Genetically Modified Organisms and Regulations Concerning Biotechnological Products

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To Ada Kaya, my beloved daughter

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Sometimes I used to wish I were a poet to write poems about all my closest friends, who have been with me for decades; they did all their best to contribute to the life I have today and I am very grateful. I have always known that writing a book was not an easy task to undertake, I wonder how indeed difficult it would have been, if it were not the sacrifice of those persons so dear to me who selflessly offered their time to me when I needed it the most. I cannot list all their names here but especially I cannot forget to recognize the role played by my dear husband, Halil Kaya, for being there anytime he was needed as a partner to fuel my reflection. I cannot also afford to neglect all commitments by Dr Mustafa ÇAKIR, who provided me with the necessary tools for legal instruments I have used in this work. I want to thank especially Jacques KABANO, who gave me his support for sources in foreign languages, without him this extensive work on global situation of genetically modified products would have been more difficult to complete.

Assoc. Prof. Dr. Iraz HASPOLAT KAYA

PREFACE

The world today is exposed to insufficient food that does not adequately feed its inhabitants. More solutions have been formulated to fight this problem but no suggestion is better than plant biotechnology where, with modern genetically engineering, plants and seeds are modified to grow faster and in greater numbers.

Today, the market of GMOs is characterized by three different approaches; the first is the idea that GMOs are not healthy and are dangerous to human life, the position that is held by most fundamentalist ideologies; the second approach is the idea that GMOs do have positive sides and negative sides, features that anything can have. The last approach is non-discriminative insight where people in this category do not have to care which is GMO and which is not.

The market of GMOs at the global level is a game of perception and mentality that consumers have, concerning a certain product. Due to their productions in high numbers, GMOs tend to be at a lower price than non-GMOs on the global marketplace.

In this book, we will enlighten on the importance of GMOs and risks, consumer perception, GMO restriction as well as relevant regulations regarding them, and the place GMOs have on the global market where we will divide the global market into two parts – developing countries and developed ones. The developments in biotechnology continue to make headlines about organisms other than human beings: the first form of synthetic life is close – cloned animals will soon be on our dining menus – without considering the myriad of genetically modified animals and plants that inhabit our laboratories and our "natural" environment. These technologies are not without creating strong controversy, but it is their application to human beings that raises fundamental questions: a genetically modified human being or cloned, for example, do they deserve to be called a human?

The science behind biotechnology is packed with wonders that are waiting to be revealed and yet undoubtedly it is a challenge to the international community and a hard task for international law. It challenges lawmakers in almost at all structures of the law with so many worries; should manipulated genomes count as property rights that would make private high-tech companies rich? This question is not simple to answer since this kind of ownership would affect all basic needs for the health and welfare of billions of people around the world. On the export issues, international law has concerns on regulations regarding the information that could be given to the states of import about any biotech products which are about to be exported to their territories and what would be the grounds to prohibit such transactions.

This work consists of three main chapters: Chapter one will explain GM products and their benefits; Chapter two will provide the reader with details of the situation of GMOs around the world; Chapter three will focus on the regulations of biotechnological products and on the concerns that the international community has regarding the development of this field.

LIST OF ABBREVIATIONS AND ACRONYMS

ABNE	African Biosafety Network of Expertise
AIA	Advance informed agreement
BCH	Biosafety clearing-house
BT	*Bacillus Thuringiensis*
CFT	Confined field testing
DNA	Deoxyribonucleic acid
DR	Disease resistance
EU	European Union
FFP	Feed or for processing
FT	Field trials
GATT	General Agreement on Tariffs and Trade
GMO	Genetically modified organism
HT	Herbicide tolerance
IR	Insect resistance
ISAAA	International Service for the Acquisition of Agri-Biotech Applications
LMO	Living modified organisms
MLT	Multi-location trials
N/A	Not applicable
RNA	Ribonucleic acid
SPS	Sanitary and phytosanitary
ST	Stacked traits
TBT	Technical barriers to trade
UN	United Nations
UNECA	United Nations Economic Commission for Africa
USDA	United States Department of Agriculture
WTO	World Trade Organization

CHAPTER ONE

GENETICALLY MODIFIED ORGANISMS

Scientists, farmers, agribusinesses and public authorities have always striven to develop crops, animals and more resistant species, with increased nutritional qualities and a more attractive presentation to consumers. This approach is part of the usual improvement process that is practised in our societies. So why are genetically modified organisms regularly causing concerns today? To answer this question we need to first explain what GMOs are.

Genetically modified organisms (GMOs) represent all organisms whose arrangement of genomes respond to a laboratory plan to fit the wanted physiological features. Under modern biotechnology, recombinant DNA technology and reproductive cloning are considered to be the main techniques used to produce GMOs.

Figure 1-1 below shows the techniques of recombinant DNA as manipulated by geneticists in a biotech laboratory. Recombinant DNA technology means the act of joining two DNAs from different species in order to obtain a new kind of organism made with predicted compositions under laboratory conditions. This technique serves as the main tool used by geneticists to select a portion of a desired gene or any other division of DNA with the aim of studying the sequence of its nucleotide and change it in a highly specific way so that it can be ready to be reinserted into a living organism.[1]

It is a result of manipulation of genetic code of an organism by humans in order to make it more resistant, to improve its nutritional qualities, or to give it properties that prevent a disease. This research focuses mainly on plants (corn, rice, rapeseed, soybean, etc.); the disadvantage is that transgenic plants often cannot reproduce on their own; one-year seeds cannot be used for the next year, thus increasing seed producers' control over their distribution.

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[1] Julia Diaz and Judith Fridovich-Keil, "Genetically modified organism", *Encyclopaedia Britannica*, 7 June 2019.
https://www.britannica.com/science/genetically-modified-organism

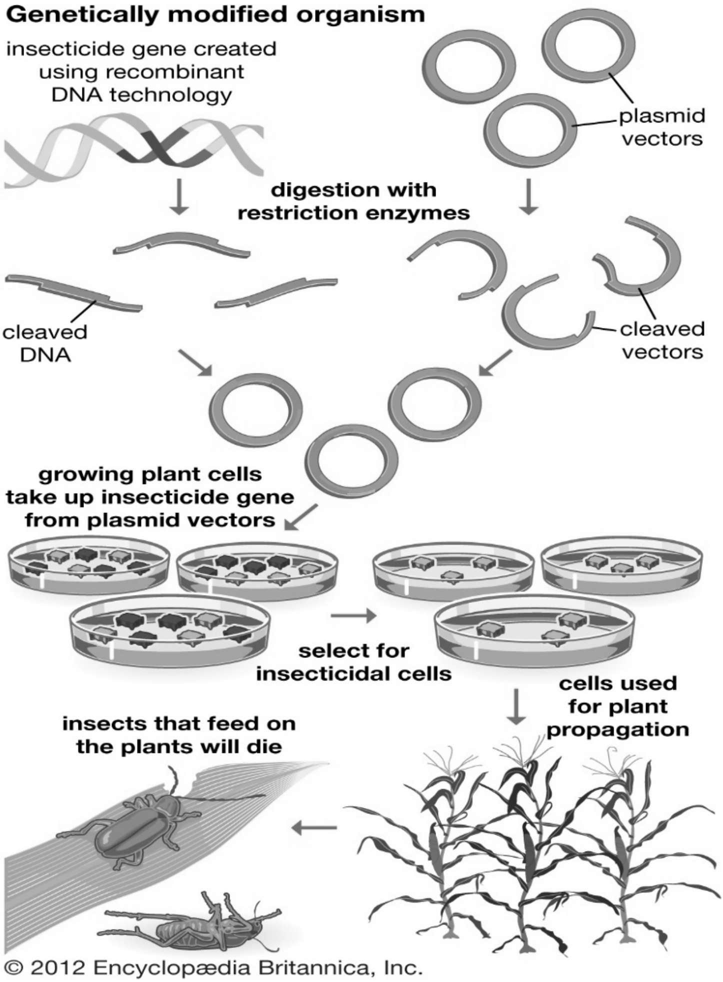

Figure 1-1: GMP Production[2]

Transgenesis is a technique that involves introducing into a body a gene (or a small number of genes) from another organism, whatever the origin of these genes (microorganism, plant of the same species or of another species,

[2] This is a representation of GMO production by the way of recombinant DNA technology. Anthony Griffiths, "Recombinant DNA", *Encyclopaedia Britannica,* 5 June 2019. https://www.britannica.com/science/recombinant-DNA-technology

animal or human) and by a method other than sexual reproduction. The organism obtained is described as a genetically modified organism (GMO). This chapter will focus on the application of transgenesis to plants, but animals, vertebrates or invertebrates and microorganisms may also be modified by these methods, as we will see in the last chapter.

The gene transfers between different species – or even between different kingdoms – which are carried out by transgenesis are made possible by the universality of the genetic code[3] and its transcription mechanisms in the cells of living organisms. Mechanisms of regulation and expression, still rather poorly known, modulate the expression of this genetic code between different species, depending on environmental conditions.

The gene, or the few genes, introduced into the recipient genome are included in a complex genetic construct called a transgene, which sets various functional elements side by side that aim to correctly express the foreign transgene:[4]

- one or more promoters, which are genes that allow the initiation of the reading of the information, either permanently and ubiquitously, or in a more limited manner (for example only in the leaves or in the seeds or at a given moment);
- regulatory sequences, which act by modulating the level of appearance of a particular gene;
- one or a few genes of interest, which contain the character that one seeks to give to the GMO (genes of interest which can themselves be modified, even synthesized);
- marker genes, which are used to select, after the transgenesis operation, the target cells having integrated the transgene;
- termination sequences, which mark the end of the informative segments of the transgenes.

In plants, the introduction of the transgene into the recipient genome is done either by mechanical methods (biolistic = bombardment of target cells

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[3] Universal coding system of genetic information at the DNA level, ensuring the correspondence between the nucleotides constituting the sequence of the DNA and the amino acids constituting the sequence of the proteins synthesized from this DNA. Each amino acid is encoded by a set of three successive nucleotides, called the codon; this correspondence is valid for all living beings.

[4] Marie-Pierre Arlot, et al., "OGM et agriculture: options pour l'action publique", (in French) accessed 14 November 2018 https://www.ladocumentationfrancaise.fr/var/storage/rapports-publics/014000692.pdf.

by a large quantity of transgenes) or by bacterial vectors, which inoculate the transgene with the target cells of the recipient plant. In the current state of techniques, the implantation site and the number of similar transgenes in the genome of the recipient cells are not controlled and may be variable from one cell to another. It is therefore necessary to go through a phase of selection of the cells having integrated the transgene, then to regenerate whole plants from the transformed cells, to sort out the plants having the desired characteristics and to locate in these plants or the site(s) insertion of the transgene. The proportion of transformed cells that give plants with the expected characteristics remains rather low, of the order of a few per thousand to few per cent of the treated cells. However, for these plants, the transformation event is a transgene placed at a specific place in the genome, which is described by its border fragments.

Different technical variations as to the components and vectors of the transgene can be developed; those that seem to open new perspectives of evolution of transgenesis will be detailed in the second part of this book. At present, the very broad a priori possibilities of transgenesis are only partially exploited. In order to understand the topic concerning the importance of GMOs on the global market, we first need to understand their historical path and why they have been developed from time to time.

1.1 Historical Background of Genetically Modified Organisms

GM crops are a very recent step in a crop improvement practice that began more than 12,000 years ago and includes corn, wheat, tobacco, grapes and so on. These traditional and empirical techniques of plant breeding, which lasted until the dawn of the twentieth century in Europe, continue to be practised widely in the world for many species. Plant breeding involves a variety of techniques, starting from traditional plant crosses to in vitro crosses and reproduction. It also uses artificial induction techniques of plant genome mutation to look for interesting traits, practises different sterilization techniques to control crosses, and is already making extensive use of molecular genetic techniques with genetic markers.[5]

[5] A marker gene is a portion of known sequence DNA and/or localization that is used as a reference to locate other genes.

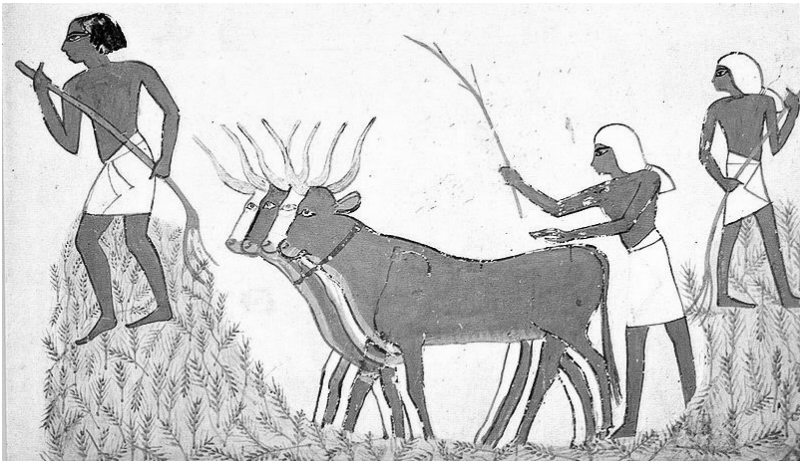

Figure 1-2: Illustration of agriculture in Ancient Egypt[6]

Humans have arguably been trying to think about how their crops will be good almost from the time they knew they could grow something from the soil. From the discovery of agriculture approximately 12,000 years ago, humans never ceased to search for durability in their crops by even intervening with food and their genes. By choosing some qualities over others, humans manipulated their harvest into something greater than what they had before; for example to be tastier, bigger and juicier. As a researcher in biotechnology at the University of Illinois, Bruce Chasey noted in his 2007 paper, “Plants such as strawberries, wheat, cabbage, corn, and almost all the rest of our crops descended from ancestors that were nothing like strawberries or wheat or corn from back in the day”.[7] Interestingly, sweet potato is an example of one of food that only existed because humans bred it; humans bred sweet potatoes out of swollen regular potato roots 8,000 years ago.[8]

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[6] Figure 1-2 shows how Ancient Egyptians started to modify their seed expecting a better crop. https://images.medicaldaily.com/sites/medicaldaily.com/files/styles/full_breakpoints_theme_medicaldaily_desktop_1x/public/2015/07/21/ancient-egypt.jpg

[7] Lecia Bushak, “A brief history of genetically modified organisms: from prehistoric breeding to modern biotechnology”, 22 July 2015, https://www.medicaldaily.com/brief-history-genetically-modified-organisms-prehistoric-breeding-modern-344076

[8] Bushak, “A brief history”.

Below we are going to establish a short chronological development of GMOs from the nineteenth century, because this century was the start of modern genetic engineering.

In the 1800s one of the most popular biologists, Charles Darwin, published his book on the origin of species (*The Origin of Species Through Natural Selection*) in 1858 with which he provoked a revolution in the thoughts of biologists of his time. He proved that species are unstable – they change and evolve – and they have evolved from the simplest to the most complex plants, animals or humans. According to Darwin, the driving force of evolution is in natural selection in which only the strongest species will survive. However, it is Darwin's contemporary, the Czech Gregor Mendel, who described the laws of heredity by observing the results of crossing peas and transmitting characteristics such as size, shape or colour.[9] By crossing hybrids, he described the so-called classical selection method. Gregor Mendel then found other ways to improve cultivated plant species.

In the 1950s, James Watson and Francis Crick discovered the structure of DNA (deoxyribonucleic acid, the molecule that carries the genetic code) in 1953, which was an important turning point in the genetic field. This discovery laid the foundation for a new discipline called molecular biology. In 1958, Edward Tatum confirmed the concepts of the young discipline:[10]

- All biochemical processes in all organisms are under genetic control;
- These biochemical processes are reducible to sequences of individual reactions;
- Each isolated reaction is controlled by one gene.

The 1970s showed the potential of genetic modification. Genetic engineering had brought a first practical use, the manufacture of new drugs, for example insulin that is used even in our time. The topic of GMOs was widely discussed and this debate was not limited to the issue of risk alone. Beside the particular successes, this method brought many questions that were not answered, especially those related to potential consequences of genetic modification on the variety of life on earth or human safety. **Chemist John Franz** developed glyphosate as an herbicide in 1970, the product that is being used in major GMO-producing mega companies to this day.

From 1972 to 1973 two American biochemists, Herbert Boyer and Stanley Cohen, invented a method to separate DNA pieces from one main

[9] Orel Vítězslav, *Gregor Mendel, Founder of Genetics* (Blok Brno, 1965), 43–45.
[10] Hervé Kempf, *La guerre secrète des OGM*, (Paris: Le Seuil, 2003), 16.

DNA and inserted those specific fragments to the DNA of other different organisms, which took contemporary biotechnology to another chapter of its history. This invention happened at exactly the same time the first debate about the health-related risks of genetically modified products was taking place. Biotechnology became commercialized in 1976, when permission was given to companies to conduct experiments on genes for various applications including food, medicine and chemistry.

In 1982, the decision of the United State Supreme Court concerning patent rights over GMOs gave Exxon Oil Company permission to use an oil-eating microorganism in its business.[11] In 1983, biochemists who were working for Monsanto were the first to pioneer the genetic modification of plants and tested their first GMOs five years later. In 1988, scientists inserted genes into soybeans, which gave rise to the most common GMO: glyphosate-tolerant soybeans. Soon after, scientists manipulated other GMO seeds such as potato, cotton, rice, sugar beets, sugarcane and tomatoes in order to make them more resistant to diseases, herbicides, insects, antibiotics and pesticides.

In 2003 in the framework of the UN, the first international agreement on GMOs, the *Cartagena Protocol on Biosafety Relating to the Convention on Biological Diversity* was established with the aim to "establish appropriate procedures to improve biotechnology security in line with the overall objective of the Convention, which is to reduce all potential threats to biological diversity, also taking into account risks to human health".[12] This is a very useful document in regulating biotech products, as we will see later in this book.

1.2 Benefits of Genetically Modified Crops

The benefits of GMOs can be found in different levels but here we will focus on two types of benefits: economic benefits and environmental benefits. According to a British agency for agriculture and other related resource sectors, PG Economics, the global benefits of genetically modified crops since they were first planted has reached $150.3 billion.[13]

[11] David Biello, "Silk solution: How Microbes will Clean up the Deepwater Horizon Oil Spill". *Scientific American,* 25 May 2010. https://www.scientificamerican.com/article/how-microbes-clean-up-oil-spills/

[12] The preamble of the *Cartagena Protocol on Biosafety to the Convention on Biological Diversity*, Montreal 2000.

[13] Graham Brookes and Peter Barfoot, *GM Crops: Global Socio-economic and Environmental Impacts 1996–2014*. Dorchester: PG Economics May 2018.

1.2.1 Economic Benefits

Genetically modified technology played a key role in raising farm-based income from a mixture of strengthened output and efficiency advantages. The above report argued that in 2014, the direct farm income benefits reached $17.7 billion, which suggests that worldwide production of crops of cotton, corn, soybeans and canola had increased by 7.2%.

The maize sector for 2014 produced the largest gains in farm income, over $5 billion; insect-resistant GM (GM IR) was the creator of this massive income. The maize sector alone is responsible for adding 6.1% of the value of the crop in the developing states. We summarize the farm income from 1996 until 2014 in the table below:

Table 1-1: Worldwide GM crops income between 1996 and 2014 (US$M)[14]

Features	**Income as of 2014**	**1996–2014**	**Percentage (2014)**	**% of benefit**
GM herbicide-tolerant soybeans	5,221.4	46,643.4	4.6	4.2
GM herbicide-tolerant and insect-resistant soybeans	853.5	1,174.7	0.75	0.69
GM herbicide-tolerant maize	1,600.1	9,050.4	1.8	1.0
GM herbicide-tolerant cotton	146.5	1,654.2	0.5	0.3
GM herbicide-tolerant canola	607.1	4,860.0	6.6	1.8
GM insect-resistant maize	5,296.0	41,407.3	6.1	3.2
GM insect-resistant cotton	3,940.8	44,834.3	12.5	8.9
Others	79.7	652.4	–	–
Totals	17,745.1	150,276.7	7.3	7.2

[14] Brookes and Barfoot, "GM crops, environmental impacts".

After a look at the global scale, we can see what happened in selected countries from 1996 up to 2014. The US heads the list and is followed by Argentina among the countries that have profited more in our time frame; India occupies third place on the list even though its data on the most verified GMOs are unknown. The fact that the production of GM IR cotton has been multiplying over time make it one of the leaders in this list.[15]

[15] WHO, "20 questions on genetically modified foods". May 2014. http://www.who.int/foodsafety/publications/biotech/20questions/en/index.html

	HT soybeans	HT maize	HT cotton	HT canola	IR maize	IR cotton	HT/IR soybeans	Total
US	*21,400.3*	*6,106.1*	*1,074.1*	*311.4*	*32,198.3*	*4,750.2*	*N/A*	*65,840.4*
Argentina	*16,435.6*	*1,243.0*	*145.0*	–	*678.3*	*803.0*	*33.5*	*19,338.4*
Brazil	*6,317.0*	*1,368.3*	*133.3*	–	*4,787.1*	*72.3*	*1,100*	*13,778.2*
Paraguay	*1,029.2*	*0.9*	–	–	*13.1*	–	*26.3*	*1,069.5*
Canada	*613.3*	*137.4*	-	*4,492.8*	*1,229.5*	–	–	*6,473.0*
South Africa	*18.1*	*48.3*	*4.2*	–	*1,711.9*	*30.9*	–	*1,813.4*
China	–	–	–	–	–	*17,537.6*	–	*17,537.6*
India	–	–	–	–	–	*18,268.4*	–	*18,268.4*
Australia	–	–	*91.5*	*55.8*	–	*801.7*	–	*949.0*
Mexico	*6.1*	–	*183.2*	–	–	*194.3*	–	*383.6*
Philippines	–	*141.6*	–	–	*418.3*	–	–	*559.9*
Romania	*44.6*	–	–	–	–	–	–	*44.6*
Uruguay	*143.2*	*1.2*	–	–	*24.8*	–	–	*183.3*
Spain	–	–	–	–	*231.7*	–	–	*231.7*
Other EU	–	–	–	–	*22.2*	–	–	*22.2*
Colombia	–	*3.8*	*23.0*	–	*82.5*	*19.0*	–	*128.3*
Bolivia	*636.0*	–	–	–	–	–	–	*636.0*
Myanmar	–	–	–	–	–	*185.0*	–	*185.0*
Pakistan	–	–	–	–	–	*1,954.0*	–	*1,954.0*
Burkina Faso	–	–	–	–	–	*177.6*	–	*177.6*
Honduras	–	–	–	–	–	–	–	*9.6*

Why did genetically modified crops bring a big economic benefit? The boost in dollars did not just come by itself; GMOs showed a difference in comparison with non-GMOs because the former are proven to be insect resistant (IR), herbicide resistant (HR) and disease resistant (DR).[16] Other benefits can be that genetic engineering can produce plants that are nutritionally enriched in vitamins more than in natural crops,[17] plus they do not need as long in the fields and are able to grow during any season, which all show why the economic benefit is remarkable.

1.2.2 Environmental Benefits

Any agricultural activity, including the cultivation of a given plant, produces an obvious effect on the environment. Cropping patterns determine the weed and insect species that invade the fields, agricultural machinery squeezes the soil, consumes fuel and releases CO_2, while excessively applied fertilizers stay in the soil. A plant producing a large amount of pollen and nectar is able to draw pollinators such as bees, while another plant will tend to proliferate and stifle local vegetation.

For example, abandoning oat farming to maize directly affects the environment. Additionally, properties of plants (such as insect resistance) can also affect the environment. It is possible to obtain new properties by applying plant breeding methods that use the most old-fashioned methods, such as crossbreeding or genetic manipulation, or even newer ways with even more targeted action in the DNA of plants.[18] However, the environmental impact of a plant, whether genetically modified or not, or a property of the plant obtained by means of GMO technology or not, depends in the first instance on the plant or the property per se and not the technology that was used to develop it.

With regard to GMO plants, four important properties feature in what is now available on the market. Some properties such as resistance to viruses, insects and drought aim to mitigate the influence of farming activities on the environment. Further properties, such as herbicide resistance, have the primary purpose to improve the efficiency of food production. In other words, these properties are not all likely to promote environmentally

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[16] WHO, “20 questions”.

[17] WHO, “Modern food biotechnology, human health and development: an evidenced-based study”, 1 June 2005, http://www.who.int/foodsafety/publications/biotech/biotech_en.pdf

[18] VIB, “Van plant tot gewas: Het verleden, heden en de toekomst van plantenveredeling” (in Dutch), 2016, http://www.vib.be/nl/educatie/Pages/Dossier-plantenveredeling-.aspx

friendly farming. However, and contrary to the alarming news relayed by the media, the figures of the environmental impact of GMO plants give a different view. Overall, GM crop cultivation has provided a significant environmental benefit over the last eighteen years.[19] Insect-resistant crops have shrunk the utilization of insecticides by up to 230 million kilograms. From the introduction of zero tillage, herbicide-tolerant plants reduced fuel consumption and CO_2 releases by 6.3 billion litres and 16.8 million tonnes, respectively. All GM plants combined, the environmental benefit can be as high as 37%.[20]

The current environmental situation that can be easily seen is the increasing population, a high rate of loss in biodiversity and global warming. As often predicted by different reports, the world population could reach 9 billion by 2050 which means that in only 32 years (from 2018) 1.3 billion people will join the 7.7 billion[21] we have today.

Even if we number about 7.7 billion, cases of hunger exceed 850 million today.[22] We have to expect in 32 years' time, more hunger and more deaths if nothing different is done. Among others, strategies aimed at generating more to eat and a fair distribution of it will allow us to maintain security of food on earth. However, with the high rate of population and the day-by-day decrease in arable land in the search for human habitat, the only solution lies in using technology by producing more food from smaller portions of land.

On the environmental level, GM crops do have benefits for the environment: research on the worldwide cost-effective and ecological impact of manipulated crops showed that from 1996 until 2015 within 20 years of using GM crops, thanks to the implicated technology pesticide spraying shrank by 6,191 million kilograms. The study also demonstrated that genetic engineering contributed to an 18.6% decrease in environmental impact associated with pesticide utilization. Furthermore, the study

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[19] Graham Brookes and Peter Barfoot. "Environmental impacts of genetically modified (GM) crop use 1996–2015: Impacts on pesticide use and carbon emissions." *GM Crops & Food*, 8, No. 2 (May 2017) https://www.researchgate.net/publication/316174866_Environmental_impacts_of_genetically_modified_GM_crop_use_1996-2015_Impacts_on_pesticide_use_and_carbon_emissions

[20] Brookes and Barfoot, "Environmental impacts".

[21] "Current world population", Worldometers, accessed 13 October 2018, http://www.worldometers.info/world-population/

[22] World Hunger Education Service, "2018 World Hunger and Poverty Facts and Statistics", accessed 7 February 2018, https://www.worldhunger.org/world-hunger-and-poverty-facts-and-statistics/#produce1