36th Plenary meeting of the EPA Network, 25-26 November, Prague

TITLE: Work Programme 2022-2026 for the Joint EPA ENCA Interest Group on Genetically Modified Organisms (IG GMO)
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OBJECTIVE OF THE PAPER:
Provide information for the ENCA Plenary (online, 16/17 November 2021) and EPA Plenary in Prague (25/26 November 2021) in order to decide on the continued work of the Interest Group on Genetically Modified Organisms (IG GMO).

The EPA and ENCA Networks are invited:

- To give advice on the proposed activities;
- To decide to continue the work of the Interest Group and, to consider and endorse its strategic work programme for the period 2022-2026;
- To consider participation in the IG GMO

The last work programme ran from 2017 to 2021 and the activity report for this period is available in Autumn EPA and ENCA Network plenaries. The paper stems from the preparatory discussions of the IG GMO members.

IG GMO WORK PROGRAMME 2022-2026

Content

1 INTRODUCTION

Deliberate releases of genetically modified organisms (GMOs) 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, ecological functions or ecosystem services. Hence, it is essential that prior to such releases, an environmental risk assessment (ERA) is performed and in parallel with such releases an environmental monitoring is implemented, both on a case-by-case basis, as required by Directive 2001/18/EC on the deliberate release of GMOs into the environment.

Risk assessment and monitoring are key elements of the regulation concerning the introduction of GMOs into the environment. Since ERA are limited and based on assumptions and estimations (risks scenarios), it is essential to verify their validity. Environmental monitoring is a means to test the 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). For this reason, ERA and monitoring should be the target of due attention prior to GMO-releases.

The EPA Network plenary endorsed the establishment of the joint EPA ENCA Interest Group on Genetically Modified Organisms (IG GMO) in Locarno (Switzerland in May 2009). The group held its first meeting in Bern (Switzerland) in September 2009. After the separation of the ENCA Network from the EPA Network, ENCA members joined the IG GMO; hence its current name “Joint EPA-ENCA

Interest Group on Risk Assessment and Monitoring of GMOs" (IG GMO). Since 2010, the group has prepared several documents regarding environmental risk assessment and monitoring of GMOs, which were welcomed and supported by both EPA and ENCA Networks.

The IG GMO is composed of members from environmental protection agencies and nature conservation agencies or institutions with competence and expertise in ERA and monitoring. Their participation is voluntary. Based on the group's informal character and because it is not directly involved in approval procedures, the IG GMO is ideally suited to pinpoint and outline essential questions regarding the impacts of GMOs on the environment and interactions of GMOs with the environment. Furthermore, the IG GMO regularly addresses EU entities to voice its concerns regarding the impact of GMOs on the environment 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.

2 MANDATE

The IG GMO promotes the exchange of information and experience on environmental risk assessment and monitoring of GMOs between the EPA[1] and ENCA[2] networks. The overall aim of the IG GMO mandate is to develop joint and consolidated views and positions of the EPA and ENCA networks in order to add additional emphasis to environmental aspects in the course of GMO approval procedures, ERA and environmental monitoring programs.

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 that their use poses in the context of environmental protection and conservation. 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.

3 BACKGROUD INFORMATION

3.1 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[3]*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 instruments 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 created a large number of fully sequenced 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 (e.g., herbicide resistance, pest resistance, stress tolerance, nutritional content) or remove (e.g., unwanted metabolites) specific traits into existing varieties.

[1] 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.
[2] 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.
[3] Clustered Regularly Interspaced Short Palindromic Repeats

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 for changes due to natural limitations (reproductive isolation). For example, there are areas of the genome that are particularly well protected against mutations by the cell's own repair mechanisms[4].

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 new 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 lower gluten content[5].This property has not yet been achieved in wheat by conventional breeding. Recent developments made possible by those technologies such as non-bruising potatoes[6] and maize with a higher amylopectin or less acrylamide content[7] 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 modifying also such complex metabolic pathways.

3.2 Gene Drives

Gene Drive Organisms are a special application of *Genome Editing*, where the genome is modified by means of site-directed nucleases in such a way that the desired genetic modification is passed on to all offspring and thus rapidly spreads in wild population. When *Gene Drive* organisms are created, not only is the desired genetic modification created, but also the nuclease complex, - the instrument for the genetic modification- is incorporated and inherited. The goal might be, for example, 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.

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 specific interests such as animal and human health, crop protection, and livestock production. Being a promising tool, *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 desired impact and 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 2017-2021on *Gene Drives* and relevant environmental issues.

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

[5] 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

[6] Innate Potatoes modifies by Crispr-Cas

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

3.3 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) synthetic organisms or biological active material. Besides genome modification and complex biochemical pathways, entire genomes can be redesigned and synthesized. 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, inexpensive and accurate genome assembly[8].

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[9].

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 focused on possible challenges of ERA procedures for GMOs, in particular where the familiarity principle is not applicable.

4 RESULTS OF THE PREVIOUS PERIOD 2017-2021

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. The IG GMO has focused its work in particular on monitoring of GMO and *Gene Drive.* In accordance with the precautionary approach, and in view of the use of *Gene Drive* on wild organisms and biodiversity, the group has decided to provide its recommendations and expertise in the early stages of development of this modification process.

The IG GMO developed two technical papers: one technical paper on ERA regarding Genome Editing with special focus on specific Gene Drive 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.

The complete *Activity Report 2017-2021* with all results in detail can be found under the following link (available after publication).

[8] 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

[9] 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 NEW WORK PROGRAMME 2022-2026 AND KEY ACTIVITIES

In its previous work programme (2017-2021), the IG GMO worked on the issue of *Genome Editing*, with a focus on the *Gene Drive* modification processes. Since, the awarding of the 2020 Nobel Prize in chemistry for the discovery of CRISPR/Cas9 in 2012, the field of *Genome Editing* has been experiencing special attention and unparalleled interest. *Genome Editing* has rapidly developed from being a niche group of technologies to mainstream methods and a new generation of tools used by many researchers and industries for the development of various potential applications; on the other side an intense debate has continued both at regulatory and legal level.

The areas of use are broadening and the interactions with biodiversity and wildlife is intensifying. This highlights the importance of examining and monitoring the risks, using a system approach, aiming in anticipating negative impacts and further loss of biodiversity at species, population and genetic level. There is a clear need of clarity on the regulation of the products of *Genome Editing* techniques and on how to put in place methods and processes to assess potential risks, to verify the potential benefits connected and to ensure an effective environmental monitoring and traceability.

In face of the climate crisis and the rapid erosion of biodiversity that we are experiencing, the use of biotechnology might be seen a promising tool by some stakeholders that need to be carefully examined in the light of their long-lasting or even irremediable effects. The emergence of zoonotic diseases reveals how biodiversity loss is a key driver of emerging infectious diseases. Protecting biodiversity is vital for avoiding the next pandemic. The current pandemic crisis has given rise to the idea that biotechnology could help manage the risks of zoonotic diseases. It is therefore critical that countries integrate biodiversity considerations into their COVID-19 response plans.

5.1 Topic 1 – Setting the Scene

Meanwhile, the debate on the topic of *Genome Editing* and its applications, in particular *Gene Drives*, is discussed and addressed in several frameworks and fora worldwide. At EU level, on 29 April 2021, the European Commission published a study[10] regarding the status of New Genomic Techniques (NGT) under Union law that includes *Genome Editing* techniques; furthermore, on 20 October 2020 the European Parliament Intergroup on "Climate Change, Biodiversity and Sustainable Development" (https://ebcd.org/intergroup/) has organised a webinar on: "Research and Innovation for biodiversity: what role for *Gene Drive* research?" to address any questions different stakeholders may have with regards to *Gene Drive* and to stimulate an open debate on the safe and responsible development of the research in this field.

Furthermore, the topic is addressed by different Multilateral Environmental Agreements (MEAs):

- The Convention on Biological Diversity has established an Ad Hoc Technical Expert Group (AHTEG) to discuss this issue within the Synthetic Biology item, the topic of *Genome Editing* is also discussed under the item “Risk Assessment and Risk Management of living modified organisms” in the framework of the Cartagena Protocol on Biosafety.

- In 2016, the International Union for Conservation of Nature (IUCN) in 2016 passed a resolution (WCC-2016-Res-086) calling for an examination of *Gene Drive* systems and their relationship with biodiversity conservation. The topic of *Genome Editing*, with particular reference to *Gene Drive* systems, has been addressed in at least two further documents. In the Guidelines for invasive species planning and management on islands (IUCN, 2018) the use of genetic techniques, including the use of organisms containing *Gene Drive*, is considered a potential useful tool for the management, control and eradication of established invasive alien species (IAS). In 2019 the IUCN Synthetic Biology and Biodiversity Conservation Task Force published a technical assessment where *Gene Drives* are presented as a new challenge to the conventional

[10] https://ec.europa.eu/food/plant/gmo/modern_biotech/new-genomic-techniques_en

conservation tools called for them to be considered by conservationists and biologists alike, to chart a path forward.

- The IPBES's “Scoping document for a thematic assessment of invasive alien species and their control», considers the use of *Gene Drive* technology as one of the options for the management and eradication of IAS.

Several further documents and position papers have been published by NGOs and researchers and scientist organizations on this issue.

During the working period 2022-2026 the IG GMO intends to confirm its commitment in participating in the debate on the topic of *Genome Editing* (GE) addressing the issue by different activities and products.

- The IG GMO will address the identified knowledge gaps, the aspects to be further developed and challenges for risk evaluation, monitoring and risk management measures focusing on and highlighting the importance of biodiversity and nature conservation. Furthermore, the IG GMO will carry out the activities identified and described in the following paragraphs of the working programme 2022-2026.

- The IG GMO will emphasize the importance of focusing not only on the level and accuracy of the intervention on the genome that GE techniques allow, but rather on the resulting organism produced as a whole and on the potential associated changes in the interactions between that organism and the receiving environment. Although *Genome Editing* allows site-specific modifications, the application of *Genome Editing* techniques does not necessarily lead to the stable integration of recombinant constructs in the genome and may lead to non-target, unpredictable and pleiotropic effects and epigenetic phenomena. The IG GMO plans to develop tools and solutions to evaluate the potential consequences to the organism and to the environment resulting from the genetic modifications.

- The wide range of applications of *Genome Editing* leads to further aspects that need to be considered. In fact, *Genome Editing* applications may produce large-scale and long-time changes and effects on the environment that imply further societal evaluations including socio economic evaluation.

- Crops, including genetically modified crops, are typically less well adapted than wild varieties to conditions outside the controlled and managed systems that are the agricultural environment, and tend to fail to thrive and are out-competed by wild types. The modification of wild type species (e.g. invasive rodents, *Gene Drive* mosquitoes for the control of malaria) selected and adapted to survive in nature and in unmanaged conditions, would lead to new and unpredictable consequences for biodiversity and nature conservation. The IG GMO will address the challenges, for risk assessment and monitoring, associated with the shift of biotechnological applications from agricultural systems to natural habitats.

- The IG GMO will analyse and assess the issue of *Genome Editing* by an environmental protection and nature conservations perspective, following the “One health” approach that recognizes that the health of people is closely connected to the health of animals and our shared environment.

The IG GMO could provide material for discussion and decision at EU level and ask EU-entities (DG ENV, EFSA) about prioritization of the identified topics. What are the relevant topics for DG environment? It has been proposed using existing contacts and channels (e.g., EPA, ENCA).

As further communication activity the IG GMO could develop a short report / a statement to set the scene regarding *Genome Editing* and future challenges to finally send it as open letter to entities:

EU Commission, EFSA, IUCN European Regional Office (https://www.iucn.org/regions/europe), IPBES, Europe & Central Asia Network of organizations engaging in IPBES (ECA-Network, http://www.eca-ipbesnetwork.org/).

5.2 Topic 2: Genome Editing – Definitions and Terminology

Genome Editing is a new and rapidly evolving technology comprising a variety of methods, whereby further developments in the next years are to be expected. *Genome Editing* allows for a multitude of modifications in the genome, a variety of traits and the application in various organisms, including plants and animals. Although those applications are in various stages of research and development, several are expected to enter the market in the next years (with SU canola already available in the US and Canada). Given the environmental relevance of those applications, corresponding considerations and challenges need to be discussed. This is especially important since the regulation of products produced by *Genome Editing* is still under discussion, with several stakeholders pressing for a loosening of respective regulation in Europe. In that regard the study of the European Commission on "new genomic techniques" (NGT), published on 29 April 2021, is of political importance[11].

Currently, there is no clear and harmonised definition of *Genome Editing*. In addition, *Genome Editing* is discussed in the context of various other terms such as 'new genomic techniques' or 'new breeding techniques', which are often used synonymously. This lack of clarity could hinder information exchange as well as discussions on environmental considerations and associated legal issues. Thus, the IG GMO wants to close this gap by preparing a background paper on definitions and terminology used.

Based on current developments (including methods, applications, regulatory proposals and negotiations) an overview of the definitions used will be presented and a definition adapted to the state of development shall be proposed. Furthermore, an overview on the most relevant terminology used in the context of *Genome Editing* will be given for the sake of clarity, facilitating the upcoming discussions. This overview on definitions and terminology will also be considered in relation to the judgement of the Court of Justice of the European Union in 2018 and the study of the European Commission which also include a legislative proposal. Thus, the regulative coverage of methods, modifications and applications of *Genome Editing* can be assessed. This should facilitate a precise and comprehensive exchange of experiences and information within the IG GMO and enable to:

- present environmental concerns associated with techniques, modifications, applications and developments of importance for the IG GMO as best possible;
- critically observe, in a timely manner, the developments in the EU including the outcome and respective follow-up of the above-mentioned study of the European Commission which will be of major political relevance with the potential for great environmental consequences;
- evaluate legal developments and uncover consequences for the environment, biodiversity and nature conservation as a result of possible regulatory changes and;
- identify need for action due to technical or legal developments as well as applications and manufactured products.

5.3 Topic 3 – Genome Editing: Key questions regarding Environmental Risk Assessment for genome edited organisms

The IG GMO will address various aspects related to the wider use of genome edited organisms in agriculture as well as the possible future release of genome edited (GE) organisms into the environment. The group will address key questions associated with such applications, such as requirements for an appropriate environmental risk assessment and explore further consequences for biodiversity and nature conservation strategies, which may be associated with applications of GE organisms.

[11] European Commission study on new genomic techniques

A part of the work of the IG GMO will focus on GE organisms for use in agriculture and food production, which are developed at a high pace with the objective to address the increasing food demand and in response to ongoing climate change and the associated challenges for agricultural production. However, safe use of GE organisms will require proper risk assessment before release into the environment.

Members of the IG GMO were invited to publish their considerations regarding the ERA of GE organisms in a peer-reviewed scientific journal. Based on this publication, the IG GMO will work on a paper on environment risk assessment (ERA) of GE crop plants as an output of the 2022-2026 work programme.

5.4 Topic 4: Monitoring of Genome Edited organisms

Genome Editing (GE) techniques allow the highly specific introduction of novel traits into a novel spectrum of species compared to classical GMO. In the EU, organisms deriving from the application of GE techniques are legally GMO and thus a monitoring of environmental effects has to be performed following Guideline 2001/18/EC. It is well known that some agricultural exporting countries such as the U.S. and Canada are cultivating GMO on a large scale. As a result, genetically modified plants may (unintentionally) contaminate goods imported into the EU and Switzerland and eventually enter the environment. In the EU, the monitoring of environmental effects only takes place for authorized GMO and the authorization holder must provide the methods for detection.

GE organisms can possess novel effect pathways and interactions with the environment and thus place new demands on the monitoring. Therefore, the monitoring concepts for classical GMO need adaptations. To this end, the group will provide an overview of the GE organisms that are currently generated for placing on the market internationally and will elaborate the novel effect pathways of GE organisms on the environment. Furthermore, the IG GMO will address topics such as detectability and traceability of GE organisms in the environment. The technical paper will give input about the suitability of monitoring concepts for classical GMO, as well of environmental monitoring programmes, for the monitoring of GE organisms and will point out the need for adaptation. The insights provided in this paper will serve as valuable information for the development of suitable monitoring concepts for GE organisms on an international level.

5.5 Topic 5 – Horizon Scanning – Emerging Gene Technologies and Applications

CRISPR/Cas is a central tool in biotechnology that has opened up fundamentally new possibilities for modifying and redesigning living organisms. At the same time, the CRISPR/Cas technology itself is constantly and dynamically developing and gaining importance in all areas of biotechnology. CRISPR/Cas technology can be used both for the planned design of organisms and in combination with artificial intelligence and automated testing procedures to produce novel genetic combinations and unexpected characteristics. The range of genetically modified organisms (GMOs) currently being researched and developed is already vast, ranging from genetically modified viruses and GM algae to *Gene Drive* organisms designed to genetically modify wild populations outside the laboratory. Many characteristics of CRISPR/Cas and other *Genome Editing* applications thus go far beyond those of GM crops released into the environment to date. The spectrum of species as well as potential applications is broadened. In addition to crops, microorganisms (including viruses and algae), livestock, wildlife and fish are increasingly being targeted. Releases are planned outside agro-ecosystems (wild populations and protected species) and/or have a high rate of spread and potential global reach (GM viruses, gene drives). In addition, research is increasingly being conducted on traits with far-reaching ecological impacts (e.g. stress tolerance) and more complex traits (incorporation of entire synthetic pathways, extensive transformation). The insertion of genetic engineering tools into GMOs (RNAi, gene drives) also represents a new dimension. Besides these new *Genome Editing* applications novel random mutagenesis techniques like TEgenesis or in vitro mutagenesis are new developments that need to be evaluated from an environmental perspective.

Horizon Scanning is a process for detecting early signs of potentially important developments through a systematic examination of potential threats and opportunities, with emphasis on new technology and its effects on the issue at hand (OECD n.d.a).

This potential range of applications of novel organisms, traits and fields of application is contrasted by a hitherto almost non-existent consideration of the ecological impacts and risks of *Genome Editing* applications. In order to be able to assess the intended and unintended new properties of the organisms and their ecological effects, the methods of risk assessment and risk management must be adapted and further developed in many cases. Keeping track with the fast-paced development of biotechnology is crucial to be prepared for the upcoming challenges for environmental protection and nature conservation. To give this developments justice the COP 14 in 2018 parties of the CBD agreed to establish a broad and regular horizon scanning, monitoring and assessment of synthetic biology to review new information regarding the potential impacts of synthetic biology vis-a -vis the three objectives of the CBD and those of its Protocols. The IG GMO will observe and exchange views about these new developments and the horizon scanning process of the CBD.

5.6 Topic 6 – Genome Editing – technology assessment and socioeconomic considerations

Advances in Genome Editing make genetic engineering more accessible and powerful and diversify the range of possible applications (e.g., use in agricultural, nature conservation or disease prevention). This raises not only the question whether current protocols are sufficient to carry out a comprehensive environmental risk assessment, but also whether a wider range of potential impacts, e.g., social, cultural or ethical, should be considered. Thus, there is a need for a broader discussion that includes also other relevant aspects like sustainability issues or the discussion of alternative approaches. In addition, questions like uncertainties, goals, or conceptual and societal challenges need to be addressed. Currently, those aspects are discussed in relation to the terms “technology assessment” and “socio-economic considerations”.

Technology assessment is an interdisciplinary field of research in which risk assessment is embedded in a broader societal perspective. It can include perspectives like the effects of a given technology on socio-economic dynamics or what the alternatives to this technology could be. The term “technology assessment” was first introduced into the discussion of synthetic biology under the Convention on Biological Diversity. Amongst others the AHTEG on Synthetic Biology noted, that the assessment of potential impacts on the environment and human health needs to be complemented by an assessment of cultural and socio-economic aspects.

The wider issues mentioned above are also included in the term “socio-economic considerations”, used in the framework of the Cartagena Protocol on Biosafety, which regulates GMOs on the international level. The Article 26 of the Protocol allows Parties to take socio-economic considerations into account in decision making. The interpretation of the term and the respective assessment scope varies, reflecting different existing national regulatory frameworks. This was taken into account in the voluntary guidelines that are available since 2018 and that contain the following operational definition, reflecting the broad possible scope and the possibility to included ecological aspects as well as specific goals of protection (depending on concept an value of nature) in the risk assessment process of GMOs:

“Socio-economic considerations in the context of Article 26 of the Cartagena Protocol may, depending on national or regional circumstances and on national measures to implement the Protocol, cover economic, social, cultural/traditional/religious/ethical aspects, as well as ecological and health-related aspects, if they are not already covered by risk assessment procedures under Article 15 of the Protocol”.

The *Farm to Fork Strategy* is at the heart of the European Green Deal aiming to make food systems fair, healthy and environmentally-friendly. In the debate about redesigning our food systems which today

consume large amounts of natural resources and result in biodiversity loss and negative health impacts, the use of genetic engineering, new technologies and scientific discoveries as a sustainable solution for food and feed production is hotly debated.

In the context of the current discussion on *Genome Editing,* several stakeholders emphasize the potential benefits and call also for a weighing of risks and benefits. However, it needs to be stated that 1) most regulatory frameworks (including the Cartagena Protocol) do not foresee an analysis of benefits of GMOs, and 2) an assessment of (economic) benefits needs to be complemented by comprehensive assessment of other socio-economic effects, as e.g. outlined in the voluntary guidelines mentioned above. In conclusion, technology assessment can rather be an additional tool to better evaluate the wider impacts of the technology. However, sound methodologies, e.g. for the assessment of economic risks and benefits, are currently lacking.

Practical experience in the implementation of technology assessments and assessments of socio-economic aspects in the context of gene technology, as well as available methods and data are scarce. This applies especially for non-economic issues and environmental aspects that go beyond those covered in the environmental risk assessment including sustainability issues and the assessment of alternatives. Thus, more experience and discussion is needed in these fields.

In light of current developments, the IG GMO will discuss broader issues going beyond the current risk assessment of GMOs and the possibilities to cover those issues by a technology assessment or an assessment of socio-economic considerations. This discussion may focus on issues related to environmental aspects, such as sustainability and nature conservation, but might also touch on related societal aspects, like the intrinsic value of nature and biodiversity. The outcome may deliver valuable input to the discussion regarding wider analysis in the field of GMOs and *Genome Editing*.

5.7 Topic 7 – Applications of novel techniques of genetic modification to wild organisms

Novel techniques of genetic modification are no longer used in domesticated organisms (e.g. crops) only, but also to modify wild organisms such as mosquitoes or mice (e.g. *Gene Drive* organisms with new inheritance mechanisms). Some of these have been proposed for use in nature conservation in order to introduce a permanent genetic modification into wild populations, e.g. to suppress invasive species. Many different taxa of wild species have already been considered as potential targets, with mosquitoes and invasive rodents being the most likely first candidates in the future.

The genetic modification of wild organisms can pose novel and unprecedented risks to the environment and nature conservation. New risk assessment and monitoring approaches will be needed to address these novel risks. In addition, these applications pose conceptual challenges. A broader comprehensive technology assessment and international oversight of these applications will also be required before environmental release can be envisaged.

The IG GMO's technical report on *Gene Drive Organisms – Implications for the environment and nature conservations*[12] has been a first step to start the discussion on specific risks and uncertainties and resulting regulatory needs when using genetically modified wild populations, specifically *Gene Drive* organisms. A corresponding opinion paper (link to download) has been elaborated by the group and was submitted to and endorsed by the plenaries of EPA/ENCA in 2021.

Based on preceding work and reports on the topic elaborated by IG GMO members (e.g. Umweltbundesamt, BfN, FOEN) novel risks and challenges of these applications with focus on wild organisms will be evaluated. The focus shall be on specific risk scenarios for the environment, biodiversity and nature conservation by use of example applications and include implications for risk assessment and post-release monitoring. This should facilitate discussions regarding novel risks and pathways to harm for environmental protection goals and set the scene for necessities regarding

[12] Technical Report on Gene Drive Organisms – Implications fort he environment and nature conservation

risk assessment, risk management, monitoring and decision-making. The specific attention required for environmental aspects shall be highlighted as well as the necessary involvement of the European commission/DG Environment in the ERA and authorization process of applications with nature conservation implications.

5.8 Topic 8 - Change of Paradigm; Challenges due to Applications of Genome Editing in Nature Conservation

Genetic engineering applications are currently also being discussed in connection with biodiversity and nature conservation, which would represent a paradigm shift in these fields. It is therefore important to classify and evaluate these proposals and to come to a decision if such applications would be acceptable from a nature conservation point of view. Since the first release of a genetically modified organism more than 30 years ago, the number of genetically modified crops used in agriculture at global level has steadily increased. The intended release of GMOs outside agro-ecosystems, on the other hand, has been very sporadic. If these applications are discussed intensively in the IUCN context and if some scientists now propose the active use of GMOs as an instrument in nature conservation outside agroecosystems, this represents a novel approach for nature conservation and leads to fundamental challenges on two levels:

First, the environmental risk assessment and risk management of GMOs beyond agricultural applications quickly reaches its limits with the current knowledge already due to the complexity of the receiving ecosystems. This holds true for environmental monitoring as well. It also represents a paradigm shift in addressing risks. So far, one of the main aims of risk mitigation was the limitation of the spread of GMOs in nature in space and time. However, when GMOs are used in wild populations, the permanent spread of genetic modification is intended. The impact of this new direction has not been evaluated so far.

Secondly, some basic questions concerning nature conservation need to be taken into considerations. For example, what are the impacts on current nature conservation practices, if *Genome Editing* becomes a tool in nature conservation? Secondly, using an untried and potentially risk technology for nature conservation might for example jeopardize conservation goals. Furthermore, the question whether species keep their status as wild/natural if they are genetically modified needs to be addressed.

The topic has already been explored in the technical report and the opinion paper on *Gene Drive* Organisms. The IG GMO will elaborate on these issues. It is of special importance that this evaluation is driven by a nature conservation perspective, since basic principles of nature conservation might become affected and challenged. With its basis in the ENCA and EPA network the IG GMO is the genuine place to perform the scientific work on these founding questions, to inform both networks.

6 THE JOINT EPA-ENCA INTEREST GROUP ON GMOs (IG GMO)

The EPA Network plenary endorsed the establishment of the Joint EPA-ENCA 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 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 foundation, the IG GMO has met every year, hosted by different group members. The IG GMO is composed by 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 members from environmental protection agencies and nature conservation agencies or institutions with competence and expertise in ERA and monitoring in different regulatory fields.

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

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7 LINKS TO OTHERS ACTIVITIES

The IG GMO shall promote collaboration with and participation of EPA and ENCA network members interested and involved in this topic. Depending on subjects and activities, the IG GMO shall develop partnerships and exchange information with other Interest Groups (e.g. EPA IG Green and Circular Economy, EPA IG Better Regulation, ENCA IG Monitoring & Assessment, ENCA IG Sustainable Land Use) to ensure that surveillance strategies are coherent and any duplications avoided.

8 WAYS OF WORKING

The IG GMO will meet annually, appropriately timed with the EPA and ENCA Network plenary meetings. The meetings will take place in the different member countries or virtually. The participants will define the content, priorities, type and intervals for work exchange on a case-by-case basis. Products (e.g. technical papers, opinion papers) will be elaborated by correspondence and at the meetings and, when agreed upon, will be presented at the following EPA / ENCA Network plenaries. When agreed, the group's output is published on the EPA and ENCA websites or is directly made accessible on the institutional websites of the group members. The IG GMO welcomes new participants to complete its expertise. At each plenary session an invitation is issued to join the group.