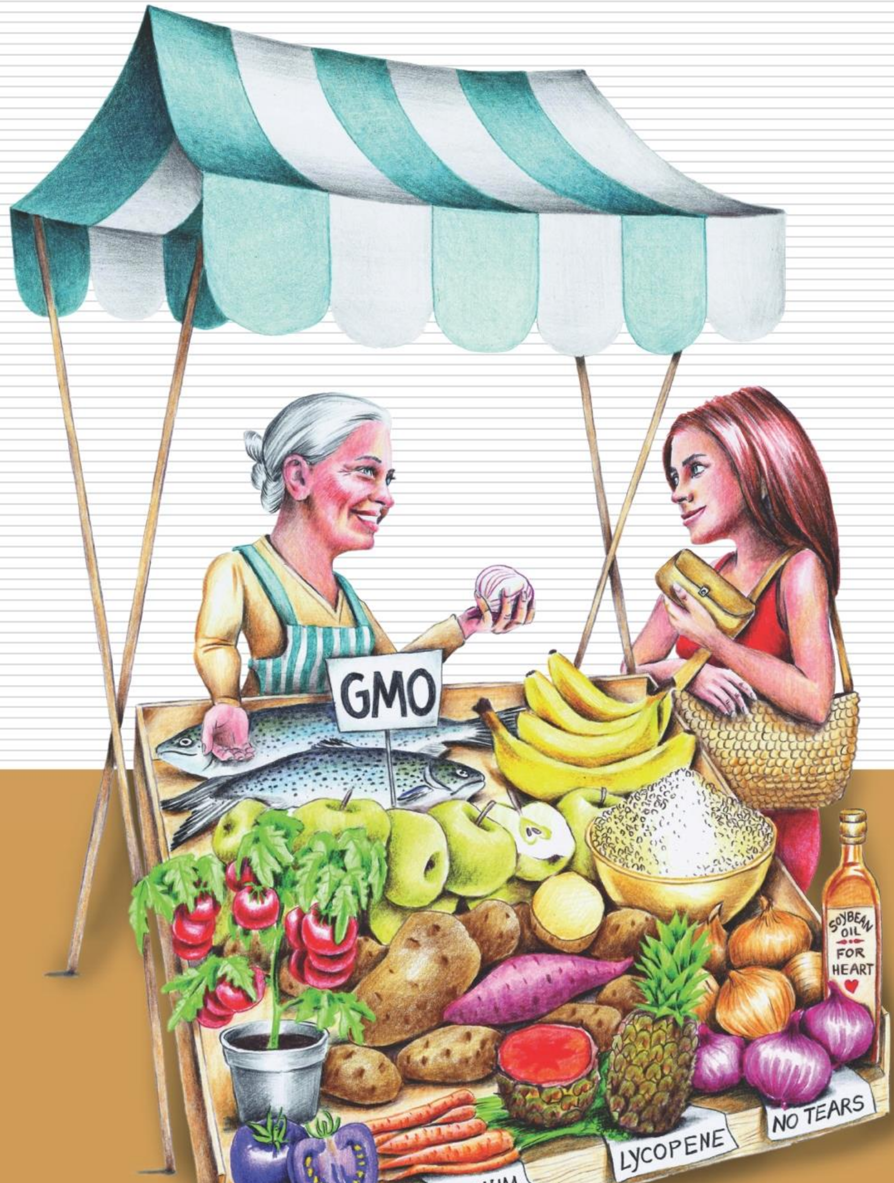
YES TO GMOs!

For us and the environment



B. Bohanec & M. Alkalaj

Yes to GMOs!

For us and the environment

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Glyphosate causes deformation of embryos
Study links glyphosate with autism, Parkinson's and Alzheimer's diseases
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Foreword

People were afraid of railways but countries built them anyway and eventually they became a popular form of transport. People were afraid of cars but there were more and more of them on the roads, so today we cannot imagine a world without them. People were afraid of electricity but, although people die from it even today, governments around the world have done everything possible to bring it to every village. The aforementioned technologies still cause injuries or even death but we all understand that the benefits greatly outweigh the harm. People are afraid of GMOs but, even when numerous advantages are known to scientists, governments do nothing to promote them. This is despite the fact that, even after countless analyses and twenty years of safe use, not a single case of harm from GMOs has ever been documented.

The present situation actually perpetuates itself. In half of the world, both farmers and consumers are strictly prevented from gaining their own experience with these modern varieties and convincing themselves of their benefits.

Are we facing neo-luddism? Imagine a world in which we could all enjoy the myriads of wonderful GMO products that already exist, which are currently kept off the shelves by senseless regulations. This YES to GMOs book is a small contribution intended to break this stalemate, so that wisdom will finally prevail and the world will leap forward, to the benefit of both US and THE ENVIRONMENT.

Introduction

What's a GMO?

GMO is short for genetically modified organism. The terms genetic technology, recombinant DNA technology or genetic engineering are also in use. What is meant is the transfer of isolated genes between usually unrelated organisms by a laboratory procedure. The World Health Organisation retains the definition of a GMO: "organisms with which the genetic material (DNA) has been changed in a way that does not naturally occur«[1]. Sadly, even that definition doesn't stand up to serious examination, since a great majority of laboratory genetic engineering is based precisely on mechanisms taken from nature. If we accept the definition »GMO organisms include genes from unrelated organisms inserted by horizontal (asexual) paths« we are again in trouble, since by that definition people would also be GMOs[2]. In a recent study, Crisp et al.[3] discovered 145 genes that humans have gained in the course of evolution, from completely unrelated species, such as bacteria, fungi, plants and other animals. The same applies to plant species that we've been eating for millennia. There was an interesting recent discovery[4]; humans selected from nature precisely the genotypes of sweet potato into which the bacterium *Agrobacterium tumefaciens*, very often used in laboratories as a "DNA transferring microbe", had inserted its own genes by means of genetic transformation.

Quite simply, we've been eating GMOs food for millennia. So describing GMOs as unnatural is more the fruit of fertile imagination than the reality.

[1] Frequently asked questions on genetically modified foods. World Health Organization

[2] Gene-swapping means that you have alien DNA inside you. BBC Earth 19 June 2015

[3] Expression of multiple horizontally acquired genes is a hallmark of both vertebrate and invertebrate genomes. Crisp A. *et al.* Genome Biology 2015, 16: 50 doi:10.1186/s13059-015-0607-3

[4] The genome of cultivated sweet potato contains *Agrobacterium* T-DNAs with expressed genes: An example of a naturally transgenic food crop Kyndt T. *et al.* PNAS 2015, 112: 5844–5849 doi:10.1073/pnas.1419685112

Structure of the book

Discussion around GMO varieties – for now mainly of plant and much less of animal origin – usually revolves around innovations for which predominantly multinational companies have succeeded in getting permission for cultivation. This book, in addition to describing these achievements, provides a description of many very little known GM innovations, most of which have actually been kept off the sales shelves by the extremely demanding and expensive statutory regulations. We also try to deal with the commonest criticisms of GMOs and refute them with scientific arguments. Finally, we explain who benefits from genetic engineering research. Who needs GMOs.

Note: references that appear as sources from the internet are given as title since domains often change. Using internet search engines all are easily traced.

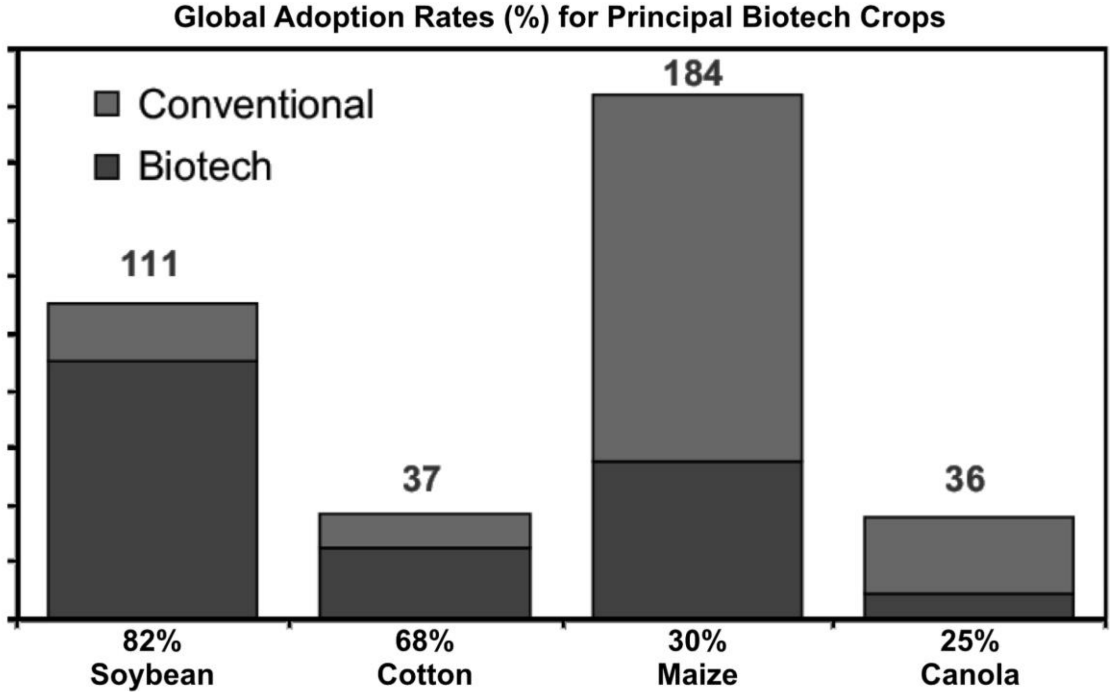
Part 1: What's the reality about GMOs?

GMOs are spreading throughout the world

Agriculture has always tended to be conservative, a branch of the economy that only slowly adapts to innovations. Nevertheless, as far the introduction of contemporary GMO varieties is concerned, it can fairly be claimed that it would be hard to find a technology that has become established faster. This can only be understood on the presumption that GMO technology brings producers some objective benefits. Some of them are described below.

The international non-profit organisation *International Service for the Acquisition of Agri-biotech Applications* (ISAAA) has published annual key data from this field since 1996. Data for 2014 show that 18 million farmers from 28 countries cultivated GM varieties on more than 181 million hectares. To give some idea of what this means, it's an area that greatly exceeds the entire arable land of the European Union. It has been an exceptional success story, especially since there's been a partial or complete ban on cultivation in many countries of the world during these 18 years, the product of media lynching. The leading countries are thus USA (73 million ha), Brazil (42 million ha), Argentina (24 million ha), India (12 million ha) and Canada (12 million ha). At the same time, it needs to be said that, for the most part, this concerns only four key field crops: soybean, maize, rapeseed and cotton. Data on these four species are impressive: on a world scale in 2014, 30% of maize, 82% of soybean, 25% of rapeseed and 68% of cotton were already transgenic[5].

[5] ISAAA Brief 49: Global status of commercialized biotech/GM Crops: 2014



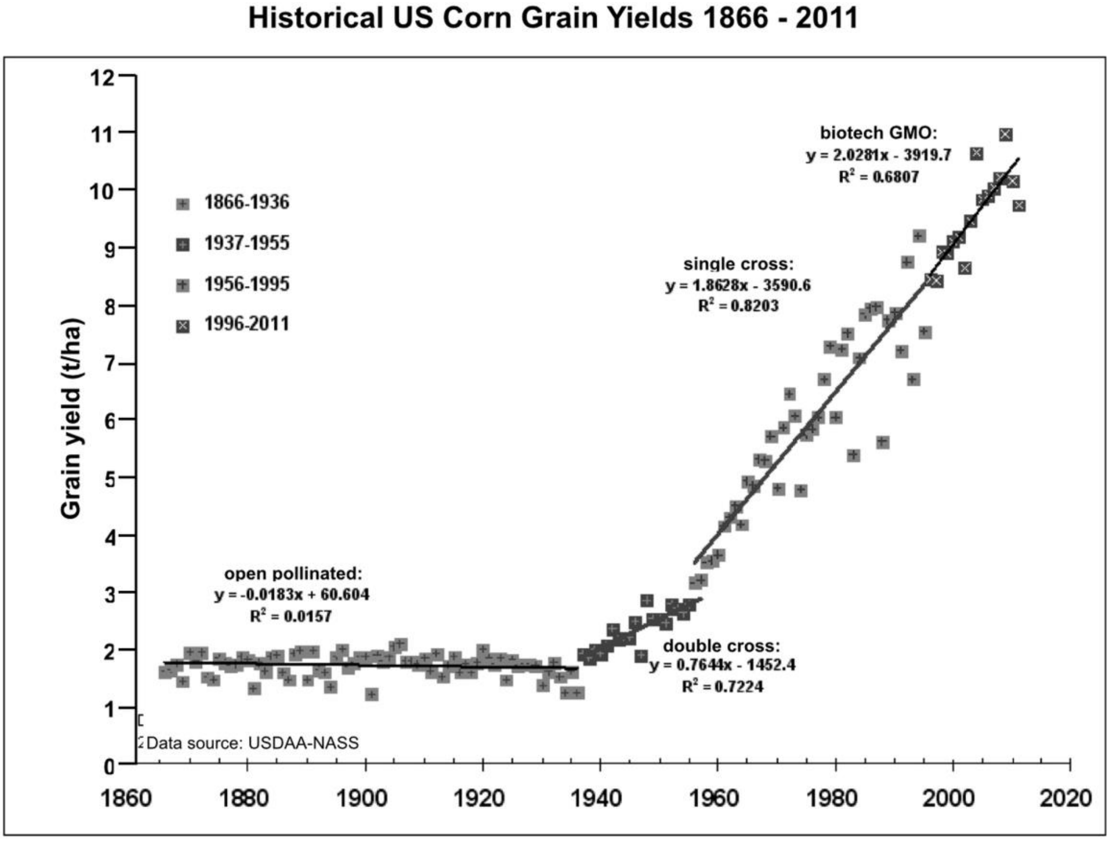
According to data from the USDA, the percentages in the USA are even higher: 8% of maize varieties have inserted genes for resistance to pests and 89% to herbicides[6]. It is worth stressing that modern varieties contain several inserted genes at the same time, so that they combine various agriculturally important traits. In 2014, there were 77% such in the USA.
The bottom line? GMOs are here to stay. They are the future. Below we explain briefly why.

GMOs increase yield per hectare and production

It's hard to understand on what basis anyone can deny it, since GMOs have been deliberately developed mainly to give higher yield, to be more resistant to diseases, pests, drought etc.; and, of course, a farmer wouldn't buy and sow them if he didn't get some economic benefit from GMOs.

This is confirmed by specific data from the USA, where GM field crops have been in cultivation for the longest and are most widespread. The table below gives figures for GM varieties of maize in the USA. Similar results are available for other field crops.

[6] Recent trends in GE adoption 1996-2015. USDA



adapted from: R.L. Nielsen 2012[7]

The graph by **Robert L. Nielsen** clearly shows the increase in grain yield of maize, which was a result of advances in the 20th century linked to breeding methods. Traditional open pollinated varieties have prevailed since the 1930s but yields were drastically increased by the first major innovation in plant breeding - the appearance of double and later single cross hybrids. Since 1996, the continued increase in maize yield can also be attributed to the second major innovation, the introduction of GM varieties.

GMOs have not just had an impact on yields in the USA but everywhere that they've been introduced, as is shown by, among others, a study by *PG Economics* for the period 1996–2007[8]: e.g., the greatest success has been shown by the introduction of GM cotton in India, where yield increased by 54.8% and transformed the country from a predominant importer to an exporter of this raw material.

GM field crops can't by themselves ensure sufficient food for the growing human population but it's clear from the above data that the contribution of GMOs is crucial if future agricultural production is to feed 10 billion people.

[7] Historical maize grain yields for indiana and the U.S. R. L. Nielsen, Purdue University, Agronomny Department, August 2012

[8] PG economics, focus on yield - biotech crops; evidence, outcomes and impacts 1996-2007

Cultivation of GMOs needs fewer phytopharmaceutical means for the same increase in yield

GMO opponents who claim the opposite often cite a key article by **Charles M. Benbrook** in the journal *Environmental Sciences Europe* 2012[9], but only in part: "*The technology of herbicide and pest resistant field crops from 1996–2011 led to increased use of herbicides in the USA by 239 kilograms ...*" This is an increase in the *entire* use of herbicides in the period of 16 years; it says nothing about the increase in total cultivation in this time. The author continues: "*... while Bt field crops reduced the use of insecticides by 56 million kilograms...*" The author concludes "*total use of pesticides increased by 183 million kilograms or around 7%.*" In the same period, for example, rice cultivation in the USA increased by 7.56%, soybean by 30.25%, grain maize by 33.70% and legumes (except soybean) by 255.64%[10]. The whole article that GMO opponents like to cite thus states indisputably that GMO cultivation *reduces* the use of chemicals for the same or greater yield – though it cannot of course have any impact on the use of such means in the cultivation of other cultures.

A report by USDA[11] states that the use of pesticides has remained more or less the same since 1986, despite the increase in total yield. Relatively, the use of herbicides has increased and the use of insecticides decreased. The change is in line with the introduction of GMO cultures, which to date have been predominantly of two types: those with inbuilt additional resistance to harmful insects (e.g., *Bt*-maize), which does not of course affect the use of herbicides; and those that are resistant to more effective herbicides (e.g., glyphosate), which of course does not reduce the use of insecticides.

Wilhelm Klümper and **Matin Qaim** evaluated the effects of the introduction of GMOs on the basis of scientific articles published between 1996 and 2014[12] with data on maize, soybean and cotton. The results show indisputably that cultivation of GMOs increases yield, reduces the use of pesticides (in both quantity and price terms) and essentially increases the producer's profit.

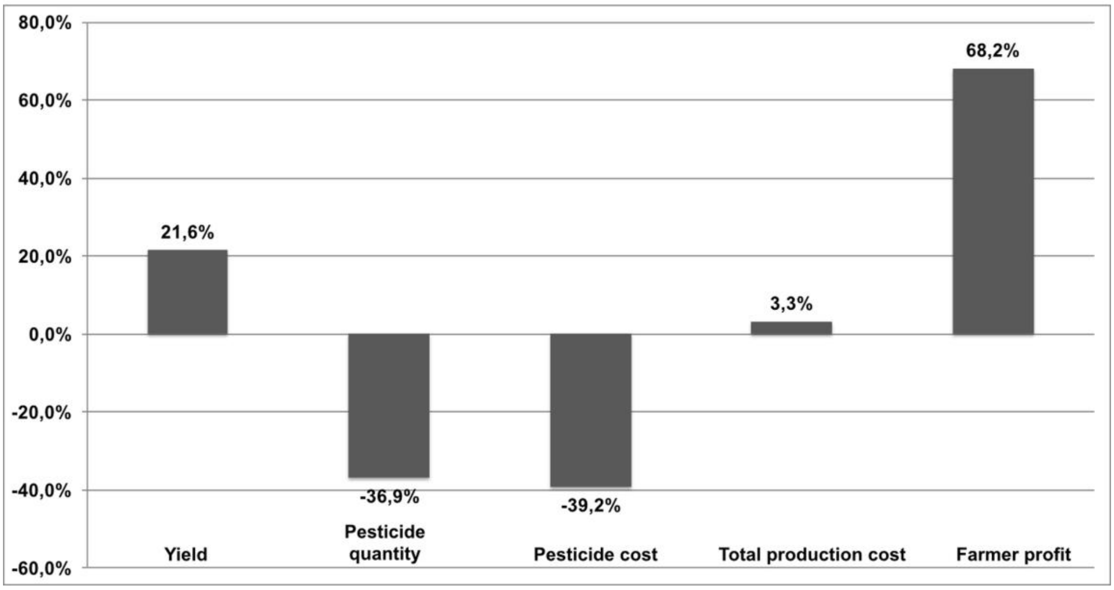
[9] Impacts of genetically engineered crops on pesticide use in the U.S. -- the first sixteen years. Benbrook C.M. Environmental Sciences Europe 2012, 24: 24 doi:10.1186/2190-4715-24-24)

[10] usda national agricultural statistics service, charts and maps, charts and maps by commodity

[11] United States Department of Agriculture, pesticide use in U.S. agriculture: 21 selected crops, 1960-2008. Fernandez-Maizeejo J. *et al.* 2014

[12] A meta-analysis of the impacts of genetically modified crops. Klümper W. and Qaim M. PLOSone 2014, DOI: 10.1371/journal.pone.011162

A Meta-Analysis of Genetically Modified Crops1996 - 2014



Source: Wilhelm Klümper & Matin Qaim

It has been shown that extending field crops that have built-in resistance to pests on the basis of toxins from *Bacillus thuringiensis* (Bt) results in pests that feed on plant sap (order Hemiptera) becoming established as the main field crop pests. Bt toxins, in other words, are mainly expressed in plant tissue (leaves, stem, roots) so do little harm to insects, such as leaf lice, that suck sap[13]. However, solutions can already be found in the scientific literature that enable the development of GM plants that are also resistant to sucking insects[14, 15].

Genetic changes for protection against pests

Pests, particularly insects, have always been one of the major threats to agriculture, so breeders have constantly tried to breed varieties that are as resistant as possible to them. Their success, not just by methods of genetic technology, also by classical crossing and inter-species hybridisation, means that we can produce more food today than ever before in human history.

However, classical methods, such as crossing and inter-species hybridisation, are limited: a close relative of the plant into which we

[13] Toxins for transgenic resistance to hemipteran pests. Chougule N. P. and Bonning B. C. Toxins 2012, 4: 405-429 doi:10.3390/toxins4060405

[14] Resistance to sap-sucking insects in modern-day agriculture. VanDoorn A. and de Vos M. Frontiers of Plant Science 2013. 4: 222. doi: 10.3389/fpls.2013.00222

[15] Recent advances in plant biotechnology and its applications. Kumar, A. and Sopory S.K. *et al.* IK International Publishing House 2008, ISBN-10: 8189866095

want to build resistance must be found that has this property and that can be crossed with our plant. Some important field crop cultures, maize for example, have almost no wild relatives. With many others, there are no natural relatives with suitable resistance. So a wider choice of suitable genetic structures for many varieties used for food or industrial purposes today has been created by radiation. The method of causing genetic change by radiation was described in 1927 by the American geneticist **Hermann Joseph Muller**[16]; he received the Nobel Prize for his work in 1946.

With any protection against pests (or other harmful organisms) there is a considerable probability that sooner or later variants will evolve with resistance to individual means of protection. This is particularly clear with the use of insecticides, which generally lose their effectiveness within a few decades, if not sooner. The same also applies for resistance created by classical methods.

Genetic technology enables (in principle) a suitable gene that confers resistance to pests to be transferred from any organism. Because there are a large number of plants and micro-organisms in nature that have developed protection against insects, the choice of possible protective mechanisms in breeding using genetic engineering methods is large. Stacking (pyramiding) not just one but a few resistance genes together may provide durable resistance and therefore provide a new type of environmentally friendly agricultural crop.

GM plants that express protective *Bt*-toxins

GM plants into which a suitable gene from the bacterium *Bacillus thuringiensis* (normally designated by the prefix *Bt*-)[17, 18] had been inserted were among the first and exceptionally successful GMOs. So-called *Bt*-toxins (formally named *Cry*-toxins) are already effective in very small concentrations[19] and people can't be harmed in quantities that could be ingested with food[20]. Their action is also very specific, so that they only work against the target insect and not against all species. In particular, they have no effect on useful insects such as bees. So *Bt*-varieties of agricultural plants are greatly spreading

[16] Artificial transmutation of the gene. Muller H.J Science 1927, 66: 84-87 doi: 10.1126/science.66.1699.84

[17] *Bacillus thuringiensis* toxins: an overview of their biocidal activity. Palma L. *et al.* Toxins 2014, 6: 3296-3325 doi:10.3390/toxins6123296

[18] *Bacillus thuringiensis* as a specific, safe, and effective tool for insect pest control. Roh JY *et al.* Journal of Microbiological Biotechnology 2007, 17:547-59

[19] *Bacillus thuringiensis* insecticidal crystal proteins affect lifespan and reproductive performance of *Helicoverpa armigera* and *Spodoptera exigua* adults. Zhang Y *et al.*, Journal of Economic Entomology 2013, 106: 614-624

[20] AgBioWorld, Safety of *Bacillus thuringiensis* proteins used to control insect pests in agricultural crops

throughout the world: varieties of *Bt*-maize protected against the commonest pests are the commonest.

The larvae of *Ostrinia nubilalis*[21] and *Helicoverpa zea* attack the ears and stalks of maize; the first causes the most damage to maize, the second also attacks tomatoes, millet etc. but is most dangerous to cotton. The beetles *Diabrotica virgifera virgifera*, *D. barberi* and *D. undecimpunctata howardi* do harm in two ways: the larvae chew the roots and the adult beetles eat the maize 'husks' and leaves[22]. The maize beetle has also been causing ever greater damage in Europe since its introduction in 1992. Wireworms, the larvae of click beetles (Coleoptera, Elateridae), which also cause damage to other crops, have increasingly been appearing in Europe in recent years.

Bt-maize is the most effective protection against European maize borer *O. nubilalis* and western maize rootworm *D. virgifera virgifera*, although after more than 20 years of production of *Bt*-maize the latter is effectively developing its own resistance[23, 24]. The loss of resistance is being fought in two ways: a mandatory refuge zone, something uniquely required of GM crops, not others, and, at the same time, inserting more than one gene for resistance.

The effects of the gene for resistance to maize borer have already been studied in detail and published in the eminent journal Science. We mention the article because it clearly identifies a drop in the occurrence of this pest over the entire cultivation zone in the 14 years since the introduction of resistant varieties. Everyone has had the benefit of this, 3.2 billion dollars' worth of benefit, including some 2.4 billion farming enterprises that sowed ordinary non-transgenic varieties[25].

Today, 93% of American and 80% of world production of soybean is already GMO. Although with soybean a gene for resistance to herbicide predominates, the use of Bt genes for resistance to pests is increasing. *Bt*-cotton in particular has proved itself with resistance to the most dangerous pest, the larvae of the moth *Helicoverpa*

[21] University of minnesota extension, maize production, Bt maize and European maize borer

[22] Purdue University, Field crops IPM, Maize Rootworms

[23] Effects of refuges on the evolution of resistance to transgenic maize by the western maize rootworm, *Diabrotica virgifera virgifera* LeConte. Deitloff J. *et al.*, Pest Management Science 2015 doi: 10.1002/ps.3988.

[24] Resistance evolution to the first generation of genetically modified *Diabrotica*-active Bt-maize events by western maize rootworm: management and monitoring considerations. Devos Y. *et al.* Transgenic Research 2013 22: 269-99 doi: 10.1007/s11248-012-9657-4.

[25] Areawide suppression of european maize borer with bt maize reaps savings to non-bt maize growers. Hutchison W.D. *et al.* Science 2010 330: 222-225, doi: 10.1126/science.1190242

armigera[26] and enabled an increase in and lowering of the cost of cultivation of cotton in USA, India, Australia and China.

A few years ago, a variety of *Bt*-potato was released for production in USA, which was resistant to Colorado beetle[27]. However, professional environmentalists managed to have the variety withdrawn from cultivation by threats against the largest producers[28]. So potatoes still have to be sprayed with insecticides.

Environmentalists also achieved a ban on the cultivation of a Bt-variety of eggplant (*Bt-brinjal*) in India[29], which later became a field and commercial success in Bangladesh[30].

The technology can also be used for the protection of tomatoes[31] and many other plant species against pests.

Defence against insects with RNA interference (RNAi)

RNA interference (RNAi) is a method that is based on post-transcriptional gene silencing. For easier understanding of the achievements mentioned later, we provide a short explanation of how they work, although it is difficult to present such complex knowledge in a few sentences.

In contrast to DNA, RNA molecules are single chain but if they nevertheless occur in a cell in a two-chain version, a series of events is triggered that leads to their split. It's a mechanism by which the cells of higher organisms defend themselves against viruses and other insertions, such as transposons. The phenomenon was discovered in 1998 and the Nobel Prize was awarded for this exceptional discovery in 2006[32].

The method is also attractive because inactivation of the gene already happens on the level of the RNA molecule, which prevents the target

[26] Suppression of cotton bollworm in multiple crops in china in areas with bt toxin–containing cotton. Wu K.M. *et al.* Science 2008, 321: 1676-1678, doi: 10.1126/science.1160550

[27] Transgenic-Bt potato plant resistance to the colorado potato beetle affect the aphid parasitoid *Aphidius nigripes*. Ashouri A. Communications in Agricultural and Applied Biological Sciences 2004, 69:185-189

[28] McDonald's GMO dilemma: why fries are causing such a fuss. Gunther M. The Guardian 4 December 2013

[29] How Jairam Ramesh's luddite ban on Bt brinjal has set us back several years. Fernandes V. F. Business Feb 17, 2015

[30] Bt brinjal in Bangladesh – the true story. Lynas M. 8 May 2014

[31] Production of transgenic tomato plants expressing *Cry 2Ab* gene for the control of some lepidopterous insects endemic in Egypt. Saker M.M. *et al.* Journal of Genetic Engineering and Biotechnology 2011, 9: 149–155 doi:10.1016/j.jgeb.2011.08.001

[32] The nobel prize in physiology or medicine 2006. Nobelprize.org Nov 25, 2015

protein being created at all. Inactivation of the gene is achieved with gene transformation by inserting a construct that creates a short two-chain RNA molecule, part of which is identical to the target mRNA molecule. The cell mechanisms split both, resulting in gene inactivation.

It has been established that this method can be used for various purposes, including combatting insect pests[33]. In comparison with inserting Bt-genes, it has the advantage that there are no toxic proteins in the plant; the chain RNA itself destroys the insect[34]. It is possible to direct plant defence with RNAi at a target, so that it only works against very specific insects[35].

The new technology is important because the most widespread method to date, using *Bt*-toxins, doesn't work on all insect pests. In addition, RNAi provides a 'reserve' for cases in which pests develop resistance to *Bt*-toxins.

GM plants resistant to nematodes

Nematodes, or roundworms, are small worms that can live over a very wide range of habitats. Around 25,000 species are known, of which half are parasitic. Biologists reckon that there are more than a million species of nematode. Some parasitize plants and can affect the yield of maize, potato, soybean, sugar beet, fruit trees and grape vines, garden vegetables etc. In classical cultivation, the damage is contained mainly by crop rotation and, with some species, also with chemical means against nematodes, such as fumigants, organophosphates and urea. All have undesirable environmental side effects[36] and, of course, destroy all nematodes.

Fortunately, (at least for countries that don't surrender to prejudices against GMOs) methods are already known for developing transgenic plants that are resistant to nematodes[37] and have no toxic effects on

[33] RNAi for insect-proof plants. Karl H J Gordon K. H. J. and Waterhouse P. M. Nature Biotechnology 2007, 25, 1231 – 1232 doi:10.1038/nbt1107-1231

[34] Recent advances in RNA interference research in insects: Implications for future insect pest management strategies. Gu L. and Knipple D. CV.; Crop Protection 2013, 45:36–40, doi:10.1016/j.cropro.2012.10.004

[35] Control of coleopteran insect pests through RNA interference. Baum J. A. *et al.* Nature Biotechnology 2007, 25: 1322 – 1326 doi:10.1038/nbt1359

[36] Chemical control of nematodes: efficiency and side-effects.. Gowen S.R, FAO Corporate Document Repository

[37] Engineering broad root-knot resistance in transgenic plants by RNAi silencing of a conserved and essential root-knot nematode parasitism gene 2006, Huang G. *et al.* PNAS vol. 103: 14302–14306 doi: 10.1073/pnas.0604698103

people[38]. It is thus already possible to achieve resistance to nematodes in rice, potato and bananas (for cooking)[39], wheat[40] etc. In these cases, the investigators used a number of possible approaches, from RNAi technology to the insertion of specific genes isolated from rice or potato. In Europe, for example, nematode resistant sugar beet would be of particular importance. Currently, sugar beet can only be grown on the same field once every four years, just because of nematodes, which greatly increases the transport distance to the factory. Unfortunately, already developed herbicide resistant sugar beet is produced only in USA[41]. Because of resistance to GM varieties, research on which was already reported in 2000, work has been halted.

In other words, we've closed sugar factories because of the uncompetitiveness of European sugar production from beet compared to production from sugar cane. This state of affairs has already completely transformed breeding of new varieties.

Genetic changes for protection against fungal diseases

Fungal diseases can significantly reduce yields or even destroy affected plants. Some moulds also produce dangerous mycotoxins. Conventional defence is spraying with fungicide - even in the 17th century, farmers in Europe sterilised seed with cow's urine or mercury to prevent the transmission of infection by common maize bunt, caused by the fungus *Tilletia tritici.* However, the usefulness of an individual fungicide is limited, since target organisms sooner or later develop resistance to it. Because of the new popular ecological farming, whereby disinfection of seeds with synthetic preparations is forbidden, a number of already almost forgotten diseases are again being spread[42]; they are appearing in more virulent and in pesticide

[38] Prototype demonstration of transgenic resistance to the nematode *Radopholus similis* conferred on banana by a cystatin Atkinson H. J. *et al.* Transgenic Research 2004, 13: 135-142 DOI 10.1023/B:TRAG.0000026070.15253.88

[39] Research highlight: Genetic transformation for nematode resistance in rice, potato and cooking bananas for developing countries. PSP Annual Report 2004. Section 2: Introduction. Research Highlights. 17-19.

[40] Assessment of nematode resistance in wheat transgenic plants expressing potato proteinase inhibitor (PIN2) gene. Vishnudasan D *et al.* Transgenic Research 2005, 14: 665-675 doi 10.1007/s11248-005-5696-4

[41] Bred for Europe but grown in America: the case of GM sugar beet. Koen Dillen *et al.* New Biotechnology 2013, 30: 131-135 doi:10.1016/j.nbt.2012.11.004

[42] Smut diseases. Fuentes-Dávila G. *et al.* FAO Corporate Document Repository

resistant variants[43]. The same applies to infection by *Fusarium* species.

GM wheat for protection against rust and other fungal diseases

Wheat is the third most-produced cereal after maize and rice and world trade in wheat is greater than for all other crops combined but, so far, nowhere in the world has the cultivation of any GM variety been approved. The worst threats to wheat cultivation are rusts, caused by fungi of *Puccinia* spp. Infection can reduce the yield by 50-80% or even destroy an entire crop. New variants of *Puccinia* spp. that are resistant to ever more known fungicides[44] have already been identified in the Near East and in Africa, Germany, France, Australia and Canada.

Efforts to develop rust resistant GM wheat are going on in many laboratories. Among the first to succeed with the transfer of one gene from a relative of wheat, *Aegilops tauschii,* into wheat, was the Australian state institute CSIRO[45]. Unfortunately, on 14 July 2011, Australian activists of the international environmental organisation Greenpeace broke into the closed greenhouse in which they were experimentally cultivating rust resistant wheat and destroyed the entire crop[46].

Fungi of *Septoria* spp., *Tilletia tritici* and *Fusarium* spp. also cause harmful fungal diseases of wheat; the last is especially dangerous for people since some of them, in addition to damage to the plant and reduction in yield, also leave very poisonous mycotoxins in the grains.

GM grapevine with increased disease resistance

In countries such as France, vineyards cover 4% of arable land and they use 60,000 tons of pesticides on them annually, which is 20% of all pesticides used. *B. cinerea,* known in viticulture as »noble rot«, gives predicate wines such as dry berry selections their characteristic

[43] A New Pathogenic Race of Tilletia caries Possessing the Broadest Virulence Spectrum of Known Races. Matanguihan J.B. and Jones S.S. Plant Management Network 2011 doi:10.1094/PHP-2010-0520-01-RS

[44] Epidemiology and control of stripe rust [*Puccinia striiformis* f. sp. *tritici*] on wheat. Chen X.M., Canadian Journal of Plant Pathology 2005, 27: 314-337 DOI: 10.1080/07060660509507230

[45] The Gene Sr33, an Ortholog of Barley Mla Genes, Encodes Resistance to Wheat Stem Rust Race Ug99. Periyannan S. *et al.* Science 2013, 341: 786-788. DOI: 10.1126/science.1239028

[46] Australian Greenpeace activists destroy GM wheat crop. Owens B., Nature Biology & Biotechnology, 14 Jul 2011

aroma. In the French vineyard region of Sauternais they even spray the vines in autumn with a fine mist to encourage the growth of *B. cinerea*, which is essential for the production of the famous sweet Sauterne wines. In other periods, *B. cinerea* is a dangerous and destructive mould against which vines have to be sprayed regularly[47]. Scientists recently discovered a method of genetic modification that would insert into the vine a gene for resistance to *B. cinerea*[48]. What is interesting is that the grape's own gene was used, which thus enables the creation of an increased concentration of resveratrol.

Tests over ten years of resistance to bacterial Pierce's disease *Xylella fastidiosa* have been less successful[49] since these inserted synthetic genes were not retained. There are other similar experiments, such as the inserted gene for stilbene synthase from the Chinese species *Vitis pseudoreticulata* into the variety 'Chardonnay', which promises increased resistance to powdery mildew (*Botrytis cinerea)*[50] and thus less spraying.

GM chestnut returns to American forests

American chestnut (*Castanea dentata*) used to amount to 20% of all trees in American forests, so it was an important source of both timber and food. Around 1900, the fungus *Cryphonectria parasitica* was accidently imported, probably from Asia, and in the following 50 years it destroyed the majority of American chestnuts. Attempts to replace American chestnut with hybridised Chinese (*C. mollissima*) and Japanese chestnut (*C. crenata*), which were more resistant to *C. parasitica*, were for the most part unsuccessful.

A genetic method for achieving resistance was developed within the framework of a national project for the restoration of American chestnut[51], and trial planting of the first genetically modified *C.*

[47] Gosenice, peronospora, oidij, sedaj še botritis in kap vinske trte. Vtič M., Štajerski tednik 25 Aug 2014

[48] Enhanced resistance to *Botrytis cinerea* in genetically-modified *Vitis vinifera* L. plants over-expressing the grapevine stilbene synthase gene. Dabauza M. *et al.* Plant Cell, Tissue and Organ Culture 2015, 120: 229-238 doi 10.1007/s11240-014-0598-x

[49] Overexpression of antimicrobial lytic peptides protects grapevine from Pierce's disease under greenhouse but not field conditions. Li ZJT *et al.* Transgenic Research 2015, 24: 821-836 doi: 10.1007/s11248-015-9876-6

[50] Establishment of a picloram-induced somatic embryogenesis system in *Vitis vinifera* cv. Chardonnay and genetic transformation of a stilbene synthase gene from wild-growing *Vitis* species. Dai L.M. *et al.* Plant Cell Tissue and Organ Culture 2015, 121: 397-412 doi: 10.1007/s11240-015-0711-9

[51] Transgenic American chestnuts show enhanced blight resistance and transmit the trait to T1 progeny. Newhouse AE *et al.* Plant Science 228: 88-97 doi:10.1016/j.plantsci.2014.04.004

dentata trees started in 2014[52]. It appears that a wheat gene that decomposes oxalic acid released by the pathogen of the fungus will save the chestnut. Researchers under the leadership of **William Powell** have already obtained permission for a trial reintroduction of chestnut[53].

The story of saving the American chestnut is particularly interesting for Europe because chestnut is also dying out in European forests. Although *C. parasitica* is slightly less destructive for the European *C. sativa*, it is distributed throughout Europe[54] and weakens trees (that are not destroyed) sufficiently for many to succumb to attacks by insects, now also the introduced chestnut gall wasp (*Dryocosmus kuriphilus*). In contrast to the USA, for the moment it is not possible in the EU to solve the problem with genetic modification.

It is worth mentioning that new diseases are constantly appearing in other species; for example, in Britain a mould caused by the fungus *Chalara fraxinea,* is destroying ash trees [55] and even the environmentally conscious The Guardian finds that the only solution may be GM[56]. Similarly, in the south of Italy the bacteria *Xylella fastidiosa* is wiping out olives[57].

GM potato resistant to mould

Potatoes can be affected by potato blight caused by infection by *Phytophthora infestans* (in distinction from early blight, which is caused by *Alternaria solani*). Infection by *P. infestans* caused a major drop in production in Europe in the middle of the 19th century, when Ireland was worst affected, where it caused the Great Famine in 1845-1852. Damage can be prevented with suitable genetic modifications to potato[58, 59, 60], which also create greater resistance to frost. The gene

52 Blight-resistant american chestnut trees take root. Science Daily, November 6, 2014

53 Government approval next step in GM revival of American chestnut. Genetic Literacy Project

54 Chestnut blight in Europe: Diversity of *Cryphonectria parasitica*, hypovirulence and biocontrol. Robin C. and Heiniger U., For. Snow Landsc. Res. 2001, 76, 3: 361–367

55 Ash dieback 'could affect 75% of trees in worst-hit areas'. Vaughan A., The Guardian 30 April 2014

56 With 90% of the UK’s ash trees about to be wiped out, could GM be the answer? Vidal J., The Observer, Saturday 31 October 2015

57 Europe’s olive trees threatened by spread of deadly bacteria. Neslen A. The Guardian 8 January 2015

58 Analysis of late-blight disease resistance and freezing tolerance in transgenic potato plants expressing sense and antisense genes for an osmotin-like protein. Zhu B. *et al.* Planta. 1996, 198:70-77.

59 Performance of transgenic potato containing the late blight resistance gene *RB*. Halterman D.A. *et al.* Plant Disease 2008, 92: 339-343

for resistance can be found in wild relatives of potatoes, from which it is possible to insert it into potato by crossing or with the aid of genetic technology. The first GM plants are already in the testing procedure. Dutch and Belgian investigators recently reported a particularly interesting approach. In a project entitled Durable Resistance against *Phytophthora* through cisgenic marker-free modification [61], they simultaneously inserted three completely different genes, each of them derived from a different relative of potato. Why is this important? Only the simultaneous insertion of a number of independent genes can ensure that the achieved resistance is more likely to be durable, if not permanent. Insertion of individual genes for resistance normally only lasts a short time, which breeders have known for decades.

It is additionally worth mentioning that in this approach, the genes are introduced by a procedure of cisgenesis. Briefly, cisgenesis[62] is genetic transformation by which an entire gene from a related species is inserted, without being in any way altered. There is the conviction throughout the world that it will be easier to achieve consumer acceptability, or silence the always negative criticism, with such an approach.

Bananas are attacked by destructive fungal diseases

As is said below, a number of bacterial diseases attack bananas, but fungi are even more destructive. Among the fungal diseases, the most dangerous in the past was fusarium wilt (*Fusarium oxysporum* f. sp. *cubense* race 4), which destroyed the then most popular variety of banana 'Gros Michel'. Another variety, 'Cavendish', is now cultivated throughout the world, which is also only partially resistant to fungal diseases. The large majority of plantations are therefore regularly sprayed from the air but success is not assured.

The world media often report that perhaps even within a few years, we will no longer see bananas, one of the most popular fruits, in the shops[63].

The reason are two new destructive diseases known as yellow sigatoka (*Mycosphaerella musicola*) and black leaf streak (*Mycosphaerella fijiensis*), variants of which have become ever more resistant to fungicides. Even spraying a crop fifty times is no guarantee.

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[60] Development of late blight resistant potatoes by cisgene stacking. Jo K.R. *et al.* BMC Biotechnology 2014, 14:50 doi:10.1186/1472-6750-14-50

[61] Novel approaches to achieve durable disease resistance. Wageningen UR September 3, 2015

[62] Cisgenesis and intragenesis, sisters in innovative plant breeding Schouten H.J. *et al.* Trends in Plant Science 2008, 13: 260-261 DOI: 10.1016/j.tplants.2008.04.005

[63] Bananas facing extinction, scientists warn. Wutje E. DW made for minds. Dec 13, 2015

Bananas cannot be bred by classical methods since the result is sterile triploids, which form fruit without fertilisation. Many experiments based on the use of artificial mutations have been predominantly unsuccessful and crosses are difficult to make. It is very likely that the only realistic solution to the further cultivation of bananas is the insertion of genes from unrelated organisms by genetic transformation.

Numerous approaches can be found in the scientific literature by which researchers have attempted to insert genes required for resistance into leading varieties of bananas, which is clearly a major problem. We describe them briefly below.

An unusual attempt – isolation of the gene for magainin – was made in India[64]. It is a synthetic gene similar to the gene found in African clawed frog (*Xenopus laevis*). Resistance to both the aforemention fungal diseases has been reported. Another research group used seed defensin gene (Sm-AMP-D1) of common chickweed (*Stellaria media*), synthesized artificially, and demonstrated improved resistance to fusarium wilt[65]. Chinese scientists achieved resistance to fusarium wilt by the insertion of the human gene for lysozyme[66]. Similar resistance to the same disease has also been achieved by excessively expressed self genes of the banana, *MusaDAD1*, *MusaBAG1* and *MusaBI1*[67]. With the introduction of two genes for the creation of hitinase isolated from rice, researchers from Belgium[68] achieved increased resistance of the variety 'Gros Michel' to the fungus *Mycosphaerella fijiensis*. Israeli scientists have inserted two different genes[69]: the *ThEn-42* endochitinase gene from the fungus *Trichoderma harzianum* and grape stilbene synthase (*StSy*) gene.

It appears this approach will enable more environmentally and people friendly production of bananas. The situation at the moment is that,

[64] MSI-99, a magainin analogue, imparts enhanced disease resistance in transgenic tobacco and banana Chakrabarti A. *et al.* Planta 2003, 216: 587-596 doi: 10.1007/s00425-002-0918-y

[65] Transgenic banana plants expressing a *Stellaria media* defensin gene (Sm-AMP-D1) demonstrate improved resistance to *Fusarium oxysporum* Chag S.B. *et al.* 2014, Plant Cell Tissue and Organ Culture 119: 247-255 doi: 10.1007/s11240-014-0529-x

[66] Creation of transgenic bananas expressing human lysozyme gene for Panama wilt resistance. Pei X.W. Journal of Integrative Plant Biology 2005, 47: 971-977 doi: 10.1111/j.1744-7909.2005.00141.x

[67] Native cell-death genes as candidates for developing wilt resistance in transgenic banana plants. Chag S.B. *et al.* 2014AOB Plants 6: Article Number: plu037 doi: 10.1093/aobpla/plu037

[68] Expression of a rice chitinase gene in transgenic banana ('Gros Michel', AAA genome group) confers resistance to black leaf streak disease. Kovacs G. *et al.* Transgenic Research 2013, 22: 117-130 doi: 10.1007/s11248-012-9631-1

[69] Improved tolerance toward fungal diseases in transgenic Cavendish banana (*Musa* spp. AAA group) cv. Grand Nain. Vishnevedsky J. *et al.* Transgenic Research 2011, 20: 61-72. doi: 10.1007/s11248-010-9392-7

because of resistance to GM varieties, the majority of the aforementioned studies for the moment remain on the level of laboratory and greenhouse; field trials have not for the most part been performed.

Genetic changes for protection against bacteria and viruses

Plants do not have an immune sytem (like animals) so they cannot be 'vaccinated' for prior resistance to bacteria and viruses. Partial and limited protection can be achieved with some phytopharmaceutical means but the causative agents quickly develop resistance. Some species, such as bananas, are also very difficult to spray effectively.

GM banana with resistance to *Xanthomonas campestris* pv. *musacearum*

While a banana is more or less an exotic fruit to us, it's a basic food source in many countries of the world. In 2001, banana plantations in central and east Africa began to be threatened by the bacterium *Xanthomonas campestris* pv. *musacearum* (BWX), which destroys the crop and often also the whole plant. *X. campestris* can be spread atmospherically or through the ground, so in areas of affected plantations new bananas cannot be planted unless they are resistant to this bacterium and there are none such in Africa.

By transferring a suitable gene from paprika, bananas have been cultivated that are resistant to this bacterial infection[70]. Similar can be achieved with the transfer of a gene from rice[71], which is a useful reserve if *X. campestris* develops new resistance.

GM oranges resistant to the bacterium *Candidatus Liberibacter* spp.

[70] Expression of sweet pepper Hrap gene in banana enhances resistance to *Xanthomonas campestris* pv. *musacearum*. Tripathi L. *et al.* Molecular Plant Pathology 2010, 11: 721-31. doi: 10.1111/j.1364-3703.2010.00639.x.

[71] Transgenic expression of the rice Xa21 pattern-recognition receptor in banana (*Musa* sp.) confers resistance to *Xanthomonas campestris* pv. *musacearum*. Jaindra N. *et al.* Plant Biotechnology Journal 2014, 12: 663–673 doi: 10.1111/pbi.12170

The bacterium (*Candidatus Liberibacter asiaticus*), which already previously threatened citrus plantations in Asia and Africa, causes improper ripening (»greening«) of the fruits and the death of the trees. It was only recently introduced to the USA. It is vectored by the insect *Diaphorina citri* in Asia and America and *Trioza erytreae* in Africa, which feeds on the sap of citrus and thus transfers the bacteria from infected trees to healthy ones. The disease appeared in Florida in 2005 and in 2012 in California. No known citrus species is naturally resistant to the disease.

The only solution for orange plantations in Florida and California (which among other things produce the most orange juice in the USA) was the development of a GMO resistant to this pest[72, 73]. Perhaps the most promising solution succeeded with the transfer of two genes from spinach[74] and it is already under the testing procedure and preparation for release. It is amusing to hear the question being asked of whether oranges will therefore taste of spinach. Another research group provides a similar solution[75], inserting a gene from thale cress into orange. GM citrus will most certainly be grown in the USA one way or another, because there probably won't be any at all otherwise.

Thale cress (*Arabidopsis thaliana*) will be mentioned several times. This small weed species is very popular among geneticists. It has a small genome and fast development life cycle, so is often used in studies of the function of genes in improving agricultural plants.

GM apples resistant to fire blight

The bacterium *Erwinia amylovora* causes leaf desiccation and even the death of whole trees. It attacks apple, pear, quince and some ornamental plants, in particular[76]. The disease has caused damage mainly in America but has been spreading in Europe since 1957[77]. Outbreaks of the disease are unpredictable and it is often necessary to fell an entire orchard.

A GM variant of the apple variety 'Gala' has been developed in the Swiss development institute ETH, which is resistant to the activity of

72 A race to save the orange by altering its DNA. Harmon A. The New York Times JULY 27, 2013

73 Can genetic engineering save the florida orange? Voosen P. National Geographic SEPTEMBER 13, 2014

74 Spinach genes may stop deadly citrus disease. Rod S.A. AgriLife Today March 26, 2012

75 UF creates trees with enhanced resistance to greening. IFAS News, University of Florida

76 Scientific opinion on the pest categorisation of *Erwinia amylovora* (Burr.) Winsl. *et al.* EFSA Journal 2014, 12: 3922 -3959 doi: 10.2903/j.efsa.2014.3922

77 Invasive species compendium. CABI Datasheet

E. amylovora. The gene for resistance was isolated from the related species *Malus* x *robusta*. Trial planting of the variety is supposed to start in spring 2016 on a protected field in Zurich[78].

»Rainbow« papaya

The pathogenic plant virus Papaya ringspot virus (PRSV) first appeared in Hawai in 1937 and a more aggressive mutation started to spread around 1950 and at that time destroyed 94% of papaya plantations. Papayas were then only cultivated under strict isolation in the region of Puna (on the main island) but in 1992 the virus also invaded there and since 1995 the cultivation of papaya has been impossible throughout Hawaii.

A group of researchers under the leadership of **Dennis Gonsalves** developed a GM papaya called "rainbow" papaya – so called because of the colour of the skin, with an added gene for resistance to the PRSV virus[79].

Despite the opposition of environmentalist groups, producers quickly accepted the GM papaya and by 2000 the yield had returned to the level prior to the appearance of the virus disease. Today, it is already also being grown in China.

As has already become normal today, activist groups of Greenpeace tried to prevent the introduction of rainbow papaya in Thailand. They first tried with a lawsuit, which they lost[80]. Then they simply destroyed the GM papaya plantations[81].

GM potato resistant to the PVY virus

The PVY virus belongs to the Potyviridae family, which threatens a range of crops. Depending on the variant, it can cause only a fall in the potato yield but can also cause necrotic blotches on the tubers so that they can't be marketed.

The problem is by no means unimportant in Europe. A variant of the virus, Y^{NTN}, began to threaten the whole of Europe in the 90s. Many

[78] Feldversuch geplant mit cisgenen Apfelbäumen, die gegen Feuerbrand resistent sind. Field trial planned with cisgenic apple trees, which are resistant to fire blight. Agroscope 27.10.2015

[79] Pathogen-derived resistance provides papaya with effective protection against papaya ringspot virus. Lius S. *et al.* Molecular Breeding 1997, 3: 161-168 doi: 10.1023/A:1009614508659

[80] Thai supreme court dismisses genetically modified papaya case. Thai Law Forum October 27, 2014

[81] Greenpeace decontaminates GMO-tainted Thai papaya farm. NW Resistance Against Genetic Engineering, 19. May 2006

previously popular varieties of potato disappeared from production. Researchers at the National Institute for Biology of Slovenia had already developed a variant of the traditional popular variety 'Igor' in 1998, which had become resistant to the Y^{NTN} virus but, because of extremely negative attitudes to GMOs in Europe, it has not been possible to grow. Finally, potato cultivation in Europe has been saved by resistant varieties such as 'Sante', which gained resistance to PVY^{NTN} with hybridization to a wild potato species, *Solanum stoloniferum*. Resistance genes from these varieties were then crossed into the majority of modern resistant varieties.

They recently behaved more reasonably in Argentina, in contrast to European authorities: in September 2015, they approved GM potato resistant to PVY for cultivation (together with a range of other GM plants)[82].

Increased resistance of local bees to *Varroa destructor*

At the beginning of the 21st century, first in the USA and then also in Europe, there was a dramatic increase in the death of whole colonies of bees. Environmental organisations ascribed the so-called colony collapse disorder (CCD) to new types of insecticides, which are known as neonicotinoids. The EU adopted the environmental explanation and temporarily banned the sale and use of clothianidine, thiametoksam and imidachloprid in the EU[83].

The facts have shown that neonicotinoids cannot be a significant cause of CCD. In the USA, where neonicotinoids weren't banned, the number of bee colonies remained stable and there were actually more in 2012 than in 2006[84]. An official report by EURL (*European Union Reference Laboratory for honeybee health*), in a pan-European study of colony collapse in 2012-2013, does not mention the influence of neonicotinoids[85] - the commonest cause of CCD is the parasitic mite *Varroa destructor*, which sucks bees' body fluids[86].

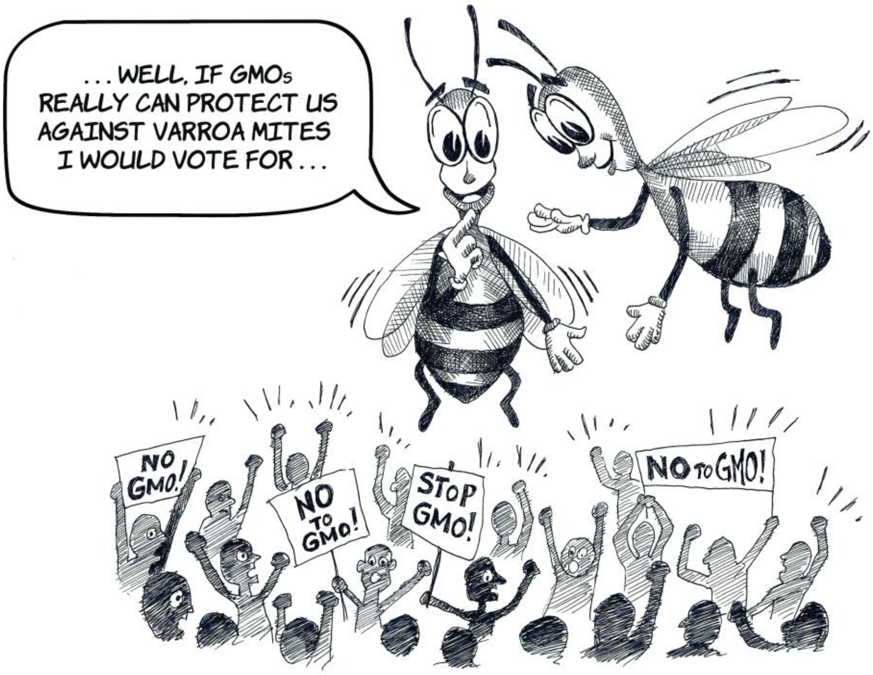
[82] Argentina approves GM potato for human consumption. Fresh Plaza.com, 10/9/2015

[83] Commission implementing regulation (EU) No 485/2013. Official Journal of the European Union 25.5.2013

[84] Bee deaths reversal: as evidence points away from neonics as driver, pressure builds to rethink ban. Jon Entire, Forbes Magazine 2/05/2014

[85] European Union Reference Laboratory for honeybee health (EURL): A pan-European epidemiological study on honeybee colony losses 2012-2013

[86] *Varroa destructor* is the main culprit for the death and reduced populations of overwintered honey bee (*Apis mellifera*) colonies in Ontario, Canada. Guzman-Novoa E. *et al.* Apidologie 2010, 41: 443-450 doi http://dx.doi.org/10.1051/apido/2009076



A report by USDA (*United States Department of Agriculture*) in October 2012[87] found similarly: the most important factor in the appearance of CCD is *Varroa destructor* and a series of viruses the effect of which is intensified by the presence of *V. destructor*[88].

Identification of a link between *V. destructor* and CCD was a very important discovery. Honeybees are threatened by paralysis caused by viruses from the family Dicistroviridae, which are transferred by the mite. In 2007, the action of a new variant was described for the first time, in Israel, known as IAPV (*Israeli Acute Paralysis Virus*)[89], and a recent genetic analysis of bee colonies shows that the common feature of collapsed colonies is the presence of IAPV, carried by *V. destructor*[90].

Given current knowledge of the causes of CCD, it seems clear that the harmful activity of the mite *V. destructor* must be restricted. Fortunately, at least one effective method for this is known, previously described RNA interference: if bees are fed with RNAi that is homologous to the genetic sequence in IAPV, they become immune to

[87] Report on the national stakeholders conference on honey bee health. USDA, October 2012

[88] Varroa-virus interaction in collapsing honey bee colonies. Francis R.M. *et al.* PlosOne 2013 doi: 10.1371/journal.pone.0057540

[89] Isolation and characterization of Israeli acute paralysis virus, a dicistrovirus affecting honeybees in Israel: evidence for diversity due to intra- and inter-species recombination. Maori E. *et al.* Journal of General Virology 2007, 88 :3428-38.

[90] Genetic survey finds association between CCD and virus. Kaplan K. USDA, September 6, 2007

this virus infection[91]. The insertion of RNAi sequences, which exclude vital genes only in mites and do not harm bees or people, has also been studied. Reduction in the parasite (*Varroa* mite) population by 60% was achieved in this way[92]. It is noteworthy that in the case of feeding with manufactured RNA molecules no DNA is integrated into bee's genome. The Israeli company Beeologics, since 2011 owned by Monsanto, has been developing a treatment for practical application[93].

Controlling dengue fever and zika virus by GM mosquitoes

Mosquitos have often been called the deadliest animals on Earth[94] because of the number of fatal diseases they carry. Reducing the population of life threatening mosquitoes has long been a goal, and various approaches have been used. An almost complete elimination of malaria transmitting mosquitos from developed countries of the northern hemisphere was achieved by extensive spraying with insecticides after the Second World War, with DDT playing a crucial role. Nevertheless, even today, mosquitoes transmitting malaria alone kill two to three million people and infect another 200 million or more *every year*. Several other diseases are spread by various species of mosquitos, including yellow fever, dengue fever and even typhoid fever. *A. aegypti* has again come to the attention of the public recently: in addition to spreading dengue, yellow fever and chikungunya virus, it has recently been identified as the vector for zika virus. Infection with the deadly viral disease can occur via a single bite of a female mosquito. This poses an increasing problem, because *A. aegypti* populations have increased during the past 2-3 decades worldwide, and it is today considered to be among the most widespread mosquito species[95].

Past and existing mosquito control measures have been insufficient, and some (e.g., DDT) were discontinued due to environmental concerns.

91 Prevention of Chinese sacbrood virus infection in *Apis cerana* using RNA Interference. Liu X. *et al.* Current Microbiology 2010, 61: 422-428

92 Bidirectional transfer of RNAi between honey bee and *Varroa destructor*: Varroa gene silencing reduces *Varroa* population. Garbian Y, e*t al.* PLoS Pathog. 2012 8:e1003035. doi: 10.1371/journal.ppat.1003035.

93 Monsanto's plan to help the honeybee. Rojahn, S.Y. MIT Technology Review, Biomedicine News July 9, 2013

94 Mosquitoes and disease. Illinois Department of Public Health, Prevention and Control

95 *Aedes aegypti*. European Centre for Disease Prevention and Control

A new and very promising was approach has been developed by the Oxitech company[96]. The method is actually a variant of an existing strategy based on the release of male sterile insects into the environment that, following mating with wild females, cause the death of the offspring. Since the 1950s, such a method used heavy irradiation of male insects but was never successfully applied in mosquito control since the damage caused by the appropriate irradiation dose was too severe to mosquitos themselves.

Oxytec's patented technique[97] involves the insertion of a dominant lethal gene producing tTA protein into insect embryos. Although technically fairly complex, its use is actually very simple. In technical terms, based on the promotors used, relatively little tTAV protein is produced in the presence of the antibiotic tetracycline, while in the absence of tetracycline, tTAV stimulates its own expression in a positive feedback loop. In practice, this means that scientists rear the modified mosquitoes in a laboratory, keeping them alive by supplementing their diet with the antibiotic tetracycline. In addition to genes controlling sterility, a GFP gene (causing insects to fluoresce green) or DsRed (causing insects to fluoresce red) was inserted, allowing visual identification of GM mosquitoes under specific illumination. Before release into the environment, male and female mosquitos are separated at the pupal stage. Male pupae are smaller than female pupae, which allows them to be sorted. The process is very efficient: tests have shown that only app. 200 female GM mosquitoes are released for every million males. The few females that are accidentally released pose no danger, since they carry no disease and the introduced GM proteins cannot harm humans; in fact, they are not even present in the salivary glands of the mosquitoes.

Large scale tests have been ongoing since 2010 and they have demonstrated that an 80% reduction in *A. aegypti* populations is usually achieved, with the most successful reduction of over 90% (Itaberaba, Brazil). Commonly used chemical control of mosquitoes rarely reduces their population by more than 20-30%.

While efficiently tested on the Cayman Islands, in Brazil and elsewhere, a planned test in Florida Keys (USA) has not so far received a green light, due to public mistrust in GM technology. The situation might change with the appearance of zika virus. Notably, according to the New York Times[98], a representative of the FDA agency, **Luciana Borio**, told a United States congressional subcommittee that the agency was “greatly expediting” Oxitec’s application to test the mosquitoes in the Florida Keys. This response indicates that the real

[96] TED Talk – Hadyn Parry: Re-engineering mosquitos to fight disease Nov 2012

[97] Expression systems for insect pest control. EP 1649027 B1

[98] A biotech evangelist seeks a zika dividend. Pollack A. March 5, 2016

reasons for common delays in releases of GMOs by the regulating agencies are more public mistrust and political fear than real risk.

The Oxitec company is testing the same approach for the control of agriculturally important insects, such diamondback moth (in *Brassica* crops),pink bollworm (in cotton),medfly (in several fruit species), mexfly (in citrus, mango, avocado) andolive fly (in olives).
It should be stressed that these first large scale trials are not the only approach tested against mosquitos, but the described one is the most developed and closest to application. An overview of several others is given by Achee et al.[99]

GMOs for more efficient meat production

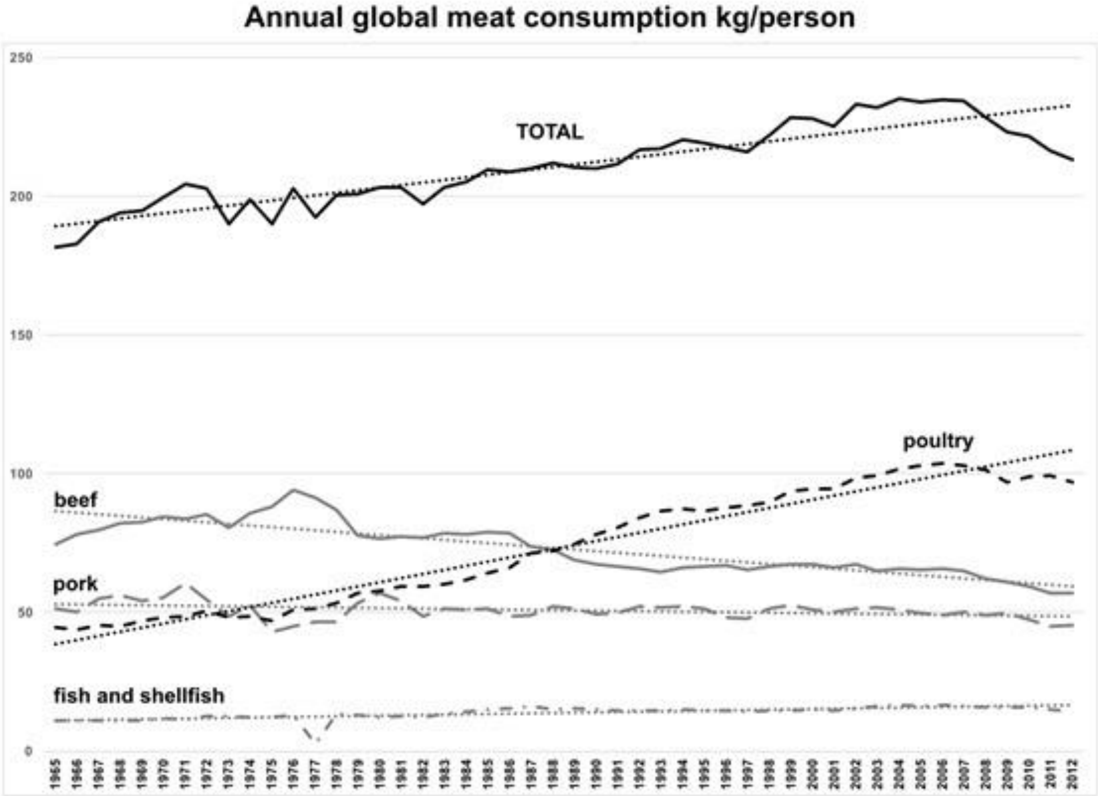
Meat contains proteins we need that the human body doesn't know how to produce itself. Judging by the most recent findings, it is possible to obtain everything needed by a human body through a completely vegetarian diet if it is suitably rich and balanced[100, 101], which can be more expensive in the end than normal food with meat, so a really healthy vegetarian diet is more or less available only as a privilege of the rich. For most of the world, meat is the most important source of proteins, as well as being a high energy food. So the national use of meat became a measure of development.

[99] A critical assessment of vector control for dengue prevention. Achee N.L. *et al.* 2015 PLoS Neglected Tropical Diseases 9(5): e0003655.

[100] The contribution of vegetarian diets to health and disease: a paradigm shift? Sabaté J., The American Journal of Clinical Nutrition 2003, 78: 502S-507S

[101] Nutritional Update for Physicians: Plant-Based Diets. Philip J. and Tuso P.J. The Permanente Journal 2013, 17: 61–66 doi: 10.7812/TPP/12-085

Global use of the most important kinds of meat 1965-2012



The use of meat is thus growing more or less in line with global GDP (the fall after 2008 is connected with the financial crisis) but ratios are changing: with a fall in the use of beef, slightly less pork, the growth in total use is more or less entirely due to poultry. This is reflected in its own way by rearing costs: the basic indicator is the FCR (Feed Conversion Ratio), which says how many kilos of dry feed is needed to produce one kilo of meat. The FCR for raising beef is 7-8, for pigs 3-4, for poultry 1.3-2. The best FCR can be achieved in raising fish in fishfarms, 1.1-1.8, but the great majority of fish that we eat are still caught in the wild.

Since the human population is growing and because we want to ensure both sufficient and the highest possible quality of food, we must exploit all possibilities to increase meat production and do it more efficiently.

GM beef resistant to *Trypanosoma brucei*

The single cell parasite *Trypanosoma brucei* is better known for causing sleeping sickness in people, which is carried by tetse fly (*Glossina* spp.), but it can also infect other mammals. There are actually African wild animals (more or less) resistant to it, such as the *zebu*, an African variant of domestic cattle. Domestic animals from other parts of the world that could be of interest for rearing in Africa are there quickly infected and succumb to a disease that at best greatly weakens the animal and often kills them. So it is not possible to raise beef over most of Africa and in many places not even *zebu*.

An extensive group of researchers from Great Britain, Ireland, Kenya and Korea has discovered a way of inserting resistance to the parasite *Trypanosoma* by a genetic modification to European beef cattle[102]. Stephen J. Kemp succeeded with the addition of a gene from baboons to raise GM beef that has been confirmed as resistant to *Trypanosoma brucei*[103], which could essentially change the possibilities of raising beef cattle in Africa.

GM pigs resistant to African Swine Fever

In addition to sleeping sickness, livestock rearing in Africa is threatened by ASFV (African Swine Fever Virus), which, although it regularly infects warthog, an African species of the pig *Potamochoerus larvatus,* and many other autochthonous species, does not cause the symptoms of illness in them. In European and Asian species of pig, however, it causes hemmorrhagic fever with a high mortality rate. So there 's practically no pig breeding in Africa.

At the University of Edinburgh, by transferring a gene from warthog into the genome of European pig, they have developed a variant that is resistant to ASFV[104]. Trial breeding of the first animals is already taking place[105].

GM pigs with less fat and more muscle tissue

Animal fats are not wanted in a modern western diet. So animal breeders try to raise as lean meat as possible because the fat is more or less a waste product.

Chinese and Korean scientists have developed a pig by a method of genome editing (CRISPR/Cas9), which has a higher share of muscle

[102] Genetic and expression analysis of cattle identifies candidate genes in pathways responding to *Trypanosoma congolense* infection. Noyesa H. *et al.* PNAS vol. 108 no. 22, 9304–9309, doi: 10.1073/pnas.1013486108

[103] Transgenic cows might help struggling farmers in Africa. Fobar R. Popular Science, May 7, 2015

[104] Species-specific variation in RELA underlies differences in NF-κB activity: a potential role in african swine fever pathogenesis. Christopher J. *et al.* Journal of Virology 2011, 85: 6008–6014 doi: 10.1128/JVI.00331-11

[105] Could these piglets become Britain's first commercially viable GM animals? Hannah Devlin, The Guardian, 23 June 2015

tissue and thus little subcutaneous fat, so that its muscles are clearly seen through the skin. They hope to get permission for commercial breeding quickly since, as the leader of the group, Jin-Soo Kim, says, the same pig could also be bred by classical selection but it would take much longer[106].

Bulls with no horns

Dairy cattle develop horns that are usually removed early in a calf's lifetime in order to prevent piercing other cattle and handlers. Some breeds of cattle and sheep are naturally hornless but this is not the case of most common breeds used in dairy. Although dehorning has evident economic and safety reasons, the procedure is unethical and painful.

Using another genome editing technique, known as TALENs, a group of researchers from Recombinetics, a Minnesota lab, disrupted a key gene for horn growth, thus enabling the birth of the first two calves that do not grow horns[107]. We can expect this major event to reduce suffering and, at the same time, be economically viable.

Enviropig® – GM pig that better exploits plant phosphorus

Phosphorus is an essential element for all forms of life on earth. A grain of maize, soybean and wheat contains 50 – 75% phosphorus in the form of phytic acid. Ruminants have bacteria in their digestive organs that enable the phosphorus to be obtained from the phytic acid, but pigs, poultry, fish and many other reared animals do not. So farmers everywhere supplement feed with phosphates, which are obtained by mining and are a non-renewable and ever more exploited source. In addition, the phytic acid remains in the feed undigested and is excreted as water soluble waste, which pollutes water and the phosphorus becomes an irretrievable swill in the depths of the ocean. Another approach that only the rich can afford is to mix an enzyme phytase in the feed, which deconstructs the phytic acid and is commercially produced on the basis of GM bacteria.

Scientists at the University of Guelph have developed a variant pig which expresses phytase in saliva[108]. They achieved this with the

[106] Super-muscly pigs created by small genetic tweak. Cyranoski D. , Nature 2015, 523, 13–14 doi:10.1038/523013a
[107] UC Davis welcomes campus' first gene-edited calves. Sadlowski E. The California Aggie 18 January 2016
[108] University of Guelph, Enviropig™ Technology

insertion of gene PSP/APPA from the bacteria *Eschericia coli.* Because an enzyme that decomposes phytic acid is mixed in the feed, it exploits the plant phosphorus better, reducing the content in excretion by up to 75%[109].

The problem can also be solved differently by the plants on which animals are fed already containing phytases. Such an approach is described below.

AquAdvantage™ – GM salmon that grows twice as fast as normal

Fish contain Omega-3 fatty acid, which is particularly beneficial for the human organism, so they are a very good source of proteins. Most of the fish that we eat are still caught in the sea and, because they are mainly at the top of the food chain, it is as if among land animals we chose mainly lions and tigers for food. With the growing needs of mankind, we have already hunted many wild species to the limit at which commercial fishing is no longer viable.

However, many fish species can be farmed. Indeed, the ratio between the cost of feed and weight increase (FCR) is best for fish of all animals. The best FCR has been achieved with farmed salmon: in Scotland 0.99 kg feed for 1 kg of meat and in Chile 1.1 kg for 1 kg of meat[110].

Efforts to achieve faster growth of salmon with the aid of genetic technology date to 1989, when at the Canadian University Memorial University of Newfoundland they inserted a suitable genetic construct. In the genome of Atlantic salmon (*Salmo salar*), whose genome contains around 40,000 genes, they inserted another gene, one from Pacific salmon (*Oncorhynchus tshawytscha*) fitted with a regulatory (promotor) region from the Northwest Atlantic ocean pout (*Zoarces americanus*). Such an artificial gene enables the fish uninterrupted growth, which doesn't apply to normal salmon, which only grow in the warm half of the year. The fish thus reach market weight in 16 to 18 months and not in three years, as is normal, and they need 25% less feed to achieve the same weight[111].

After purchase of the licence, efforts at commercialisation were taken over by the company AquaBounty Technologies Losos AquAdvantage™, which in November 2015, after 19 years of

[109] Pigs expressing salivary phytase produce low-phosphorus manure. Golovan S.P. *et al.* Nature Biotechnology 2001, 19: 741 - 745 doi:10.1038/90788

[110] Evaluation of closed-containment technologies for saltwater Salmon aquaculture. B. Sayavong, E.M.P. Chadwick, G.J. Parsons (ed.): Canadian Science Publishing (NRC Research Press) January 2010. ISBN-13: 978-0660199689

[111] Chronology of aquadvantage® salmon and aquabounty technologies. www.aquabounty.com

verification, obtained a permit from the American Food and Drug Administration (FDA), that it is suitable for human consumption[112]. Salmon has thus become the first GM animal whose meat is approved for human consumption in the USA and worldwide.

Genetic technology enables adaptation of plants to abiotic stress

In the first period of the use of genetic technologies, plants resistant to biotic stresses predominated, thus resistant to insects or the more effective herbicides – these two measures in themselves have greatly alleviated cultivation. Varieties resistant to abiotic stresses are increasingly appearing today. By »abiotic stress« is meant all forms of unfavourable natural circumstances that can affect growth or fruiting but are not connected with disease or pests, weeds and other biological factors: salt contents in soil, heat or cold, drought or excessive water, too little nitrogen or phosphorus in the ground etc.

Just imagine: genes that prevent frost resistance have been known for several years. Do we really need to fear a late and devastaing frost each spring, particularly since they have become so frequent lately?

GM eucalyptus for resistance to frost and faster wood growth

Eucalyptus globulus is a fast growing tree of tropical and sub-tropical zones. A lot is grown for timber and cellulose in Australia, Chile and other warm places. It cannot survive frost in its natural form.

Chilean scientists have therefore developed a genetically modified form of *E. globulus* that can be grown at higher altitudes since it is resistant to freezing[113]. The company ArborGen in USA has developed a GM variety of eucalyptus that can withstand temperatures down to -8°C and they have already begun trial cultivation in Florida[114].

The Israeli company FuturaTech, by transfer of a gene from thale cress, has developed an eucalyptus with essentially faster growth.

[112] FDA has determined that the aquadvantage salmon is as safe to eat as non-GE salmon. FDA Consumer Health Information / U.S. Food and Drug Administration November 2015

[113] RAPD and freezing resistance in *Eucalyptus globulus*. Fernández M.R. *et al.* Electronic Journal of Biotechnology 2006, 9 doi: 10.2225/vol9-issue3-fulltext-9

[114] Cold-tolerant trees win. Walt E. Nature Biotechnology 2011, 29: 1063 doi:10.1038/nbt1211-1063b

With plantations in Israel, South Africa, Brazil and elsewhere, they intend to produce wood for processing into biofuel[115].

Rice resistant to flooding and drought

Although rice seedlings are planted in a flooded field, the seedlings must not be submerged in water for more than three days or they disintegrate. So floods in countries such as Vietnam, India and Bangladesh often destroy a considerable part of the crop.

In 1996, **Pamela Roland** began genetic research leading to rice resistant to flooding[116]. Technically, her approach (use of genetic markers) is not considered genetic manipulation but it enables faster selection of plants with the desired properties[117]. After a number of trial variants, her group succeeded in developing rice capable of surviving submersion up to 14 days[118, 119]. Following backcrossing to a variety of cultivars, rice Sub1 is now cultivated by millions of poor farmers throughout Southeast Asia and they do not have to pay royalties for its use.

Japanese scientists have developed a type of GM rice that survives flooding in the ripening phase without loss of crop[120].

Rice cultivation requires a lot of water, e.g., in China some 50% of all sources of fresh water are used. So varieties are being developed that will require less irrigation for high yield[121].

GM maize more tolerant to drought

Developed in 2012, DraughtGuard™ was the first GM maize to be resistant to drought[122]. Success was achieved by inclusion of a gene for resistance obtained from the soil bacterium *Bacillus subtilis*.

[115] The GM tree plantations bred to satisfy the world's energy needs. Vidal J., The Guardian 15 November 2012

[116] Submergence tolerant rice: SUB1's Journey from Landrace to Modern Cultivar. Bailey-Serres J. Rice 2010, 3:138–147 doi 10.1007/s12284-010-9048-5

[117] Selection theory for marker-assisted backcrossing. Frisch M. and Melchinger A.E., Genetics 2005, 170: 909–917 doi: 10.1534/genetics.104.035451

[118] *Sub1A* is an ethylene-response-factor-like gene that confers submergence tolerance to rice. Xu K. *et al.* Nature 2006, 442: 705-708 doi:10.1038/nature04920

[119] Flood tolerance mediated by the rice SUB1A transcription factor. Jenks M.A. *et al.* Plant Abiotic Stress 2014, Second Edition doi: 10.1002/9781118764374.ch1

[120] Mechanisms for coping with submergence and waterlogging in rice. Nishiuchi S. *et al.* Rice 2012, 5: 2 doi:10.1186/1939-8433-5-2

[121] Breeding for water-saving and drought-resistance rice (WDR) in China. Luo L.J. Journal of Experimental Botany 61: 3509-3517.

Various approaches are known today[123] for the cultivation of varieties resistant to abiotic stress. The African Agricultural Technology Foundation (AATF) considers that a combination of varieties improved by classical breeding and genes added with GM technology could essentially improve the extent and stability of crop yield in Africa[124]. Decreasing the concentration of trehalose-6-phosphate in developing corn ears by overexpression of the appropriate gene obtained from rice has been shown to be a promising approach[125]. According to the authors »*the engineered trait improved yields from 9% to 49% under non-drought or mild drought conditions, and from 31% to 123% under more severe drought conditions, relative to yields from nontransgenic controls*«.

Drought resistant tomato

In January 2013, Indian scientists reported that they had developed a tomato that is more resistant to drought[126]. They did this by using the tomato gene *BcZAT12*, which when overexpressed enabled the tomato to survive drought.

Drought resistant GM soybean has obtained a permit for cultivation in Argentina

Argentinian scientists, in collaboration with the American company Arcadia Biosciences, have developed a variety of soybean that is (more) resistant to drought[127]. The Argentine authorities recently approved cultivation of soybean HB4®[128]. Varieties with the construct

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[122] Monsanto’s GM drought tolerant maize. DiLeo M. Biology Fortified 25 August 2012

[123] Overexpression of maize *SDD1* (*ZmSDD1*) improves drought resistance in *Zea mays* L. by reducing stomatal density. Yanbo Liu Y. *et al.* Plant Cell, Tissue and Organ Culture 2015, 122: 147-159

[124] AATF: combining breeding and biotechnology to develop water efficient maize for Africa (WEMA). Concept Note

[125] Expression of trehalose-6-phosphate phosphatase in maize ears improves yield in well-watered and drought conditions. Nuccio ML *et al.* Nature Biotechnology 2015, 33, 862–869 doi:10.1038/nbt.3277

[126] Engineering drought tolerant tomato plants over-expressing BcZAT12 gene encoding a C2H2 zinc finger transcription factor. Raia A.C. *et al.* Phytochemistry 2013, 85: 44–50. doi:10.1016/j.phytochem.2012.09.007

[127] Stress-tolerant soybeans to be advanced through new collaboration by bioceres, Arcadia Biosciences, and TMG. Arcadia Biosciences, July 7, 2015

[128] Bioceres and Arcadia biosciences receive regulatory approval for stress-tolerant soybeans in argentina through Verdeca Joint Venture. BusinessWire, April 27, 2015

HB4 (its composition has not been revealed) have thus become the first abiotic stress resistant soybean varieties in the world[129].

GM rice that does not produce the greenhouse gas methane

Methane absorbs radiation emitted from the earth up to 84 times more effectively than carbon dioxide, which makes it a potential greenhouse gas. Rice paddie fields are the largest anthropogenic methane source and produce 7–17% of atmospheric methane[130]. Su *et al.* recently reported in the journal Nature [131] an important improvement of rice achieved by insertion of a single transcription factor gene, barley *SUSIBA2*, which was able to shift the carbon flux in GM rice plants from the roots to the aboveground leaves and grains. Such an allocation resulted in increased biomass and starch content in the seeds and stems, while methanogenesis was simultaneously supressed, possibly through a reduction in root exudates.

GM rice that better exploits nitrogen

Rice is cultivated on specially irrigated fields, because of which the water leaches nutrients and, mainly in Asia, producers must add a large amount of nitrogen fertiliser. For some time now, breeders have been studying approaches by which to increase the efficiency of nitrogen use and thus reduce the need for fertilisers.

Researchers from the company Syngenta, in cooperation with scientists at the University of Guelph, have published a study of many genes that could affect better exploitation of nitrogen[132]. Early nodulin gene *Os06g05010*, similar to genes included in nodulation with legumes, successfully increased yield with a limited supply of nitrogen. In a more recent study, they confirmed that this gene can increase yield by 23%[133]. Such research is intensively continuing,

[129] Stress-tolerant soybeans to be advanced through new collaboration by bioceres, Arcadia Biosciences, and TMG. Arcadia Biosciences July 7 2015

[130] Metabolic, phylogenetic, and ecological diversity of the methanogenic archaea. Liu Y. and Whitman W.B. Annals of the New York Academy of Sciences 2008, 1125: 171–189 doi: 10.1196/annals.1419.019

[131] Expression of barley SUSIBA2 transcription factor yields high-starch low-methane rice. Su J. *et al.* Nature 2015, 523: 602–606 doi:10.1038/nature1467

[132] Increased nitrogen-use efficiency in transgenic rice plants over-expressing a nitrogen-responsive early nodulin gene identified from rice expression profiling. Bi YM *et al.* Plant Cell & Environment 2009, 32:1749-1760 doi: 10.1111/j.1365-3040.2009.02032.x.

[133] Identification of regulatory genes to improve nitrogen use efficiency. Guevara D.R. et al. Canadian Journal of Plant Science 2014, 94: 1009-1012 doi: 10.4141/CJPS2013-154

also with the aid of contemporary genomics approaches[134] and is being extended to other species[135].

GM plants that exploit phosphorus better

Phosphorus is an essential element for plants and is actually a non-renewable (or at least difficult to renew) resource: it is constantly leached into the sea in water soluble form, from where it can only return through volcanic eruptions. So phosphorus fertiliser needs to be added with practically all forms of cultivation, and in especially large quantities in lands that are phosphorus poor (e.g., Australia). An additional problem is that sites with a sufficiently high concentration of phosphorus are rare and increasingly depleted.

Some specific genes have been discovered that enable plants to exploit sources of phosphorus more efficiently[136]: normal plants can draw the necessary phosphorus from salts on the basis of orthophosphate PO_4^{3-}, and genetically modified plants can also exploit phosphyte PO_3^{3-}. Using the *ptxD* gene from the soil bacterium *Pseudomonas stutzeri*, the authors created an unique opportunity for crops that can now for the first time utilize this form of phosphorus. In experiments, such genetically modified plants used 30-50% less added phosphorus for the same yield than normal ones, they created 2-10 times more biological mass and thus »overtook« weeds. So such a modification simultaneously reduces the need for herbicides.

Chinese scientists succeeded with another approach, which enabled the survival of rice with small stocks of phosphorus by modifying the promotors of key regions[137].

Phillipine and South Korean scientists report improved exploitation of anorganic phosphorus; by increased activity of the rice gene *OsACP1* they enabled rice to exploit existing anorganic phosphorus essentially better and plants achieved up to 200% improved growth[138].

[134] Transcriptome analysis of nitrogen-starvation-responsive genes in rice. Yang W.Z. *et al.* BMC Plant Biology 2015, 15: Article Number: 31 DOI: 10.1186/s12870-015-0425-5

[135] Mining for low-nitrogen tolerance genes by integrating meta-analysis and large-scale gene expression data from maize. Luo B.F. *et al.* Euphytica 2015, 206: 117-131 DOI: 10.1007/s10681-015-1481-5

[136] Engineering phosphorus metabolism in plants to produce a dual fertilization and weed control system. López-Arredondo D.L. and Herrera-Estrella L. Nature Biotechnology 2012, 30: 889-893.

[137] Genetic manipulation of a high-affinity PHR1 target cis-elementto improve phosphorous uptake in *Oryza sativa* L. Ruan W. et al. Plant Molecular Biology 2015, 87: 429-440 doi: 10.1007/s11103-015-0289-y

[138] Enhanced organic phosphate utilization by over-expression of OsACP1 and OsPAP1 genes in rice (*Oryza sativa* L.). Hwang WH et al. Philippine Journal of Crop Science 2015, 40: 17-23

GM plants resistant to salt

One of the potentially interesting challenges for contemporary gene technology is modifying plants into a form that can grow in high salinity conditions – halophytes. The majority of normal food plants, wheat, rye, soybean etc., have a genetically close relative among natural halophytes, which provides the possiblity of the transfer of key genes[139, 140, 141]. “Halophytisation” of food plants could essentially extend possible land for cultivation, not only on sea coasts, saltwater marshes and similar areas unused today but also on farmland on which poor quality accelerates salination.

The first GM plants that can grow on land with an increased salt content are already in trial plantings, e.g., wheat[142] and alfalfa[143]. For the salt tolerance of wheat, they drew on gene *AtNHX1* from thale cress, and in alfalfa they built in gene *rstB* from the nitrogen fixing soil bacterium *Rhizobium* sp.

GMOs for the production of medically active ingredients

Even people who reject on principle any kind of food of GMO origin, will not refuse medicine made with the aid of genetically modified bacteria when they’re ill. This applies most today to the majority of antibiotics, biological medicines and a number of other medically active ingredients.

The next step in the development of medicines is clearly to cultivate the necessary active ingredients or raw materials for them more cheaply in genetically modified plants. Some approaches have already been developed.

[139] Living with salinity. C.S. and Munns R. New Phytologist 2008, 179: 903–905 DOI: 10.1111/j.1469-8137.2008.02596.x

[140] Learning from halophytes: physiological basis and strategies to improve abiotic stress tolerance in crops. Shabala S., Annals of Botany 2013, 112: 1209–1221 doi: 10.1093/aob/mct205

[141] Halophytes: a precious resource. Gamal E.I *et al.* In : A. Hamdy (ed.), Non-conventional water use: WASAMED project. Bari : CIHEAM / EU DG Research, 2005. p. 119-128 (Options Méditerranéennes : Série B. Etudes et Recherches; n. 53)

[142] Enhanced salt tolerance of transgenic wheat (*Triticum aestivum* L.) expressing a vacuolar Na+/H+ antiporter gene with improved grain yields in saline soils in the field and a reduced level of leaf Na+. Zhe-Yong Xue *et al.* Plant Science 2004, 167: 849–859 doi:10.1016/j.plantsci.2004.05.034

[143] Enhanced salt tolerance of alfalfa (*Medicago sativa*) by rstB gene transformation. Zhanga W.J. Plant Science 234: 110–118 doi:10.1016/j.plantsci.2014.11.016

It is worth stressing that the production of GMOs for medically active ingredients is typically a 'boutique' activity, i.e., suitable for small, fragmented areas, which could particularly suit farming in countries that cannot compete in size of arable areas.

GM tobacco for producing a medicine against ebola

On 6 December 2013, a two-year old boy died in Guinea, the first victim of a catastrophic epidemic of ebola, which spread to a large part of eastern and central Africa; 70% of those infected died, the death toll to June 2015 was more than 11,000[144].

In all kinds of experiments, they tried a new experimental medicine ZMapp, first on monkeys, with which there was 100% success[145]. They then, with their consent, injected some patients with explicit symptoms of ebola with ZMapp, which proved to be the most effective means against ebola in humans[146]. ZMapp was created in a genetically modified wild relative of tobacco, *Nicotiana benthamiana,* in which it creates neutralizing antibodies needed for the treatment. ZMapp is for the moment still experimentally produced by a small firm *Mapp Pharmaceuticals*, which can afford the strictly regulated conditions for the production of this tobacco only to a very limited extent; the first planting of the necessary GM tobacco has already been used. It is not yet clear which production organisms the US regulatory organs will allow. Meanwhile, researchers have already observed that ebola has mutated into a new form, which could spread to a wider area[147], so constant upgrading of the constituents of the medicine will of course be necessary.

GM beef produces human antibodies for the treatment of ebola

There are reports from the USA of cows to which they have added human DNA and which can then develop in the blood an antibody to the ebola virus[148]. Serum from the blood of such cattle is completely equivalent to human. It has already been shown that it helps in the treatment of ebola if it contains a suitable antibody.

[144] Ebola death rates 70% - WHO study. Briggs H. BBC News Health 23 September 2014

[145] Experimental Ebola drug cured 100% of monkeys tested. Szabo L. USA TODAY August 29, 2014

[146] Reversion of advanced Ebola virus disease in nonhuman primates with ZMapp. Xiangguo Qiu X. *et al.* Nature 2014, 514: 47–53 doi:10.1038/nature13777

[147] The ebola wars. Preston R., The New Yorker, October 27, 2014 issue

[148] Genetically modified cattle with human dna might hold ebola cure. Fox M., NBC News, Jan 19 2015

GM goats, rabbits and hens: »walking drug producers«

Goats have been engineered to produce milk that can prevent blood clots. The human anticlotting protein is produced by a herd of 200 bioengineered goats[149]. To make its protein, the company took the human gene for antithrombin and used a goat promotor sequence to ensure its production only in milk.

The genetic disorder, hereditary angioedema, which is caused by having insufficient amounts of a plasma protein called C1-esterase inhibitor, can now be treated by a human recombinant enzyme produced in milk of transgenic rabbits[150].

Another genetic disorder, called lysosomal acid lipase deficiency, is now treated from the whites of GM chickens' eggs[151]. The product is called Kanuma and works by replacing a malfunctioning enzyme in people with lysosomal acid lipase deficiency.

GM yeasts and tobacco for making antimalarial artemisinin

Throughout the world, 198 million people suffer from malaria and 584,000 of them die of it annually, the majority of them children in Africa. The commonest forms of malaria are caused by the microorganisms *Plasmodium vivax* and *P. fulciparum*, the latter being the cause of the deadliest form[152].

The most effective treatment for infection by *P. fulciparum* is based on the use of artimesinin and its derivatives, which were originally obtained from a plant native to China, *Artemisia annua* (a relative of absinthe). Treatment is essentially more accessible today since they have begun to produce it with genetically modified yeasts[153], and

[149] F.D.A. approves drug from gene-altered goats. The New York Times Pollack A. 6. Feb 6 2009

[150] FDA approves new product to treat rare genetic disease. FDA News Release, July 17 2014

[151] FDA approves genetically modified chicken — but not as food. Duhaime-Ross A. The Verge Dec 9 2015

[152] World Health Organization, Media Center, Malaria Fact sheet N°94 (Reviewed April 2015)

[153] High-level semi-synthetic production of the potent antimalarial artemisinin. Paddon C. J. et al. Nature 496, 528–532 (25 April 2013), doi:10.1038/nature12051

scientists have already found a method for generating artemisinin in GM tobacco[154].

GM tobacco against HIV

A similar approach [155] to that which enabled the development of ZMapp, gave rise to the creation of a medicine against HIV, which has already entered the clinical testing phase[156].

GM *E. coli*, yeasts and safflower (*Carthamus tinctorius*) for making insulin

According to WHO data, in 2014 9% of adults over 18 had diabetes. In 2012, diabetes directly caused 1.5 million deaths[157]. The majority of sufferers need a daily dose of insulin, which could originally only be obtained from cattle, pigs and fish. Since 1978, a method has been known of generating insulin in yeasts[158]; the most recent method of obtaining insulin is based on GM safflower (*Carthamus tinctorius*)[159].

GM yeasts, potato, tomato and bananas for inoculation against Hepatitis B

Hepatitis B is a virus infection that attacks the human liver; 240 million people are infected annually, 780,000 of whom die [160]. Hepatitis B cannot reliably be treated, so the main means against the disease is timely vaccination. Most vaccines today are made in genetically modified yeasts[161] and the most recent approach enables expression of the vaccine in genetically modified derivatives of some

[154] Generation of the potent anti-malarial drug artemisinin in tobacco. Farhi M. Nature Biotechnology 29: 1072–1074 doi:10.1038/nbt.2054

[155] Influence of Antiviral Factor on Tobacco Mosaic Virus RNA Biosynthesis in Tobacco. Šindelářová M. and Šindelář L. Biologia Plantarum 2003, 46: 95-100

[156] Anti-HIV drug made by GM plants begins trials in humans. Boseley S. The Guardian 19 July 2011

[157] World Health Organization, Media Center, Diabetes Fact sheet N°312 (Updated January 2015)

[158] Secretion of human insulin by a transformed yeast cell. Hansen T.L. and Sørensen M.T. FEBS Letters 1987, 212: 307-312.

[159] SemBioSys achieves major insulin milestone. PR Newswire July 18 2006

[160] World Health Organization, Media Center, Hepatitis B Fact sheet N°204 (Updated March 2015)

[161] Human hepatitis B vaccine from recombinant yeast. McAleer WJ *et al.* Nature 1984, 307:178-180.

species of fruit and vegetable that we eat regularly[162]. Antibodies were created in this research in potato, which the tested persons ate raw.

GM rice for making lysozyme and lactoferrin (treatment for diarrhea)

Lysozime and lactoferrin are important immunity enzymes mainly in the human intestine and human milk, where they prevent infection with undesirable microorganisms. Adults get enough of both enzymes in a normal diet; it is found in milk and eggs etc. Lack of the enzymes typically causes diarrhea (which further reduces the enzyme content in the intestine) and the condition is primarily typical in babies fed with babyfood lacking added enzymes. The enzymes are also key components of medicines against diarrhea. Both enzymes can now be generated in GM rice[163, 164], which has still not obtained a permit for production in USA precisely because of resistance to GMOs.

GM carrot and rice against Gaucher's disease

Gaucher's disease is a rare genetic disorder, a genetic deficiency of the enzyme glucocerebrotidase. The effects are deposition of fat in some organs, enlarged liver and salivary gland, liver failure, bone defects etc. The disease is untreatable; the patient can only be helped by injections of an equivalent to the lacking enzyme[165]. Such therapy is essential, life-saving and extremely costly.

[162] Immunogenicity in humans of an edible vaccine for hepatitis Thanavala B.Y. *et al.* PNAS 2005, 102: 3378–3382 doi: 10.1073/pnas.0409899102

[163] Expression and localization of human lysozyme in the endosperm of transgenic rice. Yang D *et al.* Planta 2003, 216:597-603

[164] Expression of human lactoferrin in transgenic rice grains for the application in infant formula. Nandi S. et al. Plant Science 2002, 163: 713–722 doi:10.1016/S0168-9452(02)00165-6

[165] Mayo Clinic, Diseases and Conditions, Gaucher's disease

In May 2012, the American FDA – to the general disapproval of environmental activists – approved a new treatment for Gaucher's disease[166], which is made in a bioreactor with cells from GM carrot[167].

[166] Protalix, Pfizer report FDA approval of plant-derived Gaucher disease ERT Elelyso. GEN News Highlights May 2, 2012

In Italy they have succeeded in developing a GM rice that expresses in the grain the human undamaged gene for beta-glucosidase[168], for the treatment of Gaucher's disease[169]. We know from experiments carried out in greenhouses that this rice very successfully generates the necessary protein, a few hectares would be enough for all patients and the cost of treatment would dramatically fall. In order to register the medicine, a two-year test cultivation on open fields should be performed but because of the extreme European legislation against GMOs, they were unable do this in either Italy or Spain. They linked with the Biotechnical Faculty of the University of Ljubljana but the result was the same in Slovenia: legislation based on prejudice again defeated science[170].

GM diatomeae for precise delivery of means for destroying cancer cells

Chemotherapies, treatments that can destroy cancer cells, are very toxic. People that have to receive them feel very bad throughout the treatment, they often lose their hair – even at concentrations that do not guarantee complete destruction of the cancer cells.

For decades, researchers have been trying to discover a way of enclosing the active chemo ingredient in high concentrations in a microscopic carrier, which would release the content precisely on the cancer cell and nowhere else. Considerable success has been achieved by the use of peptides but these methods are mainly suitable for chemo active ingredients that are easily water soluble.

To deliver chemo active ingredients that are poorly water soluble, the most successful method has been shown to be delivery of the medicine with semi-permeable silicate nanoparticles[171, 172]. The difficulty of this method is that the production of such particles is very expensive and requires the use of a range of strongly poisonous chemicals.

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167 Gaucher's disease treatment option rides on carrot cells' biologic power. Morrow T, Managed Care 2012, 21:45-46.

168 Endosperm-specific expression of human acid beta-glucosidase in a waxy rice. PattiT. *et al.* Rice 2012, 5: 34 http://www.thericejournal.com/content/5/1/34

169 Endosperm-specific expression of human acid beta-glucosidase in a waxy rice. Patti T. *et al.* Rice 2012, 5:34 doi:10.1186/1939-8433-5-34

170 Nezaželeni riž. Undesired rice. Zgonik S., Mladina 27, 7. 7. 2011

171 Mesoporous silica nanoparticles as controlled release drug delivery and gene transfection carriers. Slowing I.I. Advanced Drug Delivery Reviews 2008, 60: 1278–1288

172 Biocompatibility, biodistribution, and drug-delivery efficiency of mesoporous silica nanoparticles for cancer therapy in animals. Jie L. Small 2010, 16: 1794–1805. doi: 10.1002/smll.201000538

However, there are suitable semi-permeable silicate carriers in nature: they are skeletons of diatoms, single cell algae that live in both salt and fresh water. They are already key for the existence of life on Earth: they represent some 45% of basic production of nutrients in oceans, which ensures the existence of higher forms of life.

The diatom species *Thalassiosira pseudonana* has an almost circular skeleton of a diameter of 4-6 µm (micrometres) and lives in the North Atlantic. A group of researchers from the USA, Australia and Germany succeeded in modifying the genetic structure of *T. pseudonana* so that the skeleton can be used as a carrier for the delivery of poorly water soluble chemo active ingredients. In addition, they succeeded in creating a trigger in the skeleton of this diatom, which releases the medicine in the presence of specifically determined proteins (cancers)[173].

GMOs with direct benefit for the final consumer

Genetic technologies also enable the development of plants that carry clear benefits to the final consumer, since they contain compounds that act positively on human health.

Golden rice

On 31 July 2000, the title page of Time magazine carried the picture of the Swiss **Ingo Potrykus**[174], who, together with the German **Peter Beyer,** had developed a GM rice with provitamin A (β-karotene, from which our body produces indispensible vitamin A).

There is not generally any difficulty with a lack of vitamin A in western countries since almost all food of an orange colour contains sufficient β-karotene, and above all we eat enough vitamin A with meat. It is a serious problem, though, in countries in which rice is a main part of the diet. Rice does not contain β-karotene. A lack of vitamin A causes, among other things, xeroftalmia (from the Greek "dry eyes"), which is least expressed in night blindness but with longlasting deficiency causes complete blindness. Mainly in Southeast Asia, from 250,000 to

[173] Targeted drug delivery using genetically engineered diatom biosilica. Delalat B. *et al.* Nature Communications 2015, 6: Article number: 8791 doi:10.1038/ncomms9791

[174] Dr. Ingo Potrykus, Time July 31, 2000

500,000 children go blind every year because of a lack of vitamin A and half of them die each year[175].

Ingo Potrykus and Peter Beyer succeeded in the first experiments in obtaining golden rice that contained β-karotene, by inserting a *psy* gene from narcissus and *crt I* gene from the soil bacterium *Erwinia uredovora*. The quantity was a bit low for normal dietary needs for vitamin A. Opponents of GMOs still exploit this today when they explain that it is necessary to eat several kilos of golden rice to satisfy daily needs for vitamin A[176]. The company Astra-Zeneca (today Syngenta) developed another variant in which, instead of narcissus, they used a similar gene from maize and thus achieved an essentially higher quantity of product. Such golden rice has now been shown to contain enough biologically available β-karotene for normal dietary needs[177].

Golden rice was planned from the very start to help people, so free access for family and small production in places with the highest deficiencies of dietary provitamin A ensures food for the majority. Golden rice has already been thoroughly tested at the international institute IRRI in the Phillipines and has been shown to be completely safe.

175 World Health Organization, nutrition, micronutrient deficiencies, vitamin A deficiency
176 Golden Illusions - The broken promises of golden rice. Greenpeace, October 2013
177 Golden Rice is an effective source of vitamin A. Tang G. *et al.* The American Journal of Clinical Nutrition 2009, 89: 1776–1783. doi: 10.3945/ajcn.2008.27119

Unfortunately, mainly thanks to propaganda [178, 179] and even vandalism[180] by »green« activists, the rice has still not reached those for whom it was intended, although recently the first testing intended for release into production began in Bangladesh[181].

It is also now possible with genetic changes to increase the content of β-karotene in soybean[182] and bananas[183] and in many other species.

GM rice with more iron and zinc

Iron deficiency is actually the commonest nutritional problem in the modern world. It can hinder the functioning of our body in various ways and, in extreme cases, even lead to death[184]. Researchers are seeking possibilities of increasing the amount of available iron in several of the more agicultural species. At least two successful experiments with rice have been reported, by which they succeeded by genetic modification in providing more biologically available iron[185, 186]. In both cases, they over-expressed the rice gene *OsNAS1*, which increases the creation of nicotianamine. This rice was recently tested on fields in two countries, showing 15 µg g^{-1} Fe and 45.7 µg g^{-1} Zn in polished grain[187]. No harmful heavy metals were detected in the grain. The trait remained stable in different genotype backgrounds. The authors concluded that "We have successfully accomplished the proof of concept on attaining Fe/Zn nutritional targets under flooded field conditions to fulfill 30% of the estimated average requirement in the human diet, in a well-characterized GM event in the widely consumed indica rice cultivar, without a yield penalty.«

178 Take action: Stand up for your rice! Greenpeace International, October 15, 2009

179 Hands off our rice! Greenpeace International

180 GM protesters cut down crop. BBC News, 18 May, 2003

181 Bangladeshi scientists ready for trial of world's first 'Golden Rice' The Daily Star Oct 8 2015

182 Genetic modification of the soybean to enhance the β-carotene content through seed-specific expression. Kim M.J. et al. PLOSone 2012, 7(10): e48287 DOI: 10.1371/journal.pone.0048287

183 GM banana designed to slash African infant mortality enters human trials. Milmo C., The Independent 10 JULY 2015

184 Iron deficiency anaemia: assessment, prevention and control. World Health Organization 2001

185 Nicotianamine, a novel enhancer of rice iron bioavailability to humans. Zheng L. *et al.* PLOS one 2010, 5(4): e10190 doi: 10.1371/journal.pone.0010190

186 Constitutive overexpression of the OsNAS gene family reveals single-gene strategies for effective iron- and zinc-biofortification of rice endosperm. Johnson A.A.T. *et al.* PLOSone 2011, 6(9): e24476. doi: 10.1371/journal.pone.0024476

187 Biofortified indica rice attains iron and zinc nutrition dietary targets in the field. Trijatmiko KR et al. 2016, Scientific Reports 6, Article number: 19792 doi:10.1038/srep19792

GM cassava with increased content of vitamin B_6

Cassava (*Manihot esculenta*) is a rare exotic vegetable in western kitchens but, in tropical places, it is the third most important source of carbohydrates. Unfortunately, cassava contains little other than starch, above all very few vitamins: for the recommended daily dose of vitamins, a person would have to eat some 1.3 kg of cassava. It contains most vitamin B_6, but even a normal daily dose of this would require at least 1 kg of cassava. So in places where cassava is an essential part of the diet, illnesses that are a result of vitamin B_6 deficiency are common: from inflammation, eczema and skin flaking similar to dandruff (seborrheic dermatitis), painful ulcers on the soft tissue in the mouth, inflammation of the eye (conjunctivitis), to damage to the nervous system (peripheral neuropathy).

Researchers at the Swiss institute ETH therefore developed a GM variety of cassava that contains more B_6, in both the leaves and rhizomes[188]. They achieved this by the insertion of two genes, *PDX1.1* and *PDX2*, from thale cress. The content of B_6 in the first bred variants was still too small to solve the problems of deficiency of this vitamin in the undeveloped world[189] but it is an important first step towards modifying cassava into a better food crop.

GM wheat and barley with less gluten

Gluten causes an autoimmune reaction with some people, known as celiac disease. A gluten-free diet is increasingly popular in developed countries, often even without any scientific basis.

Anyway, with genetic technology it is possible to produce wheat that contains essentially less gluten[190], so that it cannot trigger an autoimmune reaction. We can look forward to completely gluten-free wheat soon being available, which will greatly alleviate the diet of patients that already have celiac disease.

A group from the Spanish *Instituto de Agricultura Sostenible, Córdoba*, in cooperation with scientists at the University of Oslo, have already developed and patented GM wheat without gliadin (patent no. EP 2 395 089 B1), the protein within the framework of glutein that triggers

[188] Increased bioavailable vitamin B6 in field-grown transgenic cassava for dietary sufficiency. Li K.T. Nature Biotechnology 2015, 33: 1029–1032 doi:10.1038/nbt.3318

[189] A cure for vitamin B6 deficiency. Rüegg P. ETH Zurich News 09.10.2015

[190] Structural genes of wheat and barley 5-methylcytosine DNA glycosylases and their potential applications for human health. Wen S. *et al.* PNAS 2012, 20543–20548, doi: 10.1073/pnas.1217927109

the celiac autoimmune reaction[191]. They achieved this by the insertion of target RNAi sequences that prevent the creation of target proteins on the level of the RNA molecule. The technology is supposed to achieve 97.3% reduction in the content in key glutein proteins in the patented GMO wheat, which is undoubtedly progress, although it has not yet been proven that the remainder could not cause an autoimmune reaction among people with celiac disease.

In this case, it was again shown how harmful is the extremely restrictive EU legislation. The institute cannot find any European company interested in cultivating this wheat in the EU. It looks as if the patent will be bought by the British consultancy company Plan Bioscience Limited, which does not intend to grow the wheat itself but will sell the patent or license it for production outside the EU[192].

Milk from GM cows that does not cause allergies and protects from microbes

Cow milk contains the protein β-laktoglobulin, which is not present in human milk and which causes an allergic reaction in 2-3% of children. Although most children lose this allergy as they grow up, it is a problem that more and more children today are fed child food that is often made precisely on the basis of cow milk.

New Zealand scientists, with the aid of RNAi technology, have succeeded in developing GM cows that do not express β-laktoglobulin in milk[193] and would therefore be safer for feeding newborns. Many people are intolerant of lactose, which cow milk contains. The successful insertion of genes that are supposed to reduce the content of lactose in cow milk has been reported[194] but final results have not yet been reported in the scientific literature.

Chinese scientists have modified the milk of cows so that it is as similar to human as possible. They have established that added genes for lactoferrin and lysozyme possess antimicrobial properties. In a further study, in non-transgenic and transgenic cloned cattle, specifically expressed human α-lactalbumin, lactoferrin or lysozyme in

[191] Effective shutdown in the expression of celiac disease-related wheat gliadin T-cell epitopes by RNA interference. Gil-Humanesa J. PNAS 2010, 107:17023-17028. doi: 10.1073/pnas.1007773107.

[192] La patente española del trigo para celíacos tendrá que buscarse la vida en el extranjero. Benavente R.P., El Confidencial, 11.11.2015

[193] Targeted microRNA expression in dairy cattle directs production of β-lactoglobulin-free, high-casein milk. Anower Jabed A.. PNAS 2012, 109: 16811–16816, doi: 10.1073/pnas.1210057109

[194] Cows genetically modified to produce healthier milk. The Telegraph 17 June 2012

milk was shown to have essentially similar protein profiles in all groups[195].

Tomato with delayed ripening

Flavr Savr (pronounced "flavor saver") tomato was the first commercially available GMO variety released onto the US market in 1994[196, 197]. This GM variety included an antisense copy of a gene that coded for enzyme polygalacturonase. By suppressing enzyme activity, the tomatoes expressed delayed ripening, thus enabling them to be picked when vine-ripe. It was sold with a clear label »Genetically engineered« and was initially a success story. At the same time, (1996 to 1999) canned tomatoes sold by Zeneca under license were introduced in the United Kingdom as paste from these tomatoes. The grocery chains Sainsbury and Safeway sold 1.8 million cans. Following publication of scare stories calling GMOs »Frankenfood«[198] the cans were removed from the shelves. Production in the US was later discontinued following purchase of the license by the Monsanto company.

Similar results have been achieved more recently by several research groups, such as Indian scientists[199] who delayed ripening of tomato by inactivating two other N-glycoprotein modifying enzymes by an RNAi approach.

“Black” GM tomato reduces the risk of cancer

Antocianins are plant colours that colour fruit or flowers red, blue or violet (depending on the pH and concentration) and have already been known for a long time to reduce the risk of cancer in people[200]. They are contained naturally in cranberries, red and black currents, cherries, red cabbage, the skins of eggplant etc.

[195] Comprehensive Assessment of Milk Composition in Transgenic Cloned Cattle Zhang R. *et al.* Plos ONE 2012, 7(11):e49697 doi: 0.1371/journal.pone.004969697

[196] The case of the FLAVR SAVR tomato. G. Bruening and J.M. Lyons. *California Agriculture* 54:6-7. July-August 2000.

[197] https://www.youtube.com/watch?v=kv5TlkAN3z8

[198] The original Frankenfoods: origins of our fear of genetic engineering. Aneela Mirchandani, Genetic Literacy Project 10. Feb. 2015

[199] Enhancement of fruit shelf life by suppressing N-glycan processing enzymes. Meli VS et al. PNAS 2010, 107: 2413-2418

[200] Anthocyanins and their role in cancer prevention. Wang L.S. *et al.* Cancer Letters 2008, 269: 281–290 doi: 10.1016/j.canlet.2008.05.020

In Great Britain, researchers from the John Innes Centre in Norwich, under the leadership of **Cathy Martin**, in 2008 developed a transgenic tomato that contains enough antocians to be more resistant to over-ripening, rotting and mould, so that it lasts twice as long after picking than normal tomato[201].

Genetically modified »black« tomato cannot of course be cultivated or bought in the EU. So many breeders wanted to exploit the confirmed positive properties of transgenic tomato with a high antocian content and sought other, non-GMO methods of achieving a similar aim. They actually had partial success by complex inter-species crossing. Because »black« tomato so cultivated is not GMO, it can be grown and sold in the EU – although there is a sufficient concentration of antocianin only in the skin and less in the meat of the fruit.

With the most recent discoveries of the aforementioned laboratory, it is also now possible to increase the content of other secondary metabolites in tomato. In addition to antocian, GM tomatoes now also express stilbenoid - resveratrol and izoflavone - genistein[202]. The authors claim that the content of reservatrol in one tomato fruit is the same as the content in 50 litres of red wine or the same genistein as 2.5 kg of soybean »cheese« tofu. For this achievement, we have to thank above all the regulatory gene *AtMYB12* from thale cress, fitted with a promotor that enables the creation of the desired substances only in the fruit and not in the plant cells of tomato.

GM carrots against osteoporosis

In 2004, an American research group transferred gene *sCAX1* from thale cress into carrot in order to achieve a higher content of organically bound calcium[203]. In 2008, they tested the carrot on mice and on 30 volunteers and established that people received 42% more calcium from the test carrots than from normal ones[204]. The trial was intended to prevent osteoporosis and the emphasis was on its bioavailibility in target tissues.

[201] Anthocyanins double the shelf life of tomatoes by delaying overripening and reducing susceptibility to gray mold. Zhang Y. *et al.* Current Biology 2013, 23:1094–1100 10.1016/j.cub.2013.04.072.

[202] AtMYB12 expression in tomato leads to large scale differential modulation in transcriptome and flavonoid content in leaf and fruit tissues. Pandey A. Scientific Reports 2015 5:Article number: 12412 doi:10.1038/srep12412

[203] GM carrot may help treat osteoporosis. Roger Highfield, The Telegraph 14 Jan 2008

[204] Nutritional impact of elevated calcium transport activity in carrots. Jay Morris *et al.* PNAS 2008, 105: 1431–1435 doi: 10.1073/pnas.0709005105

GM pineapple with pink flesh Del Monte Rosé

The company DelMonte took a similar approach as with black tomato, with a pink pineapple. They wanted to grow it in Costarica and export it throughout the world, to begin with to USA. The pineapple is pink because they have inserted a gene from mandarine and, at the same time, excluded two of the pineapple's own genes. A further gene is added that causes more even ripening of the fruit. The pink colour is caused by the dye lycopene, better known from tomatoes. A number of medically beneficial effects are ascribed to lycopene[205] but, just as with others of this kind of secondary metabolite, science has still not had the last word. In April 2013, the American USDA approved import of the pink pineapples into USA[206], although it still doesn't have a permanent marketing permit.

Del Monte Rosé GM pineapple was subjected to all the required experiments, so the ideological opponents of GMOs could not reproach it in terms of safety requirements. So they set about a well tried method guaranteed to attract the media[207]: they threatened a boycott of retail chains that wanted to sell the fruit. Not for the first time (and sadly also not the last), ideologically obsessed environmentalists are forcing their own opinions on us, opinions that conflict with science and the consumer's best interests.

GM Purple Limes and Blood Oranges

So far red or »blood« oranges have been known to be grown in moderate climates such as Italy or Spain, while their cultivation in warmer regions has been limited. The red color can be derived from anthocyanin contents. Just as in »black tomato« described above, researchers from the University of Florida have produced dark red citrus fruits expressing a high anthocyanin content. These new limes were developed using genes isolated from the red grape 'Ruby Seedless' and the Blood Orange 'Moro'. The authors claim that such fruits will have direct health benefits, such as preventing a number of human health issues, including obesity and diabetes.

205 Carotenoids and their isomers: Color Pigments in Fruits and Vegetables Hock-Eng K. *et al.* Molecules 2011, 16: 1710-1738 doi:10.3390/molecules16021710

206 Del Monte gets GM pineapple green light. Carl Collen, AmericaFruit 25th April 2013

207 Boycotts are a crucial weapon to fight environment-harming firms. Bill Laurance, The Conversation April 6, 2014

Healthier cooking oil from GMOs

Two American companies succeeded by genetic transformation in greatly improving soybean cooking oil for frying. In both cases, they blocked the functioning of undesirable genes, and thus a change in the structure of the oil, by the RNAi technique.

The oil is marketed by DuPont under the trademark Plenish®. It contains more than 75% oleic acid, the main component of olive oil. Because of gene-silencing it contains few polyunsaturated and many mono-unsaturated fatty acis and the share of saturated fatty acids is reduced by 20%. The oil thus has great stability during baking, which means that the chemical process of hydrogenation, which causes undesirable transformation of fats, is unnecessary.

Under the trademark Vistive®, Monsanto markets soybean oil with a more than three times increased content of oleic acid, which now represents up to 70% of components of the oil, while linolenic, stearinic and palmitic acids (unstable polyunsaturated acids) are greatly reduced.

GM oil with omega 3 fatty acids

Omega-3 fatty acids are polyunsaturated fatty acids (PUFAs) needed by the human body. They provide the starting point for making hormones that regulate blood clotting, contraction and relaxation of artery walls and inflammation. Probably due to these effects, omega-3 fats have been shown to help prevent heart disease and stroke, may help control lupus, eczema and rheumatoid arthritis and may play protective roles in cancer and other conditions[208].

Omega-3 long-chain polyunsaturated fatty acids EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) are recognized for their strong health benefits. Terrestrial plant precursors of these fatty acids, α-linolenic acid (ALA) and stearidonic acid (SDA), need to be converted by our bodies to longer forms but conversion occurs at surprisingly low levels[209]. Cold-water fatty fish such as salmon (but not tuna, mackerel or sardine) have so far been the optimal source. It should be noted that fish do not produce PUFAs by themselves but obtain them from algae.

[208] Omega-3 fatty acids: an essential contribution. Harvard T.H. Chan School of Public health

[209] Alpha-linolenic acid supplementation and conversion to n-3 long-chain polyunsaturated fatty acids in humans. Brenna J.T. *et al.* Prostaglandins, Leukotrienes and Essential Fatty Acids 2009, 80: 85–91 doi:10.1016/j.plefa.2009.01.004

By the addition of seven genes mainly from sea algae fitted with predominantly plant regulatory sequences, the British research centre Rothamsted Research has succeeded in making a close relative of rapeseed, camelina (*Camelina sativa* or false flax) express the acids of omega-3 [210]. Because of the large number of inserted genes and necessary balance of their products, the research lasted some 15 years. It appears currently to be the most complex product made with the technology of genetic transformation. A similar achievement has also been reported from Australia[211].

In Great Britain, the first crop from this GM camelina has already been harvested[212]. The oil is suitable for direct human consumption but, for the moment, it is being tested as food for farmed salmon. In contrast to wild salmon, these consume omega 3 fats in aquaculture if they are fed small fish[213].

In environmental »announcements«, Monsanto, frequently demonised, has combined with the food company DSM, to provide the market with cooking oil with omega-3 fatty acids[214] on the basis of GM soybean.

GM oil rape (*Brassica napus*) from the company BASF also contains omega-3 fats; it is supposed to be ever closer to cultivation (in USA)[215]. Modification was achieved by the insertion of five genes from sea algae.

In addition to plant oil, cow milk can also contain omega-3 fatty acids. Chinese scientists reported this success in 2011[216].

210 Transgenic plants as a sustainable, terrestrial source of fish oils. Napier J.A. European Journal of Lipid Science and Technology 2015, 117: 1317–1324 doi: 10.1002/ejlt.201400452

211 Metabolic engineering *Camelina sativa* with fish oil-like levels of DHA.Petrie J.R. et al. PLoS ONE 2014, 9, e85061. doi 10.1371/journal.pone.0095409

212 Field trial evaluation of the accumulation of omega-3 long chain polyunsaturated fatty acids in transgenic *Camelina sativa*: Making fish oil substitutes in plants. Usher S. et al. Metabolic Engineering Communications 2015, 2: 93–98 doi:10.1016/j.meteno.2015.04.002

213 New GM cereal crop produces fish oil in its seeds. Connor S. The Independent 09 JULY 2015

214 DSM, Monsanto Partner to Deliver SDA Omega-3 Soybean Oil. FPD April 08, 2013

215 Cargill and BASF Plant Science join forces to develop EPA/DHA canola oil. Cargill News Release Nov. 2, 2011

216 Production of cloned transgenic cow expressing omega-3 fatty acids. Wu X. *et al.* Transgenic Research 2012, 21: 537-543

GM apple Arctic® doesn't brown

Apples brown on being cut because of oxidation. So they are first soaked in anti-oxidant in the commercial preparation of dried apple.

Under the trade name Arctic® Apple, in 2012 Canadian researchers began the release of two popular varieties of apple 'Golden Delicious' and 'Granny Smith' and they are also working on 'Gala' and 'Fuji'. The aforementioned varieties include a number of genes but key is the part that, on the basis of RNAi technology, prevents the functioning of the enzyme polyphenol oxidase and thus prevents browning of the cut apples.

It is interesting that some varieties already previously expressed this non-browning property, including the Slovene variety 'Majda'. Because of other properties, none of these varieties was a commercial success. The GMO approach is therefore completely new, by which already established varieties are given properties that they did not previously have.

It is particularly interesting for small countries that this success was achieved by a small company, which showed that it is possible to improve established patent-free old varieties with this procedure, giving them new properties and thus increasing market interest in them.

Healthy GM onions that don't make us cry

A research group in New Zealand under the leadership of **Colin Eady** in 2008 successfully developed a GM onion that doesn't make us cry when cut. By silencing a single gene for lacrimatory synthase by the RNAi method, they prevented the functioning of the enzyme that causes tearing and, at the same time, also achieved a still greater content of healthy sulphur containing compounds[217].

GM rice with increased resveratrol

Resveratrol is a natural phenol that plants produce when they are damaged or are attacked by bacteria or moulds. The skins of grapes, blueberries, cranberries, the fruits of mulberry etc. contain some of it. In 2013, scientists discovered that resveratrol helps prevent

[217] Silencing onion lachrymatory factor synthase causes a significant change in the sulfur secondary metabolite profile. Eady C.C. *et al.* Plant Physiology 2008, 147: 2096-2106, doi: 10.1104/pp.108.123273

cardiovascular diseases and in their treatment, but only in larger doses than can be obtained under normal conditions from fruit that contain it [218]. Chinese scientists have succeeded in developing transgenic rice that contains 1.9 µg resveratrol per gram of kernel[219]. They achieved this with the insertion of a gene for stilben synthase isolated from peanuts. Experiments with such rice on mice additionally showed that it could also help in the treatment of obesity[220].

GM potato that produces less acrylamide during frying

Acrylamide is considered a probable carcinogen[221]. Since 2002 it has been known that it can be created during boiling or frying some kinds of starchy food[222]. In 2014, the USDA approved release of a transgenic potato by the company Simplot, which contains less asparagine, amino acids from which acrylamide is created during frying[223].

The second generation (2015) of potatoes sold under the 'Innate' brand name contains four beneficial traits of relevance to potato growers, processors and consumers: in addition to the already mentioned reduced asparagine, reduced bruising and black spots, resistance to late blight (*Phytophthora infestans)* and enhanced cold storage capacity. They achieved resistance to phytoftora by transfer of a gene from the wild American species *S. venturii*, and other properties were achieved by silencing target genes with the aid of RNAi methods. So far insertions have been made into the well known 'Russet Burbank' variety, while insertions into several additional varieties – 'Ranger Russet', 'Atlantic' and 'Snowden' are planned to be submitted in coming months.

GM potato for industrial use

[218] Resveratrol in primary and secondary prevention of cardiovascular disease: a dietary and clinical perspective. Tomé-Carneiro J. *et al.* Annals of the New York Academy of Sciences 2013, 1290: 37–51, doi: 10.1111/nyas.12150

[219] Creation of resveratrol-enriched rice for the treatment of metabolic syndrome and related diseases. Baek S.H. *et al.* PLoS One. 2013, 8(3):e57930. doi: 10.1371/journal.pone.0057930

[220] Treatment of obesity with the resveratrol-enriched rice DJ-526. So-Hyeon Baek *et al.* Nature Scientific Reports 2014, 4: Article number: 3879. doi:10.1038/srep03879

[221] The carcinogenicity of acrylamide. Rice J.M. Mutation Research 2005, 580:3-20.

[222] Maizeell chemist explains how acrylamide, a possible carcinogen, might be formed when starch-rich foods are fried or baked. Friedlander B., Maizeell Chronicle Dec. 19, 2002

[223] US approves low acrylamide spud. Trager R., Chemistry World 25 November 2014

While with potatoes, it is worth mentioning the contrasting experience from the EU. The transgenic potato by the company Amflora contains a reduced content of amylose in starch and increased amilopectin and is thus suitable for industrial use. BASF lodged an application for the release of this potato in August 1996. In March 2010, on the basis of a positive opinion from EFSA the European Commission approved release[224] but in December 2013 the General Court of the EU annulled the approval[225]. The rejection did not have any tangible consequences since the company BASF, because of the complicated and time-consuming procedures in the EU, had already begun moving its plant development department to the USA in 2012[226] and it has also abandoned efforts for marketing GMOs in the EU[227]. As a point of interest, a potato with the same properties but by the technique of mutation and the TILLING method was developed at a German institute[228], which allows production of industrial potato without all the mentioned restrictions.

Genetically modified content of amylose in cereals

Amylose is one of two components of starch (the other is amylopectin), which, in unmodified kernels, creates 20-30% of the starch. Amylose is insoluble in water and difficult to digest. By varying the content of amylose in the grain, therefore, we can develop a range of varieties of the same species, with variants that are more or less easily digested.

Chinese scientists have developed a technology for genetically modifying rice[229] and wheat[230], which reduces the level of amylose (both rice and wheat are therefore digested more quickly and are thus more nutritious).

High-amylose wheat also produces a high level of resistant starch, which is important in bowel health. It also has a lower glycaemic index than other starches, with benefits for managing body weight and stabilising blood glucose levels.

[224] Commission announces upcoming proposal on choice for Member States to cultivate or not GMO's and approves 5 decisions on GMO's. European Commision Press Release Database IP/10/222

[225] E.U. court annuls GM potato approval. Rabesandratana T. Science Insider 13 December 2013

[226] European vacation: BASF Moves Plant Science HQ to U.S. McCurry J.W., Site Selection January 2012

[227] BASF to stop selling genetically modified products in Europe. Kanterjan J. The New York Times Jan. 16, 2012

[228] Precision breeding creates super potato. ExzellenzNRW 16. Nov. 2009

[229] Stable inheritance of the antisense waxy gene in transgenic rice with reduced amylose level and improved quality. Qiaoquan Liu *et al.* Transgenic Research February 2003, 12: 71-82

[230] RNA silencing of Waxy gene results in low levels of amylose in the seeds of transgenic wheat (*Triticum aestivum* L.). Li JR et al. Yi Chuan Xue Bao. 2005, 32:846-54

Several studies on various cereals have therefore focused on altered starch composition, which has most often been achieved by an RNAi approach[231, 232, 233].

GM alfalfa with reduced lignin content

Alfalfa (*Medicago sativa*) is mainly grown for feeding livestock. The longer alfalfa grows, the more lignin it creates, mainly in the stem, which preserves the structure of the plant. Unfortunately, this lignin is hard to digest so it is not wanted in animal feed. Alfalfa growers therefore harvest the alfalfa well before it gains its maximum weight because, despite the smaller yield, the product is more digestible.

In USA in April 2014, GM alfalfa was released into cultivation[234] that, because of RNAi silencing of the *CCOMT* gene, contains 10–15% less lignin[235]. Producers can thus harvest the alfalfa later so as produce higher quality feed on the same area, which in the end also means higher production of milk and meat.

GM plants with a more suitable protein composition

Carbohydrates and proteins are major constituents of diet for both farmed animals and human beings. In animal husbandry, proteins are commonly provided as seeds, usually from legume or cereal grains. However, the amino acid composition of the proteins in seeds can have a sub-optimal composition. Of the 20 protein amino acids, 10 are classified as 'essential' because animals are unable to synthesize them and they must be therefore supplied in the diet. Missing essential amino acids can be a cause of malnutrition in humans or limit the efficiency of animal production. Among them, the amino acids methionine and lysine are most frequently below recommended

[231] Comparative proteomic analysis of kernel proteins of two high amylose transgenic durum wheat lines obtained by biolistic and *Agrobacterium*-mediated transformations. Sestili F. *et al.* Journal of Cereal Science 2013, 58: 15-22 doi: 10.1016/j.jcs.2013.05.001

[232] The differential effects of genetically distinct mechanisms of elevating amylose on barley starch characteristics. Regina A. *et al.* Carbohydrate Polymers 2012, 89: 979–991 doi:10.1016/j.carbpol.2012.04.054

[233] Suppression of starch synthase I expression affects the granule morphology and granule size and fine structure of starch in wheat endosperm. McMaugh S.J. *et al.* Journal of Experimental Botany 2014, 65: 2189–2201 doi:10.1093/jxb/eru095

[234] Determination of nonregulated status under 7 CFR Part 340 for Monsanto company and Forage Genetics International KK179 alfalfa

[235] Forage Genetics International the development of HarvXtraTM Alfalfa

values. Animal feed is therefore often supplemented with synthetic amino acids.

Scientists have used various approaches to increase essential amino acids in plants. Using genetic engineering, as far back as 1997 Keeler and coworkers inserted a synthetic protein containing 31% lysine and 20% methionine residues in GM tobacco seeds [236] . Since then numerous other achievements have been published, ranging from the insertion of proteins from Brazil nut, sesame or sunflower into lupins, soybean or narbon beans[237].
The first released brand to be cultivated in the USA was Mavera maize with increased lysine content[238], due to a bacterial gene that regulates lysine synthesis.

Altering the amino acid composition in proteins is not limited to plants. As a point of interest, using synthetic biology Yale scientists recently created a completely new strain of bacteria whose metabolism is altered in such a way that it requires synthetic amino acids for growth that cannot be found in nature[239].

The research team expects these novel »genomically recoded organisms » to be used in the production of pharmaceuticals, fuels and new chemicals, since such bacteria cannot survive in nature. They explained to the media that: »This new method of bio-containment, solves a longstanding problem in biotechnology«[240].

GM farmed plants with phytase

As was already mentioned in the description of Eviropig, kernels of maize contain up to 75% of phosphorus in the form of phytic acid. Only ruminants can exploit this, because they have special intestinal bacteria for the production of the enzyme phytase, which decomposes the phytic acid. It is similar with other cereals.

Scientists at the Chinese Institute for Biotechnological Research developed a GM variant of maize that expresses phytase in the

[236] Expression of de novo high-lysine alpha-helical coiled-coil proteins may significantly increase the accumulated levels of lysine in mature seeds of transgenic tobacco plants. Keeler S.J. et al. Plant Molecular Biology 1997, 34: 15–29. doi:10.1023/A:1005809900758.

[237] Genetic contributions to agricultural sustainability. Dennis E.S. Philosophical Transactions of the Royal Society 2008, 12;363:591-609

[238] Renessen receives final regulatory clearance for world's first crop-based biotechnology quality trait for animal feed industry February 6, 2006

[239] Recoded organisms engineered to depend on synthetic amino acids. Rovner A.J. et al. Nature 2015, 518: 89-93

[240] Synthetic amino acid enables safe, new biotechnology solutions to global problems. Science daily

kernel [241] and thus enables also non-ruminants to exploit the phosphorus from phytic acid. A number of tests have already shown that such maize is completely safe for feeding pigs and poultry[242, 243]. China has been announcing for a number of years that it will release this variety of maize for cultivation but it has not yet happened. As well as maize, there are reports in the scientific literature of the insertion of a gene for phytase into other species but they do not mention attempts at release. With barley, phytase was achieved[244] by the insertion of the barley's own gene, with soybean[245], oilseed rape[246] and cotton[247] by the insertion of the genes *PhyA* or *MPHY2* from the fungus *Aspergillus* sp.

GM plants without allergens and toxins

Some allergens and toxins can be removed from plants using contemporary methods of genetic manipulation[248]. They have thus already developed soybean that does not have a dominant allergen[249]; and reduced the allergic nature of Indian hazelnuts[250]; tomato[251] and many others. These technologies, which are for the most part based

[241] Transgenic maize plants expressing a fungal phytase gene. Chen R. *et al.* Transgenic Research 2008, 17: 633-43.

[242] Phytase transgenic maize does not affect the development and nutrition utilization of *Ostrinia furnacalis* and *Helicoverpa armigera.* Zhang Y. *et al.* Environmental Entomology 2010, 39:1051-1057 doi: 10.1603/EN09380.

[243] Effect of dietary phytase transgenic maize on physiological characteristics and the fate of recombinant plant DNA in laying hens. Gao C. *et al.* Asian-Australasian Journal of Animal Sciences 2014, 27: 77–82 doi: 10.5713/ajas.2013.13265

[244] Cisgenic barley with improved phytase activity. Holme I. B. *et al.* Plant Biotechnology Journal 2012, 10: 237-247 doi: 10.1111/j.1467-7652.2011.00660.x. Epub 2011 Sep 29.

[245] Transgenic soybean with low phytate content constructed by *Agrobacterium* transformation and pollen-tube pathway. Yang S.H. *et al.* Euphytica 177: 375-382 doi: 10.1007/s10681-010-0262-4

[246] Codon-modifications and an endoplasmic reticulum-targeting sequence additively enhance expression of an *Aspergillus* phytase gene in transgenic canola. Peng R.H. *et al.* Plant Cell Reports 25: 124-132 doi: 10.1007/s00299-005-0036-y

[247] Agrobacterium-mediated transformation of cotton (*Gossypium hirsutum* L.) with a fungal phytase gene improves phosphorus acquisition. Liu J.F. *et al.* Euphytica 2011, 181: 31-40 doi: 10.1007/s10681-011-0370-9

[248] Inactivation of allergens and toxins. Morandini P. Nature Biotechnology 2010, 27: 482-93. doi: 10.1016/j.nbt.2010.06.011.

[249] Genetic modification removes an immunodominant allergen from soybean. Herman E.M. *et al.* Plant Physiology 2003, 32: 36-43 doi: 10.1104/pp.103.021865

[250] Alleviating peanut allergy using genetic engineering: the silencing of the immunodominant allergen Ara h 2 leads to its significant reduction and a decrease in peanut allergenicity. Dodo HW *et al.* Plant Biotechnology Journal. 2008, 6:135-45.

[251] Reduced allergenicity of tomato fruits harvested from *Lyc* e 1-silenced transgenic tomato plants. Le LQ *et al.* Journal of Allergy and Clinical Immunology 2006, 118:1176-83. doi: http://dx.doi.org/10.1016/j.jaci.2006.06.031

on RNAi silencing, are already so far developed that in a few years all known potential allergens could be removed from food products of plant origin; if, of course, methods of breeding with genetic modifications didn't experience such political and ideological opposition.

GM silkworms produce silk that is as strong as a spider's thread

The thread from which spiders spin their webs is a natural miracle: for the same thickness it has a bearing power similar to that of steel but, because a spider's thread is essentially lighter, for the same weight it is five times stronger than steel cable. Their way of life means that it is not possible to breed spiders in sufficiently large groups for the commercial production of their thread.

Silkworms (*Bombyx mori*) have been bred in China for at least 5000 years. When the caterpillars pupate, they are wrapped in a protective cocoon made from silk thread. These cocoons were formerly unwrapped by hand but today mainly by machine and the result is strong thread from which valuable material is made. The silk thread is made from similar proteins to that of spiders.

Researchers from USA and China discovered a method in 2011 of genetically modifying silkworms so that they produce thread from spider proteins – such silk thread is up to fifty times stronger than normal[252]. The company Kraig Biocraft developed a procedure on this basis for the commercial production of »spider thread«[253].

Actually, scientists had already reported in 2002 the possibility of producing proteins of spiders' thread from GM mammalian cell lines[254]. They used two genes, *ADF-3/MaSpII* and *MaSpI*, from two different species of spider. They actually used the method on goats[255] but in this case the proteins are dissolved in the milk, from which they first had to be separated and then spun into thread.

Clothing woven from such "spider silk" would be proof against small caliber bullets and knives and, at the same time, would have all the aesthetic advantages of natural silk: rope from "spider's thread" could replace steel etc.

[252] Silkworms transformed with chimeric silkworm/spider silk genes spin composite silk fibers with improved mechanical properties. Teuléa F. *et al.* PNAS 2012, 109: 923–928, doi: 10.1073/pnas.1109420109

[253] Kraig Biocraft Laboratories Spider Silk

[254] Spider silk fibers spun from soluble recombinant silk produced in mammalian cells. Lazaris A. *et al.* Science 2002, 295: 472-476 doi: 10.1126/science.1065780

[255] "Biosteel": an exciting product from nature that is superior to many manmade alternatives. Majumder S. *et al.* Reviews in Chemical Engineering 2015, 31: 509-519 doi: 10.1515/revce-2014-0055

Improvements in plant breeding procedures

Production of hybrid seed

As was mentioned in the introduction, the introduction of hybrid varieties of maize signified an exceptional agricultural leap forward; thus also benefiting the whole world. Hybrid varieties were then introduced in a number of field crops, vegetables and even ornamental plants. Breeders choose the most suitable parent lines and cross them each year to obtain hybrid (F1) seed. The procedures that enable this are anything but simple. In some species they use various traits such as pollen incompatibility or genetic or cytoplasmic male sterility. In such cases, lines do not have to be manually crossed, although this very time consuming work is still performed with some plant species, for instance in tomatoes. Manual crossing makes seeds much more expensive, of course, even though this affects a limited number of species.

GM procedures have long made it possible to produce hybrid seed without manual work. A number of procedures have already been developed to do this. The majority of procedures are based on the fact that expression of the GM property can be restricted to a particular organ, for example only the layer of the anther containing the pollen. The same is thus achieved as with normal hybrids, infertility of the pollen of the seed line.

Thanks to the European company Plant Genetic Sytems, hybrid oilseed rape, including by the GMO method, has already been cultivated since 1996[256] and since 2005 such varieties have been allowed to be sold in the EU. The company used four elements in order to achieve a male sterile line, and its pollinators and the procedure worked with many plant species. Such hybrid rapeseed is grown in North America on at least 800,000 hectares. It is not the only GM system for obtaining hybrid seed. Already developed but not yet in use, for instance, is a system that causes male sterility in the seed line by combining two separately created parts of proteins, in which each derives from a different line[257].

[256] Engineered genes for fertility control and their application in hybrid seed production. Reynaerts A. *et al.* Scientia Horticulturae 1993, 55: 125–139. doi:10.1016/0304-4238(93)90028-O

[257] Split-gene system for hybrid wheat seed production. Kempe K. *et al.* PNAS 2014, 111: 9097–9102 doi: 10.1073/pnas.1402836111

The company Pioneer, now part of the Dupont company, has been using entirely its own system since 2005, in which infertile pollen is coloured red and disintegrates with the seed of the parents. This system is particularly interesting because only the parentals are GM; the F1 hybrid does not contain inserted genetic elements and so, at least in the USA, it is not marketed as GMO[258]. In the EU, similar cases are only being debated; because of political obstruction there's still no decision.

Reverse breeding

As was explained above, breeding hybrid varieties is an optimal solution for several reasons. Unfortunately, the procedure is extremely laborious. Breeders first cross several parent lines, then induce inbred lines by selfing or with the aid of induced haploidy, which gives them thousands of lines. They then have to make a series of test crosses to identify a particular two lines that combine in a final hybrid. This last step in particular is a major limitation.
Researchers of the Rijk Zwaan company led by Rob Dirks, with help from other labs, patented and published[259] a novel approach called reverse breeding. By this procedure, a breeder would first obtain a large number of F_1 hybrids by crossing parental lines, then select the obvious best ones and finally reconstruct new parental lines that reproduce the same F_1 hybrid. This is achieved with three key steps: inactivation of a gene that regulates a process called crossing over (in meiosis), production of doubled haploid lines and identification of individual chromosomes by molecular fingerprinting. Although the method might be limited to crops with rather low chromosome numbers (which would generate reasonable probabilities of identifying appropriate complimentary lines), it is clear that the innovation is a game changer in hybrid production.

GMO specialities: for better appearance, smell, commercial interest

Mankind could probably survive without blue roses and carnations, black tulips etc. but visual pleasure is an important part of daily life. Modern genetic technologies enable the development of flowers with

[258] Petition for the determination of nonregulated status for maize 32138 spt maintainer used in the Pioneer seed production technology (SPT) process

[259] Hybrid recreation by reverse breeding in *Arabidopsis thaliana*. Wijnker E. *et al.* Nature Protocols 2014, 9: 761-772

interesting colours[260]. Objections based on suspected risk with such GMOs are merely political, not scientific.

GM blue carnations

Moonlite™ blue carnations, developed by the Australian company **Florigene** (since 2003 majority owned by the Japanese concern **Suntory**), are a fine example of how complicated and lengthy procedures are in the EU for approving GMOs. Moonlite® carnations contain an added gene for colour, so that they flower from pink to explicitly blue; in addition, they contain a gene for increased resistance to herbicides. In 2006, Florigene filed an application for a permit to important *cut* flowers of these carnations into the EU[261]; they received the permit on 24 April 2015[262].

GM blue roses

The first blue roses were presented at a horticultural fair in Tokyo in October 2008 [263] . They had been developed by Suntory and Florigene[264] using similar technology as used for the development of blue carnations. They are not allowed to be cultivated in the EU, of course. Not even cut flowers can so far be imported.

Blue and violet GM chrysanthemums

The Australian company Filippa Brugliera developed GM chrysanthemums that express blue or violet in the flowers[265]. It is worth mentioning that chrysanthemums here are only an ornamental flower but they are an important spice in Asian cuisine.

[260] Recent progress of flower colour modification by biotechnology. Tanaka Y. International Journal of Molecular Sciences 2009, 10: 5350–5369. doi: 10.3390/ijms10125350

[261] Carnation Moonaqua GMO Compass

[262] European Commission - Press release. Commission authorises 17 GMOs for food/feed uses and 2 GM carnations. Brussels, 24 April 2015

[263] World's first blue roses after 20 years of research. Demetriou D. The Telegraph 31 Oct 2008

[264] Suntory global innovation center, research & technology, challenge for “blue roses”

[265] Patentdocs: Patent application title: genetically modified chrysanthemums

Petunia Circadia, GM petunia that changes colour through the day

With the aid of technology partly developed at the University of California, Davis [266], the company Revolution Bioengineering has produced a petunia that changes colour from blue to dark pink in relation to exposure to sun[267].

GM flowers with an unusual smell

A group of researchers at the University of Florida has discovered a genetic mechanism that enables changing the smell given off by flowers. As first proof of the technology, they developed a petunia that smells like roses. However, the aim of the research is not just to produce flowers with unusual smells: among other things they also discovered that the same gene as that which gives roses their scent is also responsible for giving tomatoes a better taste[268].

GloFish® - GM fish that »light up«

Genes that create fluorescent proteins are well known in genetic laboratories since they provide a simple way to monitor gene expression in various cells in an non-destructive manner. A particularly popular fluorescent protein was originally found in jellyfish *Aequorea victoria,* its brighter modifications are now used in various organisms. The Nobel prize was awarded in 2008[269] for the discovery of this green fluorescent protein (GFP)!

Insertion of GFP gene into aquarium fish resulted in an interesting commercial product GloFish® which was the first successful genetic modification on animals on the market. In 1999, a group under the leadership of **Zhiyuan Gong** at the National University of Singapore successfully transferred a *GFP* gene into the common river fish from India and Bangladesh, *Danio rerio*[270] which was at that time already popular among owners of tropical freshwater aquariums. Following transformation the fish express the fluorescent proteins mainly in the

[266] UC Davis. Today, color-changing petunias on their way. Nelson D
[267] Revolution bioengineering, the science of color changing flowers
[268] PhDAHP1 is required for floral volatile benzenoid/phenylpropanoid biosynthesis in *Petunia* x *hybrida* cv 'Mitchell Diploid'. Langer K.M. et al. Phytochemistry 2014, 103: 22-31 doi: 10.1016/j.phytochem.2014.04.004. Epub 2014 May 6.
[269] ttp://www.nobelprize.org/nobel_prizes/chemistry/laureates/2008/press.html
[270] Green fluorescent protein expression in germ-line transmitted transgenic zebrafish under a stratified epithelial promoter from keratin. Gong Z. *et al.* Developmental Dynamics 223:204–215 (2002)

epidermis so they display fluorescence when lightened by short wavelenghth light. Later on, company inserted various variants of the gene resulting with extended palette of colours. Today GloFish® exists in green, orange, red, blue, yellow and violet colours.

Using the developed technology, they transformed also the species *Gymnocorymbus ternetzi* and *Puntius tetrazona*, which are now extremely successful among aquarium owners. Nice presentation of achievements is available in the following video[271].

[271] GloFish® fluorescent fish video! (Includes our new GloFish Tetras!)

Part 2: Common misconceptions about GMOs

GM maize NK603 causes tumours (Séralini affair)

Gilles-Éric Séralini, professor of molecular biology at the University of Caen (France), gained »international fame« when in September 2012 he presented the results of his research to chosen journalists[272], according to which Monsanto's GM maize NK603, resistant to the herbicide glyphosate, caused tumours in rats that had been fed on it for two years. He warned that prior to the writing of the article they were not allowed to consult other experts. He showed some rats at the presentation with giant tumours and the media throughout the world published the sensational news on their front pages[273].

[272] Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Séralini GE *et al.* Food and Chemical Toxicology 2012, 50:4221-4231 doi: 10.1016/j.fct.2012.08.005

[273] Shock findings in new GMO study: Rats fed lifetime of GM maize grow horrifying tumors, 70% of females die early. Adams M. Natural News, 19. 9. 2012

Séralini's results immediately seemed suspicious to other scientists because in no other experiments on NK603 maize had anything similar been noted, although this GM plant had had to go through a mass of official tests in order to get a permit at all as food, fodder and production outside the EU [274, 275] and as food and fodder for production in the EU. More detailed analysis of Séralini's research showed that rats of the breed Sprague-Dawley had been used, which are naturally inclined to tumours or, put another way, a fair number of Séralini's rats would have developed tumours anyway in two years, even if they had been fed babyfood. Séralini had only used one control group of rats (of 10) in his »research«, which is already methodologically unacceptable. Séralini demonstrated the carcinogenicy of NK603 maize with a very small sample of ill rats, which could certainly not justify his conclusion. The French Academy of Science condemned Séralini's study as sensationalist and scientifically inadequate [276]. Regulatory bodies, including EFSA, discussed the study[277].

[274] Test Biotech Event NK603

[275] Safety assessment of roundup ready maize event NK603

[276] Joint advice note issued by the French national academies of agriculture, medicine, pharmacy, sciences, technologies and veterinary sciences in regard to a recent publication by G.E. Séralini *et al.* on the toxicity of a GM

[277] Séralini et al. study conclusions not supported by data, says EU risk assessment community. EFSA 28 November 2012

The scientific journal *Food and Chemical Toxicology*, which originally published the article, officially withdrew it in November 2013[278]. This sad story became known as the Séralini Affair in scientific and even in more general circles[279].

Séralini's »results« are often exploited by GMO opponents to ascribe carcinogenicity to all genetically modified organisms. However, no confirmation at all of this thesis can be found in the scientific literature.

GM potato (Árpád Pusztai)

Árpád Pusztai, a biochemist of Hungarian birth who worked in the Rowett Research Institute in Aberdeen in Scotland, in 1998 claimed, first on television[280] and then in 1999 in a published scientific article[281], that the genetically modified potato developed by the biotech company *Cambridge Agricultural Genetics*, caused damage to the digestive tissue of rats on which the potato was tested. An international media sensation developed from Pusztai's publication[282] and his claim that genetically modified food is harmful is still repeated today by some »green« media. The truth is not so simple.

First, nobody produced the potato that Puzstai tested for food – they had sent it for testing as an experimental product of genetic technology, from which they could collect enough data for the decision on whether it was suitable for commercial production. Second, the damage that Pusztai established was not caused by some unenvisaged property of this transgenic potato but a known and intentionally caused content of lectin, which was achieved by transfer of the appropriate gene from common snowdrop (*Galanthus nivalis*); lectins, of course, are a familiar poison.

Why would anyone want to develop a potato that contains poison? Because lectins are a well known toxic substance that are also present in some types of completely »natural« food, such as beans. A raw bean is poisonous, so it is always cooked – lectin completely decomposes with cooking (10 minutes in boiling water is enough). A healthy potato

[278] Retracted: Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize; Food and Chemical Toxicology 2012, 50: 4221-4231

[279] Does the Seralini maize study fiasco mark a turning point in the debate over GM food? Forbes, 30. 9. 2012

[280] Genetically modified plants and human health; Key S *et al.* Journal of the Royal Society of Medicine 2008, 101: 290-298, doi: 10.1258/jrsm.2008.070372

[281] Effect of diets containing genetically modified potatoes expressing *Galanthus nivalis* lectin on rat small intestine; Ewen S.W. and Pusztai A. The Lancet 1999, 354: 1353-1354 doi:10.1016/S0140-6736(98)05860-7

[282] Dr Arpad Pusztai: GM potatoes damage gastrointestinal tract in rats. GMO evidence

tuber contains no dangerous amounts of toxins but, in the stems, leaves and other green parts, there are poisonous glycoalkaloids – and if tubers are exposed to light or damaged, these toxic substances are expressed in them. So we don't eat potatoes raw. Lectin would additionally protect potato tubers from pests, as it does with beans; it is one of the naturally developed insecticides that protect plants from the majority of potential attackers. Such food is not harmful to people because we cook it and the lectin thus decomposes, with beans and potatoes. The basic aim of testing this transgenic potato would thus have been to establish the effects that could be caused by cooked potato, to check whether perhaps the content of lectin would not decompose quickly enough etc.

Instead of processing the obtained results and preparing them for publication in the scientific literature, Pusztai appeared on one of the British television national networks with alarming claims. He claimed that the GMO had an essentially more negative effect on the test rats than normal potato, despite the fact that lectin had been added to normal potato. The story about later reactions of the institute, publications in the scientific press and investigations of the method of work and results by the prestigious Royal Society (the Academy of Science of the UK and Commonwealth) and a UK parliamentary commission, is very long. A subsequent serious review of Pusztai's work found a variety of deficiencies in the research: among other things, Pusztai used too few test animals, testing was not blind etc. The expert review by the Royal Society therefore found that »the study is compromised in many aspects of design, implementation and analysis« and that therefore on its basis »one could not derive any conclusions”[283].

The author's statements for television were contradicted by the later published results and testimony before the parliamentary commission. Pusztai was fired for scientifically improper behaviour but, because of his »courage« (because, on completely unfounded suspicion, he »warned« the public of harmful effects of GMOs), he became a martyr of the green movement[284]. Even though his claims were scientifically entirely unfounded, he attracted sensationalist attention and harmed the reputation of British science[285], his “findings” (and consequencies for his career) are still today “proof” for professional environmentalists of the harmfulness of GMOs and the evil intentions of the »agro-industrial lobby«.

[283] Review of data on possible toxicity of GM potatoes; The Royal Society, June 1999

[284] Arpad Pusztai: Biological divide - James Randerson, The Guardian, 15 January 2008

[285] The Pusztai affair - science loses”; BBC News Online's Science D. Whitehouse (Ed), BBC News, October 15, 1999

Pollen of GM maize kills monarch butterflies

The pollen of genetically modified maize kills the larvae of the monarch butterfly (*Danaus plexippus*) [286] was published in the prestigious journal Nature[287]. It doesn't really: the claim was based on laboratory experiments carried out in completely unrealistic conditions. The article provoked extensive, in-depth scientific research, which did not support the original conclusions[288]. The only example of mortality of the larvae in nature, which came about in conditions of severe drought, could not be ascribed to GM maize[289, 290].

The media interpreted a more recent article connecting the reduced number of monarch butterflies to GM maize[291] as evidence that GMOs threaten these butterflies. However, the article says something different: because of the ever more widespread cultivation of maize that is resistant to glyphosate, the use of this herbicide has also spread, destroying weeds in fields and in their immediate surroundings. These weeds include silkweed (*Asclepias syriaca*), on which monarchs lay their eggs. Less silkweed thus also means fewer monarchs – but the effect would be the same if weeds like silkweed were pulled by hand.

However, it is indisputable that monarch populations are still falling, which environmental groups regularly exploit for their claim that all GMOs destroy these butterflies. However, the reality is different: scientists who study monarchs say that the main reason for the reduction of their population is the fast disappearance of forests in Mexico in which the monarchs overwinter. The most recent research shows that increasing losses during migrations are very important for the fall of monarch populations[292].

It is worth mentioning in this case that such an emphasis on the threat to monarch butterflies in USA has a particularly powerful

[286] Toxic pollen from genetically modified maize kills monarch butterflies, researchers find in lab tests. Friedlander B. Jr, Maizeell Chronicle, May 20, 1999

[287] Transgenic pollen harms monarch larvae. John E. Losey *et al.*, Scientific, Correspondence, Nature 399, 214 (20 May 1999) | doi:10.1038/20338

[288] Gensko spremenjena hrana. Genetically modified food. Bohanec B. et al. Univerza v Ljubljani, Biotehniška fakulteta, Ljubljana, 2004, ISBN 961-6379-06-2

[289] Three years later: Genetically Engineered Maize and the Monarch Butterfly Controversy. Pew Initiative on Food and Biotechnology

[290] Impact of Bt maize pollen on monarch butterfly populations: A risk assessment. Sears M.K. PNAS 2001, 98: 11937-11942 doi: 10.1073/pnas.211329998

[291] Milkweed loss in agricultural fields because of herbicide use: effect on the monarch butterfly population. Pleasants J.M. *et al.* Insect Conservation and Diversity 2013, 6: 135–144 doi: 10.1111/j.1752-4598.2012.00196.x

propaganda effect. There are no such butterflies in Europe (there is the apparently similar species, the swallowtail, *Papilio machaon*) but in USA the monarch is especially famous: if an American knows the name of at least one species of butterfly it will probably be the monarch. They are taught about them in all primary schools. The attractive feature of the monarch is its long migration, with up to four generations during the course of a year; the first flies from the south northwards, all the way to Canada and later generations turn and fly again south. So for the average American, the claim that »GM maize threatens the monarch« has a similar emotional charge as, for example, in Slovenia the claim that GMOs threaten the Carniolian honeybee.

Suicides of Indian farmers because of GM cotton (Vandana Shiva)

The Indian environmental activist, **Vandana Shiva,** claimed in a number of articles that the sale of Monsanto's GM cotton seed had caused a rise in the number of suicides among Indian farmers[293]. The high price of such seed was claimed to have forced poor farmers into debt and the crop was not so much bigger that they could pay off the debt, so many of them are supposed to have decided on an extreme way out. Vandana Shiva also claimed that Monsanto cotton seed also contained a »terminator« gene, which caused sterility in the harvested seed and the farmer was thus obliged constantly to buy new patented seed[294, 295].

Vandana Shiva's propaganda campaign was actually a pack of lies, which is easiest to prove from his claim that Monsanto seed contained a »terminator« gene: Vandana Shiva herself had to admit that it's just not true[296].

Another piece of Vandana Shiva's disinformation is the link between the increase in rural suicides »from the mid nineteen-nineties« and the sale of Monsanto's seed: GM cotton seed was only approved for sale in 2002. Indian farmers have been growing GM cotton in large numbers throughout the country. Why then was the »epidemic of suicides« because of GM cotton limited to only 5 of the 28 Indian federal states? Furthermore, the increased level of suicides in the countryside

[293] Seeds of suicide and slavery versus seeds of life and freedom. Shiva V. Al Jazeera 30 Mar 2013

[294] From seeds of suicide to seeds of hope: why are Indian farmers committing suicide and how can we stop this tragedy? Vandana Shiva, The Huffington Post, April 28, 2009

[295] The seeds of suicide: how Monsanto destroys farming. By Shiva V. Global Research, March 13, 2014

[296] Vandana Shiva admits: There is No Terminator. SkeptEco

continued after 2012, when equivalent GM seed was also provided by Chinese and Indian firms and the price fell by half[297]. More detailed analysis of this disinformation can be found in many articles, such as those by **Paul Raeburn**[298] or **Michael Specter**[299].

The increased number of suicides among Indian farmers is an "…unanticipated result of bank reforms that the country enacted in the early nineteen nineties. The reforms made banking more competitive … and reduced the extent of loans to farmers…"
These were forced to take loans from private individuals, who charged up to 45% interest[300]. India reformed the financial system at that time but did not reform farming[301].

Despite the lobbying of Vandana Shiva and professional environmentalists, *Bt*-cotton is also successfully grown in China, Sudan and in the poor African country of Burkina Faso[302], where it brings tangible economic benefits to the producers in all cases.

GM soybean causes the death of young rats, stunted growth, sterility (Irina Ermakova)

The Russian neurologist **Irina Ermakova** presented the surprising results of her research at an environmental conference in Germany in 2005: young rats that Ermakova had fed on genetically modified soybean from the American company Monsanto are supposed to have died en masse in the first days after birth or to have had stunted growth or be sterile[303, 304, 305]. The truth was rather different.

Scientists were first surprised by the fact that Ermakova presented her results, such as no laboratory had previously discovered, only in the media and at environmental meetings; she never sent an article

297 The GMO-Suicide Myth. Kloor K. Issues in Science and Technology, Volume XXX Issue 2, Winter 2014

298 Demolishing the myth that Monsanto's engineered crops drove 270,000 Indian farmers to suicide. Raeburn P. Knight Science Journalism Tracker March 11, 2013

299 Seeds of doubt. Specter M., The New Yorker August 25, 2014

300 Political economy of suicide: financial reforms, credit crunches and farmer suicides in India. Anoop Sadanandan , The Journal of Developing Areas, Volume 48, Number 4, Fall 2014 pp. 287-307 | 10.1353/jda.2014.0065

301 Farming in India: In a time warp. The Economist, Jun 27th 2015

302 Massive economic boost from biotech cotton. Crop Life, October 7, 2015

303 Influence of genetically modified soybean on the birth-weight and survival of rat pups. in Proceedings of the Conference Epigenetics, Transgenic Plants and Risk. Ermakova, I.V. Assessment, Frankfort am Main, Germany, December 1, 2005 (ed. Moch, K.) 41–48 (Öko-Institut, Freiburg, 2006).

304 GM soybean fed rats: stunted, dead, or sterile; Dr. Mae-Wan Ho, ISIS Report 28/11/06

305 What biotech doesn't want you to know about GMOs; Food Freedom, September 17, 2010

for publication in any peer reviewed journal. Because of the great media interest in the presumed findings on the dangers of GMOs, the prestigious journal *Nature Biotechnology* asked Ermakova for a detailed report on her work and published it together with commentaries from four leading experts in biotechnology[306]. The experts' conclusion was: "*... we find that it is not possible to draw any definitive conclusions from these results. The experiment was not carried out in accordance with internationally accepted protocols ... The nature of the original material (soybean) is unknown; the amounts individual animals consumed are unknown; the composition of their diet is unknown ... The abnormally high mortality and slow growth in control groups indicates poor care of the animals.*" Ermakova thus starved *all* the rats – and ascribed the normal effects of undernourishment to GM soybean! No other laboratory that keeps the rules on the conduct of experiments has managed to reproduce the »research results« - but that doesn't bother professional environmentalists at all: Ermakova (predictably) became a hero of the fight against GMOs and environmental media publish her articles as undisputed science.

Austrian scientists published similar alarmist news of the death of rats in a multi-generational experiment; the article went out on the internet in 2008[307]. They studied feeding rats with maize that contained the Bt gene for resistance to European corn borer and a gene for resistance to herbicides. All leading media published the findings of the study, that GM maize negatively effected the fertility of rats. This prompted a more detailed analysis of the study by the scientific community, including EFSA[308]. They drew attention to a number of deficiencies in the design of the experiments and their implementation. Two years after the warnings, in October 2010 the Austrian government officially revoked the study because of mistakes found in the statistical analysis of the data. The corrected data did not show the negative effect. The revocation did not of course reach the media.

GMO fruits cause allergies

Such claims keep on appearing and it is impossible to answer them all.

[306] GM soybeans and health safety—a controversy reexamined; Marshall A. Nature Biotechnology 25, 981 - 987 (2007); doi:10.1038/nbt0907-981

[307] Biological effects of transgenic maize NK603xMON810 fed in long term reproduction studies in mice. Velimirov A. et al. 11. November 2008

[308] EFSA GMO unit, bilateral technical meeting between members of the EFSA panel on genetically modified organisms and Austrian delegation, Austrian safeguard clause on GM maize mon810 and maize T25. EFSA Meeting report of the meeting of 02 December 2008

StarLink maize from the European company Aventis causes allergies in people[309]? No, it doesn't. *StarLink* maize was originally developed and approved only as animal fodder. However, environmental organisations have concluded »on the basis of their own research« that GM maize was also found in human food, mainly (in USA) in popular maize chips, and that it causes allergies. Because of the intensive media campaign by professional environmentalists, several tens of people actually reported allergic reactions, supposedly caused by maize chips – but clinical studies rejected this assumption and the thesis of the allergenicity of *StarLink* maize[310, 311].

Brazil nuts and soybean are another example[312]. The presumed »evidence« that GMO opponents quote is a report on GM soybean research by the company Pioneer itself, who, in order to have a better protein composition, added a gene from the Brazil nut. Despite the fact that they had developed it only as food for chickens, they ended further research when they found that the added gene could cause allergies in *people* – the »dubious« soybean was never cultivated, not even as animal feed. The case well illustrates the extremely high level of care taken in testing GMOs. Even if such a variety of soybean were grown, it could cause an allergic reaction but only in people who were already allergic to Brazil nuts since the allergenic substance would be exactly the same[313]. The company published the data entirely of its own volition, it didn't have to. The Brazil nuts containing the studied allergenic substance entirely naturally are not banned anywhere.

GMO pollen "pollutes" other plants and can cause patent suits (Percy Schmeiser)

The multi-national giant Monsanto is supposed to have extracted huge compensation from a Canadian farmer **Percy Schmeiser** for growing patented rapeseed, which Schmeiser claimed was found on

[309] Comments on the Assessment of Scientific Information Concerning StarLink Maize (Cry9C *Bt* Maize Plant-Pesticide) EPA Docket Number OPP-00688; By Michael Hansen, Ph.D. Consumer Policy Institute/Consumer Union November 28, 2000

[310] CDC: No StarLink allergies; CBSNews, February 11, 2009

[311] A negative, double-blind, placebo-controlled challenge to genetically modified maize. Sutton S.A. *et al.* Journal of Allergy and Clinical Immunology 2003, 112: 1011–1012

[312] Food, the environment and genetically modified organisms; Greenpeace

[313] Identification of a brazil-nut allergen in transgenic soybeans; Nordlee J.A. *et al.* The New England Journal of Medicine 1996; 334: 688-692, doi: 10.1056/NEJM199603143341103

his field only because it had been »polluted« by the pollen of other cultivated GMO plants[314].

Explaining this media manipulation could start in the style of answers on radio Erevan “in principle yes, but…”. First, Percy Schmeiser was not a small farmer but owner of a large estate, who earned well from growing rapeseed for wholesale to industrial processors. Second, Schmeiser's suit against the compensation claimed was rejected at all court levels. His claim that the patented rapeseed on his fields only appeared because of »pollution« with pollen from elsewhere, stands on weak foundations: the nearest fields on which patented GM rapeseed was grown were 8 km away from Schmeiser's “polluted” fields – but they nevertheless managed to “pollute” 95% of Schmeiser's rapeseed! Oilseed is self-pollinating, although bees can carry its pollen quite large distances. However, the proportion pollinated with alien pollen would be extremely small[315].

The court also found that Percy Schmeiser had bought a huge quantity of the herbicide Roundup. Why, if he had intended only to grow his own rapeseed, which the Roundup would destroy? The Roundup could only be used with Monsanto's GM rapeseed, which is specifically developed for resistance to this herbicide[316].

A similar case – **Hugh Bowman** against **Monsanto** – was heard in court in 2012[317]. The case, in which a producer of organic rapeseed sued his neighbour (who sowed GM rapeseed), on the grounds that his crop had been polluted, was concluded judicially in Australia in June 2014. The organic farmer lost the suit[318].

This is fairly frequent reproach of GM varieties: that the cultivation of GM varieties prevents the cultivation of organic food on nearby farms. The rules of what organic food may or may not contain are based on postulates that such producers set themselves and most are not scientifically supported. Among them is that organic food may not contain GMOs. To what purpose only they know, since viewed scientifically it should be precisely the opposite, if they actually wanted to produce food unburdened by chemical protection. Let me illustrate: on the publication of this book in the Slovene language, a farmer from the surroundings of Ljubljana contacted us: »Several

314 Percy Schmeiser vs Monsanto: The story of a canadian farmer’s fight to defend the rights of farmers and the future of seeds; By Democracy Now! , September 18, 2010

315 Series on harmonization of regulatory oversight in biotechnology No.7 consensus document on the biology of *Brassica napus* l. (oilseed rape), OCDE/GD(97)63

316 Gensko spremenjena hrana; Genetically modified food. Bohanec B. *et al.* Univerza v Ljubljani, Biotehniška fakulteta 2004

317 Supreme Court of The United States Syllabus. Bowman v. Monsanto co. *et al.* certiorari to the united states court of appeals for the federal circuit No. 11–796. Argued February 19, 2013—Decided May 13, 2013

318 GM farmer wins landmark canola contamination case in WA Supreme Court. Charlotte Hamlyn and Rebecca Trigger, ABC News 14 Jun 2014

times a year I spray the wheat with fungicide but, because of the content of mycotoxins, the crop on purchase is still often ranked in the second or third class. My neighbour is an organic farmer and doesn't spray the wheat at all. He sells milled grain and flour at the local market and for that receives a higher price and double subsidy. What am I supposed to think about that?«

Leaving such thinking aside and looking at whether the coexistence of two cultivation methods is really not possible, there has actually been research that defines in detail the necessary distance between fields so that undesired intermixture does not occur[319]. For maize, therefore, a 40 m distance is enough to ensure a probability of 99% limit values in a neighbour's maize will not be exceeded and with silage maize, the necessary distance is already five times smaller. This knowledge did not stop European legislators from setting the boundaries a lot wider. In Slovenia, fields with GM maize must be a whole 600 m from normal fields.

The neighbour influence can also be looked at in another way. It's been known since 2010 that, for example, producers of normal maize should be grateful to their neighbour for growing GM maize resistant to European corn borer[320], since 3.2 million dollars was saved on account of 14 years production, of which farmers growing normal maize got some 2.4 million benefit. What benefit? In the wider region, because of fields resistant to European corn borer, the occurence of this pest markedly dropped. It is easy to find examples of the reverse, when organic farmers spread pests and diseases, though no-one is held responsible[321].

»Alien« genes from GMOs can spread to local varieties even more than a hundred kilometres away

In October 2001, **David Quist** and **Ignacio H. Chapela** published a letter (which is not subject to such scientific strict review as an article) in the journal *Nature*, which was supposed to prove that "artificially added" genes for producing the toxin Cry1 were found in a local variety of maize, *criollo*, in the province of Sierra Norte de Oaxaca (southern Mexico), more than a hundred kilometres from fields in

[319] Adventitous presence of GMOs in maize in the view of coexistence. Kozjek P. *et al.* Acta agriculturae Slovenica 2011, 97: 275-284

[320] Areawide suppression of European maize borer with *bt* maize reaps savings to non-*bt* maize growers. Hutchison W.D. 201, Science 330: 222-225 doi*:* 10.1126/science.1190242

[321] Myth busting on 'contamination': GMO farms' halo effect often protects organic farms. Genetic Literacy Project Nov. 23, 2015

which they grew genetically modified *Bt*-corn[322]. A series of protests followed, which drew attention to unsuitable technology, inadequate evaluation of the results and the unfounded conclusions of Quist and Chapela, which could not be drawn from the measurements [323, 324, 325]. "What is very surprising," wrote **Paul Christou**, director of the molecular biotechnology unit at the John Innes Centre in Norwich, UK, on behalf of the Transgenic Research editors, "is that a manuscript with so many fundamental flaws was published in a scientific journal that normally has very stringent criteria for accepting manuscripts for publication."

Finally, in April 2002, the journal *Nature* published a very unusual editorial comment in which it distanced itself from the claims of Quist and Chapela: "*Nature has concluded that the available evidence does not justify publication of the original article*"[326] – which was the first such case in the journal's 133 year history.

It is worth mentioning that claims of a supposed uncontrollable spread of "alien" genes from GMOs are constantly reappearing, despite there being no sort of scientific basis for them – even during debates in the European Parliament[327, 328].

GMOs contain genes for resistance to antibiotics, which could spread dangerous bacteria to people

These genes could then, for example, leap from plants to bacteria and thus destroy the usefulness of antibiotics for treating a range of illnesses[329, 330]. Like many claims by professional environmentalists,

322 Transgenic DNA introgressed into traditional maize landraces in Oaxaca, Mexico. David Quist & Ignacio H. Chapela. *Nature* 414, 541-543 (29 November 2001) | doi:10.1038/35107068.

323 Biodiversity (Communications arising): Maize transgene results in Mexico are artefacts. Nick Kaplinsky, David Braun, Damon Lisch, Angela Hay, Sarah Hake & Michael Freeling. Nature 416, 601-602 (11 April 2002) | doi:10.1038/nature739.

324 Conflicts around a study of Mexican crops. Matthew Metz & Johannes Fütterer. Nature 417, 897-898 (27 June 2002) | doi:10.1038/417897c.

325 The Case of Mexican Maize. Johannes Wirz. In Context #9 (Spring, 2003, pp. 3-5).

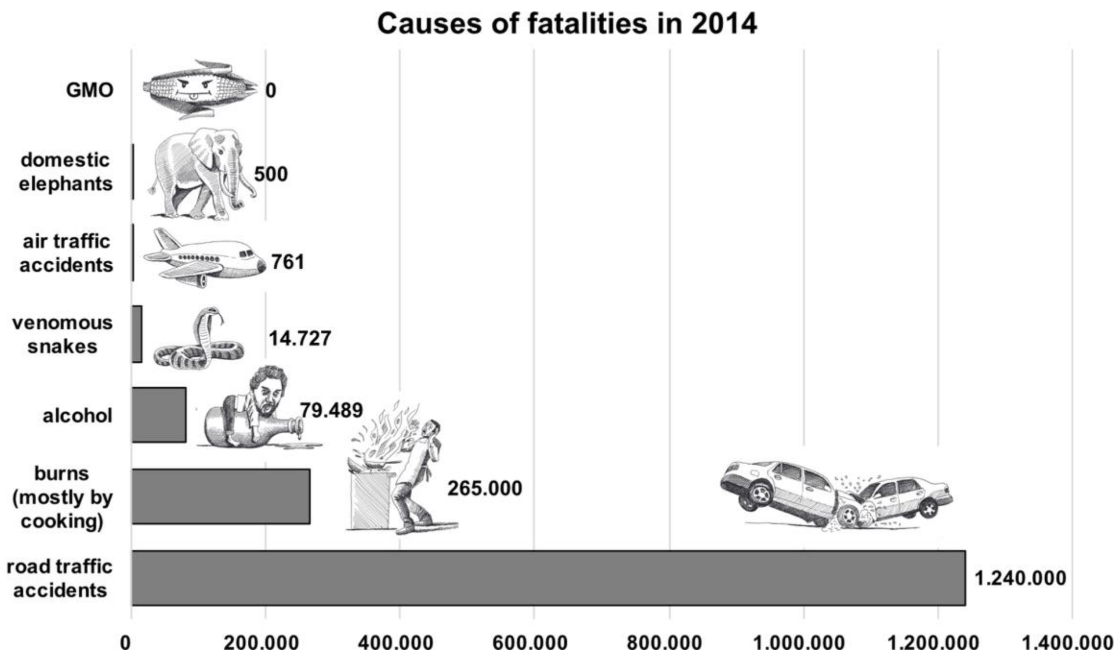
326 Biodiversity (Communications arising): Suspect evidence of transgenic contamination (see editorial footnote). Metz M and Fütterer J Nature 2002, 416: 600-601 doi:10.1038/nature738.

327 No credible scientific evidence is presented to support claims that transgenic DNA was introgressed into traditional maize landraces in Oaxaca, Mexico. Christou P. Transgenic Research 11: iii-v 2002

328 European attitudes towards GMO – an overview of the current opinions BlogActiv.eu, June 29, 2015

329 Antibiotic resistance in genetically modified plants; Caplan R. June 2002

which still today provide the basis for propaganda against GMOs, this one also contains a grain of truth: some genetically modified plants of the first generation actually contained (in addition to functional inserted genes) gene for resistance to the antibiotic kanamycin. However, with the more recent technologies for genetic manipulation, the inclusion of these »selection genes« is not inevitable, there are many undisputed selection genes available so that, at least in Europe, the objection only applies to older GMOs.



EFSA, in fact, in 2009 officially rejected the possibility that genes for resistance to antibiotics that are built into some older GMOs could represent a real risk of increasing resistance[331]. In the EFSA official statement in relation to the use of *Npt*II gene for resistance to the antibiotic from 2007[332] can be read that the likelihood of a functional transfer of this gene to bacteria is extremely low. A special scientific group of EFSA in 2004 officially analysed the consequences of growing such GMOs and found in their report that these GM plants have a "13 year history of safe use for food"[333].

In the same document, though (and elsewhere), can be found data

[330] Antibiotic resistance genes in transgenic plants, in particular ampicillin resistance in bt-maize; Executive summary; Oekoinstitut Freiburg on behalf of Greenpeace Germany

[331] Statement of EFSA, EFSA-Q-2009-00589 and EFSA-Q-2009-00593

[332] EFSA statement of the scientific panel on genetically modified organisms on the safe use of the nptII antibiotic resistance marker gene in genetically modified plants (adopted on 22-23 March 2007)

[333] Opinion of the scientific panel on genetically modified organisms on the use of antibiotic resistance genes as marker genes in genetically modified plants1 (Question N EFSA-Q-2003-109); Opinion adopted on 2 April 2004; The EFSA Journal (2004) 48, 1-18

that puts the thesis of the danger of possible transfer of genes for resistance to antibiotics in a completely different light: "*resistance to these types of antibiotic is generally widespread with species, naturally present microbes, with people and in the environment in general*". Selection genes that are used in genetic technology are not artificial creations that do not appear in nature – such genes have been present in completely natural organisms for millions of years! In fact, the likelihood of transfer of such a gene between species is very small[334] but, even if it happened[335], it could have been completely natural and have already appeared long before man's use of genetic technology, so the use of GMOs does not increase the risk.

GMO contain formaldehyde

In July 2015, **V. A. Shiva Ayyadurai** and **Prabhakar Deonikar** published an article that claimed that carcinogenic formaldehyde accumulates in GM plants [336] and the media published their conclusion on a grand scale, of course with added exaggeration.

The veracity of the article was already a little weak because it was published in the journal **Agricultural Sciences**, which is known for its "*pay for play*" policy, so it does not have great influence. If Ayyadurai and Deonikar had really scientifically correctly discovered something so revolutionary they could have published the article in one of the more prestigious scientific journals, who seriously review contributions. This suspicion in itself does not negate the published claims, though.

Merely the fact that formaldehyde is found in field crops (and in other food) is neither unknown nor surprising: formaldehyde is one of the key chemicals in the photosynthesis process[337] – with both "natural" and GM plants – and it is completely unavoidable that it will also be found in fruits and seeds. So, for example, 6.3-22.3 milligrams of formaldehyde per kilogram of fruit is found in apples; in onions 11 mg, in cauliflower 22.4, in pears 38.7-60 mg, in dried shiitake

[334] Horizontal transfer of dna from GM crops to bacteria and to mammalian cells; J.A. Thomson, Journal of Food Science 2001, 66: 188-193 doi: 10.1111/j.1365-2621.2001.tb11314.x

[335] Transformation of *Acinetobacter* sp. strain bd413(pfg4δnptii) with transgenic plant DNA in soil microcosms and effects of kanamycin on selection of transformants. Kaare M. *et al.* Applied and Environmental Microbiology 2000, 66: 1237–1242

[336] Do GMOs accumulate formaldehyde and disrupt molecular systems equilibria? Systems biology may provide answers. Shiva Ayyadurai V.A. and Deonikar P. Agricultural Sciences, 2015, 6, 630-662, http://dx.doi.org/10.4236/as.2015.67062.

[337] Studies in photosynthesis: The formaldehyde hypothesis.Barton-Wright E.C. and Pratt M.C. Biochemistry Journal 1930, 24: 1210–1216

mushrooms even 100-406 mg[338]. If you wanted to avoid formaldehyde in food completely, you could eat almost nothing. Small quantities of formaldehyde can't harm us because the compounds very quickly decompose in the body (and thus cannot accumulate)[339, 340].

More suspicious is the fact that Ayyadurai and Deonikar did not actually measure the amounts of formaldedhyde (in soybean) but drew their conclusions on the basis of a mathematical model that took as input data actual measurements, in none of which did they find dangerous concentrations of formaldehydes in soybean. They concluded merely on the basis of the model that in "natural" plants the formaldehyde decomposes but not in GM plants and it thus accumulates; so, at most, their finding could be considered a hypothesis that had to be confirmed in real measurements. These actually negated the thesis.

"Unnatural" genes can jump from GMOs to other plants and create "superweeds"

In July 2005, many media reported that transgenic DNA from oilseed is supposed to have jumped to wild mustard (*Sinapis arvensis*), descendents of which are supposed to have become »superweeds«, resistant to all field crop herbicides[341].

The claim of professional environmentalists was immediately suspect simply because »mixing« of genetic designs between sexually incompatible species (such as *Brassica* and *Sinapis*) is not very likely. On a more detailed examination of the suspect wild mustard, it appeared that the claim of the crossing of a transgenic plant with a »natural« one was no more than a flight of fantasy[342]. The appearance of wild mustard as a »superweed« is of course in no way surprising for objective scientists, since field mustard is already a strongly invasive species[343] and obtained additional resistance to herbicides by a completely »natural« path: the use of herbicides caused the selection of *S. arvensis* in resistant forms.

Nevertheless, would it be possible with the development of new genes in the laboratory by chance or deliberately to create "superweeds" that

338 Foods known to contain naturally occurring formaldehyde I. Fruits & vegetables
339 ATDSR toxic substances portal - formaldehyde
340 Scientific report of EFSA: Endogenous formaldehyde turnover in humans compared with exogenous contribution from food sources.
341 GM crops created superweed, say scientists; Modified rape crosses with wild plant to create tough pesticide-resistant strain; Brown P. The Guardian, 25 July 2005
342 Claims of GM-field 'superweed' are dismissed. Hooper R. New Scientist, 26 July 2005
343 *Sinapis arvensis* - Weed Research and Information Center

could overgrow arable surfaces and suppress other plants? Theoretically, it is probably possible but it's highly unlikely. All wild plants are the victors of hundreds of millions of years of evolutionary competition in which those that fell behind only a little inevitably died out. As the Nobel prize winner **Francis Crick** pithily put it: “Evolution is smarter than you!” So it is no surprise than man can exert the same selection pressure with the use of herbicides. »Superweeds« already exist and have developed by entirely natural pathways: field mustard, daisy (*Bellis perennis*), dandelion (*Taraxacum sp.*), green bristlegrass (*Setaria viridis*) etc. That none of these species has yet taken over is because the entire (Eurasian) biological environment has developed in a competition of (also these) species, so that (for the moment) a balance has been established among the many aggressive plants. There is no evidence that such a balance could be destroyed by the introduction the GMOs.

Phillip J. Dale *et al.* stated in the journal *Nature*[344] that “…the impact of free DNA (chains) of transgenic origin will probably be negligible in comparison to the entire amount of free DNA (in nature)«. “We find no valid scientific argument to show that GM cultures are basically different from non-GMOs. Possible environmental impacts of GMOs can only be precisely those that are known from the cultivation of non-GMOs (e.g., invasiveness, weeds, toxicity, impact on environmental diversity)”.

The creation of superweeds resistant to herbicides is actually most effectively limited by a professional farming approach: suitable rotation, including with phytopharmaceutical preparations, ensures that undesirable resistant forms do not occur.

Seeds produced on GM plants don't germinate because they contain a terminator gene

In the nineteen nineties, the company **Delta Pine and Land,** in cooperation with **USDA** (*United States Department of Agriculture*) actually developed genetic technology that would ensure that GM plants would remain infertile. They developed the technology mainly because of the objections of GMO opponents, who claimed as a potential danger of GMOs that such plants could »escape« into the natural environment [345]. The TPS (*Technology Protection System*)

[344] Potential for the environmental impact of transgenic crops. Dale P.J. *et. al.* Nature Biotechnology 2002, 20: 567 - 574 doi:10.1038/nbt0602-567

[345] Technology protection system http://www.agbioworld.org/newsletter_wm/index.php?caseid=archive&newsid=266

system was patented in 1998 and in 2006 Monsanto bought the company Delta Pine and Land and thus obtained the patent for TPS.

Because of public opposition to the ***"Terminator" gene*** – or GURT (*Genetic use restriction technology*) – neither Monsanto nor any other company that sells GM seed ever built it into any field crop[346]!

Seeds that create the GMO are not of course sterile, which does not apply to all normal varieties. For instance seed of hybrid onion has been possible to breed by classical methods for a long time so that the F2 generation does not bear seed.

Seed companies have been acting to protect their intellectual property, i.e., developed varieties, for decades. The most successful are with species in which hybrid varieties are established, thus without any kind of genetic technology. The seed of hybrids (F2 generation) germinate the following season but the crop is low and very uneven, so new seed has to be bought each year.

Why, can be shown with some basic genetics knowledge. A hybrid (F1 generation) is the progeny of two pure lines, let's say genotypes AAbb and aaBB, and occurs through the combination of their sexual cells with genotypes Ab and aB. The hybrid will only have one genotype AaBb but its progeny (generation F2), because of gene split, will have 16 different genotypes. Plants of the F2 generation will thus be very uneven.

The seed company is therefore protected on a completely biological level. With normally selected plants, the key combination is essentially more complicated and so the share of seed of the second generation that carries the original genetic design is essentially smaller. A farmer who wants a large crop therefore does not sow his own seed but buys it each year, whether it is a GM or »naturally« selected culture.

DNA from GMOs can be transferred to people who eat such food

A study that opponents of GMOs cite does not claim that this can happen only with GMO genes but that it is possible to find genes from any food eaten in the human organism. These genes are not built into the human genetic structure but can be found in the blood[347]. The study that discovered this received many comments, since it is otherwise confirmed that DNA structures are chemically fairly unstable and that they quickly decompose even in a mildly acidic

[346] Terminator genes. Wright K. and Clark J. Discover Magazine August 2003

[347] Complete genes may pass from food to human blood. Spisák S. *et al.* PLOS One 2013, doi: 10.1371/journal.pone.0069805

environment[348] (such as the human stomach), and pepsin also degrades them[349]. Despite everything we accept that it is so.

Which, put more simply, means that genes from Bt maize or from beef can be found in human blood if we eat them. Nobody who eats beef then grows horns, though. The possibility of such a genetic structure from GMOs being inserted in humans in that way is equally unlikely.

Horizontal transfers of genes – meaning between completely different species – happen in nature but they are very rare. There could also be transfer through food but, as a series of studies has shown, genomes (including ours) contain extensive protection against accepting alien genes. In general, as the history of evolution shows, such a horizontal transfer is anyway not restricted to genes from GMOs[350].

Food from GM plants causes a reduction in the male sperm count

As evidence of the claim that GMOs cause partial infertility, opponents of GMOs often cite a French study[351] that actually found such a reduction. It did not ascribe the reduction in the sperm count to any specific cause, still less to GMOs. Much in the modern life style, in fact, demonstrably reduces the sperm count: working a lot with a computer, shift work, smoking and alcohol[352]; tight underwear and pants[353]; and in general the "western diet", more sweet drinks and salt[354].

Toxins from GMOs have been discovered in the blood of pregnant women and foetuses

348 Instability and decay of the primary structure of DNA. Lindahl T. Nature 1993, 362: 709 - 715 doi:10.1038/362709a0

349 Digestion of nucleic acids starts in the stomach. Liu Y. *et al.* Scientific Reports 2015, 5: Article number: 11936 doi:10.1038/srep11936

350 Gene-swapping means that you have alien DNA inside you. Henriques M. BBC Earth

351 Gene linked to low sperm count; Nursing Times 10 November, 2010

352 Mayo Clinic, diseases and conditions, low sperm count

353 WebMD, Infertility & reproduction health center, Boxers vs. Briefs: Increasing Sperm Count

354 The association between dietary patterns and semen quality in a general asian population of 7282 Males. Chin-Yu Liu C.Y. *et al.* Plos One, July 28, 2015 doi: 10.1371/journal.pone.0134224

It should first be noted that the plural (toxins) in this claim is not entirely justified. The media articles[355], [356], [357], which explicitly stressed this presumed harmful feature of GNOs, referred to one study only "*Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada. Aziz Arisa, Samuel Leblancc, Reprod. Toxicol. 2011*"[358]. The authors actually described the detection of only one toxic (for insects) protein *Cry1Ab* and ascribed its origin to GMOs that contain genes from *Bacillus thuringiensis* (e.g., maize MON810).

The article received a number of criticisms[359], [360], [361], the most important being that the authors used the ELISA method for measuring the concentration of toxin in people, which was not suitable for that purpose. The authors provide no data on the diet of the trial subjects, so the claim that the noted *Cry1Ab* derives from GMOs is unjustified – the bacterium *Bacillus thuringiensis* is very often found in the soil entirely naturally; live cells of this bacteria are even permitted for suppressing pests in organic production[362]!

Even if the article had been entirely scientifically correct, though, which it was not, it remains a fact that that the detrmined concentrations of Cry1Ab were too low (average 0.19 ng/ml) even to harm insects – and the human organism doesn't have receptors for this protein. Different substances act differently on an organism: e.g., cherries are poisonous for dogs, cats and horses, but not for people[363].

Despite the well-founded scientific objections, which completely devalue the study on the presence of the *Bt* toxin Cry1Ab in the blood of pregnant women and fetuses, the French government of **Nicolas**

355 GM food toxins found in the blood of 93% of unborn babies. Poulter S. Daily Mail 20 May 2011

356 Toxic pesticides from GM food crops found in unborn babies. Bloxham A. The Telegraph 20 May 2011

357 Study: GMO toxins found in nearly all pregnant women, unborn babies. Benson Journal of Natural News October 10, 2012

358 Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada. Arisa A. and Leblancc S., Reprodive Toxicology 2011, 31:528-33 doi: 10.1016/j.reprotox.2011.02.004. Epub 2011 Feb 18.

359 If you record noise, you don't get music – you get nonsense. Tribe D. Biology Fortified 29 April 2011

360 Comment: Aris and Leblanc "Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada". Daniel A. Goldstein D.A. *et al.* Reproductive Toxicology 2012, 33: 120–121. doi:10.1016/j.reprotox.2011.10.007

361 Comment on "Maternal and fetal exposure to pesticides associated to genetically modified foods in Eastern Townships of Quebec, Canada" by A. Aris and S. Leblanc [Reprod. Toxicol. 31 (2011) 528–533]. Utz Mueller, Janet Gorst, Reproductive Toxicology 2012, 33: 401–402 doi:10.1016/j.reprotox.2012.01.012

362 Council Regulation (EEC) No 2092/91 of 24 June 1991 on organic production of agricultural products and indications referring thereto on agricultural products and foodstuffs, p. 42

363 ASPCA pet care Cherry

Sarkozy banned cultivation of MON810 maize and in February 2012 informed the EU Commission of supposedly "new information on the environmental risks of GM maize MON810". As an analysis of the French measure, in June 2013 scientists from three French institutes published an analysis entitled "What the French ban on MON810 means for assessing risk on scientific bases"[364] in the journal Nature Biotechnology. What does it mean? That politicians respect science only when it fits their preconceptions and opinions that bring votes.

GMOs are connected with celiac disease and other undesirable reactions to gluten

As with many similar claims, this one is not based on any kind of scientific research. The source is a single article on the website of the *Institute for Responsible Technology*[365], an American non-governmental organisation that advocates a complete ban on GMOs. The article's conclusion is based on very strange logic: the number of allergies has increased in the last two decades (which is true[366]) and, similarly, the amount of food from GM sources that we eat has also increased (which is also true); to ascribe a causal link to this is logically unfounded – the number of personal computers has also increased in recent years but probably nobody would claim that *this* causes celiac disease.

The claim is even more absurd because nowhere in the world has any GM variety of wheat been approved that could be a main cause of gluten connected problems.

Even the American *Celiac Disease Foundation* rejected the study[367].

364 What the French ban of Bt MON810 maize means for science-based risk assessment. Kuntz M. *et. al.* Nature Biotechnology 2013, 31, 498–500 doi:10.1038/nbt.2613

365 IRT can genetically engineered foods trigger gluten sensitivity?

366 The 'hygiene hypothesis' for autoimmune and allergic diseases: an update. Okada H. Clinical and Experimental Immunology 2010, 160: 1–9. doi: 10.1111/j.1365-2249.2010.04139.x

367 Celiac Disease Foundation, plant geneticist, challenge report linking GMOs to celiac disease, gluten sensitivity. Hennessy M. Celiac Disease Foundation 03-Dec-2013

Professional bodies check the safety of GMOs only on the basis of 90-day tests, which is too little to discover possible longterm risks

As with all products that require official approval for use, based on professional judgement, the time for carrying out a procedure is inevitably limited. How could any regulatory procedure work if the time to approval were to be unlimited?

However, this doesn't mean that GMOs are not subject to other studies and scientific verification, including over periods of years – actually, GMOs are more thoroughly studied than other »natural« food[368]. A good example is a review of studies lasting more than two years and multi-generational studies (2-5 generations) published in the journal *Food and Chemical Toxicology* in 2012[369]: the study is a review of articles on the effects of GM maize, soybean, cotton etc. on the health of people and animals, which found that GM field crops are from all nutritional aspects of equal value to the non-GM equivalent and can thus be safely used for the diet of people and animals. A three-generational study of Bt maize on rats[370], GM soybean on mice[371], GM soybean on rats[372], GM soybean on Atlantic salmon[373], a ten-generation study on *Bt* maize on quail[374], a 25-month study on MON810 maize on milking cows[375, 376], a three generation study of GM

[368] With 2000+ global studies affirming safety, GM foods among most analyzed subjects in science. Wendel J. Genetic Literacy Project October 8, 2013

[369] Assessment of the health impact of GM plant diets in long-term and multigenerational animal feeding trials: A literature review. Snell C. *et al.* Food and Chemical Toxicology 2011, 50: 1134–1148 doi:10.1016/j.fct.2011.11.048

[370] A three generation study with genetically modified *Bt* maize in rats: Biochemical and histopathological investigation. Kılıç A., and Akay M.T., Food and Chemical Toxicology 2007, 46: 1164–1170 doi:10.1016/j.fct.2007.11.016

[371] Histochemical and morpho-metrical study of mouse intestine epithelium after a long term diet containing genetically modified soybean. Battistelli S. *et al.* European Journal of Histochemistry 2010, 54: e36. 2010 Sep 26. doi: 10.4081/ejh.2010.e36

[372] Organic and genetically modified soybean diets: Consequences in Growth and in Hematological Indicators of Aged Rats. Daleprane J.B. *et al.* Plant Foods for Human Nutrition 2009, 64: 1-5. doi: 10.1007/s11130-008-0101-0.

[373] A long term trial with Atlantic salmon (*Salmo salar* L.) fed genetically modified soy; focusing general health and performance before, during and after the parr–smolt transformation. Sissenera N.H. Aquaculture 2009, 294: 108–117 doi:10.1016/j.aquaculture.2009.05.002

[374] Long term feeding of Bt-maize – a ten-generation study with quails. Flachowskya G. Archives of Animal Nutrition 2005, 59: 449-451

[375] Effects of long-term feeding of genetically modified maize (event MON810) on the performance of lactating dairy cows. K. Steinke *et al.* Journal of Animal Physiology and Animal Nutrition 2010, 94: e185–e193, October 2010. DOI: 10.1111/j.1439-0396.2010.01003.x

rice on Sprague–Dawley type rats[377], a four-generational study of GM maize (*Bt*) on laying chickens[378] etc. A preliminary list of more than 300 scientific articles with studies on feeding GMOs to chickens, laying hens, pigs, seafish, beef cattle etc. [379], collected by the Federation of American Societies of Science (FASS), should perhaps be mentioned.

Anyone claiming that there are no longterm studies just hasn't tried looking.

The objection also implies that once a GMO is approved on the basis of a 90-day study, its cultivation and use is permanently allowed, regardless of later discoveries – which is absolutely not true. Many countries even have an official program of monitoring GMOs after registration, which is actually mandatory for GMOs; EU legislation in this field prescribes compulsory post-monitoring of GM food or field crops[380].

Why must GMOs go through such demanding and time-consuming (and for environmentalists never sufficient) tests to show their safety – while no such tests are needed for the production and marketing of products bred by crossing, selection etc.? In an article in the journal *Nature*, Laura DeFrancesco[381] summarised tests for GMOs and found that ever new disputes about testing the safety of food (which primarily revolves around GMOs) further incites public fear of transgenic products.

The results of the EU-funded project »GMO Risk Assessment and Communication of Evidence (GRACE)[382]« were published very recently, discussing 90 day and one year feeding results. The authors suggest a need to reconsider the value of rat feeding trials for a safety assessment of genetically modified (GM) plants. When presenting their final results for the project, the team reported that they found no

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376 Long-term feeding of genetically modified maize (MON810) — Fate of cry1Ab DNA and recombinant protein during the metabolism of the dairy cow. Guertlera P. *et al.* Livestock Science 2010, 131: 250–259 doi:10.1016/j.livsci.2010.04.010

377 A three generation study with high-lysine transgenic rice in Sprague–Dawley rats. Zhou X.H. *et al.* Food and Chemical Toxicology 2012, 50: 1902–1910 doi:10.1016/j.fct.2012.04.001

378 A four-generation feeding study with genetically modified (*Bt*) maize in laying hens. Halle I. and Flachowsky G., Journal of Animal and Feed Sciences 2014, 23: 58–63

379 FASS References - Feeding Transgenic Crops to Livestock

380 European Commission, PLANTS, Monitoring plans and reports

381 How safe does transgenic food need to be? DeFrancesco L., Nature Biotechnology 2013, 31: 794–802 doi:10.1038/nbt.2686

382 Conclusions and recommendations on animal feeding trials and alternative approaches and on the use of systematic reviews and evidence maps for GMO impact assessment. GRACE project 1st June 2012 – 30th November 2015

indication that routine 90-day feeding studies with whole food / feed would provide additional information on the safety of MON810 maize compared to *compositional comparison of the GM line and its closest conventional comparator*. Of course, such an argument is also in line with the general European goal of reducing animal testing.

Finally, the safety of GMOs is also testified by the fact that they have been in use for 20 years or more without any harmful effects; not on people nor animals nor the environment.

Tests for the registration of GMOs are commissioned by the producers themselves

… which would imply, of course, that the tests were not impartial. No other approach is possible: completed applications with which the regulator deals must contain all the tests that the regulators demand and the proposer must pay for them himself.

Leaving aside the fact that applicants commission GMO tests from independent laboratories, often universities, it is more important to stress that the same applies for the majority of industry. Vehicle safety tests and measurements of consumption and exhaust gases required for homologation are always carried out by the maker himself. The same applies for the registration tests of medicines, household appliances, furniture etc. and also all food products that do not contain GMOs

Only with GMOs, though, is such an objection *casus belli* for a complete ban.

Patenting GMOs ensures the monopoly of a small number of multinationals

It is probably not generally known that the initiators of exaggerated regulation of GMOs were actually seed company conglomerates. In the 1980s, agricultural giants such as Monsanto, Ciba-Geigy and Pioneer achieved the first GM field crops (they mainly bought the technology), and lobbyists of the largest company pursuaded the US authorities that the release of GMOs for general cultivation must be regulated as strictly as possible[383, 384]. Because they were aware that they carried risks? Absolutely not.

383 Bootleggers and biotechs. Miller H.I. and Conko G. Regulation 2003, 26:12-14

384 Biotechnology Food: From the Lab to a Debacle. Eichenwald K. The New York Times, January 25, 2001

The origin of the problem is that any other seed producer could transfer key new genetic properties into their own varieties and sell the seed. The patent owner can sue for compensation through the civil courts for patent violations but court proceedings can last ten years and more; during all this time, the patented genetic properties could spread through subsequent crossing and, in the end, it would be very difficult to identify all the violators.

The complicated and, of course, expensive procedure of releasing GMOs ensures several years' advantage to the first to develop it (or obtain the technology) because a company that copies its ideas still has to go through the approval process. Additionally, because such a long procedure is extremely expensive, the system established for release actually prevented smaller competitors, who could develop new GMOs but would not have the funds to carry out the procedure. The restrictive American legislation was then copied throughout the world, including the EU.

This was the start of the business practice of large agricultural multinationals that many justifiably criticise today: it is very possible that the primary motivation for the development of new GMOs is profit for the company and not the well-being of growers. Big seed companies routinely buy up smaller companies that discover an interesting approach to GMOs and thus preserve and even increase their market share and, at the same time, prevent the emergence of competition. Scientists actually oppose such unnecessarily complicated regulations. In addition, fear of GMOs in itself generates ever more complex and costly procedures of release.

It is worth remembering that such a business approach is not characteristic only of agricultural multinationals but all profit-making commercial activities. Aided mainly by the American authorities, the profit industry (not just agricultural) has significantly extended monopolies that derive from patents or other forms of intellectual property.

Many GMOs are patent protected but many other varieties bred by classical methods are similarly protected [385]. They can also be protected by the plant variety protection system of other rights deriving from title to intellectual property[386], which has an equivalent legal effect as patent protection. The EU also guarantees legal protection based on the intellectual rights of the applicant and is equivalent to a patent[387]. In fact, the EU also has legislation that, in addition to patent protection, enables an applicant other forms of protection that are the legal equivalent of patents[388].

[385] USPTO general information About 35 U.S.C. 161 Plant Patents
[386] 28 USC Sec. 1338 https://www.law.maizeell.edu/uscode/text/28/1338
[387] European Commmision PLANTS: Plant variety property rights
[388] European Commision PLANTS: Legislation on plant protection products (PPPs)

The EU legal arrangement of owner's rights under the title of intellectual property already give the right to determine the conditions of commercial use of a protected product[389]. A small allotment holder is probably aware that, in some cases, seedlings bought in a shop can only be used for non-commercial purposes; if the flowers were to be sold, a licence fee to the owner of the author's rights must be paid.

At the same time, rights deriving from ownership of a variety are becoming more complicated by the year and typically shift towards more extensive rights for the originator. So not all producers are aware of what they are bound to with the purchase of seeds, bulbs or seedlings and in how many ways they can violate the most recent legislation by not paying a licence fee for the cultivation and/or use of seeds, flowers or fruits. Breeders also increasingly meet with similar obstacles, since ever more methods and actually minimally modified varieties are becoming protected by patent or other forms of protection of intellectual property. Even this clearly questionable trend is not actually connected only with GMOs, though; it is also happening with classically bred varieties.

The same applies for the majority of world industry. For example, a new car model can be protected with more than a hundred patents. Companies in the fields of pharmacy, computers, the entertainment industry, household appliances etc. protect their market position in the same way; it would be difficult to find a company that doesn't protect at least some elements of its products with one or other instruments of intellectual rights. Mainly under the influence of multinationals in the fields of pharmacy, computers and film, many countries have further broadened patent and related protection – for example with the international agreements TRIPS[390], ACTA[391], TTIP[392].

The argument, though, that the introduction of GMOs, especially in the EU, has caused the monopoly of a small number of multinationals is misleading. Multinationals in the agricultural field in Europe already cover the majority of the market in phytopharmaceuticals, seeds etc[393, 394]. The potential monopoly of foreign companies can only be limited by our own investment in development in this field.

389 CBI Ministry of Foreign Affairs: Which trends offer opportunities on the European cut flowers and foliage market?

390 WTO trade-related aspects of intellectual property rights

391 Office of the United States trade representative, anti-counterfeiting trade agreement (ACTA)

392 European Commision TRADE: The Transatlantic trade and investment partnership

393 Med industrijo in vrtičkarstvom. Between industry and home gardening. Staš Zgonik, Mladina 3. 7. 2015

394 Seed diversity and food security threatened by an overly concentrated EU seed market: Greens/EFA conference. The greens in the European Parliament Jan. 29, 2014

In addition, in the GMO field, there is a range of field crops that are not protected (or for which producers don't have to pay for use), among the most interesting cases being golden rice[395], rainbow papaya[396], rice that is resistant to flooding[397]… On the model of computing in the field of GMOs, too, there is an initiative for »open source seed«[398].

Anyone concerned that a dangerous monopoly of a small number of multinationals could be created through GMOs should first ask what kind of operational system he uses on his computer: very probably one from Microsoft, which is the owner of more than 92% of all operating systems on personal computers worldwide!

Glyphosate

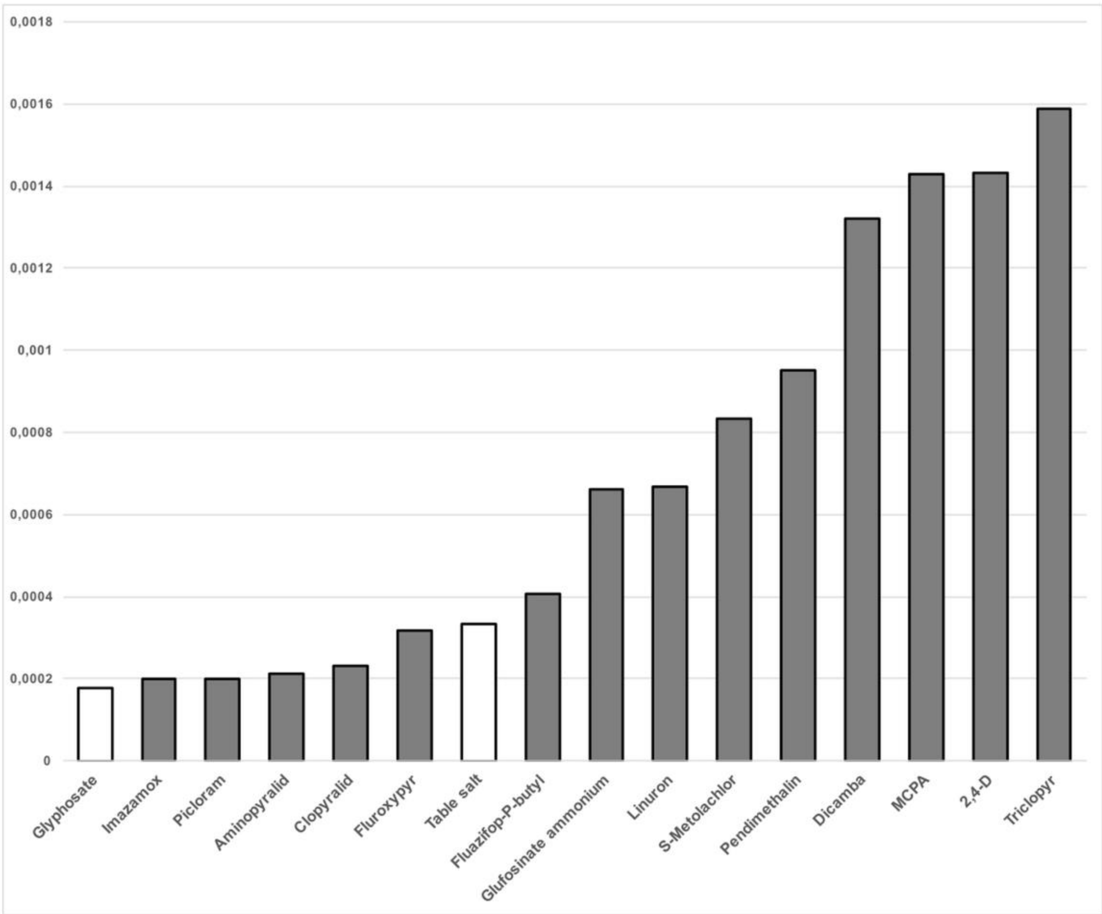
Growers use herbicides to suppress undesirable weeds and thus prevent the weeds from taking water and nutrients from the cultivated plants or even outgrowing them.

Glyphosate is currently the most effective wide spectrum, non-selective herbicide. It appears in publications on the presumed dangers of GMOs because a series of GM field crops have been specifically developed for resistance to glyphosate.

Glyphosate is actually the least toxic of commonly used herbicides and less toxic than common table salt.

395 The Golden Rice Project
396 APS transgenic virus-resistant papaya: the hawaiian 'rainbow' was rapidly adopted by farmers and is of major importance in Hawaii today
397 Ronald laboratory new flood-tolerant rice offers relief for world's poorest farmers
398 Open source seed initiative

Relative toxicity ($1/LD_{50}$) of common herbicides and table salt



(LD_{50} values used for the above graph are values for acute, oral toxicity in rats. Where multiple values were available, the lowest LD_{50} – i.e., the highest toxicity - was used)

The cited values of oral toxicity in rodents are not of course the only measure by which to judge the suitability of use of pesticides, many other factors decide on this. Nevertheless, among them there are also several reasons why glyphosate is much more suitable than other herbicides. Two of its advantages, in fact, are that the substance does not leach into groundwater and that it quickly decomposes. It could be added that a ban on the use of glyphosate would not mean a ban on the use of herbicides; quite the contrary, at best the use of environmentally less acceptable alternatives would increase.

The World Health Organisation designates glyphosate as carcinogenic for people

In March 2015, the World Health Organisation (WHO), on the proposal of the International Agency for the Research of Cancer (IARC), classified glyphosate in group 2A of carcinogens, i.e., probable carcinogens[399]. A substance obtains such a classification if (in the opinion of the IARC expert group) there is limited (but not sufficient) evidence of a carcinogenic effect on people and sufficient evidence of a carcinogenic effect on animals (irrespective of dose) or if there is insufficient evidence of carcinogenicity with people, sufficient evidence of carcinogenicity in animals and strong evidence that the same mechanism of carcinogenicity (as with animals) also acts with people.

We must leave aside the extent to which the lobbying of environmental groups and apparently scientific articles in the style of Gilles-Éric Séralini influenced the proposal of IARC. A positive opinion on glyphosate would certainly have been doubted if an employee of Monsanto had been a member of the competent commission. Strange that it didn't disturb anybody that **Christopher J. Portier** took part at that session of the IARC, who does not hide his affiliation to the American non-governmental organisation *Environmental Defense Fund*, which agitates against the use of pesticides[400].

It is difficult to understand the decision of IARC in the light of a series of articles that actually exclude a link between glyphosate and cancer: for example, a study by **Tom Sorahan** from the University of Birmingham, which analysed data on 54,315 users of glyphosate (among which in the period 1993-2001 there were 32 cases of cancerous illnesses – multiple melanomas) and concluded that »it is not possible to observe in the data any kind of convincing evidence of a link between glyphosate and multiple melanoma"[401]. Professionals of the German (government) Federal Institute for Risk Assessment (BfR)[402] and the Dutch National Agency for the authorisation of pesticides and plant protection products (CTGB) also published doubts about the soundness of the IARC decision[403]. The European Food Safety Agency (EFSA), in its assessment of glyphosate in November 2015, noted that it is not likely that it could be carcinogenic[404].

It is worth stressing here that IARC does not actually assess the *risk* that the substances in question represent for the occurence of cancer but the *possibility* that they cause cancer: the difference is crucial, since a risk assessment, in addition to a confirmed *possibility* (of the

399 Carcinogenicity of tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate. Guyton K. Z. *et. al.* on behalf of the International Agency for Research on Cancer Monograph Working Group, IARC, Lyon, France Lancet Oncology 2015, 16: 490-491. doi: 10.1016/S1470-2045(15)70134-8.

400 Christopher J. Portier, Professor, senior collaborating scientist, Environmental Defense Fund, New York, USA

401 Multiple myeloma and glyphosate use: A Re-Analysis of US Agricultural Health Study (AHS) Data. Soharan T. International Journal of Environmental Research and Public Health. 2015 Feb; 12(2): 1548–1559. doi: 10.3390/ijerph120201548

402 BfR Löst Glyphosat Krebs aus? Mitteilung 007/2015 des BfR vom 23. März 2015

403 Ctgb oordeel over IARC artikel over carcinogeniteit van glyfosaat. 27 April 2015

404 EFSA News& Events, Glyphosate: EFSA updates toxicological profile. 12 November 2015.

occurrence of cancer), must also assess the likelihood that, for example, a person could really be exposed to a dangerous dose in the environment. To illustrate with a case: it is of course very possible, probably even reliably so, that a meteor will kill us if it hits us – but what is the *likelihood* of being hit by a meteor? What therefore is the *risk* of being killed by a meteor? So the conclusion of IARC – which is ascribed to a risk assessment – is in clear contradiction to research studies, which found on the basis of real measurements that »preparations on the basis of glyphosate (GFB) do not represent a significant risk of genotoxicity for people or the environment under normal conditions of exposure[405].

In the light of the news that IARC would classify red meat and all kinds of meat products among possible carcinogens (2B)[406], critical articles are increasingly appearing asking whether it is worth taking IARC statements at all seriously[407]. In the past, they have already ranked among possible carcinogens coffee[408] and radiation from mobile telephones[409] - in both cases actual data indicated otherwise [410, 411, 412, 413].

In any case, together with glyphosates in the 2A group are also found chloramphenol (an antibiotic) and a range of other medicines (doxorubicin, azacitidin etc), bergapten (etheric oil in citrus peel), ethyl carbamat (in bread and biscuits with yeast and in most drinks made with yeast), all anorganic lead compounds, all nitrates and nitrites, trichlorethylene (organ solvent) and all types of solar ultraviolet radiation[414].

405 Review of genotoxicity biomonitoring studies of glyphosate-based formulations. Kier L.D. Critical Reviews in Toxicology 2015, 45:209-218 doi: 10.3109/10408444.2015.1010194

406 IARC Press Release N° 240: IARC Monographs evaluate consumption of red meat and processed meat. 26 October 2015

407 Meat, Coffee – Why Only Activists Pay Attention To IARC Claims. Hank Campbell, American Council on Science and Health November 2, 2015

408 International Agency for Research on Cancer (IARC) - Summaries & Evaluations. Coffee (Group 2B) VOL.: 51 (1991) (p. 41)

409 NCI Statement: International agency for research on cancer classification of cell phones as “Possible Carcinogen”. National Cancer Institute, May 31, 2011

410 The carcinogenicity of caffeine and coffee: a review. Pozniak P.C. Journal of the American Dietetic Association 1985, 9:1127-33

411 Analysis of the potential carcinogenicity of coffee and its related compounds in a medium-term liver bioassay of rats. Hasegawa R. Food and Chemical Toxicology 1995, 33: 15-20.

412 Are cell phones a possible carcinogen? An Update on the IARC Report. Trottier L. Science-Based Medicine, April 2, 2012 17

413 American cancer society: Cellular Phones

414 WHO, International Agency for Research on Cancer , Agents classified by the IARC Monographs, Volumes 1–112

Glyphosate causes breast cancer

A scientific article by **S. Thongprakaisang** *et al.*[415], the only article that advocates of this claim cite, does not say this at all. Researchers grew two types of human breast cancer cells *in vitro*: those sensitive to estrogen and those that are not. Glyphosate caused growth in the culture of cells sensitive to estrogen, but less than did estrogen. According to the results of this research, glyphosate *could* encourage the growth of cancer cells that are susceptible to estrogen, which is of course naturally present in the female body. This, though, is far from meaning that it *causes* cancer, just as estrogen doesn't.

The cited article gave rise to a series of objections, including the fact that they had already previously found that glyphosate actually *hinders* the growth of cancer cells[416].

Irrespective of the claims of S. Thongprakaisang *et al,* that glyphosate encourages the growth of cancer cells that are sensitive to estrogen is nothing special. In many food plants – e.g., soybean – estrogen-like compounds (xenoestrogens) are found that act the same[417].

Glyphosate causes chronic kidney disorder

The claim is based on a (presumably deliberate) misunderstanding of an article by **C. Jayasuman** *et al.*[418], who investigated the possible causes of chronic kidney disease in the area of northern Sri Lanka. The article is characterised as a **hypothesis**, so is not based on measured results but describes a *possible* biochemical mechanism for the occurrence of chronic kidney diseases. Neither does the article indentify specifically glyphosate but the *combined* action of hard water, metals toxic for kidneys and glyphosate.

It is worth mentioning that copper is one of the metals toxic for kidneys [419] . The commonest food sources of copper are copper hyperoxides, oxychlorides and sulphates (blue copperas), which are

[415] Glyphosate induces human breast cancer cells growth via estrogen receptors. Thongprakaisang S. *et al.* Food and Chemical Toxicology 2013, 59: 129-136 doi: 10.1016/j.fct.2013.05.057

[416] Glyphosate and AMPA inhibit cancer cell growth through inhibiting intracellular glycine synthesis. Li Q *et al.* 2013, 7: 635-43 doi: 10.2147/DDDT.S49197. eCollection 2013

[417] The role of xenoestrogenic compounds in the development of breast cancer. Safe S. and Papineni S. Trends in Pharmacological Sciences 2006, 27:447-54

[418] Hypothesis: glyphosate, hard water and nephrotoxic metals: are they the culprits behind the epidemic of chronic kidney disease of unknown etiology in Sri Lanka? Jayasumana C. *et al.* International Journal of Environmental Research and Public Health 2014, 11: 2125-2147 doi:10.3390/ijerph110202125

[419] ATSDR Toxicological Profiles. Copper

considered permissible means for weed suppression in organic cultivation[420] and in poor countries they are among the few cheap available fungicides.

Studies link feeding animals with GMOs and serious inflammation of the stomach and enlarged uterus in pigs

An article[421] based its conclusions on experiments with pigs that were separately fed with GM soybean and corn, and feed that did not contain GMOs.

Publicist **Mark Lynas** found that the authors had selectively chosen the results[422], that they had thus used only those that confirmed their previously posed hypothesis on GMOs.

The geneticist **Anastasia Brodnar** noted that the authors had not actually analysed the differences in composition of the two types of feed[423]. Previous studies, in fact, had found that the environmental conditions of production of GMOs (e.g., temperature, precipitation, water quality, soil, geographic location) had a greater influence on the composition of feed than the difference between GM and non-GM feed[424].

The geneticist **L. Val Giddings** observed that among the pigs that were the subject of the study there was an abnormally high occurrence of pneumonia, which suggests that care of the animals was inadequate[425].

Glyphosate is linked to deformations of embryos, autism, Parkinson's disease, Alzheimer's disease etc.

420 Council regulation (EEC) No 2092/91 of 24 June 1991 on organic production of agricultural products and indications referring thereto on agricultural products and foodstuffs, p. 42

421 A long-term toxicology study on pigs fed a combined genetically modified (GM) soy and GM maize diet. Carman J.A. *et al.* Journal of Organic Systems 2013, 8: 38-54 ISSN 1177-4258

422 GMO pigs study – more junk science. Mark Lynas 12 June 2013

423 Lack of care when choosing grains invalidates pig feeding study. Bodnar A. Biology Fortified 13 June 2013

424 Comparison of two GM maize varieties with a near-isogenic non-GM variety using transcriptomics, proteomics and metabolomics. Barros E. *et al.* Plant Biotechnol Journal 2010, 8: 436-51 doi: 10.1111/j.1467-7652.2009.00487.x.

425 The new pig study gets an “F” in science. Sleuth4Health June 13, 2013

Claims of this sort multiply and it is impossible to comment on all. Some are collected here in a single section because they have a common attribute: they are not based on any kind of scientific evidence. The problem of informing the public is that the media (and opponents of GMOs) keep on repeating such »research« without critically checking the source.

Glyphosate causes deformation of embryos

The claim is based on a single internet posting on the website of the non-governmental organision Earth Open Source, which advocates a complete ban on GMOs; the posting amounts (only) to a video of a discussion with **Andres Carrasco** [426] . Official data based on scientifically correct measurements explicitly state that glyphosate carries no risk of carcinogenic diseases or damage to an embryo[427].

Study links glyphosate with autism, Parkinson's and Alzheimer's diseases

The claim is based on a single publication in the journal Entropy[428], which is well-known as an example of the new »disease« of scientific publications, the so-called predator or "pay-for-play" publication. Research institutes must order all scientific publications in their field, which has encouraged the creation of mainly profit-oriented »scientific« journals that do not check articles prior to publication on the principles of scientific review but publish practically anything for payment[429].

The article was the subject of a range of critical analyses, perhaps the most popular being written by **Keith Kloor** in Discover Magazine[430], in which among other things he found that the article is "*such a mashup of pseudoscience and gibberish that actual scientists have been unable to make sense of it.*"

[426] EarthOpenSource Birth defects caused by glyphosate, Andres Carrasco

[427] NPIC National Pesticide Information - Glyphosate Technical Sheet

[428] Glyphosate's Suppression of Cytochrome P450 Enzymes and Amino Acid Biosynthesis by the Gut Microbiome: Pathways to Modern Diseases. Samsel A. and Seneff S. Entropy 2013, 15: 1416-1463 doi:10.3390/e15041416

[429] Predatory publishers are corrupting open access. Beal J., Nature Column: World View 12 September 2012

[430] When media uncritically cover pseudoscience. Keith Kloor, Discover Magazine April 26, 2013

People with chronic illnesses have higher levels of glyphosate in their bodies than healthy people

The only article[431] that is the basis for this claim was again published in a well-known »predator« journal. A proper scientific review would already have rejected it because the text nowhere states what kind of diet the test subjects were fed and what sort of »chronic illnesses« they are supposed to have had.

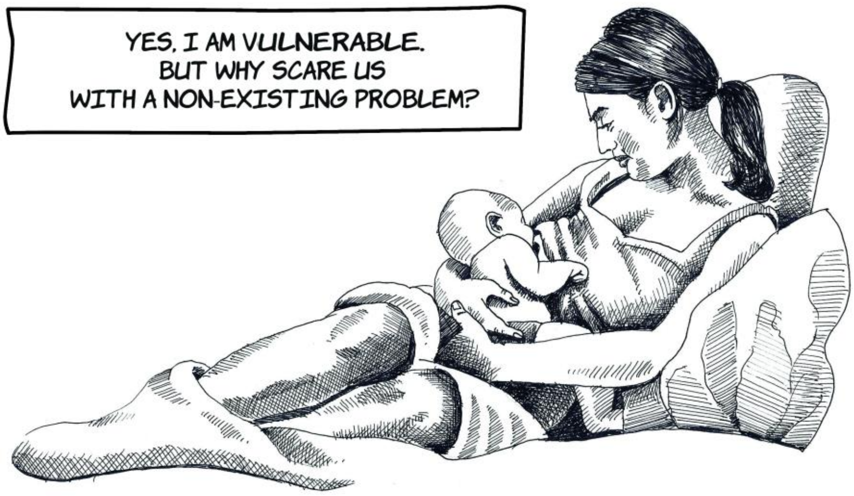
New »studies« will undoubtedly appear of this type and public opinion will continue to be formed by media that uncritically publish them.

Glyphosate has been found in mothers' breast milk

In April 2014, the organisation ***Moms Across America*** (MAA) published the sensational results of "research" performed together with ***Sustainable Pulse*** (SP), which is supposed to have shown that it is possible to find glyphosate in maternal milk[432]. At the same time, MAA and SP excused the results on the grounds that it was not actually proper scientific research. The supposed revolutionary finding was of course accompanied by an extensive media campaign, including a TV »documentary«. Both organisations are ideologically strictly opposed to any kind of GMO or use of phytopharmaceutical means and recommend only ecologically produced food.

431 Detection of Glyphosate Residues in Animals and Humans. Krüger M. *et al.*, Journal of Environmental & Analytical Toxicology 2014, 4:2 ISSN: 2161-0525

432 Glyphosate testing full report: Findings in American mothers' breast milk, urine and water. Conducted by Moms Across America and Sustainable Pulse, April 7, 2014



With the accuracy of modern analytical methods, it is of course not surprising to find some glyphosate in maternal milk. MAAA and SP, though, claimed that concentrations of glyphosate in maternal milk reach dangerous levels.

Science often finds it very difficult to respond to such accusations. It is essentially easier to launch a badly checked but alarming finding than perform proper research, which indisputably answers the questions raised.

A check of the »research« in the light of proper scientific methods immediately revealed a series of serious methodological faults that completely devalued the conclusions, including the fact that the claim on dangerously high concentrations was based only on the results of 3 samples (of 10). In addition, a large number of research studies exist and none of them to date have discovered the presence of glyphosate[433].

A sensitive and reliable method of determining glyphosate has been developed in collaboration between the company and an independent laboratory. Preliminarily published results were negative, they did not find glyphosate in maternal milk[434]. This so upset the mentioned activist groups that they initiated a media campaign against the authors, in which they tried to discredit them personally and, at the same time, refused discussion on the faults of their procedure, which

[433] Debunking pseudo science "lab testing" health risk claims about glyphosate (Roundup). Academics Review, Apr 10, 2014

[434] U.S. breast milk is glyphosate free. Science News, July 23, 2015

it appears led to the previously mentioned alarmist claims[435]. GMO opponents still cite the MAA claim as undisputed.

Many countries have banned glyphosate

A government or legislative ban is an entirely political act and generally doesn't have a great deal to do with scientific facts. In any case, there are not actually very many countries that have "banned glyphosate" and the bans are not as comprehensive as environmental organisations pretend. The actual situation is as follows.

El Salvador banned the use of glyphosate in September 2013, together with the herbicide Paraquat and insecticide Endosulfan[436].

In **Mexico,** in August 2014 a district judge of the federal state of Yucatán annulled the permit for commercial sowing of soybean that is resistant to glyphosate ("*Roundup-ready*«)[437]. The ban only applies in Yucatán, for the production of this specific GM soybean, and not for the use of glyphosate and does not apply in any of the other 6 Mexican federal states for which the Mexican Ministry of Agriculture had issued a permit in June 2012.

The Dutch parliament on 4 April 2015 passed a law by which from the end of 2015 the sale of glyphosate preparations for *non-commercial* purposes will be banned[438]. The law in no way restricts the use of herbicide based on glyphosate for commercial production, merely classifies them in the category of protective means that are not for over-the-counter sale, such as applies in Slovenia for the majority of agricultural preparations.

Columbia on 10 May 2015 issued a public statement that it would no longer use glyphosate for the destruction of coca plantations[439]. The decision has no effect on other uses of glyphosate preparations, by professionals or amateurs.

In **Bermuda** the Minister of Health **Jeanne Atherden** on 10 May 2015 issued a decision on the temporary ban on use and import of preparations on the basis of glyphosate, which will apply "until the assessment of new research"[440].

[435] Nutritionist Michelle McGuire responds to attacks in wake of 'glyphosate not in milk' study. Michelle McGuire, Genetic Literacy Project August 11, 2015

[436] El Salvador government bans roundup over deadly kidney disease. sustainable pulse, Sep 19 2013

[437] Sweet victory for Mexico beekeepers as Monsanto loses GM permit. The Guardian, 8 August 2014

438 Dutch parliament bans glyphosate herbicides for non-commercial use. Sustainable Pulse, Apr 4 2014

[439] Colombia to ban coca spraying herbicide glyphosate. BBC News, 10 May 2015

[440] Bermuda suspends glyphosate-ridden monsanto roundup indefinitely. Sarich C., Global Research, May 13, 2015

The newly elected president of **Sri Lanka**, **Maithripala Sirisena,** on 26 May 2015 promulgated a ban on the import of glyphosate preparations and a ban on sales of remaining stocks in the country[441]. The reason for the presidential decision was the hypothetical link between glyphosate and chronic kidney disease.

On 15 June 2015, the **French** minister of ecology, sustainable development and energy, **Ségolène Royal,** called on garden centres to halt sales of the herbicide Roundup®. As the sources state, the French government should legislate rules by 2022 that glyphosate preparations must be kept in shops in locked cupboards and only be sold for professional use[442].

Roundup® is the trade mark of the American concern Monsanto and, of course, contains glyphosate – but it is far from the only herbicide to contain it. Patent protection for glyphosate expired globally in 1991, in USA in 2001, so that anyone can sell herbicides today on the basis of glyphosate (but of course not under protection of the trademark Roundup®). Chinese companies are today the major providers of herbicide preparations on the basis of glyphosate.

Other claims of GM opponents of »almost« bans of glyphosate are for the moment only appeals or legislative proposals of environmental groups that have not yet been realised.

There are today 196 sovereign countries in the world.

[441] Sri Lanka's newly elected president bans glyphosate effective immediately. Sarich C. Natural Society MAY 26, 2015

[442] French minister seeks to put glyphosate products behind locked shelves. Horticulture Week, 15 June 2015

Part 3: The real need for GMOs

Why we need plant breeding

World food production grew by more than 250% in the 20th century[443]. At the start of the 21st century, the arable area actually fell slightly globally but production nevertheless is still for the moment increasing faster than the world population. We live better than any generation before us but the world is still not without hunger. In 1990–1992, 18.7% of people were undernourished and now there are 11.3% – but this is still more than 800 million people. Do we know why and how to solve hunger?

We sometimes lecture to secondary school students on plant breeding. The first thing we say is normally that we would not be sitting in the classroom together and pleasantly chatting if the work of generations of breeders in the twentieth century had not drastically increased yields of all the leading agricultural plants. The majority do not know from whence the sudden abundance of food and its variety. If they remember anything it is that today we plough with tractors and not horses. That we fertilise with mineral fertilisers and less with stable manure, that we use synthetic means of protection, that we irrigate and drain land and so on. Very rarely will anyone say: we are sitting here because we grow modern varieties of agricultural plants[444]. Nevertheles, science considers that breeding of new varieties has contributed most to the dramatic increase in yield from the same cultivated area, which is at least five times that of a century ago[445].

The history of plant breeding and animal selection did not of course start in the twentieth century. Mankind has been selecting plants for millennia and animals probably longer. After the great discoveries – let's say America – the most successful species circled the world. It is unbelievable the successes that people achieved without knowing anything about inheritance. They needed several decades to be scientifically convinced that an insignificant Mexican plant really is the unique forebear of today's mighty maize. It is similarly difficult to believe that such different vegetables as cabbage, kale, kohlrabi, brussel sprout or broccoli are actually representatives of one and the

[443] Patterns of economic growth and development

[444] Pocket K No. 13: Conventional Plant Breeding. ISAAA Nov. 2006

[445] Visionen der Pflanzenzüchtung zur Ertragssteigerung,-sicherung und Eröffnung neuer Verwertungsperspektiven. Visions of plant breeding to increase yields, securing and opening new recovery prospects.Ordon, F. 2011: In: „Landwirtschaft 2025 –Anforderungen an den effizienten Pflanzenbau“

same species, which is known botanically as *Brassica oleracea*. The history of plant breeding shows when which of now completely independent variants appeared in cultivation. The Roman Empire, for example, was responsible for a considerable number of them.

As in all other fields, progress in plant breeding was gradual. Mass crossing and selection, both within and between species, was already being done in the 18th and 19th centuries and the first modern varieties were created. We are still today growing many of the varieties of pears and grapes that originate from this period. Although the scientific foundations are ascribed to the discovery of Mendel's work in 1900, other less well-known discoveries were also actually important for plant breeding.

Progress was accelerated when they discovered how to breed self-pollinators, such as wheat or peas, cross pollinators such as rye or onions and vegatively propagated plants, such as grapevine, and all fruit species. The real entrepreneurial spirit in the seed trade caused the discovery of hybrid varieties; first maize and then a number of other species. It is noteworthy that this hybrid richness has already been known for a century. The theories that explain it are a similar age, although a series of completely new genetic discoveries only now explain the molecular background in more detail. An instructive story that shows that practice has often overtaken theory in plant breeding.

How new varieties or breeds are formed

Any plant breeding starts with selection and usually the crossing of a number of vareties. The breeder needs for this the maximum possible genetic diversity. This is concealed in modern varieties, older varieties, local populations and other wild related species. Awareness of the need to preserve agriculturally important biodiversity is around 90 years old. Numerous gene banks have been founded, which preserve millions of accessions. From them, we draw genetic diversity and then, through a lengthy process of selection, we include them in new varieties.

The basic methods of plant breeding are hybridizations, self-pollination, cross pollination, cloning or the induction of mutations. The procedures rarely last less than ten years and it is entirely normal for breeders to discard thousands or tens of thousands of lines. A group of biotechnological procedures alleviates this work. Tissue culture, for example, makes propagation easier, and obtaining haploid plants (with only one set of chromosomes) originated from pollen replaces years of inbreeding. In the transfer of genes from more or less related species we are aided by *in vitro* rescue of created embryos or by combining »naked« vegetative cells (protoplasts). It is now easier to select individual lines from thousands of crosses with the aid of DNA analysis, which is improved each year. All this enables an insight into cell processes that were formerly hidden.

Similar progress has also been made in the selection of animals, except that methods of selection are somewhat limited. The science of genetics and use of mathematical tools, known as biometrics, helps considerably. We are also carrying out progeny testing, inbreeding and crossbreeding, immunogenetics and using contemporary biotechnological methods such as cloning, sex selection and so on.

It is fair to say that the selection of animals has succeeded exceptionally in recent decades in improving domestic animal breeds. With the same food, for example, chickens reach slaughter weight in seven weeks and only 50 years ago they needed three times as long for this[446]. Many achievements are also here hidden from the eyes of the public but progress is constant and all the more directed also into the quality of meat or milk products.

Why GMOs are so important to breeders

So why do plant and animal breeders need methods of genetic engineering? Well, the answer can be quite simple – because it makes work much easier and more efficient. GMOs are sometimes used because some aims cannot be achieved by classical methods, perhaps crossing will not help because no variety of maize is resistant to corn beetle, while the insertion of a bacterial gene for resistance by means of GM has been very successful. Some aims are easier to achieve: courgettes resistant to a number of viruses can be very easily obtained by methods of genetic engineering, while being very difficult or impossible by crossing. In particular, though, because with these methods we can achieve completely new properties such as a specific species never had before. For example, no variety of rice contains vitamin A, only rice with a bacterial and maize genes will save lives. The reason can also be the desire for exploitation of plant species as a cheap supply for producers of industrial or pharmaceutical substances. Many such cases are cited above. The same applies for animals; lactose can only be excluded from cow milk by modern biotechnogical procedures.

Breeding and releasing for sale is regulated legislatively for GM varieties completely differently from releasing non-GMO varieties. This field is covered by a number of national[447], regional[448] and

[446] Havenstein, G.B., P.R. Ferket, and M.A. Qureshi, 2003a. Growth, livability, and feed conversion of 1957 versus 2001 broilers when fed representative 1957 and 2001 broiler diets. Poult. Sci. 82:1500–1508

[447] Electronic code of federal regulations http://www.ecfr.gov/cgi-bin/text-idx?c=ecfr&tpl=/ecfrbrowse/Title07/7cfr340_main_02.tpl

international[449] laws and regulations. Essentially, in the gradualness of release, in which the phases are the following: laboratory experiments, experiments in a protected environment, small field experiments, cultivation. Very detailed documentation is required from an applicant, which national scientific commissions examine in detail and also often require suitable additional material. During and at the end of the procedure, regulatory bodies publish available documentation and the final conclusion publicly. So it's no miracle that created varieties thus tend to be more[450] and not less safe than normal.

Roots of public hostility to GMOs

There is no doubt that public hostility was initially triggered back in the 1980s with the above mentioned lobbying of the main GM seed company with regulatory authorities in the USA for excessive testing required exclusively for GMO varieties. Since the process was later adopted all over the world, and particularly misused in Europe, this burdensome regulation provided the basis for public mistrust. Although deregulation based on accumulated knowledge was often later demanded, for instance by Swedish scientists[451], no regulatory action has been undertaken by goverments or international bodies.

The American public opinion polling company **PewResearch** in January 2015 carried out a poll on attitudes to more important scientific themes among members of AAAS (*American Association for the Advancement of Science*), as representatives of science, and the general public[452]. The greatest gulf was measured with GMOs: 88% of AAAS members believe that they are safe but only 37% of the public agree. Public opinion in the EU is even more disinclined to GMOs.

Part of the reason is certainly the fact that the public less and less trusts authority, since it has too often been shown in the past that governments have propagated untruths because it brought advantage to their political allies or strategic interests. Since the authorities justify their measures with science, science must also be part of the conspiracy against people – from whence scientifically completely unfounded theories of conspiracy about the harmfulness of

[448] The long road to authorisation. GMO Compass, Food and Feed from GMOs
[449] The Cartagena Protocol on Biosafety. convention of biological diversity
[450] Biotech foods are safe. Says who? [Infographic]. Sanders L. Food insight Oct 7, 2015
[451] Quasi-science prevents an environmentally friendly agriculture and forestry. Jansson S. *et al.* 5. Oct 2011

[452] Public and scientists' views on science and society. PewResearch, 29. januar 2015

vaccination[453], chemtrails[454], carcinogenic effects of power lines[455], HAARP as a weapon for controlling the weather[456] etc.

It is probably more important, though, that practically all professional environmental organisations have taken a position against GMOs. They know very well how to exploit the media's tendency for sensationalism: an American catchword says *“if it bleeds, it leads”*; and ever new "public announcements" that stress ever new supposed risks of GMOs, are more striking news than reports on successful cultivation. Unfortunately, the media are the main source of publicly available information and so crucially effect public opinion, including in relation to GMOs[457, 458, 459].

Why it is so is a question for psychologists, sociologists, politologists, media analysts and so on.

The authors consider that the real advantages of GMOs to the population are insufficiently known, so this publication is an attempt to present the more important achievements of contemporary technology. We have tried to explain them in the light of their usefulness as well as in the light of the constant accusations appearing in the media. In both cases, we state the scientifically supported evidence, by which specific claims are answered.

Rejecting GMOs has consequences

If you have read this book it will probably have become clear that scientists sharply oppose the *de facto* ban on the use of modern biotechnological methods with agricultural plants and animals that apply in many countries. Experts in the field of plant breeding and animal selection best know the limitations forced on us by such an inappropriate attitude of society. We don't just ask what could be with

[453] The anti-vaccination movement. Novella S. Sceptical Inquirer Vol. 31.6 Nov.-Dec 2007

[454] Chemtrails: Aerosol and Electromagnetic Weapons in the Age of Nuclear War. Amy Worthington, Global Research, 29. julij 2015

[455] Power Lines and Cancer FAQs. Medical College of Wisconsin Aug. 2004

[456] HAARP: Secret weapon used for weather modification, electromagnetic warfare. Fred Burks, Global Research, 18. januar, 2015

[457] Discursive struggle in the Slovenian media: journalistic representation of genetically modified organism. Erjavec K. Družboslovne razprave, XXVII 68: 45–61, 2011 UDK 608.7:316.774(497.4)"2010"

[458] Press media reporting effects on risk perceptions and attitudes towards genetically modified (GM) food. Vilella-Vilaa M. and Costa-Font J. The Journal of Socio-Economics 2008, 37: 2095–2106. doi:10.1016/j.socec.2008.04.006

[459] Mapping Boundaries of the Hostile Media Effect. Albert C. G. and Schmitt K. Journal of Communication 2004, 54: 55–70 doi: 10.1111/j.1460-2466.2004.tb02613.x

this or that GM variety but, especially, what we are losing when we reject these innovative methods.

Perhaps it is easiest to explain the unnecessary rejection by speaking of the efficiency of plant production and alternatives that are available to us. At the time of the recent ban on production of GMOs in some 19 European countries [460], the New York Times published a lucid sentence: »In essence, Europe has chosen chemistry over biology«[461].

Let's judge in the simple case of potatoes whether the claim holds. Potatoes are threatened by virus diseases. We don't spray against them but plant virus free tubers, which are again infected in a year or two with one or more known viruses, no variety is resistant to them all. This problem could have been solved a decade ago and, as we report on chapter »Rainbow« papaya, the first GM varieties resistant to only one of the viruses only entered cultivation in 2015 and for now only in one country in the world. Potatoes are threatened by the Colorado beetle. Although extremely effective resistance was already possible with Bt technology, as displayed even in the Disney Centre in Florida back in 2002, already released varieties were actually withdrawn from the market (chapter GM plants that express protective Bt-toxins). Because we know other possibilities of protection against insects, (chapter Defence against insects with RNA interference (RNAi)) potatoes could also be protected against other pests, such as click beetles (from the family Elateridae). Potato is also threatened by potato blight and a durable natural-based GM solution already exists (chapter GM potato resistant to mould). So only the problem of weeds remains. We know it is simple with GM technology to insert a gene for resistance to practically any known herbicide and, of course, it would be useful to have varieties resistant to various herbicides to avoid the exaggerated use of only one. To conclude: a farmer that planted such modern varieties would only come to the field once from planting to harvest for the application of herbicide, all other spraying (there are currently around ten[462]) would be a thing of the past. Is it therefore really worth rejecting the technology as »environmentally dubious«?

Similar applies to countless other potentials, from uses in pharmacy, cosmetics and other branches of industry. Although we summarise some briefly in the book, numerous still uncreated are only limited by the imagination of the researchers. We can confidently predict that the explosion of very varied products has barely started.

[460] It's official: 19 European countries say 'No' to GMOs. EcoWatch Oct. 5, 2105

[461] With G.M.O. policies, Europe turns against science. The New York Times Oct. 24, 2105

[462] Raba fitofarmacevtskih sredstev in preučitev možnosti za njihovo racionalnejšo uporabo v Sloveniji; The use of plant protection products and analysis of the possibilities for their rational use in Slovenia http://www.kis.si/f/docs/Publikacije/Raba_FFS.pdf

New plant breeding techniques: genome editing

We can certainly look forward to the development of completely new technologies. Synthetic biology, for instance, is knocking on the door, which promises the creation of new biomaterials such as are unknown in nature[463]. As already briefly mentioned, new methods of genomic rearrangement have been established extremely quickly recently[464]. At least four technological variants have been developed in the past decade enabling so called genome editing; currently the most popular and most recent is known under the name CRISPR/Cas9[465]. It greatly improves selection or editing of undesirable genes, since it enables chromosome breaks at chosen locations, which are followed by DNA repair but with mistakes. Finally, targeted mutation is induced at a given site. Such a consequence – gene inactivation - was formerly achieved by induced mutations (chapter Genetic changes for protection against pests), then with RNAi technology (chapter Defence against insects with RNA interference (RNAi)) and is now essentially more easily and efficiently performed. In the addition to destruction of a gene, minor nucleotide alternations have also become available. The technology is already used even in treating people, despite the fact that with people we can justifiably fear a possible action of non-target genes, which is not a problem with plants.

Genome editing will soon enable numerous useful applications, such as the complete removal of allergens from food of plant origin. This does not just apply to simple aims, when it is necessary to remove only one or two genes (such as extracting caffeine from coffee or the allergenic protein from peanuts) but also for complex and difficult aims such as complete and not just partial removal of gluten from hexaploid wheat (chapter GM wheat and barley with less gluten).

At the time that this publication was written not all regulatory procedures connected with new technologies of genome editing were yet known[466]. In 2015, for instance, USDA concluded that at least some of the described methods should not be among techniques that belong in the procedure of judgement as applies to GMOs. The EU has

[463] The promise of synthetic biology Pleiss J. Applied Microbiology and Biotechnology 2006, 73: 735-739

[464] CRISPR: cutting edge tech for plant breeders. The Western Producer Nov. 20, 2015

[465] https://en.wikipedia.org/wiki/CRISPR

[466] ZFN, TALEN, and CRISPR/Cas-based methods for genome engineering Gaj T. *et. al.* Trends in Biotechnology 2013, 31: 397-405

already been discussing this in detail for a number of years, the first report of the special commission is dated 2011[467]. Many others have followed, such as the study of the European Research Centre[468], the opinion of EFSA[469] and many other publications[470]. As is all the more characteristic of European politics, the many studies solve nothing, merely defer a political decision. Some countries have therefore already taken measures on their own, among them Germany and Sweden.

It now appears that the aforementioned USDA decision on non-regulation of methods of genome editing could be valid not only for the American but also for the global environment. Such varieties, namely, will be available throughout the world and their progeny will probably be built into many local varieties through crossing. It is important to note that such mutations or minor rearrangements of the genome in no way differ from natural or induced ones, so it is also not possible technically to exclude such varieties.

Benefits need to be understood by consumers

Nevertheless, essential progress in the field is promised through new methods and we believe that something else is crucial: sooner or later it will become clear that a different approach to GMOs is needed in public. The only real solution is that modern GM varieties begin to appear on the market, with genes the properties of which can be known by anyone and their usefulness assessed. For instance, it is not enough that we already have on the markets of the USA and EU oil pressed from GM soybean, which protects against heart and artery illnesses (chapter Healthier cooking oil from GMOs). The clear labelling »GM oil, good for your health« is needed. Similarly, why not explain on the label, that no toxic pesticides were needed by the farmer since the crop was protected by its own novel properties? Or that less water and fertilizer could be used in the process? People must recognise the benefits of new products and identify with them. Back in 1994, the first GM tomato variety actually had a similar labelling (chapter Tomato with delayed ripening), people knew that the fruit was picked ripe but, because of genetic modification, it would not

[467] New techniques working group FINAL REPORT. http://www.seemneliit.ee/wp-content/uploads/2011/11/esa_12.0029.pdf

[468] New plant breeding techniques State-of-the-art and prospects for commercial development. Lusser M. *et al.* EUR 24760 EN - 2011

[469] Scientific opinion addressing the safety assessment of plants developed using Zinc Finger Nuclease 3 and other Site-Directed Nucleases with similar function EFSA Journal 2012, 10:2943-2974 doi: 10.2903/j.efsa.2012.2943

[470] EU Perspectives on New Plant-Breeding Technique Schiemann J. and Hartung F. Julius Kühn-Institut Quedlinburg, Germany

immediately soften in storage[471] like all other tomatoes. Later on, GM varieties were not labelled in such a way. Positive labelling has only recently returned in the case of the varieties of apple (chapter GM apple Arctic® doesn't brown) and potato (chapter GM potato that produces less acrylamide during frying) described above; typically, by a small innovative company.

In short, we believe that as far as the use of GMOs is concerned, we are at a pivotal moment and we hope that this publication has at least explained it a little. Our advice would be: stay informed – not frightened.

[471] https://www.youtube.com/watch?v=kv5TlkAN3z8

About the authors

Dr. Borut Bohanec[472], professor of plant breeding and biotechnology and **M. Sc. Miso Alkalaj**[473], mathematician, computer expert and publicist, have joined forces in order to prepare a simple, understandable book which says everything that is of interest about GMOs. We have long experience in the field of modern methods of plant breeding as well as reporting for the media on various topical themes.

Borut Bohanec is a professor of plant breeding and biotechnology at University of Ljubljana, Slovenia. His expertise is development of various techniques for plant breeding. His studies so far were reported in 81 peer reviewed articles and 8 academic publications. He is also a member of the Scientific committees for GMO applications in Slovenia and occasionally of the European Union. For long he has been actively involved in promoting the societal awareness of plant biotechnology and us such frequently exposed in media.

Mišo Alkalaj is a mathematician, IT manager at the "J. Stefan" Institute in Ljubljana, Slovenia, and a writer. He has published two books and several articles highlighting the scientifically untenable claims of environmental activists, and their general ignorance of science. He has also voiced similar views in several TV appearances and is generally regarded as the bane of environmentalists in Slovenia.

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Debate about GMOs usually revolves around pesticides, corn or soybean, patenting and, of course, multinationals. Most of the discussion is actually about events in plant and animal breeding that happened more than two decades ago, as if none of the more recent achievements existed. This publication is an attempt to provide a brief but thorough insight into GMOs from the perspective of scientists. It describes various interesting traits that have been bred into crops and domestic animals in recent decades. Few people have even heard about them. In addition, a number of the more prominent scare stories are examined and a brief vision of future prospects is given. It's time to embrace knowledge, not fear.

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