

Biological Invasions And Biodiversity Threats Linked To Genetically Modified Organisms

Yuvaraj S¹, Sunita C Mesta², Sumitha.E^{3*}

¹Crescent School of Pharmacy, B.S.Abdur Rahman Crescent Institute of Science & Technology, Tamilnadu, India

²Department of Microbiology and tissue culture, JSS Academy of Higher Education and Research, Mysore, Karnataka, India

^{3*}Department of Biotechnology and Bioinformatics JSS Academy of Higher Education and Research, Mysore, Karnataka, India

***Corresponding Author:** Sumitha.E
Mail: sumithae@jssuni.edu.in

Abstract

Concerns about biological invasions and their potential impact on biodiversity have come to light due to genetically modified organisms (GMOs). The introduction of GMOs into natural ecosystems carries with it several possible risks that may result in negative effects which are, however, unintentional. That is, the GMOs having traits designed for increased productivity on the farm could also give them an added advantage in terms of invasiveness. These attributes could allow GMOs to outcompete native species by enhancing reproduction rates and providing resistance to pests and diseases, as well as improving resource utilization. The loss of indigenous flora and fauna leads to changes in welfare systems and can threaten biodiversity in a second step. The possibility of gene flow between GMOs and their wild relatives is a major concern because hybridization can lead to the creation of new species with unknown consequences for the environment. The transfer of transgenes from GMOs to wild populations relates to the stability and integrity of natural ecosystems. In addition, hybridization may take place between the introduced genes and other members of the population, leading to the production of hybrids that have a competitive advantage over their non-GMO counterparts. The implementation of regulatory measures is important in reducing these risks. Environmental risk assessments need to be ascertained to detect potential effects that could be exerted by GMOs on ecosystems and biodiversity before allowing their release. Implementing containment strategies such as geographical limits or physical barriers plays a role in stopping unintentional spread and interactions with the environment. To detect and control any unforeseen environmental variations, regular monitoring and surveillance systems are very important. Even after these steps, there are still knowledge data gaps that need more research on the long-term impacts GMOs have on biodiversity. It is important to understand how GMOs interact with other stressors as well such as habitat loss and climate change to be able to formulate complete management methods. An intricate and flexible approach is necessary as we navigate the challenging landscape of agricultural innovation to reap the benefits that GMOs can bring while maintaining the delicate balance of natural ecosystems and biodiversity.

Keywords: Genetically modified organisms, Gene drive, regulation, Biological Invasions

Introduction

Biotechnology is becoming a powerful force in the world, providing never-before-seen possibilities to tackle issues related to environmental preservation, health, and agriculture (Montagu, 2020). These developments have not come without controversy, though, since several ethical, social, and environmental issues are brought up by biotechnology's revolutionary potential. The divergent viewpoints have influenced public debate and policy decisions as they delve into the intricate terrain of biotechnology-related problems (Trump et al., 2023). Numerous cutting-edge methods, including genetic engineering, synthetic biology, and gene editing, are included in the field of biotechnology and have the potential to completely transform many facets of human existence. While the scientific community has been enthralled with the promises of increased crop yields, customized treatment, and creative environmental solutions, a parallel story has emerged, revealing concerns and scepticism in the public. One of the most divisive topics in contemporary agriculture has been the introduction of genetically modified (GM) crops and livestock, which has generated intense discussion and differing views on the advantages and disadvantages of the practice (Schnell et al., 2015). The debates surrounding genetically modified crops and animals will be examined in this introduction, which will also shed light on the intricate interactions between scientific, economic, ethical, and environmental factors that have driven the ongoing discussion. Through precise processes, genetic material is altered to create genetically modified organisms (GMOs), which are then often intended to bestow beneficial features like pest resistance, herbicide tolerance, or better nutritional content (Chen & Lin, 2013).

Genetically modified crops have been produced in the field of agriculture to tackle issues including environmental sustainability, agricultural yields, and food security (Pacher & Puchta, 2017). The possible effects of genetically modified agriculture on the environment are one of the main points of disagreement. Unintended consequences have

been brought up, including the emergence of resistant pests and the possible spread of altered genes to relatives in the wild, both of which could have unpredictable effects on ecosystems. Furthermore, the usage of herbicides has increased due to the use of some GM crops that are resistant to them, which raises concerns about the long-term impacts on soil health and biodiversity. Regarding the economy, the main topics of discussion are farmer livelihoods and corporate control. The dominance of a small number of agro-biotech businesses, according to critics, raises concerns about fair competition, intellectual property rights, and the effects on small-scale farmers. Notwithstanding these reservations, proponents of genetically modified crops and animals emphasize how they can help with global issues like hunger, malnourishment, and the demand for more environmentally friendly farming methods (Raman, 2017). Schematic representation of the generation of genetically modified crops is depicted in figure 1.

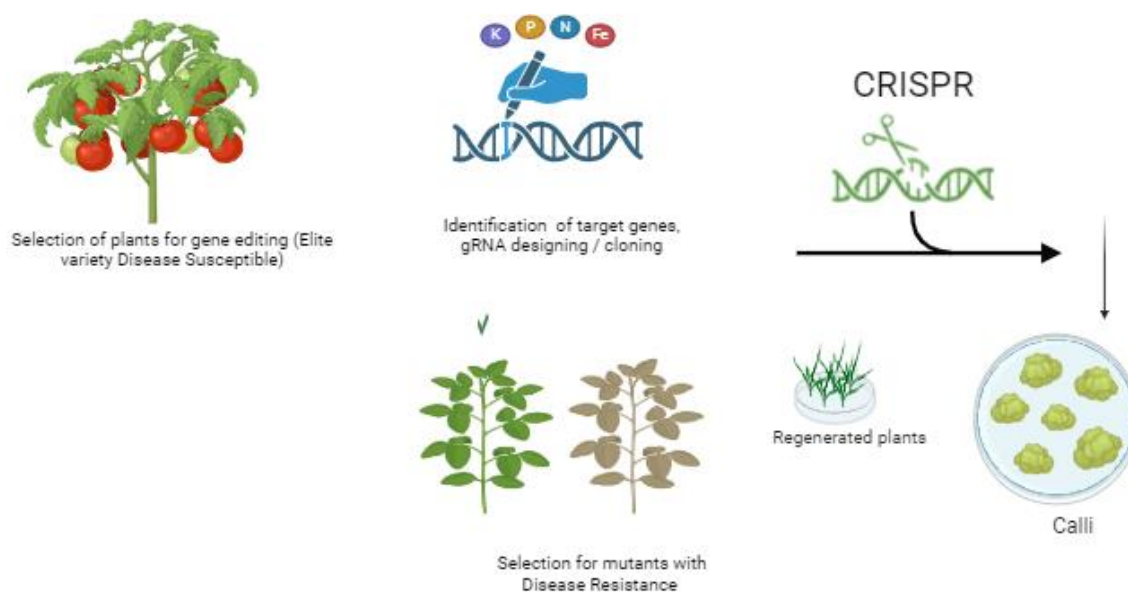


Figure: 1 Sequential event in the generation of genetically modified crops.

Need for Genetically modified crops/organisms.

To provide a sufficient and sustainable food supply for the world's expanding population which is predicted to approach 10 billion people by 2050—a major challenge must be addressed. The effects of climate change on conventional agriculture include temperature extremes, changing precipitation patterns, and unpredictable weather patterns. Many times, agriculture results in resource depletion and environmental damage because it uses a significant quantity of land, water, and energy. Pesticide-resistant pests, environmental contamination, and harm to non-target organisms are all consequences of conventional agriculture's heavy reliance on chemical pesticides. Extremely common, especially in underdeveloped nations, are malnutrition and deficiencies in vital vitamins and minerals. The loss of crops, erratic markets, and high production expenses are common problems for farmers. The use of resources inefficiently, environmental damage, and biodiversity loss are all possible outcomes of conventional farming methods (Çakmakçı, Salık, & Çakmakçı, 2023; Pérez-Escamilla, 2017; Shahmohammadloo, Febria, Fraser, & Sibley, 2021). Some communities may experience particular dietary shortages, such as vitamin A deficiency causing childhood blindness. Livestock illnesses can affect food production and have serious economic repercussions. Hence conventional farming practices will not be enough to satisfy the changing needs of the global community.

Examples of Genetically modified crops

Bacillus thuringiensis (Bt) is the bacteria from which a toxin is expressed in Bt cotton (Table 1). By acting as an insecticide, this toxin gives the plant defence against pests like the cotton bollworm (Azevedo et al., 2018; Carrière, Crickmore, & Tabashnik, 2015; Zafar et al., 2020). To make ready soybeans resistant to the herbicide glyphosate, genetic modification is used. This makes it possible for farmers to control weeds with herbicides containing glyphosate without endangering the soybean crop. Beta-carotene, a precursor to vitamin A, is produced by genetically modifying rice to generate golden rice (Azevedo et al., 2018; Carrière et al., 2015; Zafar et al., 2020). This change addresses vitamin A deficiency, especially in populations where rice is a major component of the diet. Varieties of genetically modified maize have been created to resist water scarcity. Increased drought resistance in these crops means more consistent production in areas where water is scarce (Visibelli, Roncaglia, Spiga, & Santucci, 2023). Genetically engineered Innate® potatoes have less bruising and release less acrylamide when cooked at high temperatures. One possible carcinogen that develops after cooking is acrylamide. Genetically engineered AquAdvantage® Salmon grows

to market size faster than conventional salmon. The alteration is the insertion of a gene that controls growth hormone from a different species of fish. Because of genetic modification, Enviropig™ produces less phosphorus in its dung. This change takes care of issues with phosphorus runoff from cattle activities that are relevant to the environment. Hereditary antithrombin deficiency is treated with ATryn®, a transgenic goat that generates antithrombin, a protein. One source of this healing protein is goat's milk. Genetically engineered Innate® potatoes have less bruising and release less acrylamide when cooked at high temperatures. One possible carcinogen that develops after cooking is acrylamide. Genetically engineered AquAdvantage® Salmon grows to market size faster than conventional salmon (Visibelli et al., 2023). The alteration is the insertion of a gene that controls growth hormone from a different species of fish. Because of genetic modification, Enviropig™ produces less phosphorus in its dung. This change takes care of issues with phosphorus runoff from cattle activities that are relevant to the environment. Hereditary antithrombin deficiency is treated with ATryn®, a transgenic goat that generates antithrombin, a protein. One source of this healing protein is goat's milk.

GM Crop	Advantages	Disadvantages	Species Used	Reference
Bt Corn	<ul style="list-style-type: none"> - Resistance to pests (e.g., European corn borer) - Reduced need for chemical pesticides 	<ul style="list-style-type: none"> - Potential for pest resistance development - Concerns about non-target species impact 	<i>Zea mays</i> (corn)	ISAAA (2018); James (2017)
Golden Rice	<ul style="list-style-type: none"> - Biofortified with Vitamin A - Potential to reduce Vitamin A deficiency in developing countries 	<ul style="list-style-type: none"> - Controversy over GM food safety - Limited adoption and regulatory hurdles 	<i>Oryza sativa</i> (rice)	Tang et al. (2012); Potrykus (2010)
Roundup Ready Soybeans	<ul style="list-style-type: none"> - Herbicide tolerance - Easier weed management - Reduced tillage agriculture 	<ul style="list-style-type: none"> - Increased herbicide use - Development of herbicide-resistant weeds 	<i>Glycine max</i> (soybean)	Duke & Powles (2008); Benbrook (2012)
Virus-Resistant Papaya	<ul style="list-style-type: none"> - Resistance to Papaya Ringspot Virus (PRSV) - Saved papaya industry in Hawaii 	<ul style="list-style-type: none"> - Concerns over gene flow to wild relatives - Limited global acceptance 	<i>Carica papaya</i> (papaya)	Gonsalves (1998); Tripathi et al. (2020)
Bt Cotton	<ul style="list-style-type: none"> - Resistance to bollworm pests - Reduced pesticide use - Increased yield 	<ul style="list-style-type: none"> - Potential for pest resistance - High seed costs - Ethical concerns in some regions 	<i>Gossypium hirsutum</i> (cotton)	Qaim & Zilberman (2003); ISAAA (2019)
Genetically Modified Potatoes	<ul style="list-style-type: none"> - Resistance to pests like the Colorado potato beetle - Reduced bruising and black spots 	<ul style="list-style-type: none"> - Market resistance and rejection by some consumers - Potential for unintended effects on health 	<i>Solanum tuberosum</i> (potato)	Rommens (2010); NRC (2016)

Table 1: Examples of genetically modified crops

The prospect of addressing these issues in a focused and effective way is what motivates the creation of genetically modified organisms, or GMOs. Because of the ongoing global population growth, more food must be produced to keep up with demand. It is possible to create genetically modified crops to produce more while withstanding severe environmental conditions and pest resistance (Visibelli et al., 2023). These characteristics help to guarantee food security for a growing world population by increasing agricultural production. Increased temperatures, altered precipitation patterns, and a rise in extreme weather occurrences are some of the problems brought on by climate change. Conventional agriculture frequently uses a lot of chemical pesticides and herbicides, which pollute the environment and harm organisms that are not intended targets. Genetically modified crops that are designed to resist particular pests or manufacture their insecticides might lessen the need for external chemical inputs, decreasing their negative effects on the environment and encouraging environmentally friendly agriculture (Jha & Warkentin, 2020; Ofori, Antoniello, English, & Aryee, 2022) methods. Micronutrient deficits and malnutrition are common problems, particularly in underdeveloped nations. It is possible to use genetic modification to increase the nutritional value of crops. For example, biofortified crops can alleviate nutritional deficits in vulnerable communities by offering higher levels of vital vitamins

and minerals(Visibelli et al., 2023). Livestock illnesses can affect food production and have serious economic repercussions. It is possible to genetically modify animals to resist particular diseases, which lessens the need for antibiotics and lowers the possibility of disease outbreaks in animal populations.

Certain medications and medical procedures might be costly and logistically difficult to produce. It is possible to produce useful medicinal compounds in plants or animals by genetic alteration. For instance, insulin, a vital diabetes therapy, is made by genetically engineered bacteria(Visibelli et al., 2023). Ecosystems are under attack from invasive species, habitat loss, and climate change, which is causing biodiversity to dwindle. Conservation efforts can benefit from genetic modification, which can be used to create genetically modified organisms that suppress invading species or bring back animals that have particular qualities to restore ecosystems. Industries frequently produce materials and energy from non-renewable resources. To create biofuels, enzymes, and bio-based materials, genetically modified microbes can be employed in industrial operations. This helps to promote environmentally friendly and sustainable industrial practices. Agriculture and public health are threatened by pests and disease vectors. Targeted and ecologically benign pest or disease vector management is possible using genetic modification. For instance, mosquitoes that have undergone genetic modification may be engineered to spread fewer vector-borne illnesses.- Problem: Adaptive agricultural practices are necessary due to changing environmental circumstances and emerging pests. Through the production of crops that are climate-adaptive, genetic modification ensures agriculture's sustainability and resilience in the face of changing difficulties. To address these issues, genetically modified plants and animals are necessary; nonetheless, it is important to take the ethical, environmental, and societal ramifications into account. To maximize the potential advantages of genetic alteration while reducing the risks, it is crucial to strike a balance between innovation, responsible use, and careful risk assessment.

Impact of Invasive Species on the Environment:

Invasive species outcompete native plants, the ecosystem is impacted and agricultural productivity is decreased. But they might also have a detrimental effect on people's health. As a byproduct of tainted birdseed, ragweed (*Ambrosia artemisiifolia* L.) was introduced to Europe from North America. According to Richter et al, 2013, it has expanded quickly and generates extremely allergic pollen, which affects 4-5 % of Europeans with hay fever. High economic losses or damages are also brought on by these invasive species. According to McLeod (2016), the yearly cost of pest animals in Australia was predicted to be \$597 million in 2013–14 due to lost production and control costs. Likewise, weeds were predicted to have cost Australia's economy up to \$5 billion in 2018. It is challenging to eradicate or control invasive species after they have established themselves. To implement integrated pest management strategies, weed and pest control managers require a range of instruments(Visibelli et al., 2023). The OECD Co-operative Research Programme: Biological Resource Management for Sustainable Agricultural Systems (CRP) sponsored the Genetic Biocontrol for Invasive Species Workshop in Tarragona, Spain on March 31, 2019, where a number of these biocontrol techniques, such as sterile-release, YY Males, Trojan Female Technique, and gene drive, were reviewed. The program, using gene drive approaches as a case study, increased knowledge of the advantages and hazards of controlling invasive species generally Table 2.

Invasive Species	Native Region	Invaded Region	Environmental Impact	Control Measures	Reference
Kudzu (<i>Pueraria montana</i>)	Asia	Southeastern United States	<ul style="list-style-type: none"> - Outcompetes native plants for light and nutrients - Leads to loss of biodiversity - Alters ecosystems 	<ul style="list-style-type: none"> - Mechanical removal - Herbicides - Grazing 	Forseth & Innis (2004); USDA (2019)
Zebra Mussel (<i>Dreissena polymorpha</i>)	Eastern Europe	North America	<ul style="list-style-type: none"> - Clogs water intake pipes - Displaces native mussels - Alters aquatic ecosystems by filtering water and reducing plankton 	<ul style="list-style-type: none"> - Chemical treatments - Mechanical removal 	Ricciardi et al. (1998); USGS (2021)
Cane Toad (<i>Rhinella marina</i>)	Central and South America	Australia	<ul style="list-style-type: none"> - Poisonous to native predators - Reduces populations of native species - Competes with native fauna 	<ul style="list-style-type: none"> - Physical removal - Habitat management 	Shine (2010); Phillips et al. (2007)

European Rabbit (<i>Oryctolagus cuniculus</i>)	Europe	Australia, New Zealand	<ul style="list-style-type: none"> - Causes soil erosion by overgrazing - Leads to the decline of native vegetation - Affects agriculture 	<ul style="list-style-type: none"> - Biological control (myxomatosis, calicivirus) - Fencing 	Cooke (2012); Saunders et al. (2010)
Asian Carp (<i>Hypophthalmichthys spp.</i>)	Asia	North America	<ul style="list-style-type: none"> - Competes with native fish for food - Disrupts aquatic ecosystems - Alters water quality 	<ul style="list-style-type: none"> - Electric barriers - Fishing and removal programs 	Kolar et al. (2005); Conover et al. (2007)
Brown Tree Snake (<i>Boiga irregularis</i>)	Australia, Papua New Guinea	Guam	<ul style="list-style-type: none"> - Causes extinction of native bird species - Disrupts local ecosystems - Affects power infrastructure 	<ul style="list-style-type: none"> - Trapping - Use of toxicants - Habitat modification 	Fritts & Rodda (1998); USGS (2020)
Northern Pacific Seastar (<i>Asterias amurensis</i>)	Northern Pacific Ocean	Australia	<ul style="list-style-type: none"> - Preys on native shellfish - Competes with native species - Reduces biodiversity in marine environments 	<ul style="list-style-type: none"> - Mechanical removal - Use of barriers - Monitoring 	Thresher et al. (2000); Hewitt et al. (2004)
Water Hyacinth (<i>Eichhornia crassipes</i>)	South America	Africa, Asia, North America	<ul style="list-style-type: none"> - Clogs waterways - Depletes oxygen in water, harming fish - Reduces water flow and increases flooding risk 	<ul style="list-style-type: none"> - Mechanical removal - Biological control (insects, fungi) - Herbicides 	Villamagna & Murphy (2010); Ndimele et al. (2011)

Table 2: Impact of invasive species on the environment:

Nailing down the debates around genetically modified crops and animals requires balancing innovation and caution, taking care of regulatory structures, and encouraging a transparent and educated public dialogue (Visibelli et al., 2023). This introduction lays the groundwork for an in-depth examination of the complex problems related to genetically modified crops and animals, exploring the environmental, ethical, scientific, and economic aspects that influence the continuing discussions and choices in this quickly developing subject (Visibelli et al., 2023). The capacity to alter an organism's genetic composition presents hitherto unseen opportunities for tackling global issues including food scarcity, climate change, and sustainable agriculture. Talks on GMOs however cover a wide range of viewpoints, from the scientific community's enthusiasm about the possible advantages to the public's concerns about safety and long-term effects. The complex field of genetically modified organisms goes into the science underlying their development, the wide range of industries in which they are used, and the complex web of ethical, environmental, and societal issues that surround their use. Understanding the complexities of GMOs thoroughly is essential for making educated decisions and contributing to discussions as GMOs continue to influence agriculture and biotechnology. In the fields of biology and agriculture, genetically modified organisms, or GMOs, are a revolutionary frontier wherein an organism's genetic makeup is purposefully changed to give particular traits or features. With the use of recombinant DNA techniques, genes are manipulated in this technology to improve desirable characteristics like insect resistance, environmental tolerance, or improved nutritional value. With promises of higher crop yields, less pesticide usage, and improved food security, the introduction of GMOs has generated both excitement and controversy. On the one hand, these developments have raised questions about potential health hazards, environmental effects, and ethical issues.

Gene Drive (GD) as a Specific Example of the Need for Invasive Species Control

Gene Drive (GD) refers to a range of molecular biology applications that allow the introduction of genetic elements that are inherited at frequencies higher than those predicted by Mendelian rules (López Del Amo et al., 2020), i.e., greater than the expected 50% transmission of a particular allele to the following generation. Only out-crossing sexually reproducing organisms in which GDs are active in the germline or during embryonic development can use them. Depending on the sequence targeted, gene drives may be restricted to specific regions or populations, or they may theoretically spread over a species' whole population. Many organisms naturally exhibit various forms of gene drives. Meiotic drives have been documented in plants and insects, such as the maternal-effect dominant embryonic arrest

(Medea) in flour beetles and the cytoplasmic incompatibility of *Wolbachia* bacteria in *Drosophila melanogaster* and *Silene latifolia* (López Del Amo et al., 2020). A variety of arthropod hosts get infected with the bacteria *Wolbachia*, which alters host reproduction. They produce a gene drive by killing men or by making eggs and sperm incompatible. Because the bacteria manipulate reproduction, infected females are more likely to survive. These germs are inherited from mothers.

After being injected into *Aedes aegypti* populations, *Wolbachia pipientis* significantly lowers the dengue virus's and other human infections' ability to replicate within infected mosquitoes. Field trials of this work are governed by the Australian Pesticides and Veterinary Medicines Authority under the Agricultural and Veterinary Medicines Act because the transfer of a whole organism is not thought to result in a GMO (López Del Amo et al., 2020). A variety of arthropod hosts get infected with the bacteria *Wolbachia*, which alters host reproduction. They produce a gene drive by killing men or by making eggs and sperm incompatible. Because the bacteria manipulate reproduction, infected females are more likely to survive. These germs are inherited from mothers.

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Essentials of Regulation

Most regulatory frameworks seek to safeguard the environment, and the health of people and animals, and to allow contemporary biotechnology to conduct research and generate useful products. Every action in life carries some risk, thus innovative principles and regulatory precautions must take into account the dangers associated with acting or not acting. Food instability, social catastrophes, and biodiversity loss may all be made more likely by inhibiting innovation, for example by overly cautious and stringent GMO laws. At a time when Earth is being significantly impacted by human population expansion, biodiversity loss, climate change, and declining natural resources. Since incentives and limitations play a critical role in determining whether products get past the R&D stage, regulation is key for structuring innovation. Technical development and the spectrum of economic profit are significantly influenced by political and economic settings, and technical priorities are determined by society's needs. Only when new ideas are technologically feasible, desirable, and useful for human values, commercially viable, and supported by regulations can they be considered innovative. Research initiatives on vector control and agriculture have been started as the technological viability of gene drives has advanced quickly (National Academies of Sciences, Engineering, and Medicine, 2016). For many of these, it is still too early to tell whether they will be successful, viable businesses, or well-liked by the general public. When it comes to the evaluation of invasive species, protective objectives reflect human values. The trade-off between the undesirable off-target consequences of the controlling technology and the environmental/health harm caused by the invasive species, pest, or disease determines whether control measures are appropriate. This discussion will also be influenced by the public's worries about GMOs (Adikusuma, Williams, Grutzner, Hughes, & Thomas, 2017; Teem et al., 2020).

The conflict between concern over the hazards of non-intervention and a need for prudence on intervention risk can be effectively managed with the use of a well-designed risk assessment. Malaria in Europe is a historical example of action for the beneficial eradication of a disease. In Germany and other regions of Europe, malaria was a common illness (Dalitz, 2005). With the use of chemicals and hygienic practices to destroy the mosquitoes that carried malaria, the disease was eradicated. During the eighteenth century, they included the broad-spectrum pesticide spraying in the Italian Po-Valley and the drainage of wetlands in the Oderbruch west of Berlin. What unintentional environmental harm resulted from these efforts is unknown.

Environmental Concerns in the Generation of GMO

Genetic contamination is a hazard when genes from genetically modified crops cross-pollinate with wild relatives or non-GM crops. Unintended effects may arise from this, such as changing the genetic composition of natural populations or even producing hybrid plants with undesirable features (Visibelli et al., 2023). There could be both direct and indirect impacts on biodiversity from the development of genetically engineered crops. Changes in land use patterns, modifications to agricultural attributes, and possible effects on non-target organisms can all lead to changes in local ecosystems, which may influence native plant and animal species. There could be unexpected ecological repercussions when genetically modified organisms are introduced into ecosystems. Unexpected ecological effects could result from altered creatures' behaviour or interactions with non-target species upsetting established ecological balances. Herbicide-resistant weeds have emerged as a result of the cultivation of herbicide-resistant crops (Borggaard & Gimsing, 2008;

Schütte et al., 2017). This tendency may lead to a rise in the use of herbicides, which could have negative effects on the environment and cause weed populations to become more resistant. To keep pests away, some genetically modified crops generate proteins that kill insects. Concerns exist, meanwhile, regarding possible effects on non-target creatures, such as soil microorganisms, beneficial insects, and other ecosystem elements. Concerns concerning the long-term consequences of genetically engineered features are brought up by their persistence in the environment, such as insecticidal proteins. These characteristics could linger in soil or plant matter and might have long-term effects on creatures that are not the intended targets. Genetically engineered crops may cause insects to become resistant to the new features. This may result in fewer GM crops being as effective as they may be and possibly more insect pressure. Concerns over the inadvertent alteration of wild plant populations are raised by the possibility of gene flow from genetically modified crops to their wild counterparts. This may have an impact on these species' evolutionary paths and how they interact with one another in ecosystems. The extensive production of genetically modified crops could result in modifications to land use and agricultural methods. This may lead to changes in the terrain, habitat loss, and fragmentation, which would impact the nearby ecosystems and fauna. An increasing number of genetically modified crop varieties being widely adopted could lead to a reduction in the variety of agroecosystems. Crop resilience to pests, diseases, and shifting environmental circumstances may be impacted by this decline in crop variety. It's unclear how genetically modified crops will affect the environment in the long run. Owing to the intricacy of ecosystems, questions remain about the possible long-term cumulative and synergistic effects of several genetically modified features (Borggaard & Gimsing, 2008; Schütte et al., 2017).

Human health concerns in the generation of genetically modified crop

The potential for allergenicity exists when new proteins are added to genetically engineered crops. People with pre-existing sensitivities can respond to newly produced proteins in GM crops (Visibelli et al., 2023). It's unclear what consequences eating genetically modified food will have in the long run. There are ongoing discussions on possible long-term health effects. Marker genes for antibiotic resistance are frequently used in genetic engineering procedures. Antibiotic resistance may be exacerbated by these genes being transferred to human gut bacteria, which raises concerns. Genetic alterations intended to enhance characteristics like pest resistance or shelf life could unintentionally change the crop's nutritional makeup. It is unclear how the human gut microbiome and genetically engineered foods interact. There may be health consequences for humans from changes in the gut microbiota. Insecticidal proteins are produced by certain genetically modified crops to repel pests. A health danger to humans is raised by the possibility that GM crops will have higher concentrations of these poisons (Visibelli et al., 2023). The possibility that GM crop genes may interact with gut bacterial genes and have unexpected consequences is a source of concern. Potentially unanticipated health hazards may surface with the development of new genetic editing techniques. Some regions may restrict consumer choice and awareness due to the absence of required labelling for genetically modified foods.

Measures to mitigate genetically modified crops

The regulatory approval procedure for genetically modified crops involves thorough studies of allergenicity. Crops are not allowed if considerable dangers are found. Developers discover probable allergens using laboratory testing and bioinformatics. To assess the long-term safety of genetically modified crops, research is always being done. Comprehensive research is mandated by regulatory bodies, and scientific communities keep a close eye out for any new health issues. Researchers are looking for ways to do away with the necessity for antibiotic resistance markers, and some genetically modified crops are created utilizing substitute marker genes (Visibelli et al., 2023). The possibility of gene transfer and its consequences are taken into account in regulatory assessments. Thorough nutritional evaluations are carried out in the course of obtaining regulatory approval. Developers work to minimize unintentional changes in nutritional content that could harm people's health. The relationship between genetically modified foods and the gut microbiota is still being studied. Studies on the breakdown and digestion of genetically modified organisms in the digestive system are included in this. Toxin levels in genetically modified crops are assessed by regulatory evaluations to make sure they are below safe thresholds for ingestion by humans. The processes and probability of horizontal gene transfer are still being studied. Before approving GM crops, regulatory evaluations take these factors into account. Regulations are based on the precautionary principle, and studies are being done to evaluate the safety of new genetic alteration methods (Visibelli et al., 2023). There are processes in place to monitor changes in health risks and take appropriate action. Food safety advocates contend that consumers should be informed about the ingredients in their food. Better labelling procedures and enhanced public awareness help consumers make well-informed decisions. Discussions on the creation and application of genetically modified agriculture incorporate ethical issues. The emphasis is on openness, participation from the public, and well-informed decision-making.

Frameworks for International Law

International instruments offer useful frameworks for the control of Gender Dysfunction. Since the goal of GD applications is to release organisms that might spread across landscapes and get established in the environment, nations are accountable for assessing transboundary risks and for any harm that results from these releases (Visibelli et al., 2023). The Cartagena Protocol unites many, but not all, nations in risk assessment, information sharing, and enhanced

harmonized regulation of GMO transboundary movements. It is probable that before harmonization at higher international levels, regional and bilateral systems will be adopted. According to an international custom, a nation is required to stop wrongdoing and compensate other states for harm that is unjustly caused by its territory. Draft articles regarding a nation's liability for transnational crimes have been released by the UN International Law Commission. These stipulate that "any damage, whether material or moral, caused by the internationally wrongful act of a State" must be made up for (United Nations, 2001). As far as the authors are aware, there is still some uncertainty over whether these guidelines may apply to adverse consequences brought on by GD releases. According to an international custom, a nation is required to stop wrongdoing and compensate other states for harm that is unjustly caused by its territory. Draft articles regarding a nation's liability for transnational crimes have been released by the UN International Law Commission. These stipulate that "any damage, whether material or moral, caused by the internationally wrongful act of a State" must be made up for (United Nations, 2001). As far as the authors are aware, there is still some uncertainty over whether these guidelines may apply to adverse consequences brought on by GD releases.

The Australian Regulatory Framework: GMO Regulation

Australia has laws specifically designed to control actions involving GMOs for environmental and public health protection. All GMO activities, including those involving microbes, plants, and animals, are covered by the Gene Technology Act 2000 (Commonwealth of Australia, 2000) and the Gene Technology Regulations 2001 (Commonwealth of Australia, 2001), both when the GMOs are kept in confined facilities and when they are discharged into the environment (Visibelli et al., 2023). The legislation aims to safeguard both human health and safety as well as the environment by identifying potential dangers associated with gene technology and implementing regulations to manage those risks related to genetically modified organisms. Controlling GMOs that are contained usually concentrates on the appropriateness of the enclosure. Environmental protection is necessary for a GMO that is going to be released into the environment. Generally accomplished by following a step-by-step development process (OECD, 1986): authorizations for small, short-term, confined trials, in which the GMO is removed from the environment after the trial is completed, are informed by data from initial contained research, overseas release(s), or release of a similar GMO. A case-by-case risk assessment and customized risk management plans are needed for every application for release into the environment. Mandatory consultation procedures also need to be met, including formal consultation with the Australian Minister for the Environment ('HAZARD IDENTIFICATION & RISK ASSESSMENT (HIRA)', n.d.).

Australia's Regulation of Gene Drives

The GT legislation has undergone recent modifications that have clarified the regulatory position of organisms created by various technological technologies. When working with organisms that have a functionally designed gene drive, particular risk assessment and management of the associated activities are needed. Information gathering and research progress tracking are made possible by this assessment, which may prompt future regulatory adjustments to address concerns brought up by GD GMOs, especially in the context of deliberate environmental releases. How to breed and carry out controlled studies in the target species are among the genetic and technical details that are required. To identify possible targets and create gRNAs that are specific to these loci, gene drive research also needs access to genome editing technology in the focal species or a comparable species, as well as an annotated reference genome. – Quantification of gene flow (hybridization or horizontal gene transfer) between target and non-target species, searching for potential target sites in non-target species, and suitable modelling of food web structure to predict long-term ecosystem impacts are some examples of ecological and evolutionary data on potential non-target species.

Obstacles Associated with Gene Drive Organizations

The Problem Formulation stage, which establishes the ERA scope and includes the risk hypotheses and protection goals, should be the first step in any ERA. Because of the GD's characteristics and potential for dissemination, it may be possible to bypass the phases of progressive environmental impacts. Examining the data gaps associated with this "shortcut" carefully is essential. Gene drives can be made to be geographically or functionally limited, meaning that they will only function for a certain number of generations. The limited GD persistence in the environment and the necessary efficacy of the GMO release must be taken into account while evaluating population suppression of genetically modified organisms (GDs) if they are intended to be self-limiting. The genetic components that will be distributed across the population, or the "cargo," are an essential component of gene drive technology. The main components of ERA are highlighted by the recent instance of genetic material from a transgenic mosquito strain that was released in Brazil hybridizing and introducing new genetic elements (Evans et al., 2019). What harm is involved, and how probable is it to happen? Although a gene drive was not involved in this specific situation, it does highlight a point that would apply to gene drives. Rather than being an inserted transgene, the genetic components that were introgressed came from the genetic background of transgenic mosquitoes. Therefore, genetic engineering cannot be blamed for any specific consequence that may be noticed. This paradigm is crucial to the globally accepted comparative ERA approach.

To handle uncertainty based on scientific and technological evidence, ERA employs a rational, systematic method. There is currently a great deal of doubt regarding the behaviour of GD creatures released into the environment. Even though modelling can aid in outcome prediction more information is needed to ascertain whether harm could result from

these emissions. To enhance risk assessment, additional information is needed, such as data on altered phenotypic and population data rather than molecular data, which are crucial for assessing environmental risk. Our experience with harmful creatures can guide how to recognize major hazards from those organisms. For instance, a plethora of knowledge exists regarding harmful plants, including crops. Similarly, risk assessors who now regulate pest animals have guidelines on what harms pest animals produce in various situations (e.g., SA pest animal risk assessment handbook). Gene drives could benefit from the extensive knowledge and advice gained from the release of biocontrol agents to combat invasive pests and diseases in numerous nations throughout the world (Legros et al., 2021). The majority of GMOs are now used in agriculture. GDs are unique in that the majority of suggested uses aim to alter natural populations. Though generally, various applications in plants have been proposed (Neve, 2018). Applications of GD are thought to be less applicable to plants or to use in agricultural systems.

There's little doubt that GD in wild animals that benefit the hosting individuals in terms of fitness would raise a GMO's exposure to the environment. Therefore, it is crucial to produce accurate data in the lab and from contained releases (such as islands) before the introduction of borderless/expansive surroundings. Since enzyme-based GDs are the most sophisticated, this is the main area of focus: Before putting a gene drive strategy into action, Redford et al. (2019) state that the following three categories of data concerning the target and non-target species are necessary:

"– How to breed and carry out controlled studies in the target species are among the genetic and technical details that are required. To identify possible targets and create gRNAs that are specific to these loci, gene drive research also needs access to genome editing technology in the focal species or a comparable species, as well as an annotated reference genome (Legros et al., 2021). To predict long-term ecosystem impacts, ecological and evolutionary data on potential nontarget species include quantifying gene flow (hybridization or horizontal gene transfer) between target and nontarget species, identifying potential target sites in nontarget species, and appropriately modelling the structure of the food web. A thorough understanding of the mating system and gene flow between populations is required, as is the ability to quantify both anthropogenic and natural dispersal. Spatially explicit theoretical models can aid in the prediction of gene drive dynamics. Behavioural and demographic data, such as spatiotemporal variation in size, are examples of the ecological information that is required. Population genetic models and spatial population models are the two modelling approaches that support the ERA in the (inherent) light of ambiguity.

Getting ready for impactful gene drive apps

According to Harvey-Samuel et al. (2019), risk and regulatory issues for gene-drive organisms will change depending on how quickly they are introduced into the ecosystem and where they are located. Participants in a workshop at the Lorentz Center in Leiden 20177 provided a preliminary projection for the following ten years: Timetable for GD organisms' possible initial release into the environment: *Anopheles gambiae* (2026), *Felis catus* (2028), *Mus musculus* (2023), and *Rhinella marina* (2026).

Future Directions and Research Needs

As genetically modified organisms become more prevalent in agriculture and other sectors, addressing their potential ecological risks is increasingly important. One of the key concerns is the possibility that GMOs might contribute to biological invasions, which can threaten biodiversity. To manage these risks, future efforts should focus on three main areas: ongoing monitoring and surveillance, adaptive management strategies, and filling critical research gaps. Regular ecological monitoring is crucial for understanding and managing the effects of GMOs on biodiversity. Continuous surveillance helps detect any negative impacts that might arise from introducing GMOs into ecosystems (Bauer-Panskus, Miyazaki, Kawall, & Then, 2020). This is especially important because ecological interactions are complex, and GMOs could have unintended consequences. For instance, a GMO designed to resist pests might inadvertently harm non-target species, leading to a chain reaction of ecological changes. Without proper monitoring, these effects could go unnoticed until significant damage has already occurred. Monitoring also plays a vital role in assessing the long-term impacts of GMOs (Bauer-Panskus et al., 2020). While initial risk assessments provide insight into potential risks, they can't fully predict long-term ecological consequences. Post-release monitoring fills this gap by offering real-world data on how GMOs affect natural environments over time. This information is essential for updating risk assessments, refining regulations, and guiding the development of new, environmentally safe GMOs. Technological advances are opening up new possibilities for monitoring and tracking the ecological impacts of GMOs. One promising tool is environmental DNA (eDNA) analysis, which detects organisms by analyzing DNA fragments found in soil, water, or air samples. eDNA is especially useful for tracking the spread of GMOs and identifying instances where they might hybridize with wild relatives. Remote sensing technologies, such as satellite imagery and drones, can also play a significant role in ecological surveillance (Hilbeck, Meyer, Wynne, & Millstone, 2020). These tools enable large-scale monitoring of ecosystems, providing valuable data on changes in land use, vegetation cover, and species distribution. This data can help identify areas where GMOs might be having an impact, allowing for targeted interventions to prevent or mitigate adverse effects. Additionally, advances in bioinformatics and data analysis are enhancing our ability to process and interpret large volumes of ecological data. For example, machine learning algorithms can be used to detect patterns and trends in monitoring data, helping to identify early warning signs of ecological disruption caused by GMOs. These technologies also allow for the integration of data from multiple sources, offering a more comprehensive understanding of the ecological impacts of GMOs (Hilbeck et al., 2020). Given the uncertainties surrounding the ecological impacts of

GMOs, adaptive management strategies are essential. Adaptive management is a flexible approach that allows for the continuous adjustment of management practices based on new information and changing conditions. This approach is particularly well-suited to managing the ecological risks of GMOs, where the potential for unforeseen impacts is high. A key component of adaptive management is the establishment of feedback loops, where monitoring data is used to inform management decisions. For instance, if monitoring reveals that a particular GMO is harming non-target species, management practices can be adjusted to mitigate these effects. This might involve modifying the use of the GMO, implementing containment measures, or even halting its use if necessary (Bawa & Anilakumar, 2013).

Another important aspect of adaptive management is involving a diverse range of stakeholders, including scientists, policymakers, farmers, and conservationists, in decision-making. This collaborative approach ensures that multiple perspectives are considered, leading to more effective and socially acceptable management strategies. It also allows for the integration of local knowledge and values into the decision-making process, which can enhance the success of management efforts (Mattsson et al., 2019). Adaptive management also provides a framework for balancing conservation and agricultural goals. The use of GMOs in agriculture often raises concerns about potential trade-offs between increasing food production and protecting biodiversity. Adaptive management offers a way to navigate these trade-offs by promoting the integration of conservation and agricultural objectives. For example, buffer zones could be established around areas where GMOs are used to protect adjacent natural habitats from potential gene flow. Similarly, landscape-level planning could ensure that GMO use does not disrupt ecological corridors or other critical habitats. By adopting a holistic approach that considers the broader landscape context, it's possible to develop strategies that support both agricultural productivity and biodiversity conservation. While progress has been made in understanding the ecological risks associated with GMOs, several research gaps remain. Addressing these gaps is essential for improving our ability to predict, manage, and mitigate the impacts of GMOs on biodiversity (Pichler & Hartig, 2023).

One critical area for further research is the long-term ecological effects of GMOs. Most studies have focused on short-term impacts, but the full consequences of GMO release may only become apparent over longer timescales. Long-term studies are needed to assess the cumulative effects of GMOs on ecosystems, including potential changes in species composition, ecosystem functions, and evolutionary processes. Another important research area is the risk of hybridization between GMOs and wild relatives. Hybridization can introduce novel traits into wild populations, potentially creating new invasive species or altering the genetic structure of native populations (Pichler & Hartig, 2023). Research is needed to better understand the factors that influence hybridization rates, the potential ecological consequences, and strategies for preventing or managing hybridization events. Finally, more research is needed on the socio-economic and cultural dimensions of GMO use and its impact on biodiversity. This includes understanding the perceptions and concerns of different stakeholders, the potential for conflicts between agricultural and conservation goals, and the effectiveness of different regulatory and management approaches. By taking a more interdisciplinary approach to GMO research, it's possible to develop more comprehensive and effective strategies for managing the ecological risks associated with GMOs (Pichler & Hartig, 2023). As GMOs continue to play an increasingly important role in agriculture and other sectors, it's essential to adopt a proactive approach to monitoring, managing, and researching their ecological impacts. By investing in ongoing ecological monitoring, developing adaptive management strategies, and addressing key research gaps, we can better understand and mitigate the risks posed by GMOs to biodiversity. This approach will help protect the environment while ensuring that the benefits of GMOs can be realized in a sustainable and responsible manner (Gbashi et al., 2021).

CONCLUSION

The science-driven economies will use these new, more effective, and less expensive weapons in their battle against invading species. For the good of society, the ideal ratio between caution and innovation must be determined. Without depleting or harming environmental resources, regulatory policies must strike a balance between the public's need for food, feed, and environmental safety as well as the financial costs for developers, growers, shippers, and processors. The secret to successful innovation is a globally coordinated regulatory framework. Everyone agrees that GD is an extremely potent tool that must be carefully and thoroughly evaluated before being allowed to be released into the environment.

References

1. Adikusuma, F., Williams, N., Grutzner, F., Hughes, J., & Thomas, P. (2017). Targeted Deletion of an Entire Chromosome Using CRISPR/Cas9. *Molecular Therapy*, 25(8), 1736–1738. Retrieved from <https://doi.org/10.1016/J.YMTHE.2017.05.021>
2. Azevedo, R. S. S., De Sousa, J. R., Araujo, M. T. F., Martins Filho, A. J., De Alcantara, B. N., Araujo, F. M. C., ... Vasconcelos, P. F. C. (2018). ABC transporter mis-splicing associated with resistance to Bt toxin Cry2Ab in laboratory- and field-selected pink bollworm. *Sci Rep.*, 8(1), 1–15. Retrieved from <https://doi.org/10.1038/s41598-017-17765-5>
3. Bauer-Panskus, A., Miyazaki, J., Kawall, K., & Then, C. (2020). Risk assessment of genetically engineered plants that can persist and propagate in the environment. *Environmental Sciences Europe*, 32(1), 1–15. Retrieved 4 September 2024 from <https://doi.org/10.1186/S12302-020-00301-0/TABLES/4>
4. Bawa, A. S., & Anilakumar, K. R. (2013). Genetically modified foods: safety, risks and public concerns—a review.

- Journal of Food Science and Technology*, 50(6), 1035. Retrieved 4 September 2024 from <https://doi.org/10.1007/S13197-012-0899-1>
5. Borggaard, O. K., & Gimsing, A. L. (2008). Fate of glyphosate in soil and the possibility of leaching to ground and surface waters: a review. *Pest Manag Sci*, 64(4), 441–456. Retrieved from <https://doi.org/10.1002/ps.1512>
6. Çakmakçı, R., Salık, M. A., & Çakmakçı, S. (2023). Assessment and Principles of Environmentally Sustainable Food and Agriculture Systems. *Agriculture 2023, Vol. 13, Page 1073*, 13(5), 1073. Retrieved 20 January 2024 from <https://doi.org/10.3390/AGRICULTURE13051073>
7. Carrière, Y., Crickmore, N., & Tabashnik, B. E. (2015). Optimizing pyramided transgenic Bt crops for sustainable pest management. *Nat Biotechnol.*, 33(2), 161. Retrieved from <https://doi.org/10.1038/nbt.3099>
8. Chen, H., & Lin, Y. (2013). Promise and issues of genetically modified crops. *Current Opinion in Plant Biology*, 16(2), 255–260. Retrieved from <https://doi.org/10.1016/J.PBI.2013.03.007>
9. Gbashi, S., Adebo, O., Adebisi, J. A., Targuma, S., Tebele, S., Areo, O. M., ... Njobeh, P. (2021). Food safety, food security and genetically modified organisms in Africa: a current perspective. *Biotechnology and Genetic Engineering Reviews*, 37(1), 30–63. Retrieved 4 September 2024 from <https://doi.org/10.1080/02648725.2021.1940735>
10. HAZARD IDENTIFICATION & RISK ASSESSMENT (HIRA). (n.d.).
11. Hilbeck, A., Meyer, H., Wynne, B., & Millstone, E. (2020). GMO regulations and their interpretation: how EFSA's guidance on risk assessments of GMOs is bound to fail. *Environmental Sciences Europe*, 32(1), 1–15. Retrieved 4 September 2024 from <https://doi.org/10.1186/S12302-020-00325-6/FIGURES/1>
12. Jha, A. B., & Warkentin, T. D. (2020). Biofortification of pulse crops: Status and future perspectives. *Plants*, 9(1). Retrieved from <https://doi.org/10.3390/PLANTS9010073>
13. Legros, M., Marshall, J. M., Macfadyen, S., Hayes, K. R., Sheppard, A., & Barrett, L. G. (2021). Gene drive strategies of pest control in agricultural systems: Challenges and opportunities. *Evolutionary Applications*, 14(9), 2162. Retrieved 20 January 2024 from <https://doi.org/10.1111/EVA.13285>
14. López Del Amo, V., Bishop, A. L., Sánchez C, H. M., Bennett, J. B., Feng, X., Marshall, J. M., ... Gantz, V. M. (2020). A transcomplementing gene drive provides a flexible platform for laboratory investigation and potential field deployment. *Nature Communications*, 11(1). Retrieved 20 January 2024 from <https://doi.org/10.1038/S41467-019-13977-7>
15. Mattsson, B. J., Arih, A., Heurich, M., Santi, S., Štemberk, J., & Vacik, H. (2019). Evaluating a collaborative decision-analytic approach to inform conservation decision-making in transboundary regions. *Land Use Policy*, 83, 282–296. Retrieved from <https://doi.org/10.1016/J.LANDUSEPOL.2019.01.040>
16. Montagu, M. Van. (2020). The future of plant biotechnology in a globalized and environmentally endangered world. *Genetics and Molecular Biology*, 43(1 Suppl 2). Retrieved 20 January 2024 from <https://doi.org/10.1590/1678-4685-GMB-2019-0040>
17. Ofori, K. F., Antoniello, S., English, M. M., & Aryee, A. N. A. (2022). Improving nutrition through biofortification—A systematic review. *Frontiers in Nutrition*, 9. Retrieved 20 January 2024 from <https://doi.org/10.3389/FNUT.2022.1043655>
18. Pacher, M., & Puchta, H. (2017). From classical mutagenesis to nuclease-based breeding – directing natural DNA repair for a natural end-product. *Plant Journal*, 90(4), 819–833. Retrieved from <https://doi.org/10.1111/TPJ.13469>
19. Pérez-Escamilla, R. (2017). Food security and the 2015-2030 sustainable development goals: From human to planetary health. *Current Developments in Nutrition*, 1(7). Retrieved from <https://doi.org/10.3945/CDN.117.000513>
20. Pichler, M., & Hartig, F. (2023). Machine learning and deep learning—A review for ecologists. *Methods in Ecology and Evolution*, 14(4), 994–1016. Retrieved 4 September 2024 from <https://doi.org/10.1111/2041-210X.14061>
21. Raman, R. (2017). The impact of Genetically Modified (GM) crops in modern agriculture: A review. *GM Crops & Food*, 8(4), 195. Retrieved 20 January 2024 from <https://doi.org/10.1080/21645698.2017.1413522>
22. Schnell, J., Steele, M., Bean, J., Neuspiel, M., Girard, C., Dormann, N., ... Macdonald, P. (2015). A comparative analysis of insertional effects in genetically engineered plants: considerations for pre-market assessments. *Transgenic Research*, 24(1), 1–17. Retrieved from <https://doi.org/10.1007/S11248-014-9843-7>
23. Schütte, G., Eckerstorfer, M., Rastelli, V., Reichenbecher, W., Restrepo-Vassalli, S., Ruohonen-Lehto, M., ... Mertens, M. (2017). Herbicide resistance and biodiversity: agronomic and environmental aspects of genetically modified herbicide-resistant plants. *Environmental Sciences Europe*, 29(1), 1–12. Retrieved 20 January 2024 from <https://doi.org/10.1186/S12302-016-0100-Y/METRICS>
24. Shahmohammadloo, R. S., Febria, C. M., Fraser, E. D. G., & Sibley, P. K. (2021). The sustainable agriculture imperative: A perspective on the need for an agrosystem approach to meet the United Nations Sustainable Development Goals by 2030. *Integrated Environmental Assessment and Management*. Retrieved from <https://doi.org/10.1002/IEAM.4558>
25. Teem, J. L., Alphey, L., Descamps, S., Edgington, M. P., Edwards, O., Gemmell, N., ... Roberts, A. (2020). Genetic Biocontrol for Invasive Species. *Frontiers in Bioengineering and Biotechnology*, 8, 524341. Retrieved from <https://doi.org/10.3389/FBIOE.2020.00452/BIBTEX>
26. The impact of Genetically Modified (GM) crops in modern agriculture: A review - PMC. (n.d.). Retrieved 20 2168



January 2024, from <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5790416/>

27. Trump, B. D., Cummings, C. L., Loschin, N., Keisler, J. M., Wells, E. M., & Linkov, I. (2023). The worsening divergence of biotechnology: the importance of risk culture. *Frontiers in Bioengineering and Biotechnology*, 11. Retrieved 20 January 2024 from <https://doi.org/10.3389/FBIOE.2023.1250298>
28. Visibelli, A., Roncaglia, B., Spiga, O., & Santucci, A. (2023). The Impact of Artificial Intelligence in the Odyssey of Rare Diseases. *Biomedicines* 2023, Vol. 11, Page 887, 11(3), 887. Retrieved 20 August 2023 from <https://doi.org/10.3390/BIOMEDICINES11030887>
29. Zafar, M. M., Razzaq, A., Farooq, M. A., Rehman, A., Firdous, H., Shakeel, A., ... Ren, M. (2020). Insect resistance management in *Bacillus thuringiensis* cotton by MGPS (multiple genes pyramiding and silencing). *Journal of Cotton Research* 2020 3:1, 3(1), 1–13. Retrieved 20 January 2024 from <https://doi.org/10.1186/S42397-020-00074-0>