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Joint EPA-ENCA Interest Group on Genetically Modified Organisms (IG GMO)

European Network of the Heads of Environment Protection Agencies (EPA Network)
European Network of the Heads of Nature Conservation Agencies (ENCA Network)

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Activity Report

Working Period 2017-2021

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Content

1 Colophon 2
2 Summary 3
3 Introduction 3
3.1 Context 3
3.2 The Joint EPA-ENCA Interest Group on GMOs (IG GMO) 4
3.3 Mandate 5
4 Background Information 6
4.1 Challenges of *Genome Editing* regarding Risk Assessment and Monitoring 6
4.2 Gene Drives 6
4.3 Synthetic Biology 7
5 Output of the Joint EPA-ENCA IG GMO 7
5.1 Technical Report on Gene Drives 8
5.2 Webinar on *Gene Drives* and Nature Conservation 8
5.3 Opinion Paper on *Gene Drives* 9
5.4 Recommendation on Environmental Monitoring of GMOs intended for Import and Processing 10
5.5 Scientific paper on considerations for a focused risk assessment of genome edited plants 10
5.6 Scientific paper on herbicide resistance and biodiversity regarding agronomic and environmental aspects of genetically modified herbicide-resistant plants 10
6 Exchange of experience and information on relevant topics 11
6.1 Plants developed by new techniques - comparison of existing regulation frameworks of the EU and non-EU countries and their respective requirements for risk assessment 11
6.2 Legal status of new biotechnological tools (*Genome Editing*) 11
6.3 Exchange of knowledge, views and position in the course of international processes 12
6.4 List of discussion topics during physical and online IG GMO meetings 2017-2021: 12
7 Conclusions 14
7.1 Retrospective 14
7.2 Promoting monitoring methodology 14
7.3 Perspective: Future technologies, future risks and horizon scanning 14

1 Colophon

Project management	
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2 Summary

Environmental risk assessment (ERA) of and implementation of post market environmental monitoring (PMEM) for genetically modified organisms (GMOs) have become an integral part of the assessment process for GMOs to be released into the environment. Understanding how the release of GMOs may affect the environment is a difficult task, particularly because there may be a time lag between the release and observable impacts, and because of the complexity of the receiving ecosystems. Additionally, the number of GMOs and traits, as well as their combinations, is increasing. As a result, predictions regarding the environmental impact of GMOs need to be treated with precaution. Further, the rapid emergence of new biotechnological tools like CRISPR[1] or *Genome Editing* in general will lead to new questions and challenges for risk evaluation, monitoring and risk management measures.

A prominent example for such so-called *emerging challenges* is the introduction of synthetic *Gene Drives* into organisms, resulting in *Gene Drive* organisms (GDOs). As *Gene Drives* have been proposed by some stakeholders to be employed as an instrument in the control of pathogens, pests and invasive species, GDOs have gained a lot of attention in the scientific literature and the media. Because of their unique features, the use of GDOs will represent a fundamental shift in the way GMOs will interact with the environment. GDOs are intended to spread in the environment and would be applied to modify wildlife in their natural environment instead of crops being confined to areas under cultivation. *Gene Drives* have also been suggested to be applied in nature conservation. Because of the potential far-reaching consequences for the environment and nature conservation, *Gene Drives* are currently high on the political agenda. While it is not yet clear if *Gene Drive* applications might open novel approaches to address the desired issues, they also bear the potential to cause significant and irreversible environmental harm. In order to assess *Gene Drive* applications, methods for ERA, environmental monitoring and risk management need to be developed and operational before any release of GDOs into the environment takes place. In parallel, societal and ethical issues need to be addressed.

Because negative impacts of GMOs on ecosystems are difficult to predict and detect, their deliberate release into the environment in the EU and Switzerland is performed to the precautionary principle. The implementation of the precautionary principle follows a stepwise approach, going from laboratory to greenhouse tests, field trials and eventually to releases into the intended environment. This approach generates knowledge on and experience with the interactions of a GMO with the environment at each stage and aims at testing increasingly complex risk scenarios in order to detect any harm as early as possible. However, laboratory tests and field trials are limited tools to assess the impact of GMOs on the environment. Therefore, the formulation and testing of risk scenarios for the ERA and the monitoring of the impact after the release of GMOs into the environment are crucial elements to minimize the risk of GMOs. The *Joint EPA-ENCA Interest Group on Genetically Modified Organisms* (IG GMO) has identified a need for action regarding ERA and PMEM of GMOs and has the competence to make an essential contribution.

The IG GMO is composed of members nominated by environmental protection and nature conservation agencies. The members represent agencies or institutions exercising their competence and expertise in ERA and monitoring of GMOs. They participate on a voluntary basis. Due to the informal nature of the group and because the IG GMO is neither directly involved in approval procedures nor has regulatory duties, the IG GMO is ideally suited to pinpoint and outline essential questions regarding the interactions of GMOs with the environment and potential negative impacts. Furthermore, the IG GMO regularly addresses EU entities to provide technical information and to voice its opinion and urges discussions on the subject. Thus, the work of the group significantly contributes to placing a stronger emphasis on the environment in the approval processes of GMOs.

3 Introduction

3.1 Context

Deliberate releases of GMOs into the environment may lead to unexpected and unwanted environmental impacts such as the establishment of GMOs in the environment or negative effects of GMOs on non-target organisms. To minimize the risk of GMOs, the precautionary principle is applied for their deliberate release in the EU and Switzerland. ERA and monitoring are key elements of the implementation of the precautionary principle regarding the introduction of GMOs into the environment. ERA is based on risks scenarios and, thus, based on assumptions and estimations (ex ante

[1] Clustered Regularly Interspaced Short Palindromic Repeats

evaluation). Therefore, it is essential to verify their validity (ex post evaluation). Environmental monitoring is a mean to test assumptions and conclusions drawn in the ERA (case-specific monitoring) and to detect any effects which were not anticipated in ERA (general surveillance) early, as outlined in the Council Decision establishing guidance notes supplementing Annex VII to Directive 2001/18/EC (2002/811/EC). Both ERA and monitoring have to be performed on a case-by-case basis and following a step-by-step approach, as required by Directive 2001/18/EC on the deliberate release of GMOs into the environment and the precautionary approach.

Because of their significant role in protecting the health and safety of human beings, animals and the environment, ERA and monitoring should be the target of due attention prior to releases of GMOs.

3.2 The Joint EPA-ENCA Interest Group on GMOs (IG GMO)

The EPA[2] Network plenary endorsed the establishment of the Interest Group on Genetically Modified Organisms (IG GMO) in Locarno (Switzerland) in May 2009. The IG GMO held its first meeting in Berne (Switzerland) in September 2009. In the same year, the ENCA[3] Network endorsed the preliminary work and the work programme of the IG GMO, and ENCA members joined the IG GMO; hence its current name *Joint EPA-ENCA Interest Group on Genetically Modified Organisms*. Since its establishment, the IG GMO has met every year, hosted by different group members. The IG GMO is composed of members from all over Europe. The agencies represented within the IG GMO have a broad range of responsibilities in the field of regulation, risk assessment and monitoring of GMOs. The IG GMO is composed of experts from environmental protection agencies and nature conservation agencies or institutions with competence and expertise in ERA and monitoring of GMOs in different regulatory fields.

The group currently includes members from agencies of the following countries:

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[2] Network of the Heads of Environmental Protection Agencies. The EPA Network is an informal grouping of the directors of national environmental protection agencies and similar bodies across Europe.

[3] The European Nature Conservation Agency Heads Network. The ENCA network is a grouping of actors from Europe and other countries with experience of nature conservation and nature conservation policy.

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3.3 Mandate

The IG GMO promotes the exchange of information and experience on ERA and monitoring of GMOs between the EPA and ENCA networks. The overall aim of the IG GMO mandate is to develop joint and consolidated views and positions in order to add additional emphasis to environmental aspects in the course of GMO approval procedures, ERA and environmental monitoring programmes.

During the working period 2017-2021, the IG GMO focused its activity on the topic of ERA and monitoring with regards to recent developments in gene technology, and to the challenges associated with the use of classical and new GMO in the context of environmental protection and conservation.

4 Background Information

4.1 Challenges of *Genome Editing* regarding Risk Assessment and Monitoring

While the advance of research and expertise on the use of GMOs has improved the scientific level of risk assessment concepts and practices over the last two decades, the rapid emergence of recent biotechnological tools of *Genome Editing* (such as CRISPR[4]*as the most important example)* open up new questions and challenges for risk evaluation, monitoring and risk management measures. This is for two reasons: the new techniques will change the quantity and characteristics of new GMOs as well as the type of organisms likely to be modified.

Genome Editing is a method of genetic engineering which relies on nucleases that are engineered to specifically cut targeted sites in the DNA of organism. The resulting cut is repaired with the help of the cell's own repair mechanisms, which may result in loss or gain of function in the genome.

Genome research has established complete DNA sequence information for a large number of crop genomes and described the function of numerous genes and effects of specific mutations. Because *Genome Editing* allows to introduce targeted alterations in a crop's genetic makeup, the techniques have been picked up rapidly namely by plant breeders to introduce desired traits (e.g. herbicide resistance, pest resistance, stress tolerance, nutritional content) or remove unwanted traits (e.g., unwanted metabolites) in existing varieties. Together with other recently developed gene engineering techniques, they are typically referred to as new breeding techniques (NBT) when used to genetically modify crops.

With *Genome Editing* methods, it is possible to intentionally generate changes in the genome that go beyond the possibilities of naturally occurring mutations. Thus, areas in the genome can be changed which were previously difficult to access due to natural limitations (reproductive isolation). For example, there are areas of the genome that are particularly well protected against mutations by the cell[5]. With the help of *Genome Editing*, characteristics can be inserted in crop plants that are present in wild relatives. However, it is also possible to introduce properties that were not present in the species concerned. Certain metabolites in a plant are often produced not only by one but by several genes. For example, the simultaneous modification of a series of wheat genes on all six copies of the chromosomes, which is feasible with *Genome Editing*, could produce wheat with a lower gluten content[6].This property has not yet been achieved in wheat by conventional selection means. potatoes[7] and maize with a higher amylopectin or less acrylamide content[8] follow several interests, such as farming, nutritional or industrial interests.

Complex traits such as drought or salt tolerance also require complex changes in the genome, since many genes and different parts of the plant are involved in the plant adaptation processes. *Genome Editing* allows the modification of even such complex metabolic pathways. However, while it is now possible to alter the genes, it is difficult to predict, if the plants will exhibit the desired function, since the involved metabolic processes are complex and interconnected with other functions.

4.2 Gene Drives

Gene Drive Organisms are a special application of *Genome Editing*, in which the genome is modified by means of site-directed nucleases in such a way that the desired mutation is passed on to all offspring and thus rapidly spreads in a population. When *Gene Drive* organisms are created, not only is the desired mutation created, but also the nuclease complex for the creation of the mutation is incorporated. A potential area of application of *Gene Drives* might be the introduction of a lethality factor, leading to the decimation or eradication of mosquito populations that transmit malaria. In theory, *Gene Drives* could also allow to spread traits causing a lower fitness, which would normally disappear because of the high selection pressure.

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[4] Clustered Regularly Interspaced Short Palindromic Repeats

[5] Kawall, K. (2019): New possibilities on the horizon: *Genome Editing* makes the whole genome accessible for changes. Frontiers in Plant Science, 10:525

[6] Eckerstorfer, M.; Dolezel, M.; Heissenberger, A.; Miklau, M.; Reichenbecher, W.; Steinbrecher, R. A. & Waßmann, F. (2019): An EU perspective on biosafety considerations for plants developed by *Genome Editing* and other new genetic modification techniques (nGMs). Frontiers in Bioengineering and Biotechnology. 7:31

[7] Innate Potatoes modifies by Crispr-Cas

[8] Conversion of a normal maize hybrid into a waxy version using in vivo CRISPR/Cas9 targeted mutation activity - ScienceDirect

Any use of GDOs will represent a fundamental shift in the way how GMOs will interact with the environment and the biodiversity: In contrast to classical GMOs, the purpose of GDOs is to spread and / or persist in the environment. *Gene Drive* applications intend to modify wild populations in the environment, according to the intended specific aim such as animal and human health, crop protection, and livestock production. *Gene Drives* have also been suggested to be applied in nature conservation. Due to the novelty of *Gene Drives* and their specific characteristics, there is currently limited knowledge on their intended aim, on their impact on the environment in general and on the biodiversity in particular. Taking into account the far reaching consequences for the environment and nature conservation, *Gene Drives* are an important topic to EPA and ENCA. For the above mentioned reasons, the IG GMO focused its interest during its work programme 2017-2021 on *Gene Drives* and relevant environmental issues.

4.3 Synthetic Biology

Synthetic Biology is a further area of genetic engineering that combines a number of modern techniques in the field of biotechnology with computer sciences to engineer new organisms or parts of organisms that do not occur in nature. The novelty lies in the systematic use of an engineering approach to intentionally shape, in whole or in part, (semi)-artificial organisms or biological active material. Besides genome modification and complex biochemical pathways, entire genomes can be redesigned and synthesised. In 2010, the first living bacterium (*Mycoplasma mycoides*) was created synthetically (chemically synthetized). In 2017, the new assembly of the chromosomes of the mosquito *Aedes aegypti* by the means of synthetically engineered DNA scaffolds was achieved. *Synthetic Biology* opens new doors to a fast and less expensive genome assembly[9].

Synthetic Biology is a further development and new dimension of modern biotechnology that combines science, technology and engineering to facilitate and accelerate the understanding, design, redesign, manufacture and/or modification of genetic materials, living organisms and biological systems[10].

The challenges for risk assessment in *Synthetic Biology* organisms are closely connected to the fact that the new organisms, referred to as synthetic organisms, are at least partially newly designed and have therefore no natural counterparts. The current ERA is based on a case-by-case approach, the assessment of the familiarity to natural counterparts, the known genetic basis of the introduced trait, and the characteristics of known donors and receiving organisms. Thus, the current ERA may no longer be adequate. The ERA procedure may have to be adapted, taking into account the depth of intervention, the whole organism characteristics and the limited knowledge of potential interactions. In the context of synthetic *Gene Drives*, the IG GMO focussed on possible challenges of ERA procedures for GMOs, in particular where the familiarity principle is not applicable.

5 Output of the Joint EPA-ENCA IG GMO

During the work period 2017-2021, the IG GMO promoted its scientific positions and visions regarding the protection of biodiversity and the environment with regard to recent developments in gene technology. Taking into account both, the fast-paced development of modern biotechnology and the importance of appropriate ERA and monitoring to anticipate the possible effects on biodiversity, the IG GMO seeks to work continuously on the most recent scientific evaluations for the sake of the implementation of GMO regulation.

The IG GMO developed two technical papers: one technical paper on ERA regarding *Genome Editing* with special focus on specific *Gene Drives* examples and, secondly, a technical recommendation paper on comprehensive GMO monitoring. In addition to the above mentioned technical paper, the IG GMO offered a consolidated in-depth opinion on *Gene Drives*. Furthermore, the IG GMO promoted the exchange of information and experience on ERA and risk management and provided consolidated inputs to international activities regarding these topics via different bodies at EU level. The information and knowledge gained within the IG GMO group can be used also in sharing information on biotechnology development and safety principles at national level.

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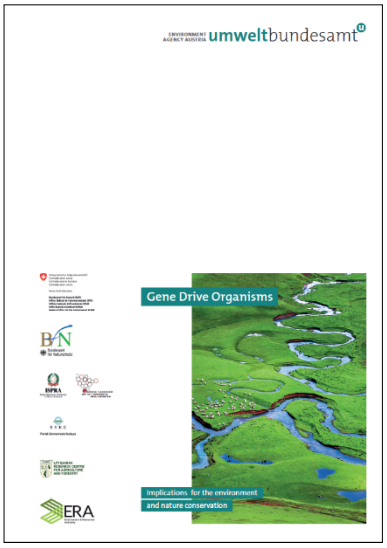
[9] De novo assembly of the *Aedes aegypti* genome using Hi-C yields chromosome-length scaffolds; O. Dudschenko *et al.*; Science. 2017 Apr 7;356(6333):92-95. doi: 10.1126/science.aal3327. Epub 2017 Mar 23, https://www.ncbi.nlm.nih.gov/pubmed/28336562

[10] Operational definition of synthetic biology as acknowledge by the COP 13, CBD/COP/DEC/XIII/17; https://www.cbd.int/doc/decisions/cop-13/cop-13-dec-17-en.doc

5.1 Technical Report on Gene Drives



The use of genetically modified organisms (GMOs) with *Gene Drives*, also referred to as *Gene Drive Organisms* (GDOs), is a rapidly evolving scientific field. As *Gene Drives* have been proposed to solve global issues in order to control pathogens, pests and invasive species, GDOs have gained a lot of attention in the scientific literature and the media.

Any use of GDOs will represent a fundamental shift in how GMOs will interact with the environment: In contrast to classical GMOs, GDOs are intended to spread in the environment and will be applied to modify wildlife in their natural environment instead of crops being modified in the lab before release. *Gene Drives* have also been suggested to be applied in nature conservation. Because of the far reaching consequences for the environment and nature conservation, *Gene Drives* are discussed in the IG GMO.

The present document provides an overview of the technical realization of *Gene Drives* and their proposed applications, including nature conservation. The main focus of the report is on three aspects: i) the environmental implications of GDOs, ii) the challenges the applications pose for the environmental risk assessment, monitoring and risk management and iii) critical uncertainties associated with the approach.

While *Gene Drive* applications might have the potential to address environmental or human health issues, they also bear the potential for significant and irreversible environmental harm. In order to assess *Gene Drive* applications, methods for ERA, environmental monitoring and risk management need to be developed and operational before any release of GDOs into the environment takes place. In parallel, societal and ethical issues need to be addressed.

The aim of this report is to delineate the potential implications of a potential use of GDOs for the environment, including nature conservation, and to address the uncertainties linked with *Gene Drive* applications. The report also analyses the challenges GDOs will pose to the ERA, risk management and the post-release monitoring.

Download technical report: link

The presentation *Genome Editing and Nature Conservation* given by Bettina Hitzfeld on behalf of the joint EPA-ENCA IG GMO during the 25th ENCA plenary in The Hague on Wednesday 13 November 2019 is available upon request from the ENCA Secretariat[11].

5.2 Webinar on *Gene Drives* and Nature Conservation

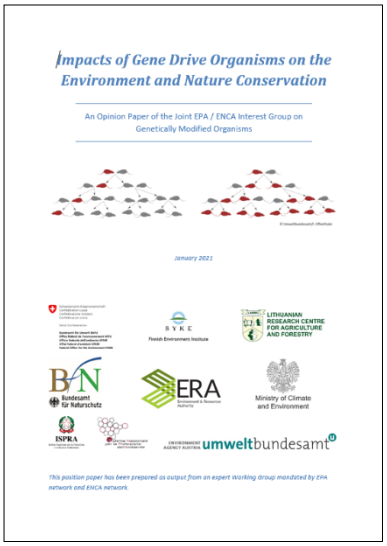
The EPA and ENCA plenaries mandated the IG GMO to conduct a webinar on the topic *Gene Drives* and implication for the nature conservation. The webinar was aimed at experts and members of interested agencies. The IG GMO produced a presentation on the topic as a base for further discussions. Due to the complexity of GDOs and their interaction with the environment, it was pointed out that it remains unclear whether and how the current practice and process of risk assessment could lead to sufficiently reliable conclusions. In parallel and in light of the fundamental questions regarding the feasibility, the implementation under current legislation, and the potentially irreversible consequence of Gene Drives, it was concluded that societal and ethical issues need to be fully addressed when considering a GDO release. The need for a technological assessment was advocated.

25 experts from many different agencies and including the European Commission (DG ENV, DG SANTE) participated to the webinar. The presentation *Gene Drive Organisms – Implications for the environment and nature conservation* given by Bettina Hitzfeld (chair IG GMO) is available upon request from the ENCA Secretariat11[11].

[11] Please contact ulrike.lamb@umweltbundesamt.at.

5.3 Opinion Paper on *Gene Drives*

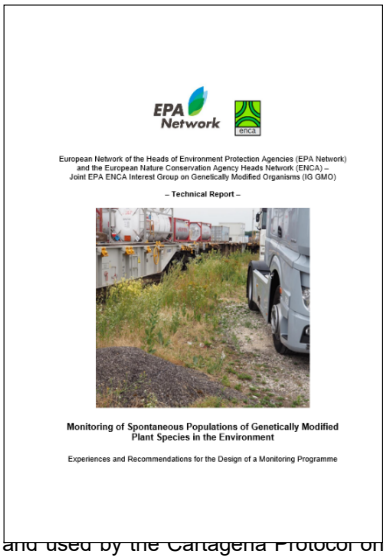
Based on the technical report on GDOs (section 5.1), the IG GMO prepared an opinion paper, stating the following recommendations:



- Current ERA, risk management and monitoring methods need to be adapted to the unique features and potential effects of GDOs in order to be fit for purpose before releases into the environment take place. Robust approaches need to be developed to characterize the specific risks related to GDOs, including the identification of potential new pathways to harm.
- Biosafety research is needed to fill existing knowledge gaps and address scientific uncertainties related to effects on biodiversity in the long and short term – this is of critical importance to the ERA of GDOs, to the development of suitable risk management measures (e.g. containment, reversal methods) and monitoring programs.
- Because of these knowledge gaps and the high potential risks of GDOs, the precautionary approach[12] and the stepwise principle[13] need to be strictly applied.
- Due to their potential for uncontrolled transboundary spread, applications using GDOs may affect other countries' biodiversity. A framework for international cooperation, information exchange and the control of research and releases of GDOs as well as internationally coordinated monitoring activities are necessary.
- Currently, too many knowledge gaps related to the spread, confinement and ecological consequences of GDOs exist. Testing potential applications with GDOs in the environment requires sufficient and robust data for the ERA as well as adequate risk management and environmental monitoring strategies.
- The consequences of applications with GDOs for the environment and nature conservation must not only be considered from a pure risk perspective. An assessment needs to include also legal, ethical and socio-economic considerations. Addressing these aspects will require novel tools in order to facilitate a broader technology assessment.
- Considering all relevant aspects, decisions for the release of GDOs need a broad interdisciplinary stakeholder involvement.

Download opinion paper: link

5.4 Recommendation on Environmental Monitoring of GMOs intended for Import and Processing



This technical report provides an overview of the experience with monitoring of spontaneous populations of genetically modified plants (GMPs) in two countries (Switzerland and Germany). The aim of the concepts and methods presented in this report is to allow for the efficient recording in the wild of spontaneous populations of genetically modified plants (GMPs) based on practical experience of GMP monitoring in Switzerland and Germany.

This report provides an overview of previous activities to monitor spontaneous populations of GMPs in Europe and contains recommendations for the planning and design of GMP monitoring programmes. Experience from these two countries shows that unintended release of GMPs to the environment regularly takes place through import of GMPs for processing or for food and feed.

[12] As defined by Principle 15 of the Rio Declaration on Environment and Development and used by the Cartagena Protocol on Biosafety

[13] According to Directive 2001/18/EC; also referred to as "stepwise approach" by EFSA

The unintended release, possible spontaneous growth and establishment of GMPs are to be addressed by risk assessors and risk managers. A well-designed monitoring programme that systematically records spontaneous populations of GMPs in the environment is able to generate data, which can be used in the decision-making process and management of GMPs.

Download technical report: [link]

5.5 Scientific paper on considerations for a focused risk assessment of genome edited plants

Schütte et al. Environ Sci Eur (2017) 29:5
DOI 10.1186/s12302-016-0100-y

Environmental Sciences Europe

REVIEW

Open Access

Herbicide resistance and biodiversity: agronomic and environmental aspects of genetically modified herbicide-resistant plants

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Abstract

Farmland biodiversity is an important characteristic when assessing sustainability of agricultural practices and is of major international concern. Scientific data indicate that agricultural intensification and pesticide use are among the main drivers of biodiversity loss. The analysed data and experiences do not support statements that herbicide-resistant crops provide consistently better yields than conventional crops or reduce herbicide amounts. They rather show that the adoption of herbicide-resistant crops impacts agronomy, agricultural practice, and weed management and contributes to biodiversity loss in several ways: (i) many studies show that glyphosate-based herbicides, which were commonly regarded as less harmful, are toxic to a range of aquatic organisms and adversely affect the soil and intestinal microflora and plant disease resistance; the increased use of 2,4-D or dicamba, linked to new herbicide-resistant crops, causes special concerns. (ii) The adoption of herbicide-resistant crops has reduced crop rotation and favoured weed management that is solely based on the use of herbicides. (iii) Continuous herbicide resistance cropping and the intensive use of glyphosate over the last 20 years have led to the appearance of at least 34 glyphosate-resistant weed species worldwide. Although recommended for many years, farmers did not counter resistance development in weeds by integrated weed management, but continued to rely on herbicides as sole measure. Despite occurrence of widespread resistance in weeds to other herbicides, industry rather develops transgenic crops with additional herbicide resistance genes. (iv) Agricultural management based on broad-spectrum herbicides as in herbicide-resistant crops further decreases diversity and abundance of wild plants and impacts arthropod fauna and other farmland animals. Taken together, adverse impacts of herbicide-resistant crops on biodiversity, when widely adopted, should be expected and are indeed very hard to avoid. For that reason, and in order to comply with international agreements to protect and enhance biodiversity, agriculture needs to focus on practices that are more environmentally friendly, including an overall reduction in pesticide use. (Pesticides are used for agricultural as well non-agricultural purposes. Most commonly they are used as plant protection products and regarded as a synonym for it and so also in this text.)

Keywords: Herbicide-resistant crops, Herbicide resistance, Genetically modified crops, Glyphosate, Biodiversity, Farmland biodiversity, Agriculture, Agricultural practice, Sustainability, Pollination

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Prof. Schroeder is the handling editor

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ment (ERA) should be conducted for plants obtained through novel genomic techniques, including genome editing (GE). Some countries have already exempted certain types of GE applications from their regulations addressing genetically modified organisms (GMOs). In the European Union, the European Court of Justice confirmed in 2018 that plants developed by novel genomic techniques for directed mutagenesis are regulated as GMOs. Thus, they have to undergo an ERA prior to deliberate release or being placed on the market. Recently, the European Food Safety Authority (EFSA) published two opinions on the relevance of the current EU ERA framework for GM plants obtained through novel genomic techniques (NGTs). Regarding GE plants, the opinions confirmed that the existing ERA framework is suitable in general and that the current ERA requirements need to be applied in a case specific manner. Since EFSA did not provide further guidance, this review addresses a couple of issues relevant for the case-specific assessment of GE plants. We discuss the suitability of general denominators of risk/safety and address characteristics of GE plants which require particular assessment approaches. We suggest integrating the following two sets of considerations into the ERA: considerations related to the traits developed by GE and considerations addressing the assessment of method-related unintended effects, e.g., due to off-target modifications. In conclusion, we recommend that further specific guidance for the ERA and monitoring should be developed to facilitate a focused assessment approach for GE plants.

Keywords: novel genomic techniques; genome editing; CRISPR/Cas; plant modification; GMO; environmental risk assessment; biosafety regulation

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1. Introduction

The ruling of the European Court of Justice (ECJ) in the case C-528/16 delivered in July 2018 clarified that plants developed by novel genomic techniques for directed mutagenesis are considered genetically modified organisms (GMOs) in the EU in accordance with Directive 2001/18/EC on the deliberate release and placing on the market of GMOs. The ruling also confirmed they are not exempt from regulations according to Article 3 in

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In June 2021, several experts from member institutions of the IG GMO (Switzerland, Germany, Italy, Poland and Austria) published a scientific paper concerning biosafety considerations for plants developed by *Genome Editing* (GE) in the journal MDPI BioTech (*Biosafety of Genome Editing Applications in Plant Breeding: Considerations for a Focused Case-Specific Risk Assessment in the EU*).

While not being a publication by the IG GMO itself, a draft had been presented and discussed at the 2021 IG GMO meeting and the paper will be used by the IG GMO as an input to the further work concerning the ERA of GE crop plants during their 2022-2026 work programme.
The publication addresses challenges associated with the current biosafety framework in the European Union (EU). In the EU plants developed by novel genomic techniques for directed mutagenesis are currently regulated as GMO and have to undergo an ERA prior to environmental release or placing on the market. However, specific guidance for this ERA is still lacking. In the review the limited suitability of general denominators of risk/safety to predict the risks associated with individual GE plants is discussed. The authors argue that there is no safety by default for whole groups of *Genome Editing* applications encompassing different individual GE organisms. They suggest integrating the following two sets of considerations into the ERA to address particular characteristics of GE plants: (1) considerations related to the traits developed by GE and (2) considerations addressing the assessment of method-related unintended effects, e.g. due to off-target modifications. In conclusion, they recommend that further specific guidance for the ERA and monitoring should be developed to facilitate a focused assessment approach for GE plants.

Download paper: [link]

5.6 Scientific paper on herbicide resistance and biodiversity regarding agronomic and environmental aspects of genetically modified herbicide-resistant plants

In January 2017, several experts from member institutions of the IG GMO (Switzerland, Germany, Italy, Finland and Austria) published a scientific paper concerning herbicide resistance and biodiversity in the journal Environmental Sciences Europe.
The scientific paper is a summary and an update of a comprehensive technical report which was previously published by the German Federal Agency for Nature Conservation BfN, the Austrian Environment Agency EAA, and the Swiss Federal Office for the Environment FOEN. Based on this technical report ([link]), some members of the IG GMO within the EPA and ENCA networks, drafted a position paper which highlights key messages regarding the environmental impacts of the cultivation of genetically modified herbicide-resistant plants ([link]). Acting upon the key messages should improve the current environmental risk assessment of these plants. The position paper was addressed to relevant EU bodies with the aim to ensure adequate protection of the environment in the future.

Download paper: [link]

6 Exchange of experience and information on relevant topics

In their current activities, the members of the IG GMO are significantly involved in exchanging information and expertise regarding the current and future situation related to regulatory framework,

ERA and monitoring of GMOs (with a special focus on *Genome Editing*). Moreover, the IG GMO encourages the exchange of information, the implementation of the GMO regulation and provides background information on these topics and positions. Thus, the network of the IG GMO members is considered to be an essential platform, interacting regularly and contributing to important outputs regarding ERA, monitoring, and adding substantial value to the topics discussed, both on the European and the global level.

To attract more attention to environment issues, the IG GMO searched and opened the dialogue with the EU entities and EFSA by addressing their technical reports on *Environmental Monitoring of GMOs* and on *Gene Drives* to EFSA and DG SANTE for consideration. At the time of submission of the *Gene Drive* paper, EFSA was in the process of a public consultation on *Gene Drive Organisms*.

6.1 Plants developed by new techniques - comparison of existing regulation frameworks of the EU and non-EU countries and their respective requirements for risk assessment

The IG GMO analysed the existing frameworks for biosafety regulation in European and non-European countries, their requirements concerning ERA, and the differences regarding the implemented regulatory triggers. In their current tasks, many IG GMO members are involved in the development or setting into force of the regulation of *Genome Editing* techniques. Within the IG GMO, emphasis was given to the fact that the current biosafety frameworks provides an appropriate approach for the ERA of new breeding technologies applications, whereas alternative general legislation does not. The IG GMO considers as very important to comment on ERA and monitoring concepts regarding products issued from the techniques discussed in the section 5.1. The group was active in consultation processes of relevant EFSA documents/guidance and OECD consensus documents/reports as well as reports issued from subsidiary bodies of the Convention on Biodiversity (CBD) and related Cartagena protocol. Within the processes of implementation of EU law, the IG GMO commented on ERA and monitoring requirements. The IG GMO has taken notice of the EFSA's evaluation of the existing regulatory framework for their adequacy for the ERA of plants developed by new techniques. After discussing the matter, the group accepted the proposal to prepare a scientific publication by IG GMO members in their own name to contribute to the public discussion and as a basis for the IG's planned work during the period 2022 – 2026.

6.2 Legal status of new biotechnological tools (*Genome Editing*)

Unlike the "classical" gene technology (transgenesis), *Genome Editing* technologies (see also section

6.3 Exchange of knowledge, views and position in the course of international processes

The novel features of GDOs also lead to challenges that are not covered by current legislation. In the

The IG GMO exchanged information and experience on ERA and risk management and discussed inputs to international activities via different bodies at EU and Convention of the Biological Diversity level.

[14] CURIA - Documents (europa.eu)

The members involved in the work within the Subsidiary Body on Scientific, Technical and Technological Advice (SBSSTA) and in the preparation of the COP 14, MOP 9 exchanged their views regarding the documents issued by the secretariat regarding *Synthetic Biology*, *Gene Drives*, ERA and risk management.

6.4 List of discussion topics during physical and online IG GMO meetings 2017-2021:

Information from the EPA and ENCA network activities, international meetings of conferences of IG GMO relevance, and organisational and procedural matters were common topics at all meetings. The following table gives a short overview of the topics dealt with during the IG GMO meetings 2017-2021:

Year and Venue	Topics
2017, Bern, Switzerland (physical)	• Finalisation of Work Programme 2017-2021 and relationship with EU-Agenda • Research on the Flow of Potentially GMO-Contaminated Agricultural Products and Recommendations on the Development of a GMO-Monitoring • Synergies between IG GMO interests and the topics on the Agenda of the COPs of the convention on biological diversity (*Synthetic Biology*) • New Breeding Technologies – Ethical Questions • ERA Requirements for GMOs with *Gene Drives* Capacity – Challenges for Regulation • Outlines of a Potential New Document on New Techniques, focussed on risk Scenarios, *Gene Drive* mosquitos, CRISPR/Cas9. • Exchange of experience regarding experimental releases of genetically modified plants on a protected site in Switzerland • Drafting the elements of the planned output on New Breeding Techniques (Risk Scenarios, *Gene Drive* Mosquitos, CRISPR/Cas9)
2018, Helsinki, Finland (physical)	• *Gene Drives* – implications and challenges for the regulation and the environmental risk assessment in Europe and globally – study presentation and proposal of options regarding a IG GMO *Gene Drives* (position) paper • Technical preparations of the CBD COP 14 and Cartagena COP-MOP 9 issues of relevance (*Synthetic Biology*, risk assessment guidance) in November 2018. Short inputs on discussion topics in the subsidiary bodies (e.g. *AHTEC Synbio 2017, Public Awareness in the context of the Cartagena Protocol)* • Elements for a technical background paper “Recommendations for the design of a GMO-monitoring” • New breeding technologies: the Italian experience • New Breeding Technologies: Results from stakeholders meeting conducted in Switzerland • Synthetic *Gene Drives*: between continuity and novelty • Exchange of views regarding an OECD document “environmental considerations document • Plants developed by New Techniques - Comparison of existing regulation frameworks of EU and non-EU countries and their respective requirements for risk assessment • Experiences on prohibiting or restricting GM-cultivation based on environmental policy objectives such as town and country planning, and land use
2019, Vienna, Austria (physical)	• GMOs with *Gene Drives* – drafting the technical report • Risk assessment: *Genome Editing* of organisms with *Gene Drives* • Brief assessment on the implementation of the Post-Market-Environmental-Monitoring report on the cultivation of genetically modified maize MON 810 in the EU from EFSA. • Discussion on the scope, significance and implications of the Decision of the European Court of Justice ECJ on new GMOs

	• Restricting or banning GMO cultivation under the new Directive (EU) 2015/412 EU, referred as opt-out measures; discussion on scope and criteria of the individual countries regarding the opt-out measures. Relevant environmental issues. • The relationship between *Genome Editing* and nature conservation • *New Genetic Modification (nGM) Techniques* – Biosafety Considerations for GM-plants and consequences for their regulation • New techniques: regulation perspectives in CH • Traceability of new techniques: the state of affairs, open questions and relevance for the IG GMO how to continue • ***Gene Drive*** opinion paper: drafting the elements for an opinion paper on *Gene Drive* organisms.
2020, spring (online)	• Opinion paper on *Gene Drive organisms* – Final discussions on the *Gene Drives* opinion paper • Overview and timeline on further IG GMO output on *Genome Editing* • Drafting the elements for the Activity Report 2017-2021 • Drafting a New Work Programme 2022-2026: important elements and relevant topics • Biosafety of *Genome Editing* Applications in Plant Breeding – Considerations for a focused risk assessment of potential environmental effects
2020, winter (online)	• Delivery and publication of the opinion paper on *Gene Drive organisms* • Elaboration of an input on risk assessment of *Genome Edited* crop plants (drafting a scientific publication in collaboration with IG GMO). • Input from the IG GMO on the EFSA opinion regarding *Gene Drives* • TEgenesis (EpiBreed) for crop breeding: Input from CH and EU • Presentation of the Swiss GMO-Monitoring App (in the context of the GM oilseed rape monitoring)
2021, spring (online)	• Preparation of the new Work Programme 2022-2026 and the Activity Report 2017-2021 • Discussion on the planned publication on risk assessment of *Genome Edited* crop plants by IG GMO members in the journal BioTech.
2021, autumn	27/28 October 2021

7 Conclusions

7.1 Retrospective

The IG GMO has completed the work planned for the period 2017-2021 by producing two technical papers and an opinion paper and by providing input regarding the topics under discussion to the relevant entities.

The accomplished work provides a fundamental understanding of the issues related to environmental aspects in the course of GMO approval procedures, ERA and environmental monitoring programmes. Due to the quality and specific features of the output, the IG GMO demonstrated its expertise and value in outlining essential questions relative to impacts on and interactions with the environment. The IG GMO's views and output are transparent and publicly available and the group gained wide recognition for raising relevant environmental questions. Moreover, transmitting these products to EU entities established direct contact to and opened the dialogue with those entities. The IG GMO provided an essential open platform, contributing to important outputs, and adding substantial values regarding ERA, monitoring programmes for GMOs and organisms issued from *Genome Editing* technologies.

7.2 Promoting monitoring methodology

The IG GMO wants to further promote its positions and visions regarding the protection of biodiversity and the environment. Therefore, the IG GMO will continue to raise the importance of performing an appropriate ERA and a suitable monitoring while enforcing the implementation of the regulation of GMOs. Based on its previous work, the IG GMO plans to develop a technical paper on *Genome*

Editing and environmental risk assessment and a supplementary technical paper on monitoring of GDOs. Further, the IG GMO wants to promote the exchange of information and experience on this topic. Finally, the translation of the two technical papers on monitoring and on GDOs, respectively, to newly emerging challenges due to the continuing evolution of gene technologies will be a further task of the IG GMO.

7.3 Perspective: Future technologies, future risks and horizon scanning

While expertise accumulates regarding ”classical” GMOs, biotechnology keeps evolving rapidly and the emergence of new tools and applications are adding new aspects to ERA and monitoring. *Genome Editing* enables the relatively accessible rewriting of the genome. Because of this, these new technologies are expected to replace the application of “classical” gene technology methods in most cases. GDOs as a specific application of *Genome Editing* and *Synthetic Biology* pose additional new challenges due to their unique characteristics. This may lead to unpredictable consequences or irreversible damages for the biodiversity and the environment as a whole.

Taking into account the rapid progress in biotechnology with potentially greater environmental impacts, the IG GMO intents to share its expertise to help adress future challenges in the area of ERA and monitoring of new emerging gene technologies.

As a further extension of its current mandate, the IG GMO will submit a new work programme for the period 2022-2026 to the EPA and ENCA Network plenaries for endorsement.