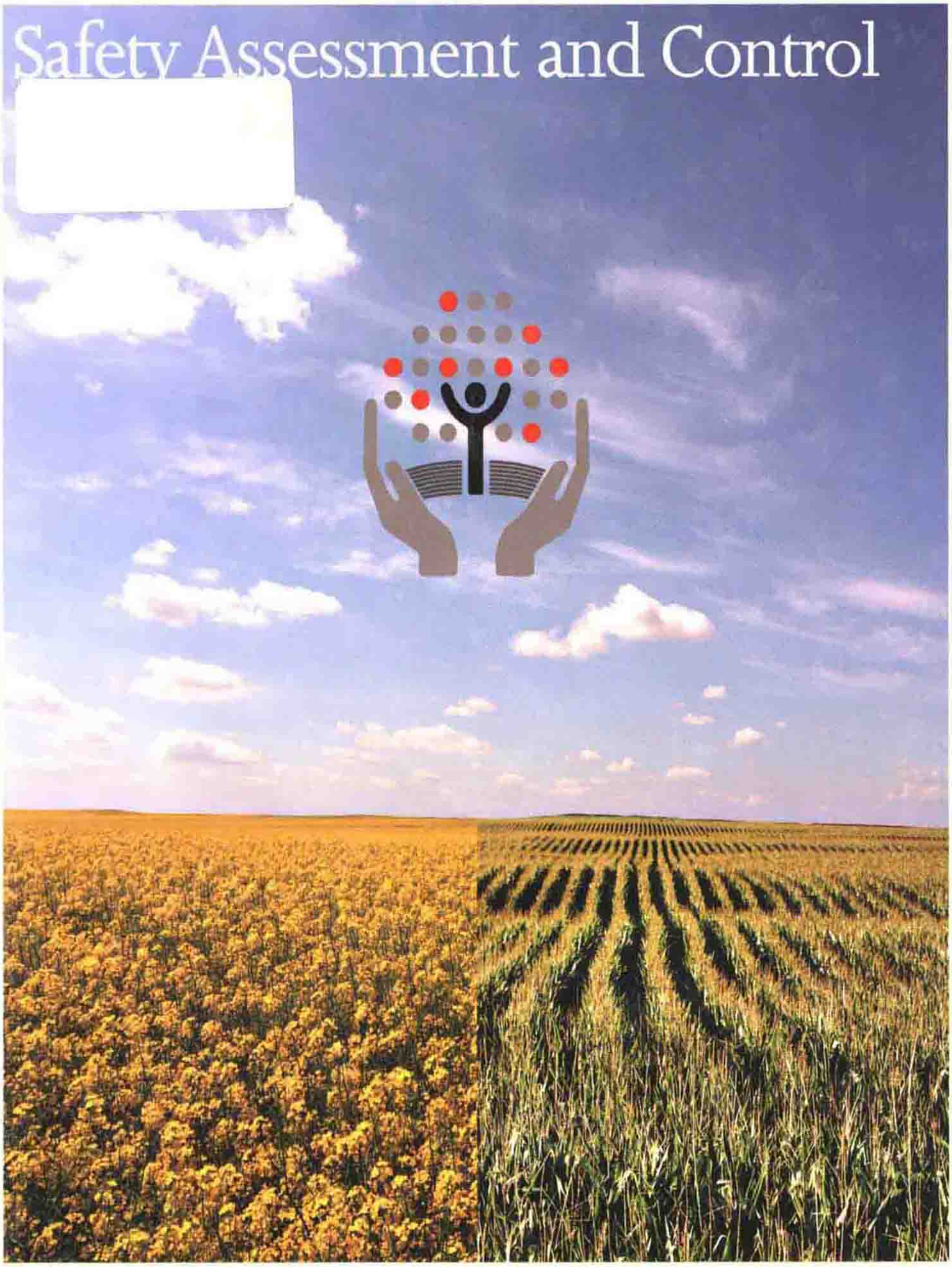
Genetically Modified Food Sources

Safety Assessment and Control



Edited By **V.A. Tutelyan**

Genetically Modified Food Sources

Safety Assessment and Control

Edited by

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Genetically Modified Food Sources: Safety Assessment and Control

Edited by Prof. V. A. Tutelyan, Ph.D., D.Sc.

This book reports for the first time the detailed results of the studies on human and animal food/feed safety assessment of 15 lines of genetically modified plants. The authors focused on issues of the basic legislative regulations of plant biotechnology in the Russian Federation, and approaches to the human and animal assessment of safety of food and feed, and control of the food produced from the genetically modified organisms. The book is addressed to a wide community of the specialists working in various fields of medicine and biology, to the students and postgraduates focusing on the problems of modern biotechnology and biological safety, and sanitary inspectors.

Abbreviations

AI	Anaphylactic Index
BV	Biological Value
CaMV	Cauliflower Mosaic Virus
DC	Diene Conjugates
DNA	Deoxyribonucleic acid
cDNA	Complementary DNA
T-DNA	Transferred DNA
ESR	Erythrocyte Sedimentation Rate
GM plants	Genetically Modified plants
GMO	Genetically Modified Organism
GMS	Genetically Modified Source
GOST	National Standards of Russian Federation
HEA	Hen's Egg Albumin
HPLC	High-Performance Liquid Chromatography
LPO	Lipid Peroxidation
MCH	Mean Cell Hemoglobin
MCHC	Mean Cell Hemoglobin Concentration
MCV	Mean Cell Volume
MDA	Malonic Dialdehyde
NPER	Net Protein Efficiency Ratio
PCR	Polymerase Chain Reaction
PER	Protein Efficiency Ratio
PFA	Polyunsaturated Fatty Acid
QMAFAnM	Quantity of Mesophilic Aerobic and Anaerobic Microorganisms
RAS	Russian Academy of Sciences
RAMS	Russian Academy of Medical Science
RAAS	Russian Academy of Agricultural Sciences
RI	Reaction Index
RNA	Ribonucleic acid
mRNA	Messenger Informational RNA
SE	Sheep Erythrocytes

SOD	Superoxide Dismutase
TLC	Thin-Layer Chromatography
TPD	True Protein Digestibility
WHO	World Health Organization

Introduction

The basic law of nature is maintenance of life by striving through reproduction to maintain survival of the biological species. This law applies to all living organisms from single-cell to human beings. The most important prerequisite to species preservation is the provision of sufficient amount and necessary assortment of nutritional elements (food for humans), which constitute the source of energy, building material, and biologically active regulatory substances. Deficiency or decrease in bioavailability of these nutritional substances lead to reduction or even to complete disappearance of population, while sufficient supply and availability of these substances results in the development, perfection, and expansion of the natural habitat of the living organisms.

Throughout history, mankind has tried to solve the fundamental problem of reliable food provision. While humans coped with this problem by persistent search for food and the means to preserve it, the vital problem of the settled population became not only production and preservation of the food, but also maximization of the output from natural food sources. While engaged in plant cultivation and cattle breeding, humans not only used all available means to enhance production of conventional varieties and livestock species, but they also searched for novel food sources.

Evidently, the cornerstone of many (if not all) political, socio-economic, military, and other cataclysms shaking human society during its historical development was the struggle to expand territory in order to gain access to additional food sources.

To resolve the present challenge to provide mankind with food, a wide variety of technical and technological means based on scientific achievements are being used. The most important responsibility of any state is to ensure availability and safety of food in the country, based on its own crop and cattle-breeding production in sufficient amounts to provide the necessary source of raw materials to meet the requirements of any human being in energy, food, and biologically active substances, thereby ensuring the nation's health. One of the most efficient and promising ways to increase food resources is based

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on application of the methods of modern biotechnology, which emerged at the interfaces between fundamental research avenues and became a powerful production force capable of contributing significantly to solution of food production challenges. Fundamental studies of the recent decades in medicine and biology, including genetics, genomics, and postgenomic technologies, opened a novel scientific field: genetic engineering. The potency of genetic engineering made feasible the replacement of the chaotic empirical search for favorable mutations by the targeted modification of genome to obtain the desired traits. First of all, it is used in plant cultivation and production of genetically modified (GM) plants with increased yield, extended shelf-life, and tolerance to various natural factors. Even now the food derived from transgenic plants, an important product of genetic engineering, significantly contributes to the global food balance.

There are several equally important aspects of the practical use of GM food sources. The first aspect relates to the technology of development and logistics of large-scale production of the new plant varieties. Until recently, it was not only an extremely sophisticated but also a very long and expensive process. However, experience acquired in the last decade, development of new methods, and improvement of the technology have recently contributed to reduction of the time and material expenditures required to bring new products to market.

At the same time, the role of the second aspect—the development and improvement of the system of human and animal health safety assessment of food derived from GM plants—has increased significantly. Currently, this aspect is the most important in decision-making about admission of GM plants to large-scale production and on their use as food and feed sources.

The third aspect concerns protection of society against intended harmful application of modern biological technologies. Any technology can be used for both welfare or detriment of man. Examples are the outstanding achievements in chemistry and microbiology that were also used to make poison gases and biological weaponry for military purposes, the use of nuclear power to provide energy as well as military applications like the atomic bomb, etc. The most important if not unique way to protect mankind from the potential unintended side effects of scientific and technological progress is to set high standards of social and industrial culture, maintain strict observance of technological requirements, and establish uncompromised control and supervisory measures.

The possibility of careless handling of projects intended to create GM food sources, and the need to assess their safety and the feasibility of obtaining genetically modified organisms (GMOs) for biological terrorism, explain the critical importance of a standardized and methodical basis for safety assessment and reliable monitoring of GMO production.

Finally, the fourth aspect unites a number of problems that seem insignificant at first glance, but become extremely important in relation to dissemination of information among professionals and the general population. Although scientific society possesses a well-developed system of scientific and technical information, the field of practical biotechnology is rather closed and does not publish broadly enough a wide variety of scientific literature on genetic engineering technology and the results of the related medical and biological studies intended to assess the safety of GMOs. Distribution of such information among the civilian population is far worse. Sad experience in Russia illustrates that insufficient attention to public relations and accessibility of information by the general population not only impedes technological progress, but also negatively impacts promising industrial applications.

The negative Russian experience of banned genetic research during the 1940s is instructive: the ignorant leadership of the country eliminated and buried genetic science at a time when it was rated highly in the world. As a result, the country was set back for decades. Now the development of some fields in this science in Russia lags behind the world level—but, one hopes, not forever. Another example is shown by the dramatic events at the end of the twentieth century. To this time, Russia had the most powerful microbiological industry in the world. Ten factories produced 1.5 million tons of fodder protein, which formed a reliable forage reserve for poultry farming and partially for cattle breeding. At this time, scientific data attesting the safety of microbiologically synthesized protein was rapidly accumulating. This problem was intensively studied in dozens of research institutes of the Soviet Union Academy of Sciences, Academy of Medical Sciences, V. I. Lenin All-Union Academy of Agriculture, Ministry of Health, Ministry of Agriculture, Central Directorate of Microbiological Industry of the USSR, and in several research institutes in East Germany. These studies yielded comprehensive data attesting to the safety of the use of microbiologically synthesized fodder protein.

However, one or two biotechnological companies producing the fodder protein identified problems related to the negative ecological effect of this production on the environment. The corresponding technological defects could be easily eliminated. Unfortunately, this was the period of election to the State Duma (Russian Parliament) characterized by especially destructive campaigns of some politicians. The problems of microbiological production became the focus of fiery speeches, which led to an absurd situation whereby a few people ignorant in microbiological science became parliamentarians and adhered to their election pledges. As a result, not only the problematic factories, but all similar production plants were closed. The country lost the entire branch of microbiological industry. Who can count the negative consequences of such forcible measures that have nothing to do with economic science and common sense? The losses of forage reserves led to persistent and progressive reduction of cattle breeding and virtually complete loss of poultry farming. Russia became dependent on food imports. Instead of the development of the domestic food industry, the country must buy foreign food. This is an example of how political ambitions can deliver a blow to food production in Russia—an event with consequences that will be experienced for a long time.

In 1994, the USA registered the first GM tomato for use as food (variety FLAVR SAVR), with enhanced resistance to rotting and increased shelf-life. Foreign countries quickly appreciated the evident advantages of agricultural GM crops and widely applied genetic engineering in plant cultivation. As a result, production of GM food sources steadily increased. At present, there is a real possibility to supply the Russian food market with GM products as well.

Consequently, the professionals of relevant ministries and departments developed the necessary legislative, normative, and methodical principles for regulation of the requirements and procedure to assess safety of GM food products and to control their presence on the food market. It is worthy of note that all the work to create the regulatory and methodological basis was prospective, as the world production of GM food was negligible at that time.

With the active participation of academician of RAS M. P. Kirpichnikov, academician of RAMS G. G. Onishchenko, academician of RAAS K. G. Skryabin, and other scientists, a system for the safety assessment of plant-derived GMOs and a system for post-market monitoring were created, and both directives are being updated in response to the requirements of modern science. For example, the medico-biological assessment of GMO safety includes the use of such modern methods as proteomic and metabolomic analyses. At present, the Russian national system of GMO safety assessment is the strictest in the world—it has more stringent requirements than those of the USA, Canada, Australia, Japan, or the European Union and is stricter than recommended by the WHO. Experience acquired during previous years has played an important role in the development of the GMO safety assessment system.

The system for monitoring of food containing GM crops secures maximum protection of the Russian food market from GMOs not registered in Russia. In 1998–2007, the Russian Consumption Inspectorate approved a number of standards and methodical directives (Sanitary Regulation, Standards, and Methodical Directives) that regulated the order and methods to control GM food products. These Directives introduced obligatory labeling of such products. Some control methods were approved as the National Standards. Due to the efforts of the Head State Sanitary Inspector of Russia, the entire system of Russian Consumption Inspectorate has the necessary instrumental and methodical basis as well as qualified specialists to efficiently monitor GMOs in all states of the Russian Federation. At present, the monitoring system for food containing GM crops carries out tens of thousands of analyses every year.

Thus, the principal problems of GMO safety assessment and control were solved, although the task of providing information for the Russian population is still pending. While the requirement to indicate the use of GM products in the label of a food product is absolutely substantiated and supported by the corresponding legislative and standard acts, the development of an adequate public education on GM sources of food is far from being achieved.

Retrospective analysis of these issues shows that pioneers of new technologies were partially "guilty" in allowing the rise of social aversion to the genetic innovations in the food industry. The public should be informed of the advent of novel technologies. Formation of public views on GM food should have been started as early as 1990s. This has nothing to do with PR actions, where persistent and annoying repetition keeps information at the subconscious level. Only open scientific information, popular science broadcasting and publications, educational programs, and explanatory work with the population allow formation of the correct social view on this issue. However, when the first GM products were placed on the market, the information on genetically modified food was confidential or highly specific, and could be used only by professionals. The reasons of confidentiality (classified know-how) and restriction of corresponding information within the limited circle of scientists (sophisticated technology, high-end scientific level) are understandable. Now it is evident that wide awareness of society about the nature of biotechnology is important; it could probably have prevented the present state of affairs in biotechnology in Russia.

Currently there are two camps in relation to biotechnology: the supporters and opponents of GM food. In those countries where the public is informed of the registration of novel GM food and placement on the agricultural market (USA, China, Australia), people have easily adopted the new technologies and relied on the state system of safety assessment of the new products. Examples of the opposite approach were shown until recently by the countries of the European Union, who limited the use of GM food for purely economic reasons, as well as some African countries. The same position is presently shared by Russia. In those countries where the public has not been sufficiently informed about the safety of GM food, people are cautious about GM food products or refuse to use them.

Unfortunately, such public opinion is unjustifiably supported by some researchers. The issue is the subject of negative propaganda that denies scientific data and arguments supporting GM food. The campaign against GM food seems profitable to some forces that seek to place barriers in the way of Russia's adoption of modern agricultural technologies. It is noteworthy that this discrediting campaign is focused only on GM crops but it does not "see" similar objects of genetic modification, the microorganisms, which for a long time have been successfully used in the pharmaceutical and food industry. In both fields, the products are meant for human consumption. Why can some GM products be used and others cannot? If the opponents care for the human genome, they should be equally concerned about GM crops and GM microorganisms. It is a good sign that, despite these opponents, the Russian Consumption Inspectorate and Russian Academy of Medical Sciences has developed an efficient system to control the safety and life-cycle of GM microorganisms. Thus, it is impossible to prevent progress in science in general and in its biotechnological branch in particular. Evidently, the future belongs to biotechnology. The next generation of GM crops is entering the market place. Some of these GM crops have improved nutritional characteristics and are able to produce higher yields under more challenging environmental conditions in the field. Biotechnology can raise the standards of human food and provide mankind with sufficient amount of vitally important minor food components such as vitamins and fatty acids, thereby improving intake of important nutrients.

More sophisticated technologies such as nanotechnology are presently being developed and introduced into modern life. To avoid the past mistakes, the developers of nanotechnologies and nanomaterials should make an effort to educate the public in these fields. The specialists should focus on the problem of safety control in nanotechnology and nanomaterials not in the future, but today. In Russia, there are some pronounced steps in this direction. However, there is a concern of potential delays in providing information to the population.

Biotechnology continues to grow and develop globally. Planting of biotechnology-derived agricultural crops has been increasing around the world. In 2010, 29 counties (the European included) planted about 148 million hectares with transgenic crops. It is expected that this figure will raise to 200 million hectares in 2015, which will account for 14% of cultivated land on the planet. Forty countries in all continents are predicted to adopt biotechnology-derived agricultural crops. In 2010, approximately one hundred lines of GM plants were registered and approved for a large-scale cultivation. Certainly, this is growing evidence indicating the considerable promise of biotechnology for the development of food and feed resources. However, in Russia we still delay the implementation of this technology and our agricultural production falls behind those countries that have adopted biotechnology. Russia has lagged the world leaders for 10–15 years. New measures should be taken to reduce this delay.

This book is an attempt to fill the informational vacuum on the safety assessment of GM crops in global scientific literature. In addition to specifics of legislative control of production and monitoring of food derived from

GM plants, as well as the principles and approaches to human and animal health and environmental assessment of their safety, this book reports for the first time the detailed results of experimental studies carried out on 15 varieties of various biotechnology-derived agricultural crops, which preceded the registration procedures in the Russian Federation. The last chapters describe important data on monitoring of the food derived from transgenic crops.

The path to production of this book met several challenges. Developers of the biotechnology-derived crops discussed herein raised confidentiality barriers which had to be overcome. The book is presented for the judgment of professionals, and we believe that it will be useful for a wide community of researchers, engineers, physicians, and biologists working in biotechnology, genetics, toxicology, hygiene, plant cultivation, etc.

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Prof. V. A. Tutelyan

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