The controversies of genetically modified food

K Blagoevska¹, G Ilievska¹, D Jankuloski¹, B Stojanovska Dimzoska¹, R Creeva¹
Nikolovska¹ and A Angeleska¹
¹Faculty of Veterinary Medicine Skopje, Food Institute, Lazar Pop Trajkov 5–7, Skopje, North Macedonia

E-mail: katerinab@fvm.ukim.edu.mk

Abstract. The increasing use of genetically modified (GM) foods and feeds attracts the interest of media and public, causing great concern among consumers about the consequences of their consumption. The issues of concern are mainly focused on the impact on consumer health and the repercussions on the environment. The biggest fears are the possible negative consequences on human and animal health, which encompass allergic reactions, side effects such as toxicity, damage to individual organs, gene transfer and differences in nutritional value. Consumers are unsure and confused as to whether consuming GM foods is harmful to their health or not. According to a Pew Research Center survey conducted between October 2019 and March 2020, 48% of respondents said GM foods are harmful, 13% responded GM foods are safe, while 37% of respondents could not express their opinion due to lack of knowledge about it. Numerous studies have been undertaken to examine the effects that GM foods and feeds exert on humans and animals. The results differ in many ways that issue numerous questions. In this paper, we will try addressing questions that concern the public, as well as the activities and measures that science and competent institutions are taking to confront them.

1. Introduction
1.1 What are genetically modified organisms (GMOs)?
GMOs are plants, animals or microorganisms with genetic material altered by gene insertion from another organism, carrying information about a desired trait not naturally present in the organism [1]. This gene manipulation results in a new organism that does not occur spontaneously by natural methods of crossbreeding. The gene with the desirable trait is introduced to the host organism by a biolistic or Agrobacterium tumefaciens mediated approach [2]. Gene transfer either can occur between two organisms of the same species or closely related species (the genes are called cysgenes), or between organisms not closely related (transgenes) [3]. An example of the latter is the insertion of a gene from marine fish into spinach, potatoes or tomatoes, which makes them resistant to frost [4].

The history of cultivating plants with higher yields, faster growth, disease resistance or containing a specific nutritional characteristic goes back to the early beginning of humankind. Ever since, humans have been producing crops by selecting those with desirable phenotypes. Because of that selection, we began to produce new varieties of plants with desirable traits much faster than they would naturally occur. Now though, our GM crops can carry genetic material, for example, for a particular trait that allows them to survive in adverse and/or extreme climatic conditions, or improves their quality. These include herbicide and pesticide tolerant crops, crops resistant to pests and viruses, drought or frost, or crops with improved yields and quality. In addition, the benefit of foods that contain these genetic modifications is the continued use and preservation of their nutritional value.
More than a hundred research studies comparing the effects of consuming traditional foods and GM foods have tried to give answers to the many questions raised around the use of GM foods. The outcomes of the studies have been published in numerous papers in professional and scientific journals. The accordance or not of GM foods with the regulations is visible in the database of GM cultures in different countries on the website of International Service for the Acquisition of Agri-biotech Applications (ISAAA) [5]. Moreover, the U.S. Department of Agriculture provides a list of bioengineered foods available to consumers throughout the world, where they can get information about the history of GM cultures, type of modification and regulation in the world [6].

1.2 Why did humans start producing GMOs?
According to the United Nations forecast, the world’s population will reach 9 billion by 2050 [7]. This will impose an increased demand for livestock products, followed by an urgent need for increased crop production. The ISAAA brief form 2018 states that per capita consumption of meat, milk and will rise by 2% per year in most parts of the developed world [8]. Therefore, the demand for feed crops will significantly increase, taking into consideration the fact that livestock unit’s average needs per kg of meat production are approximately 3 kg of feed grain and less than 1 kg of feed grain per kg of milk production [9].

Every year, we are witness to a drastically increased climate change that results in floods, droughts and spread of plant diseases, which poses a growing threat to the cultivation of many of these crops. So, in the decades to come it will be increasingly difficult to feed the world’s population, which is a big challenge for genetically modified crops – will they be able to do that?

In order to produce crops that will perform better than traditional crops and give higher yields with higher nutritional value, and are resistant to pesticides, especially insecticides, to limit the action of toxic herbicides, genetic modifications have been used. GM crops resistant to the organophosphorous herbicide glyphosate enable increased yields despite the much greater use of glyphosate during plant growth [10]. Unlike this type of herbicide-resistant GM crop, with the production of GM insect-resistant crops, the use of insecticides in crop cultivation is significantly reduced, indirectly affording better protection of the environment [10]. Furthermore, GM crops are resistant to various diseases, are more tolerant to stress factors of diverse nature, have a long storage time, and can be used in medicine and industry.

1.3 The first genetically modified food produced
The first genetically modified food was the red tomato, so-called Flavr Savr™ tomato, which contained a gene that delays ripening [11]. This prevented the softening of the tomato, making it resistant to spoilage, while maintaining its natural colour and taste. This product was approved for use in 1994 by the US Food and Drug Administration [11]. The most important commercially produced bioengineered crops are soybean, corn, cotton and oilseed rape, which are resistant to herbicides and pesticides. Such is the case with GM crops that are resistant to glyphosate, which is then widely used during crop growth to destroy weeds and grasses. A gene (CP4 epsp) is inserted into these crop plants from the bacterium Agrobacterium tumefaciens, and which reduces the affinity for glyphosate binding, thus increasing the plant’s tolerance to the herbicide. Currently, soybean, corn, alfalfa, oilseed rape, sugar beet and cotton carrying a genetic modification that gives them resistance to glyphosate are present on the market.

Furthermore, a gene from the bacterium Bacillus thuringiensis (Bt) and responsible for protein synthesis i.e. crystal toxin, referred to as Cry toxin, has been inserted into corn, cotton, potatoes and tobacco. This protein is toxic for larvae of some insects in the Lepidoptera, Coleoptera, Hymenoptera, Diptera and Nematoda classes that attack these cultures [12]. After ingestion of the GM food, in the digestive system of the insects, a protein coded by this gene is synthesized and binds to the intestinal wall. Within a few hours, the insect’s intestinal wall disintegrates, allowing the normal gut microbiota to enter the abdominal cavity, causing septicaemia followed by death. The commercial production and distribution of Bt crops were approved by the Environmental Protection Agency in USA in 1995 [12].
Another example of GM culture is the production of “Golden Rice”, with a genetic modification carrying genetic information for the synthesis of 20-fold more β-carotene than other varieties. Golden Rice is produced by inserting two genes into the rice genome: one from daffodil, responsible for synthesis of the enzyme phytoene synthase, and the second from the bacterium Erwinia uredovora, which produces the enzyme phytoene desaturase [13]. These two enzymes participate in the biosynthesis of β-carotene, which accumulates in the edible rice grains, and which in the human liver is converted into vitamin A.

Another variety of GM rice, used to fight the iron deficit in humans comprising almost 30% of the world’s population, has also been produced. The genome of this GM variety of rice contains ferritin gene from Phaseolus vulgaris, responsible for the synthesis of protein capable of binding iron, thus increasing the iron content up to twofold. To increase iron bioavailability, a gene is inserted into the rice from Aspergillus fumigatus; the gene is responsible for the synthesis of the enzyme phytase that breaks down phytate, an iron inhibitor [14].

1.4. Feeding animals with GM crops – are there implications for animal’s health and animal derived products?

As previously pointed out, in the past decade, food demand has rapidly grown, primarily because of climate change and environmental degradation that are reducing the amount of fruitful agricultural land. At the same time, the increase of world’s population creates serious challenges in food production, so making food safety a main issue. Taking into account this fact, as well as the fallout of COVID-19, and the UN Report from 2021 that clearly indicates that the number of people suffering from malnutrition is close to 811 million [15], serious measures should be undertaken. In response to supplying the growing world’s population with high quality protein, the global livestock population has grown, followed by an increased demand for feed crops. Producing feed crops able to persist in spite of a severe climate, especially in rural and dry areas with limited water resources, is laborious [16]. The use of modern biotechnology, including genetic modification techniques, has been proposed as a way to increase productivity and improve food/feed quality and at the same time, reduce the environmental footprint [17].

More than 70-90% of harvested GM crops are used in food-producing animal nutrition [18]. The question that arises is whether using GM feed crops can wield potential adverse effects on animals and consequently on humans. Therefore, it is crucial to review the safety of products such as milk, meat and eggs derived from animals fed GM crops, and this step should be a mandatory part of the regulatory process.

Independent studies have been undertaken to show if feeding GM crops affects the health and safety of animals. Some of the studies evaluated the health effects of feeding GM crops to ruminants, pigs and poultry, by observing parameters related to immune response, body condition score, organ weight, haematology, serum biochemistry, histopathology or gastrointestinal microbiota [19, 20]. Results have shown that despite the observed significant differences in some of the parameters, most of the effects measured were not of biological significance and were within normal biological ranges [19]. Studies where lactating dairy cows, pigs, poultry, lambs and rats were fed non-GM feed or GM-feed show the presence of fragments of GM DNA only in some parts of the gastrointestinal tract, while GM DNA was not detected in blood or any visceral tissue [21, 22, 23, 24, 25].

Research studies focused on analysing the safety of animal-derived products for the presence of GM DNA/genes have not proven their presence [26, 27]. Agodi et al., 2006, reported presence of GM DNA from maize and soybean in 25% and 11.7% of analysed samples respectively, during screening of milk samples from 12 different brands from the Italian market [28]. Within a normal diet, humans daily consume between 0.1 and 1 g of DNA originating from animal and plants [29]. Most of the digestion takes place in the small intestine, where nuclease and protease enzymes break down DNA nucleotides (nucleoproteins) into smaller parts. About 90% of nucleotides are absorbed by the cells of the intestinal epithelia, out of which 5% are retained for DNA or RNA synthesis, and 20-25% remains in the epithelial cells [30]. Therefore, since the GM DNA remains in the gut, concerns are expressed about the possibility
of horizontal gene transfer to the bacteria of the normal intestinal microbiota [21]. Despite the ability for horizontal gene transfer among certain bacterial species, in vivo experimental studies have not detected horizontal transfer of GM DNA/gens so far [21, 22].

2. What is the opinion about GMOs in scientific circles?

In the decades since the first use of GM foods, negative health consequences for consumers have not been registered. This does not mean they do not exist, but that they have not yet been definitively identified.

The European Union has invested more than €300 million in GMO biosafety research. The latest report from 2017 states: “The main conclusion that can be drawn from more than 130 research projects, conducted over a period of 25 years, involving more than 500 independent research groups, is that botany, especially GMOs themselves, do not pose a risk compared to plants obtained with conventional cultivation technologies”. A report by the American Medical Association, the National Academy of Sciences and the World Health Organization, based on research by independent groups around the world, also found that 90% of the scientific community believed that GMOs were safe to use. However, only a little over a third of consumers share this opinion. Fears about the side effects of GMO use still persist among consumers, as does the fear that inserting one or more genes could have a negative effect on other genes that are naturally present.

3. What are the fears that consumers face from the use of GM foods?

Most often, consumers fear GM foods that have inserted genes that improve nutritional value, primarily because they could increase the risk of allergic reactions, antibiotic resistance, toxic effects on various organs, mutations, or affect pregnancy, offspring and potential gene transfer to the consumer.

Concerning the fact, that in the past decades food allergy has become significant threat to humans, the relation with consuming GMOs, has raised many scientific questions. The transfer of genetic material from one organism to other results in the creation of a new protein, which could be a potential allergen, in the GM organism. Therefore, with the use of genetic engineering, the percentage of allergens naturally present in food increase. This was the case with a GM soy produced in the mid-1990s. Its genetic material was altered by the insertion of a gene from the Brazilian walnut coding information for synthesis of high quality protein with a favourable ratio of amino acids. The new protein in soy caused allergic reactions in people who were allergic to Brazilian nuts and consumed soy, which was proven by immunoassays. Fortunately, this GM soy was never approved or placed on the market. The review paper of Dunn et al. (2017) summarizes data from 83 studies of GM crops: corn, wheat, rice, soy, milk, peanut and others, addressing the question “Are GM products more allergenic than their conventional counterparts?” In this review, the authors thoroughly analysed studies that involved ingestion of GM food and feed by humans and animals. No animal or human study showed that consuming GM food or feed is more allergenic than its conventional counterpart [31].

In creating GMOs, antibiotic resistance genes are used as markers. This poses a concern of possible horizontal gene transfer between these genes and human and animal gut microbiota, as well as with environmental microorganisms. Scientists from China demonstrated the presence of a plasmid coding for β-lactamases in six Chinese rivers [32]. This very same plasmid is used for GMO production. To avoid even the very rare possibility of horizontal gene transfer, only genes coding for antibiotics that are not used in human and veterinary practice should be used in creating GM seeds and plants [33].

4. GMO regulation

There are differences between countries regarding GMO regulation, which are the result of different socio-economic and political factors. Constraints regarding GMO regulation are assessed through several indices, such as: approval process, risk management, labelling, traceability, coexistence and participation in international agreements. Thus, the European Union and Japan are in favour of more stringent measures in terms of GMO regulation, unlike the United States, where in some of the states currently it is not mandatory to label GMOs present in products, while other states have mandatory
labelling only if GMOs are present in quantities over 5%. However, starting from January 2022, the United States will begin to implement mandatory GMO labelling in consumer products. In the European Union, Japan and New Zealand, it is mandatory to label the presence of GMOs in food, if the authorized GMOs are present at levels above 0.9% for. Non-authorized GMOs must not be present at all.

Even though GMOs cause great controversy worldwide, especially in Europe, still in the European Union, 107 GMOs in food have been approved for use so far. After a call by the European Commission, 19 of 27 states of the European Union voted to either fully or partially ban GMOs. Spain and Portugal still allow GM corn MON 810 to be grown.

5. Detection and testing of GMOs

GM poses a huge challenge for analysts in developing methods that are precise and sensitive enough, can provide accurate data on whether or not the food or feed contains genetic modifications, and which will help consumers in their choice of products. Testing for the presence of GMOs in food is more than just screening for a few genes. The increase in GM crops, global trade routes and complex approval conditions in different countries require optimization of protocols for analysis and development of national strategies for their testing.

5.1 The strategy for classical GMO analysis

5.1.1. GMO screening – faster and more efficient detection of most GMOs

GMO analysis strategies generally begin with qualitative screening, which provides a reliable determination of whether or not there is a genetic modification in the food tested. Especially for food business operators who want to sell their GMO-labelled products, screening methods are essential.

5.1.2. GMO identification – providing product sales

In many countries around the world there is 0% tolerance or a tolerance threshold for unapproved GMOs. If the GMO is not approved in one country but is already approved and planted in another country, this asynchronous approval status can lead to problems in the sale of products that contain even traces of this GMO that is not approved in the importing country.

With the help of specific detection methods, unapproved GMOs can be identified and later excluded from market sale. Therefore, specific qualitative methods are an important aspect of confirming the status of raw materials and processed products derived from unapproved GMOs.

5.1.3. GMO quantification – is labelling required?

In addition to the approval of GMOs, the labelling of GMO content above a certain threshold is differently regulated by country. For example, in the European Union, unexpected or technically unavoidable pollution with approved GMOs of up to 0.9% is exempt from labelling. GMO quantities in food and feed above the threshold of 0.9% must be labelled according to EU Regulation no. 1830/2003 [34]. With the help of quantitative detection of GMOs, it can be determined whether the content of GMOs in the product is above or below the legal threshold. In animal feed, unauthorized GMOs are tolerated up to a threshold of 0.1% as long as they meet the requirements set out in EU Regulation no. 619/2011 [35]. For questions such as these, quantitative analysis is the method of choice for verifying sales and labelling requirements.

6. Conclusions

Although technologies for the production of genetically modified food are very promising in some areas that are challenges for the 21st century, still like all new technologies, they bear certain risks, known and unknown. The controversy and public concern over GM food and feed are primarily focused on human and animal health, as well as on environmental safety, labelling and consumer choice, intellectual property rights, ethics, food safety, poverty reduction and environmental conservation. What effects will GM food/feed have on the environment? What are the dangers to human health? Are we challenging
“Mother Nature” with these innovative technologies? These are the questions that we will leave to evolution itself to answer.

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