Damage in centres of biological diversity

Mexico is one of the centres of biodiversity for cotton but is now experiencing uncontrolled spreading of genetically engineered plants. This is the result of transgenes from herbicide-resistant and insecticidal genetically engineered cotton being transferred into natural cotton populations (*Gossypium hirsutum*) (Wegier et al., 2011). After infestation with pest insects, it was observed that both the transgenic cotton plants and their progeny differ from the wild cotton plants in terms of plant nectar production. Consequently, there is also a difference in the number and composition of associated ant populations attracted by the nectar (Vázquez-Barrios et al., 2021). In general, more ants were present in the natural cotton plants. Specific ant species useful for repelling insect pests were less abundant in cotton with inbred herbicide resistance, but were more abundant in Bt cotton. Since ants are important in pest control and also for cotton seed dispersal, these disrupted interactions between the transgenic plants and their environment can have significant long-term consequences.

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[16] https://www.efsa.europa.eu/en/supporting/pub/e200506

Amongst others, higher nectar production may cause Bt cotton progeny to acquire invasive traits. In fact, transgenic cotton plants are spreading faster in wild populations than originally expected (Wegier et al., 2011; Vázquez-Barrios et al., 2021). These results, which should be further investigated in future research, show how unintended genetic and metabolic interactions caused by genetically engineered modifications can promote the spread of transgenic plants. In this case, the damage is considerable since it threatens one of the centres of wild cotton biodiversity.

2.3.2 Accelerated spread of pests

The cultivation of Bt cotton in China has also led to altered interactions with the environment. Larvae of the moth, *Helicoverpa armigera*, infected with certain viruses have been observed to spread at an increased rate in fields with transgenic cotton (Xiao et al., 2021). The infected larvae become resistant to the insecticide more quickly, and thus have a selection advantage over their healthy conspecifics in the genetically engineered fields. Larvae infected with these viruses are hardly ever observed in conventional cotton fields.

In Brazil, whitefly (*Bemisia tabac*i) is spreading in fields where Bt soybean is grown (Almeida et al., 2021). The scale insects seem to benefit from certain biological properties of the transgenic soybean plants, especially when the genetically engineered soybean also contains transgenes against herbicides. The scale insects that feed on herbicide-resistant Bt soybean plants are more fertile and the number of their offspring is significantly increased. Whitefly infestation also favours the spread of plant diseases since viruses are transmitted when they suck the sap of the plants and their excretions increase the probability of fungal infestations. Causes for the spread could be insecticides that are non-toxic to the whitefly, but which may possibly have a stimulating effect on them. However, unexpected interactions in the genome of the soybean plants are also being considered, as these can be attributed to genetic modifications. In an earlier case, Monsanto researchers warned of such effects in genetically engineered soybean plants with both traits after observing a strong spread of pest insects (larvae of the moth *Spodoptera eridania*) in these fields (Bortolotto et al., 2014).

In Brazil, weeds that are resistant to several herbicides are spreading in the fields as a result of the cultivation of transgenic soybeans. Among them are several species of amaranth, which are a food source for certain moth larvae, S*podoptera cosmioides*, amongst others (Páez Jerez et al., 2022). If these larvae feed on both a certain species of herbicide-resistant weed (*Amaranthus palmeri*) and insecticidal Bt soybean plants, they have a higher number of offspring, and thus a higher overall fitness. These pests benefit from the combination of the two traits in the transgenic plants: the increased spread of certain herbicide-resistant weed species and the unintended effects of the genetic modifications of Bt soybean plants enable them to spread faster in these fields.

2.3.3 Uncontrolled spread

In addition to the progressive emergence of what are now several dozen, in particular, glyphosate- resistant weeds worldwide, the genetically engineered plants themselves can become 'weeds' (Fig. 9). Genetically engineered herbicide-resistant plants that spread in the environment can also interbreed, and thus become resistant to several other herbicides. In wild cotton populations in Mexico, for example, gene constructs of up to four transgenes have been found that are not present in this combination in any commercially grown genetically engineered cotton variety worldwide (Wegier et al., 2011). Such multiple resistances have presumably arisen through hybridisation of several 'single events' and have spread further into wild cotton populations. Besides genetically engineered cotton, other similar events (Vázquez-Barrios et al., 2021) have also been found in genetically engineered canola in Japan (Aono et al., 2006) and the USA (Schafer et al., 2011), amongst others.

Surprisingly, glyphosate-resistant genetically engineered plants can also display a higher fitness, and subsequently a stronger tendency to spread independently of herbicide use (Bauer-Panskus et al., 2020). The increased fitness is presumably caused indirectly by the transgenic enzyme, EPSPS, as it not only makes the plants resistant to glyphosate, but also interferes in various metabolic pathways by, amongst others, increasing the production of the plant hormone auxin. Auxin plays a key role in growth, reproductive capacity and adaptation to heat and drought stress. Genetically engineered plants may, therefore, exhibit stronger growth or increased seed production, and thus have a selection advantage (Wang et al., 2014; Yang et al., 2017; Beres et al., 2018; Fang et al., 2018). These unexpected properties of transgenic plants have been overlooked for decades, even though they can contribute significantly to their uncontrolled spread (see below). In addition to canola, cotton and maize, transgenic glyphosate-resistant grasses are also spreading rapidly and uncontrollably in the USA (Zapiola et al., 2007). The extent to which the increased fitness of the transgenic plants with additional EPSPS enzymes plays a role has not yet been investigated.

It became clear from examining, in particular, transgenic canola, that genetically engineered plants have actually established self-sustaining populations in several regions, and are thus able to persist and spread in the environment. This is also the case in countries that only import genetically engineered plants (possibly also unintentionally) or have done so in the past (Sohn et al., 2021).

In Canada, for example, hybridisation has occurred between glyphosate-resistant canola and the closely related wild species, *Brassica rapa* (bird rape mustard), which is a weed found in fields in many regions (Laforest et al., 2022). Although it has been known for a long time that transgenic hybrid plants grow close to transport routes in other countries, it was also assumed that they could not become permanently established due to reduced fertility. However, this assumption was disproved by the discovery of transgenic B. *rapa* in Canada. Glyphosate resistance is meanwhile detectable in homozygous form in these wild plants - presumably through multiple backcrossing of the hybrids - which is only possible if the plants persist in the environment for long periods of time. In these areas, further outcrosses of the transgenic glyphosate resistance were also detected in field radish (*Raphanus raphanistrum*), another wild relative of canola. The persistence and spread of these plants may be favoured by the application of glyphosate, but does not seem to be dependent on it.

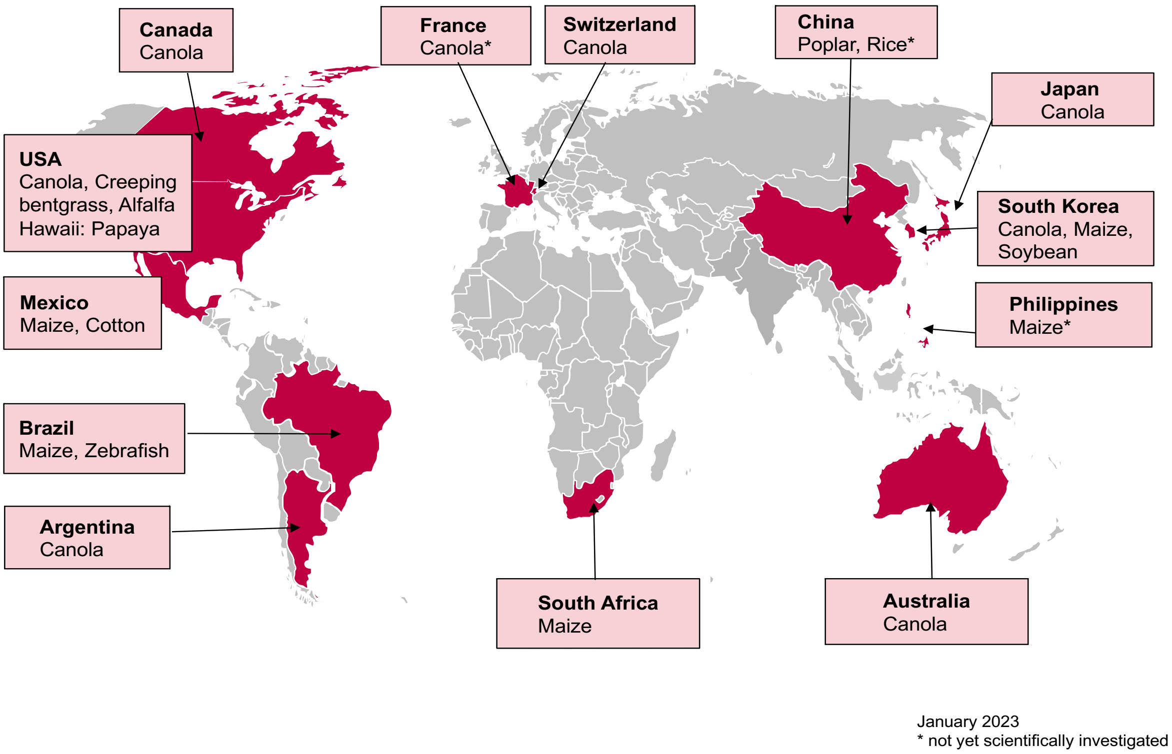

Figure 9: Uncontrolled spread of approved genetically engineered organisms: documented cases of feral populations and outcrossing into cultivated or wild species. Some cases have also been documented in countries where no genetically engineered crops are grown at all (updated according to Testbiotech 2015).

Current risk assessment does not take sufficient account of the unintended and unexpected long-term consequences resulting from spontaneous dissemination and gene transfer of genetically engineered plants able to persist and reproduce in the environment (Bauer-Panskus et al., 2020). The particular problem in this regard: the offspring of the transgenic plants can exhibit new, unexpected properties, so-called 'next generation effects'. Hybridisation effects observed in crosses of genetically engineered plants with wild populations include, amongst others, increased seed formation. Against this backdrop, some experts are calling for so-called 'cut-off' criteria, which can be used to terminate the approval assessment if there are too many uncertainties to allow conclusive risk assessment (Bauer-Panskus et al., 2020, Then et al., 2020).

2.4 Benefits for consumers?

The aforementioned OECD study (1992) also points out that the market strategy for introducing transgenic plants only works if the products have a corresponding added value for the consumer. Any cultivation of plants that is associated with herbicides or insecticides would have a very negative image. The benefits for consumers need to be shown in a more positive light if the market is to be opened up, emphasising, amongst others, "product improvements" such as "higher nutritional value, better quality and shelf life".

However, these strategic efforts suffered a serious setback very early on: the "Flavr-Savr-Tomato" introduced in the USA in 1994 was a flop. The tomato, which was supposed to stay fresh for longer, was not only more difficult to harvest, it also met with very little approval from US consumers. By 1997, the tomato had already disappeared from the market. Since then, there have been a lot of announcements made about the introduction of products derived from genetically engineered plants with special benefits for consumers. So far, however, hardly anything has come onto the market that would have any actual relevance in this respect (see also Then, 2015).

The best-known example of transgenic plants whose consumption is supposedly associated with health benefits is so-called 'Golden Rice'. Golden Rice is said to produce an increased content of a precursor of vitamin A, so-called β-carotene, in the rice grains, thus making it suitable to combat vitamin A deficiencies which are a serious problem in many so-called developing countries. However, even though the genetically engineered rice has been under development for more than 20 years, essential data on food quality and food safety are still missing. The rice was harvested for the first time in the Philippines in 2022. Further studies using this harvest will now be conducted to investigate its actual benefits.[17] There are already many questions, as the data available from the marketing authorisation applications only show low levels of β-carotene (Testbiotech 2018). High levels of loss due to storage and cooking are also expected (Bollinedi et al., 2019). Studies also confirm very different carotene contents, which depend, amongst others, on the respective varieties or their genetic background (Mallikarjuna-Swami et al., 2021). Against this backdrop, it seems doubtful whether these plants actually have any significant benefits for consumers.

The Philippines is one of the most important centres of biodiversity for rice, so it would be particularly problematic if rice fields in this region were to be contaminated with the genetically engineered rice. Cultivation of Golden Rice, therefore, poses a considerable threat to the preservation of biodiversity and regional varieties. The genetically engineered plants could, for instance, pass on their genes to wild rice. Wild rice is widespread on field borders so this would enable the transgenes to re-enter the fields, and thus be introduced into the transgene-free rice. There have already been major problems with contamination from genetically engineered rice in both the USA and China, even though it was only tested in these countries in field trials and not grown on large areas (Price & Cotter, 2014).

2.5 Summary of existing experience with transgenic plants

To summarise, it is clear that the promised benefits and high expectations raised by promoting transgenic plants have so far either completely failed to materialise, or were fulfilled only partially or temporarily. Such expectations were raised even before the introduction of genetically engineered plants, and often served as justification for their use. Once approved, there was often insufficient systematic research to objectively evaluate these promises.

In addition, there has been insufficient testing of combinatorial effects, cumulative effects and interactions between genetically engineered plants and their environment or between the genetically engineered plants themselves, including mixtures into food and feed. Since the introduction of genetically engineered crops, there has been an overall increase in uncertainties regarding the health risks of feed crops for livestock and food for humans. In addition, there are further uncertainties regarding the stability of ecosystems.

There are also questions about the sustainability of cultivating these plants when faced with challenges such as climate change, which is best addressed through diversity in the fields (FAO, 2017) and not by a one-sided approach focussing on specific plant traits, as this carries the risk of destabilisation. Findings show that the

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[17] https://ethz.ch/en/news-and-events/eth-news/news/2022/11/the-seeds-have-germinated.html

cultivation of transgenic plants with predominantly only two traits has tended to destabilise agro-ecosystems in many growing regions. The use of pesticides was reduced in some growing regions for a short time, but was then often significantly increased again - creating a 'yo-yo effect'. This is how the 'arms race' in the fields has happened and continues to happen; the plants are made resistant to more and more herbicides and, at the same time, produce an increasing number of insecticides.

The negative effects are manifest not only in increasing environmental pollution with certain toxins, but also, amongst others, in the uncontrolled spread of genetically engineered plants in centres of biodiversity, which will endanger conservation. There are, in addition, negative effects caused by genetically engineered modifications that can lead to genetically engineered crops becoming even more susceptible to, for example, insects feeding on them. These developments can cause significant agricultural damage, although their exact causes are far from being sufficiently understood.

Patents on seeds are one of the most significant driving forces behind the cultivation of transgenic plants. The market power of large corporations means that they already decide what is cultivated and harvested in many regions of the world. This gives them the power to promote bogus solutions, and sell products that they feel are especially suitable for their profit margins, but which have little chance of solving current problems in agriculture.

To ensure that these negative scenarios are not repeated with the introduction of plants developed using new genomic techniques (NGTs), the procedures for their approval should be broadened. This should include, amongst others, the introduction of a prospective technology assessment (TA). A TA assessment could be a decisive instrument enabling decision-makers to examine the actual sustainability of NGTs in agriculture, and thus effectively control or limit the type and number of genetically engineered organisms released.

3. The role of technology assessment

The introduction of transgenic plants raised many expectations regarding the benefits for plant breeding, the environment and food security (see Chapter 2). Subsequently, many of these expectations have either failed to materialise, or have only partially been fulfilled. As many aspects of genetic engineering are at best controversial, it would be useful to introduce a comprehensive technology assessment for future genetic engineering applications. This should make it possible to correctly assess the previous consequences and, if necessary, to guide further developments. It could also help to overcome the problem that, up until now, it has only been possible to fall back on data from industry or on evaluations that frequently appear questionable in their overall perspective in regard to transgenic plants. In future, data should be collected as independently as possible and according to transparent and reliable criteria.

3.1 Problems in evaluating the advantages and disadvantages of transgenic plants

A frequently cited 'meta-study' by Klümper and Qaim (2014) underlines the current problems in evaluating the advantages and disadvantages of transgenic plants. After an evaluation of almost 150 scientific studies, the study appears to show that the cultivation of genetically engineered crops has reduced the use of pesticides worldwide by 37 per cent, increased crop yields by 22 per cent and increased farmers' profits by 68 per cent. According to Klümper & Qaim (2014), these effects can be observed in all countries where genetically engineered crops are grown, but especially in developing countries.

However, the study is methodologically unsound. Since the cultivation of insecticidal or herbicide-resistant plants does not per se lead to higher yields (see 2.1), each case would have to be investigated in-depth to determine whether and under what conditions these higher crop yields actually occur. To avoid comparing apples with oranges, strict attention would have to be paid to ensuring that the conditions under which the respective studies were conducted are comparable. Factors to be considered here include:

- How long have the plants already been cultivated? With some genetically engineered plants, the results of cultivation are often better in the first few years because resistance to weeds or pests has not yet developed.
- Which seeds were used? It is possible that breeding progress is evident in the fields that is not directly related to genetic engineering.
- What management systems were available? The farmers using genetically engineered seeds may have received more detailed advice, used more fertiliser and/or irrigated more strongly.
- In which markets, as applicable, were higher sales revenues achieved? It is possible that the overall demand for certain products increased thus increasing the revenues generated.

Unless the conditions under which higher yields and/or savings in inputs are achieved are precisely recorded, the results of such meta-studies are not very reliable. The greater the number of studies included which show substantial differences in terms of methodology and initial conditions, the more questionable the result. However, the Klümper & Qaim study claims that all 'suitable' studies dealing with the cultivation of genetically engineered crops worldwide were included: *"Studies were included when they build on primary data from farm surveys or field trials anywhere in the world, and when they report impacts of GM soybean, maize, or cotton on crop yields, pesticide use, and/or farmer profits."* (Klümper & Qaim, 2014).

As a criterion for selecting 'suitable' studies, the authors mention, in particular, the requirements of their statistical methodology, which is basically the correct approach. However, it is only a necessary, but not a sufficient criterion, since it does not take into account the factors mentioned above, which are decisive for whether the respective studies are at all comparable with each other. General conclusions based on potentially non-comparable data are therefore imprecise, and at the very least questionable.

In this respect, studies such as the one by Klümper & Qaim (2014) are often just as unreliable as reports based primarily on industry data and in some cases even financed by the industry, such as publications by PG Economics[18] or the International Service for the Acquisition of Agri-biotech Applications (ISAAA).[19]

Even studies conducted independently of industry are not always convincing in terms of methodology and data availability. Overall, it cannot be denied that there is a clear lack of both sufficiently defined criteria and methods for assessing the systemic impact of transgenic plants. This further highlights the need to develop appropriate tools for an additional and comprehensive technology assessment, including the possible use of 'new genomic techniques' (see below).

3.2 Characteristics of technology assessment

Prospective technology can be an important tool to recognise as early as possible the systemic effects caused by the use of genetic engineering in agriculture and other releases of genetically engineered organisms. Important features of TA are summarised, for example, in the technology assessment Design Handbook of the US Government Accountability Office (GAO) as follows (GAO, 2021): *"New technologies can have a range of effects, potentially both positive and disruptive, that TAs can explore. GAO has broadly defined TA as the thorough and balanced analysis of significant primary, secondary, indirect, and delayed interactions of a technological innovation with society, the environment, and the economy and the present and foreseen consequences and effects of those interactions."*

In addition to the risk assessment required for the approval of individual products, questions about the potential benefits and economic consequences of using NGTs could also be examined within the framework of a TA assessment. For example, false promises could be distinguished from actual potential benefits.

Moreover, in contrast to case-specific risk assessment of individual organisms, TA can deal more systemically with (groups of) products and their overall impact(s) on ecosystems, taking into account risks, such as tipping points where the total pressure on ecosystems (or parts thereof) could be exceeded.

The primary motivation behind TA is to be able to assess possible negative effects at an early stage in order to ideally prevent them or to enable responsible handling. According to Jonas (1979), one of the founders of TA, *"for the development and use of many modern technologies, the principle of trial and error with subsequent compensation for unintended and unexpected consequences is neither politically or economically practicable, nor ethically responsible."*

3.3 Future scenarios – an important instrument of technology assessment

The development of possible future scenarios has established itself as one of the most important instruments in the methodology of TA in order to structure the conceivable consequences of a technology in terms of its (future) openness (Böschen et al., 2021). Besides the intended benefits, this would include worst-case scenarios, such as accidents, uncontrolled spread or extreme weather events. Such scenarios can be used to assess the impacts on specific areas, such as health, environmental protection, animal welfare or risk research. They can also facilitate scrutiny of food security or patents.

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[18] https://www.pgeconomics.co.uk/

[19] https://www.isaaa.org/

Important criteria for assessing and guiding the use of new genomic techniques on the basis of future scenarios could be, for example, its controllability, predictability and error-friendliness. The criteria should further take into account any available conventional breeding options, agroecology findings and traditional methods of food production. In addition, the criteria must be clear, transparent, reliable and practicable in order to make evidence-based decisions on the sustainability and potential benefits of the use of genetic engineering in agriculture.

3.4 technology assessment as an additional level of control

Experience with transgenic plants to date shows that the systemic effects of their use on ecosystems and food production have been insufficiently considered. There are good reasons to separate these issues from those of risk assessing individual organisms, which is carried out by the 'Risk Assessor' (specifically the European Food Safety Authority EFSA) and must be done independently of any potential benefits or economic impacts. Decisions on possible authorisations are currently taken by the 'risk manager' (in particular the EU Commission), who can also take other aspects into account in addition to the risks to humans and the environment: the EU Release Directive 2001/18, for example, already allows socio-economic criteria to be taken into account (see EU Directive 2001/18/EC). However, the appropriate methodology and a transparent and scientifically justified catalogue of criteria to include these aspects in the decision-making process are still missing.

An appropriate legal framework for comprehensive and prospective TA (as a complementary level of control in addition to risk assessment) could provide essential support in this context. Any such legal framework should make it possible to consider both the possible advantages and disadvantages as well as further systemic impacts of NGTs, all of which extend beyond the approval assessment of individual organisms. These assessments should take place at the earliest possible stage and well before any possible market authorisation.

TA is a vital second level of control, especially in light of the possible introduction of organisms derived from new genetic engineering (see below): the high number of possible applications filed for many different species and very different properties, makes it essential to focus more on the systemic effects. In this regard, policy-makers must be enabled to effectively control and limit the type and number of potential releases of genetically engineered organisms.

The following chapters will therefore look at some features of NGTs and their potential impacts from the perspective of prospective technology assessment.

4. technology assessment and new genomic techniques (NGTs)

Current discussions in the field of genetic engineering are considering many new potential releases of NGT organisms, e. g. in agriculture and even in nature conservation (JRC, 2021, BfN, 2022). The possible resulting impacts therefore require a comprehensive prospective analysis.

In this context, sufficient account must be taken of the technical potential in regard to possible effects on the environment and assessment of sustainability: CRISPR/Cas 'gene scissors' is the most important NGT tool in this respect; it is more precise and faster than previous genetic engineering methods, but by no means error-free. It enables much more profound changes in the genetics and biology of plants and animals (see below). Even if no additional genes are introduced, the genetic changes and gene combinations achieved often go far beyond what is known from previous breeding. NGTs could also be used to modify natural populations beyond the fields or in the laboratory, such as wild herbs, trees, bees, other insects and soil organisms (Testbiotech, 2021c). The organisms in question will not have adapted through evolutionary processes and can have a (negative) impact on ecosystems on several levels.

In the future, for example, it could happen that even within just one ecosystem, NGT plants are grown, genetically engineered soil microorganisms introduced and NGT insects released into the environment, all at the same time. Such releases would have the potential to alter the further course of evolution and disrupt mutual adaptation processes. In order to be able to assess the actual consequences, it is important to examine not only the risks for each individual organism ('event'), but also the interactions between the different genetically engineered organisms (including the interactions with their environment). There is a risk that these NGT organisms will in their entirety have a negative impact on the respective species, populations and ecosystems which reaches beyond the effects identified for the individual NGT organisms as part of the approval assessment. Developing scenarios to explore these interactions and deriving specific hypotheses about risks and risk avoidance would be a task for prospective technology assessment, without which no conclusions can be drawn about the sustainability of NGT organisms.

Another task for TA arises from the examination of the expected benefits of NGT organisms. Similar to the introduction of transgenic plants, great hopes are associated with new genomic engineering. Some of the participants in science, industry and politics are currently even giving the impression that the hypothetical benefits of using NGTs in agriculture are already a reality (see, amongst others, Leopoldina, 2019; ALLEA 2020; EU Commission 2022).

It must be taken into account, for example, that the use of NGT processes in plants and animals often leads to extreme versions of traits, which can be associated with effects and risks for the plants and animals as well as for their environment (see Chapter 6). However, it still remains to be seen whether plants that are more resistant to negative environmental influences, such as climate change and plant diseases, will really be developed with NGTs.

Whatever the case, empty promises and expectations that are too high must be distinguished from the actual possible benefits. Unless there is sufficient verifiability of the possible benefits, completely unsuitable risk technologies could be promoted as 'solutions' to problems such as world hunger, climate change and the negative impacts of (industrial) agriculture. As has happened in the past (EEA, 2001), there is a danger that supposed solutions will instead lead to new problems.

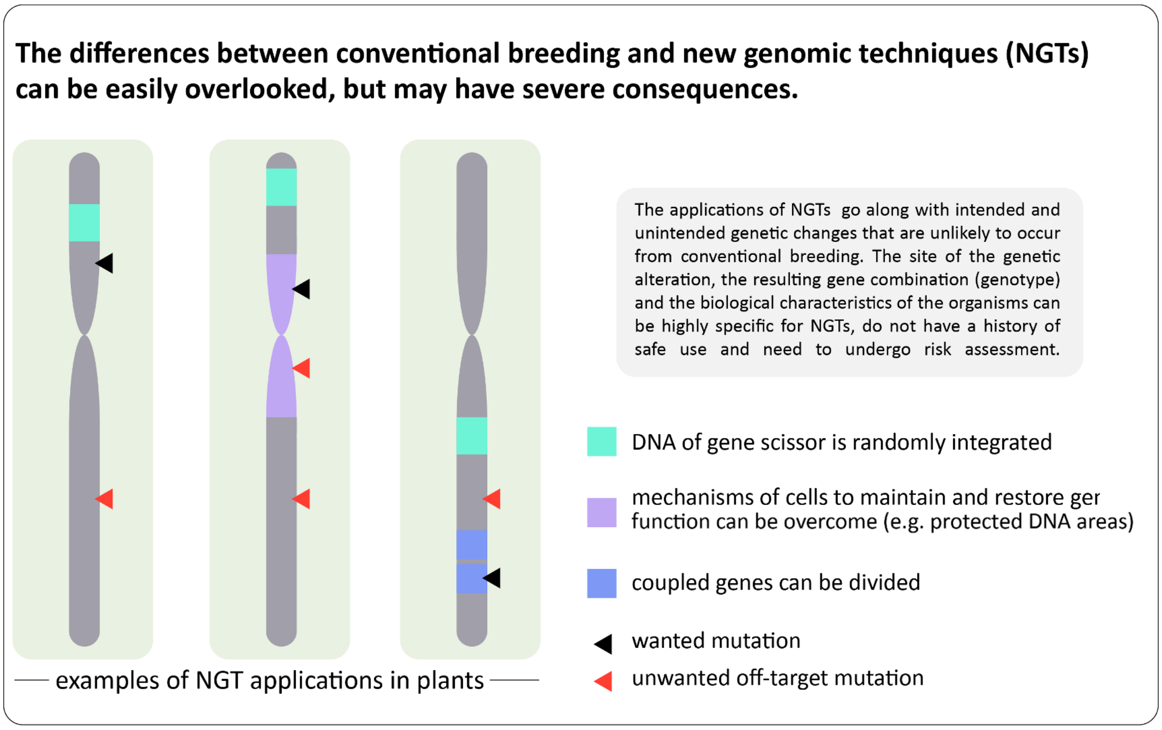
4.1 Differences between NGTs and conventional breeding

Proponents of new genetic engineering often claim that the use of NGTs, such as CRISPR/Cas or certain applications of these techniques, corresponds more or less to naturally occurring processes, especially in plant breeding, and that any related products should therefore be regarded as 'nature-identical' (e. g. Gao, 2018; Leopoldina, 2019; Eriksson et al., 2020).

However, in recent years numerous research papers have highlighted the fundamental differences between conventional breeding and genetic engineering (including Agapito-Tenfen & Wickson, 2018; Eckerstorfer et al., 2019; Kawall, 2019, Kawall, 2021b).

One reason for these differences is, for example, the natural mechanisms in cells that are particularly efficient at protecting important DNA regions and genetic information, e. g. through repair processes that can fix mutations and thereby restore original functions, so that certain gene functions are much less frequently lost or altered than others (Frigola et al., 2017; Belfield et al., 2018; Kawall, 2019; Halstead et al., 2020; Monroe et al., 2022). In addition to protecting 'essential' genes, NGTs can also be used to bypass other evolutionary mechanisms and genome organisation factors, such as gene duplications, linked genes or epigenetic mechanisms. This makes changes in the genome possible that are otherwise very unlikely to occur (Lin et al., 2014; Wendel et al., 2016; Filler Hayut et al., 2017; Jones et al., 2018; Huang & Li, 2018; Kawall, 2019; Kawall et al., 2020).

NGTs make the genome available for genetic changes to a much greater extent and the outcomes of these applications differ substantially from those resulting from previously used breeding methods (Fig. 10). For example, with the use of 'random mutagenesis', in which chemical substances or physical radiation are used to accelerate the rate of mutation, no genetic changes can be expected that cannot also occur spontaneously and naturally over longer periods of time. In contrast, NGTs can be used to alter gene functions that are otherwise protected by natural protective mechanisms such as the abovementioned repair processes. The use of the CRISPR/Cas, in particular, can prevent genetically engineered changes from being repaired by the cells, coupled genes from being inherited together or gene duplications from taking effect as backups (Kawall, 2019; Kawall et al., 2020). In addition, several different gene loci can also be changed simultaneously through so-called 'multiplexing' (Raitskin & Patron, 2016; Wang et al., 2016, Zetsche et al., 2017; Kawall et al., 2020). As a result, new genotypes and phenotypes can emerge (even unintentionally) that go far beyond what can be achieved with conventional breeding (overview and further sources: Testbiotech, 2022). This is the case even if no additional genes are inserted.



The differences between conventional breeding and new genomic techniques (NGTs) can be easily overlooked, but may have severe consequences.

The applications of NGTs go along with intended and unintended genetic changes that are unlikely to occur from conventional breeding. The site of the genetic alteration, the resulting gene combination (genotype) and the biological characteristics of the organisms can be highly specific for NGTs, do not have a history of safe use and need to undergo risk assessment.

Figure 10: Unintended genetic changes (mutations) can also occur in conventional breeding. However, NGT methods are accompanied by changes that would not be expected with conventional breeding and random mutations: both the site of mutation and the resulting gene combination can be significantly different from the results of conventional breeding. This is true not only for intentional, but also for unintentional genetic changes. Some reasons are: NGTs can overcome constraints on natural genome organization used by cells to maintain gene function (such as repair mechanisms, gene duplications, or epigenetic mechanisms). In addition, several different gene loci can be altered simultaneously (multiplexing). The introduction of NGT tools using the untargeted methods of old genetic engineering can also result in unintended changes in the genome of plants.

In summary, the higher availability of the genome enables:

- fundamental changes in the biological properties of organisms, which can be induced even if no additional genes are inserted;
- the overriding of limitations in natural genome organisation, such as repair mechanisms (or other protective factors, e. g. gene duplications), thus generating new genotypes that cannot be achieved with conventional breeding;
- more extreme versions of known phenotypes or even new phenotypes, which are often associated with side effects ('trade-offs') (see Testbiotech, 2022).

The technical potential of tools, such as CRISPR/Cas, also creates the possibility of unintentional genetic changes that could almost never be achieved with conventional breeding.

Both the intended and unintended changes associated with NGT processes (and the resulting intended and unintended effects that occur immediately, delayed or cumulatively) pose specific risks to humans and the environment (Kawall et al., 2020; Kawall, 2021a; Kawall, 2021b; Eckerstorfer et al., 2021; Yang et al., 2022; Testbiotech 2022) and need to be thoroughly assessed before approval.

There are several factors that influence the results of NGT processes in terms of intended and unintended traits, including the respective species, the intended breeding characteristics, the target genes (their position in the genome, function, number, similarity to other genes), the type of 'gene scissors' (or other genetic engineering tools) and the procedure for introducing the gene scissors into the cells (or that of other genetic engineering tools). Amongst others, it must be noted that the changes induced by NGT processes are always carried out in several stages. For example, the use of the CRISPR/Cas gene scissors in plants regularly involves the untargeted procedures used in earlier types of genetic engineering: methods such as the 'gene gun' or *Agrobacterium tumefaciens*-mediated transformation are frequently used in NGT applications to deliver the DNA necessary to form the gene scissors into the cells. In most cases, the outcome is a transgenic plant which may have a variety of unintended genetic changes as a result of this initial step (Forsbach et al., 2003; Makarevitch et al., 2003; Windels et al., 2003; Rang et al., 2005; Gelvin et al., 2017; Jupe et al., 2019; Liu et al., 2019; Yue et al., 2022). These unintended effects have also been observed in NGT plants (Braatz et al., 2017; Biswas et al., 2020). In the absence of sufficient standards in risk assessment, such unintended effects can persist unnoticed in the genome, spread rapidly in populations and possibly also accumulate.

As a result, at each stage of the process – (I) the insertion of the DNA for the gene scissors, (II) the recognition and modification of the target region, and (III) the repair processes in the cells - specific unintended changes can occur, each with its own risks. This makes risk assessment necessary for each 'event' and also raises questions for technology assessment.

4.2 Systemic effects on the environment

As explained, in the near future – and due to the technical potential of the CRISPR/Cas gene scissors - many different NGT organisms with a wide range of different properties could be released simultaneously into shared ecosystems within a short space of time.

The speed of change in the components of ecosystems is an important factor here: new traits that have emerged through evolutionary processes usually spread only gradually in natural populations. In contrast, the introduction of NGTs could rapidly expose ecosystems to mass releases of NGT organisms which have not adapted through evolutionary processes. At the same time, proponents of NGT methods are promising ever shorter development times and production cycles, thus shortening even further the intervals at which the new genetically engineered organisms with new properties are released into the environment. As a result, the ecosystems may be exposed to increased stress conditions that exceed their resilience.

Even small changes can have a considerable impact: ecosystems can be endangered just by altering individual genes that exert a particular key function within a food web. If, for example, all gene variants (alleles) of such a (key) gene are standardised with NGTs, this can lead to a reduction in the genetic diversity of a plant population, and thus have a severe impact on the composition of associated species, such as beneficial insects or pests. If these species are severely depleted or become extinct as a result of such 'gene uniformisation', even this supposedly simple intervention can lead to the destabilisation of entire food webs (Barbour et al., 2022).

There are NGT applications that could intervene in natural, non-domesticated wild populations much more profoundly and with a much broader impact than in the experiments conducted by Barbour et al., (2022). These applications include so-called 'gene drives', which can spread a new genetic trait with greater frequency in populations than would be expected according to Mendelian inheritance laws (Simon et al., 2018; Frieß et al., 2019). Further instances are the deliberate release of genetically engineered viruses to be used in agriculture for plant protection, or as vectors for the genetic engineering of crops, or even in wildlife as self-propagating vaccines. (Lentzos et al., 2022; Pfeifer et al., 2022).

Overall, releases of NGT organisms cannot generally be considered 'neutral' for the functioning of the ecosystems. In this context, both the 'degree of naturalness' of the NGT organisms (in terms of intended and unintended effects) and the magnitude of releases into the environment are crucial in determining the likelihood of undesirable interactions. Consequently, even if individual events are considered to be safe, the overall magnitude of the releases (the number of NGT organisms, the different characteristics and the species involved) must be taken into account (see also Heinemann et al., 2021).

Similar to pollution of the environment with plastics and chemicals, it does not always have to be a specific genetically engineered organism that causes the actual problems. The decisive factor may be the totality of different effects of several of these organisms on the environment. In this regard, while the release of a small number of NGT organisms over a short period of time may not have a negative impact on ecosystems, releases of large numbers of different NGT organisms over longer periods of time may lead to ecosystem overload or tipping.

These observations underline the need to look ahead at the overall impact on ecosystems in order to assess the sustainability of NGT organisms. When releasing NGT organisms, the focus should not only be on their interactions with ecosystems, but also on the interactions between the different NGT organisms. TA should therefore consider different risk scenarios involving different NGT organisms and examine, for example, the following effects: (1) disruption of ecological interactions between plants and their associated microbiomes and/or pollinators, (2) weakening of resistance (resilience) to biotic or abiotic stress factors, (3) evolutionary maladaptation that prevents further co-evolution of species and (4) threats to biodiversity from the uncontrolled or invasive spread of NGT organisms. Hypotheses can be derived from such scenarios to indicate which data and investigations would be necessary for risk assessment and approval decisions.

The introduction of appropriate termination criteria (cut-off criteria) is recommended, as definitive conclusions cannot be drawn on the safety of NGT organisms when confronted with missing data and considerable uncertainties (unknowns). The termination criteria should enable decisions to be made and, if necessary, applications for releases to be rejected if the respective uncertainties and hazards associated with the genetically engineered organisms are large scale or appear too great (Bauer-Panskus et al., 2020; Then et al., 2020).

Whatever the case, it is important that the legal regulation of genetically engineered organisms considers the number of releases, their duration, their various properties and the interactions between the NGT organisms as a whole. TA in particular can provide the necessary basis in this respect - in order to control the type and quantity of organisms that could be released into the environment and, if required, strictly limit their eventual approval.

5. Potential disruptive effects of NGTs on breeding, agriculture and food markets

Any large-scale introduction of NGT organisms into agriculture would most likely not only change the characteristics of livestock and crops, but also affect food production systems as a whole. NGTs can, therefore, be seen as disruptive technologies in this context. For example, CRISPR/Cas 'gene-scissors' is the main tool used to generate NGTs. It is a technology that was described in the Nature journal (Ledford, 2015) as a 'disruptor' in several ways: *"A powerful gene-editing technology is the biggest game changer to hit biology since PCR. But with its huge potential come pressing concerns."* While Goold et al. (2018) and Menchaca et al. (2020) highlight the disruptive potential of gene scissors in plant and animal breeding as positive, there are nevertheless concerns about possible negative disruptive socio-economic impacts on seed markets, food production and freedom of choice (Clapp, 2021, Testbiotech, 2021b).

Disruptive technologies are not per se good or bad. In the case of NGTs, however, potentially negative impacts can extend to many areas that are particularly sensitive or worth protecting. In this context, particular attention must be paid to ecosystems and biodiversity, food production, seed production and consumer choice. In this respect, TA is faced with the question of whether and how the consequences that can arise from new, disruptive technologies, especially in the area of agriculture and food production, can be assessed before they are introduced.

A comprehensive and prospective TA could be used, amongst other things, to distinguish empty promises or unprovable benefits from actual potentials. Socio-economic factors must also be taken into account, such as the redistribution of costs and profits. In particular, the impact on traditional breeding and food production, conventional- as well as organic farming and consumer choice should be included in these assessments.

The EU Commission states that in addition to risk assessment, further tools are needed to assess the potential benefits of NGT crops (EU Commission, 2021):

> *"A purely safety-based risk assessment may not be enough to promote sustainability and contribute to the objectives of the European Green Deal and in particular the 'farm to fork' and biodiversity strategies; benefits contributing to sustainability would also need to be evaluated, so an appropriate mechanism to accompany risk assessment may be required."*

In the following section we discuss possible disruptive effects triggered, in particular, by patents, and which extend to agriculture, breeding and science. The interests of food producers and consumers are also included at this point.

5.1 Disruptive effects of patents

As far as the introduction of NGTs is concerned, there are several areas that are particularly affected by patents. They include access to the technology, availability of biological diversity and the independence of science and risk assessment.

5.1.1 Access to the technology

Corteva – the former agricultural division of DowDuPont - has filed the highest number of patent applications and holds most patents granted for NGTs (Jefferson et al., 2021; Testbiotech, 2021b; Global 2000, 2022). The company succeeded in 2018 in combining a total of around 50 basic patents on CRISPR/Cas technology in a patent pool, to which it added its own patent applications (Then, 2019). This pool has been steadily expanded in recent years (IHS Markit, 2020; Jefferson et al., 2021), so that other breeding companies need access to the patent pool in order to make full use of CRISPR/Cas in plant breeding. They are thus obliged to pay licence fees, sign contracts on compliance with relevant guidelines and on confidentiality, and also disclose their breeding objectives. Such market power in the hands of a single company has no precedent in plant breeding, it not only enables control of potential competitors but also secures a dominant market position.

While it will still be possible for large corporations, such as Bayer or BASF, to conclude their own contracts with the inventors of the CRISPR/Cas technology, this is much less of an option for smaller breeding companies, even though other companies, such as KWS and Rijk Zwaan, are increasingly trying to file their own patents. However, the hundreds of patent applications already filed mean that access to CRISPR/Cas technology is either controlled, significantly restricted or blocked. This can be a major problem for small breeding companies and threatens the independence of medium-sized breeders that want to work with NGTs. As a result, it appears inevitable that the introduction of NGTs will lead to further market concentration in the field of plant breeding, and possibly have serious consequences for agriculture and food markets.

5.1.2 Access to biological material

Free access to biological resources is indispensable for both conventional breeding and NGT applications: breeders select plants on the basis of breeding (phenotypic) characteristics and genotypes (marker-assisted selection). The use of the respective biological material must, therefore, be freely available. The users of NTGs also depend on access to the natural genetic diversity they need for programming the gene scissors, both in respect to the target sites in the genome and the insertion of desired DNA components.

In this context, it is extremely worrying that, for example, patent applications filed by Syngenta claim the use of thousands of gene variants (also called 'single nucleotide polymorphisms' (SNPs)), including those found in arable crops, such as soybean and maize, which occur naturally and which can, for example, strengthen plant resistance to diseases (WO2021000878, WO202103391, WO2021154632, WO2021198186, WO2021260673). In most cases, the respective gene variants were discovered in wild relatives of the cultivated varieties (Tippe et al., 2022). The scope of the patents is, in this case, by no means limited to NGTs, it also extends to the use of the gene variants in conventional breeding.

Such patent applications represent considerable legal uncertainties for breeders. It may be almost impossible, for example, to find out whether a particular soybean plant with increased resistance to Asian soybean rust carries any of the approximately 5000 gene variants listed in the Syngenta patent application WO2021154632 in its genome. If these patents are granted, breeders will no longer be able to use all conventionally-bred varieties for further breeding. They cannot even switch to wild related species of soybean for their breeding, as any use for breeding purposes of the listed genes is claimed in the patents. This practice thus creates an impenetrable patent jungle for breeders.

Generally, patents grant a monopoly position for the economic exploitation of the claimed 'inventions'. If patents are granted on specific genetic variants, all other breeders can be excluded from using them for the production and marketing of new varieties, or made dependent on licensing agreements. Previously, breeders had the right, under the rules of plant variety protection, to use all plant varieties to breed new, improved varieties and to market them as their own breeds. This engine of innovation in plant breeding is now in danger of being blocked by an impenetrable jungle of patent applications filed to cover the genome of cultivated plants. NGTs are a major driver of this development. If patents are granted on specific gene variants and their use, this can hamper or even block conventional breeders.

Stagnation, insolvencies and upheavals in the field of conventional breeding would be the result, as the uncertainties regarding the scope of patents and their legal implications are hard for many traditional breeding companies to keep track of. Even the mere filing of patents, which may take years to be granted, can have a detrimental effect on other breeders working on similar breeding traits to those claimed in patents. These legal uncertainties are associated with an extension of patent protection from genetic engineering to conventional breeding, which increases the risk that plant breeding (also in view of the EU's "Green Deal" and "Farm to Fork" strategy) will fall far short of its potential to provide important innovations for agriculture and food production.

5.1.3 Influence on science and risk assessment

To a certain extent, patents are also appropriating science. Many scientists conducting research in the field of NGTs not only receive third-party funding from industry, but also take out patents on their research results for themselves. If these experts comment on the risk assessment of their products in connection with legal regulation, this inevitably leads to conflicts of interest. EFSA also mentions the weakening of the required independence in its guidelines.[20] Disruptive effects on scientific research are also conceivable: applications that promise to be profitable may be given priority over other (less profitable and possibly less risky) solutions proffered by research institutions.

The abovementioned special interests continue to influence the debate on the possible deregulation of plants derived from NGTs. With patents currently limited to 20 years, it is in the interest of patent holders, investor groups and companies to extract as much profit as possible from their patented technology (including resulting products such as seeds) within this narrow time window. These groups, therefore, have a strong vested interest in a possible market launch of their patented plants. From their perspective, a far-reaching deregulation of NGT products appears to be advantageous in ensuring the fastest possible access to European markets. In order to get the legislator to abolish the mandatory approval processes, attempts are being made to create the impression that there is a consensus among scientists that, for example, the cultivation of genetically engineered plants is not generally associated with risks (see e .g. Leopoldina, 2019; ALLEA, 2020; further information and sources in Testbiotech, 2021b).

5.2 Impact on food sovereignty and freedom of choice

As explained above, the use of NGTs in food production, (especially for small and medium-sized breeding enterprises, traditional and organic agriculture and regional markets), which is currently based on seed diversity and closely linked to biological diversity and ecosystems, is most likely not without consequences.

As a result, the use of NGTs may well have disruptive effects on the interests of consumers, who may, for example, be significantly restricted in their choice. If NGT organisms and related foods were to be exempt from mandatory approval procedures, this would have a negative impact on the availability of detection methods, traceability, coexistence and post-market monitoring: current legally prescribed approval procedures require that precise information is provided regarding which genetic modifications have been carried out. This information is necessary to establish appropriate detection procedures. Without these detection procedures, neither the freedom of choice for consumers nor the freedom from genetic engineering in organic agriculture and traditional food production can be maintained. A weakening or fragmentation of existing regulations and control mechanisms would, therefore, also affect the (economic) interests of many food producers and consumers.

Prospective technology assessment should take into account both food security and food sovereignty as well as freedom of choice for agriculture and consumers. In the interests of consumers, there must be an assurance that – even in future - it must remain possible for producers (in breeding, agriculture and food production) to distinguish between genetically engineered and non-genetically engineered raw materials and to keep them separate.

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[20] https://www.efsa.europa.eu/sites/default/files/corporate_publications/files/policy_independence.pdf

6. What is realistic in regard to NGTs?

Various stakeholders emphasise that the use of NGTs would lead to a considerable acceleration in plant breeding (e. g. STOA, 2022). However, it is often overlooked that conventional breeding also has many advantages, e. g. in the development of complex traits. These traits are often based on so-called quantitative trait loci (QTLs), i. e. different genetic information within a specific genome segment that is involved in the expression of certain traits, such as yield or stress resistance. The exact genetic basis of these traits is often not precisely defined at the DNA level and may in part be influenced by the genetic background of the particular variety. A necessary prerequisite for conventional breeding is a broad range of biological diversity which is present, amongst others, in existing varieties and which can be further increased by random mutagenesis if required. In contrast, breeding traits can only be generated with the help of NGTs if the corresponding DNA regions are precisely known. In many cases, it is therefore much easier to achieve complex traits based on QTLs with conventional breeding.

There are other influencing factors that can lead to expectations of NGTs being too high: in many cases, the changes brought about with the help of NGTs result in extreme versions of breeding traits, which are then often accompanied by unwanted side effects ('trade-offs').

This can also be seen in plants that are already available on the market: for example, NGT soybeans with a modified oil content produced by Calyxt (approved in the USA) only produced reduced yields, and this is probably the reason why they failed to become established in the market.[21] A further example are NGT tomatoes with increased levels of the neurotransmitter γ-aminobutyric acid (GABA) (approved in Japan) which can be impaired in their resistance to stress factors, such as plant diseases or climate change. These unwanted effects are caused by the multifunctional role of the affected genes and metabolic pathways (Nonaka et al., 2016; Santamaría-Hernando et al., 2022).

Other examples include various NGT applications that are still at the experimental stage: in a study with (hexaploid) wheat, several gene copies promoting susceptibility to powdery mildew were eliminated using NGTs (Wang et al., 2014). However, in addition to resistance to powdery mildew, unintended effects, such as leaf chlorosis (bleaching), were induced that did not occur with conventional mutagenesis techniques (Acevedo-Garcia et al., 2017). In connection with the loss of the gene functions in question, problems such as growth abnormalities, accelerated senescence, induced necrosis or increased susceptibility to other fungal diseases are also described, which may possibly be eliminated by further research (Li, et al., 2022; Spanu, 2022). However, there is some concern that not only the resistance to powdery mildew but also the above described undesirable side effects may be more pronounced in NGT plants than in conventionally bred plants. The use of CRISPR/Cas gene scissors also made it possible to switch off the function of all corresponding gene copies that are responsible for powdery mildew susceptibility in wheat, whereas this was only incompletely achieved with conventional methods (see Kawall, 2021b). However, it remains to be seen whether and how intended changes and side effects can be brought into a suitable balance in this regard.

Similar problems can be observed in another example: research is being conducted in the UK on genetically engineered wheat, which is supposed to form less carcinogenic acrylamide during baking. The researchers used CRISPR/Cas to switch off a particular gene that is decisive for the formation of the amino acid, asparagine, and thus ultimately also for the formation of acrylamide during baking. However, asparagine is also important for germination capacity, the growth of the plants, their stress tolerance and defence against plant diseases. CRISPR/Cas made it possible to reduce the content of freely available asparagine in the grains by up to 90 percent.

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[21] https://www.bizjournals.com/twincities/news/2022/09/22/calyxt-considering-sale-of-assets-merger.html

To do this, the function of several copies (alleles) of a gene (TaASN2) was blocked. As a result, the seeds of some variants of this CRISPR wheat almost lost capacity to germinate (Raffan et al., 2021). Preliminary results from a field trial also show changes in weight and number of grains derived from the CRISPR wheat (Raffan et al., 2023).

These examples show that extreme properties can be produced in plants and animals with the help of new genomic techniques that go beyond what can be achieved with conventional breeding. Unintended side effects and interactions in the complex network of genes, proteins and other biologically active molecules can occur, even if the intervention in the genome is targeted and precise. Due to these often 'inevitable' side effects, breeding progress can be considerably slowed down and certain breeding goals may prove to be unrealisable. In short, NGT techniques offer great potential for genetic modification, but it is not easy to translate this potential into actual benefits.

As a result, the necessary time span between a genetically engineered modification and the placing of the final product on the market cannot be accurately predicted. In contrast, the US company, Calyxt claimed in a presentation to investors in 2018 that it generally only takes three to six years to develop and bring plants with new properties to market.[22] Since then, however, the company has not succeeded in placing any new NGT plants at all to the market.

In fact, apart from the failed Calyxt soybean in the USA (see above), only three NGT products have been launched so far. These were in Japan: the tomato with increased GABA content,[23] the consumption of which is said to lower blood pressure (see above), and two fish (sea bream and puffer fish), which are said to gain weight faster.[24, 25] Both species of fish are affected by unintended side effects of the traits introduced by genetic engineering, e. g. misalignment of the spine (Kishimoto et al., 2018).

These trade-offs often occur together with the traits produced by the NGTs, and often go beyond what would be expected from conventional breeding. Bringing these plants or animals back into 'balance' may require more time than it would to develop a trait using conventional breeding. In addition, the question arises of whether crosses of NGT plants or animals lead to undesirable side effects accumulating and becoming more pronounced in following generations (see also Testbiotech, 2022).

If NGTs are prioritised in research and policy compared to conventional breeding, as has been proposed as a means to achieving the goals in the European "Green Deal" and the "Farm-To-Fork" strategy, amongst others, this could slow down or even prevent urgently needed solutions for breeding that actually generate real benefits.

The Swiss Federal Ethics Committee on Non-Human Biotechnology (ECNH) is also very cautious about the actual potential of plants and animals derived from NGTs (ECNH, 2022). In their report on the role of biotechnology in agriculture in Switzerland, they conclude that the chances of NGT processes contributing substantially to the necessary reduction in emissions by 2050 are very small. In their view, any realistic assessment of the chances of technological options and transparent, honest communication should avoid creating the impression that technologies, such as NGTs, will be able to make the decisive contributions to shaping the necessary transformation processes to meet the climate targets.

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[22] http://www.calyxt.com/wp-content/uploads/2018/06/Calyxt-Investor-Presentation_May-2018.pdf

[23] https://euginius.eu/euginius/pages/gmo_detail.jsf?gmoname=GE-high+GABA+Tomato

[24] https://euginius.eu/euginius/pages/gmo_detail.jsf?gmoname=GE-mstn+red+sea+bream

[25] https://euginius.eu/euginius/pages/gmo_detail.jsf?gmoname=GE-lepr+tiger+pufferfish

7. Conclusions and recommendations

This report shows that the cultivation of transgenic crops has often proved unsustainable in terms of economic and environmental impacts or systemic impacts on food production. The introduction of transgenic crops has not focused on solutions to problems that are most compatible with the environment or contribute to the stability and resilience of ecological- and food systems. The goals focussed instead on economic interests, such as increasing efficiency and/or profit, which were then made into the actual decision-making criteria.

Similar problems could be associated with the use of NGTs in agriculture. This is often promoted by highlighting sustainability aspects, or justified by the fact that new solutions are needed to secure world food supply in view of climate change. However, new solutions cannot be considered sustainable if their use can lead to an overburdening of ecosystems through mass releases of non-adapted genetically engineered organisms - or risks accumulating unnoticed in food, breeding being hindered by patents and the interests of consumers being disregarded. At the same time, many of the expectations raised around the possible benefits of plants and animals derived from NGTs appear far too high.

Large numbers of NGT organisms across numerous species with a wide range of different traits could soon be released into the environment within a short space of time. Besides many of them possibly spreading uncontrollably, complex interactions can be expected to occur both between the different NGT organisms and within their environment.

It is therefore important to maintain control over releases of NGT organisms. Against this backdrop, Testbiotech sees the need to strictly control and limit the type and quantity of organisms that may be released into the environment, in particular, to prevent uncontrolled spread. To maintain this control, all genetically engineered organisms must in future be subject to an approval assessment and traceable after being brought to market.

The concepts of nature conservation and environmental protection are largely based on the principle of avoiding interventions. These must also be applied in the field of genetic engineering. Fundamental reservations against the release of genetically engineered organisms must be given more weight in future.

Against this backdrop and in line with the precautionary principle, EU genetic engineering regulation should be adapted by updating the standards of risk assessment and introducing a complementary framework for technology assessment. The aim of a prospective technology assessment should be to examine the potential advantages and disadvantages of NGT applications - including the overall environmental and socio-economic impacts - in order to be able to distinguish empty promises from realistic expectations. This will enable policy-makers or the EU Commission in its role as risk manager, to effectively control and limit the type and number of potential releases of genetically engineered organisms.

This requires transparent, reliable and practicable criteria in order to be able to make fact-based decisions on the sustainability and potential benefits of the use of NGTs in agriculture. This could be the only way of making it possible to recognise negative effects on breeding, agriculture and food production well in advance, and thus avoid supposed NGT solutions becoming new problems for the environment, ecosystems and future generations.

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