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REPORT FROM THE COMMISSION

on the experience of Member States with Directive 2009/41/EC of the European Parliament and of the Council of 6 May 2009 on the contained use of genetically modified micro-organisms for the period 2019 – 2021

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Report on the experience of Member States with Directive 2009/41/EC of the European Parliament and of the Council of 6 May 2009 on the contained use of genetically modified micro-organisms for the period 2019 – 2021

The information contained in this document has been compiled by the Commission from individual reports submitted by Member States in accordance with Article 17 of Directive 2009/41/EC of the European Parliament and of the Council on the contained use of genetically modified micro-organisms[1] (GMMs).

INTRODUCTION

Directive 2009/41/EC ("the Directive") provides that every three years Member States are to send to the Commission a summary report on their experience with the Directive[2] and that the Commission is to publish a summary based on these reports[3]. The Commission has so far published five reports pursuant to the Directive or to the preceding Council Directive 90/219/EEC[4], for the periods 1999-2003, 2003-2006, 2006-2009, 2009-2014 and 2014-2018[5].

The present report covers the period from January 2019 to December 2021 and is based on 26 Member States[6]' and two EEA EFTA States[7]' individual reports.

The national reports are based on a questionnaire prepared by the Commission services on Member States' experience with the general implementation of the Directive, including their notification and approval systems, inspection and enforcement activities, waste disposal measures, accidents, public consultation and an overview of contained uses and premises for GMMs authorised in their territories.

The Directive does not regulate the contained use of GMOs other than GMMs, e.g. GM plants and GM animals[8]. However, in a number of Member States, the relevant national legislation regulates the contained use of GMOs as well. Therefore, the Commission extended the scope of its questionnaire to allow Member States to share their experience, good practices and challenges encountered in regulating also those organisms.

The report focuses on changes from previous reports and highlights new issues and implementing challenges raised by Member States and the way they were addressed. It

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[1] Directive 2009/41/EC of the European Parliament and of the Council of 6 May 2009 on the contained use of genetically modified micro-organisms (OJ L 125, 21.5.2009, p. 75).
[2] Article 17(2).
[3] Article 17(3).
[4] Council Directive 90/219/EEC of 23 April 1990 on the contained use of genetically modified micro-organisms (OJ L 117, 8.5.1990, p. 1).
[5] The reports are available on this European Commission webpage
[6] Malta has not provided a national report.
[7] Annex XX to the EEA Agreement (which lists, amongst others, the EU GMO legislation applicable under that Agreement) provides that *'[f]or the purposes of this Annex and notwithstanding the provisions of Protocol 1, the term "Member State(s)" contained in the acts referred to shall be understood to include, in addition to its meaning in the relevant EC acts, Iceland, Liechtenstein, Norway'*. Therefore, reference to 'Member States' in this document also includes the EEA EFTA States who replied to the questionnaire (Norway and Iceland).
[8] Article 2(4), second indent of Directive 2001/18/EC on the deliberate release of GMOs into the environment excludes from the definition of 'placing on the market' *'making available GMOs other than microorganisms referred to in the first indent, to be used exclusively for activities where appropriate stringent containment measures are used to limit their contact with and to provide a high level of safety for the general population and the environment, the measures should be based on the same principles of containment as laid down in Directive 90/219/EEC'*.

provides, in the conclusions, the Commission's views on some questions raised by Member States regarding the implementation of the Directive.

Disclaimer: The information contained in this report relating to Member States is based on Member States' individual reports.

Neither the European Commission nor any person acting on its behalf is responsible for the content of that information and of any use made of it.

Clarifications provided in the report addressing questions by Member States reflect the views of the European Commission. However only the Court of Justice of the European Union is competent to authoritatively interpret Union law.

PART I: GENERAL IMPLEMENTATION OF THE DIRECTIVE

1. Notification and approval systems (and relevant changes)

No major changes since the last reporting period were reported concerning the competent authorities responsible for applying the national legislation or in the legislation.

Germany reported changes in its national legislation to extend its notification and approval system to gene drive organisms and to keep up to date the level of academic expertise and knowledge of biological safety officers and project leaders.

France prepared new application forms including a dedicated section on new genomic techniques. Before the publication of the new forms, French authorities supported applicants in filling out application forms concerning contained uses of GMOs obtained using such techniques.

Some Member States reported challenges in the notification and approval process. Those were related to the time limits for processing notifications and following the administrative procedures, as well as to the complexity of some notifications.

Austria reported challenges related to the timely processing of a particular notification which required assessing a microwave technology for the inactivation of waste from class 2 contained uses. This notification required a time-consuming risk assessment and collaboration with the national scientific committee prior to approval.

Slovenia reported an increase in workload, particularly for biosafety class 2 notifications, due to a higher number of notifications, which almost doubled, as well as to the COVID-19 pandemic, since many research institutions started research projects on the SARS-CoV-2 virus. These developments, together with the lengthy administrative procedures of the national scientific committee, led to delays in processing notifications.

Italy highlighted the need for appropriate digital tools to reduce the staff workload, and provided an example of a collaboration project between the supervisory and safety bodies, research institutions and hospitals, to increase the knowledge and skills for the prevention of risks and the protection of health and the environment as regards the contained use of GMMs[9].

Denmark reported the presence of antibiotic resistance marker genes as a challenge in the approval process and the authorities' efforts to phase out GMO strains containing such genes which are used to produce medicines. The competent authority is currently setting up different criteria for approval of the presence of these types of genes, one of which is to identify what antibiotic the gene confers resistance to, as categorised by the European Medicines Agency.

2. Waste disposal

In general, the majority of Member States reported neither changes nor challenges in waste management during the reporting period.

Belgium reported on a new waste regulation at regional level (Brussels Capital Region).

[9] The tool for creation of the network is the website www.biotechsafety.org

Germany reported an amendment of the national legislation clarifying the rules on in-house transport of GMO waste. In particular, it now requires, as from safety level 1, that the transport of this waste takes place in labelled, sealed and shatterproof containers that can be disinfected.

Austria and Finland reported challenges in the assessment of alternative methods of GMM inactivation.

Austria reported ongoing discussions on the use of a microwave waste inactivation system as an alternative to autoclaving for the inactivation of class 2 GMO waste, with exceptions for certain types of viruses and biosafety levels.

Austria considered that general EU guidelines or an official checklist of requirements would be useful to aid the evaluation and approval process for alternative inactivation methods in the future. This guideline could, for example, include a list of inactivation parameters according to which any new inactivation method should be validated (test parameters, test organisms for different biosafety levels and groups of organisms, whether direct comparison with the standard autoclaving method is required, etc.).

Finland reported that few research institutes are willing to maintain in situ autoclaving facilities because of their costs and occupational health issues. In addition, Finland and Germany noted that operators find fewer disinfectants on the market suitable for chemical inactivation of their GMMs. Therefore, most operators prefer to send their GMM waste to municipal incineration plants, but there are difficulties with waste packaging and transportation requirements (labelling, classification, etc.). Finland considered that the relevant EU requirements are very complex and ambiguous when it comes to non-infective GMMs that are not pathogens. The competent authority is tackling this issue by giving advice to operators on a case-by-case basis considering the different sectoral requirements.

In addition, Finland reported its experience with recycling of class 1 microbial fermentation waste together with other bio-waste into compost, which required studies on the survival of GMMs and monitoring to confirm that the composting process worked effectively and no GMMs survived it.

3. Inspection and enforcement issues

The majority of Member States reported no changes in their inspection and enforcement activities.

Belgium, Czech Republic, Denmark, Germany, Spain, Finland, Portugal and Norway reported changes in this field, in several cases due to the COVID- 19 pandemic.

Those Member States established digital tools and reported a wide use of instruments for the remote surveillance of activities and facilities, for example video conferences with virtual tours, questionnaires, presentation of photographs, reports, recordings and maintenance protocols. However, Austria and Italy reported a lack of reliable and appropriate digital tools for remote inspections. Portugal adopted a guidance to support inspectors.

Some Member States reported shortages in disinfectants due to the COVID-19 pandemic.

Overall, the number of inspections varied between Member States from 6% to 100% of contained use premises.

A few countries[10] did not carry out any inspection during the reporting period, mostly because no contained use premises/activities were notified and, in some cases, due to the COVID-19 pandemic, particularly during the lockdown period[11].

In general, the impact of the COVID-19 pandemic on inspection and enforcement activities resulted in:

- a decrease in the number of on-site inspections, particularly for class 1 contained uses (Belgium, Ireland);

- changes in the way inspections were carried out in some Member States, such as a switch to remote or hybrid inspections (Germany, Finland); in many cases remote inspections were focused primarily on keeping mandatory documentation checks (Czech Republic);

- application of risk-based criteria for remote inspections, modification of inspection plans (Czech Republic and Denmark).

Some Member States acknowledged that remote inspection is an effective way to inspect laboratories performing low risk work. It saves the inspectors time as well, which gives them more time for assessing uses with higher risk to the environment and health.

The issues most frequently encountered in the course of inspections reported by some Member States[12] were related to deficiencies in:

- compliance with good laboratory practice (GLP) as regards premises (e.g. organisation, inadequacy or deficiencies in laboratory equipment, incorrect labelling of the laboratory and equipment), or users (e.g. inadequate protective clothing, missing instructions, insufficient training);

- biosafety measures (e.g. no restricted access to the premises where the contained use takes place, level of protection not corresponding to the risk class, insufficient hygiene and disinfection methods) and internal control procedures (e.g. lack of a biosafety officer in charge of implementing properly the confinement and control measures according to the class of risk);

- the administrative procedures (delayed notification of changes in persons in charge, failure to keep records of staff training, failure to notify that a premise is no longer used for contained uses) and documentation management (e.g lack of complete, up-to date, accurate documentation, incomplete records of staff working in the premises);

- waste management (inactivation method not validated);

- failure to notify activities involving the use of GMMs (Ireland).

France noted difficulties reported by applicants concerning the risk assessment of GMMs contained uses of classes 2 and 3 to file the notifications for the correct containment level. To overcome these difficulties, the competent authority and the independent expert committee

[10] Italy, Greece, Italy, Latvia, and Portugal.
[11] Spain and Austria and Spain.
[12] France, the Netherlands, Slovenia and Finland.

jointly prepared a guidance document on the principles of risk assessment for contained use of GMOs (including GMMs).

In terms of enforcement, Member States reported on action taken. When inspections identified situations requiring corrective actions, different measures were adopted (inspection reports, letters, warnings, fines, etc.) to take remedial action and bring the use back into compliance within a set timeframe. If the non-compliance could result in an increased risk for human or animal health or for the environment, all activities involving GMMs were immediately stopped and the GMMs destroyed. For minor issues (e.g. regarding documentation), deficiencies were corrected at the time of the inspection. In general, users implemented the corrective actions requested by the authorities in the given timeframe, and competent authorities controlled this with follow-up inspections or by checking the updated documentation.

Cyprus noted that since 2018 there has been only one research institute approved for the contained use of GMMs (only working with class 1 and class 2 uses), and highlighted the need for identifying and raising awareness of other premises/installations (institutes, universities, laboratories, etc.) which may have obligations under the Directive. For this reason, the competent authority published a newsletter and sent information letters to all potential operators which might work with GMMs, informing them about the regulatory requirements. The competent authority stressed the need to intensify this approach and carry out specialized inspections.

Belgium highlighted potential challenges related to the Do-It-Yourself (DIY)(Bio) practice, which aims at giving everyone with an interest in biotechnology/bio(medical) sciences the opportunity to develop research projects (open source science). Challenges arise from the difficulty to ensure oversight by professionals or competent authorities of such activities, in particular where individuals design and conduct experiments with GMOs at home ("garage biology"), without necessarily respecting biosafety regulations and standards. The Belgian Service Biosafety and Biotechnology (SBB) is currently working with the competent authorities on the potential challenges associated with the application of the Directive in relation to this practice.

4. Accidents

No accidents (according to the definition of 'accident'[13] in Article 2(d) of the Directive) were reported.

Some Member States[14] reported incidents without consequences on human health or the environment. Therefore, these incidents were not communicated to the Commission and the other Member States.

Those incidents involved classes 1 and 2 contained uses. The majority of incidents happened due to human error.

Member States who reported incidents indicated that they have a system in place to handle such situations which is based on risk analysis to establish corrective measures and avoid further incidents in the future. Concerned Member States involved experts and provided recommendations to users and training. As part of the follow-up, risk analyses were carried

[13] 'Accident' means any incident involving a significant and unintended release of GMMs in the course of their contained use which could present an immediate or delayed hazard to human health or the environment

[14] Belgium, Denmark, Germany, the Netherlands and Finland.

out by the operators/users, incident reports were drawn up and action plans to eliminate any risk were sent to the competent authorities.

All the entities where incidents took place made the necessary adjustments to improve the procedural aspects to avoid similar cases in the future, such as adapting or changing their standard operating procedures, amending the risk assessment and providing training to the staff.

5. Public information and consultation

No changes in the provision of information to the public on contained uses of GMMs since the last reporting period have been reported by Member States.

Germany reported on adaptations in its federal legislation as regards the conduct of public consultations during COVID-19 pandemic.

In Hungary questions have been raised on the handling of confidential data. A consultation mechanism between the competent authority and users was established in order to facilitate the authorisation procedure and handle confidential data.

Public consultations mainly concerned classes 3 and 4 contained uses.

In most Member States, public consultations are done via online tools and comments are rarely made by public. In Belgium (Flemish Region), the public is consulted in the framework of the request for environmental permit. There were approximately 30% of the cases of public consultations in which observations and objections were taken into consideration by the competent authority.

6. Interpretation of the Directive

Many Member States[15] did not report any specific challenges regarding the interpretation of the Directive.

However, some Member States[16] mentioned difficulties linked to the definitions in the Directive, particularly in the context of new genomic techniques and synthetic biology, the correct classification of the contained uses and the legal status of certain products obtained by new genomic techniques.

Finland considered that the definitions in the Directive are outdated and have been a major problem particularly concerning new genomic techniques and in the current research environment. According to Finland, this creates legal uncertainty as both the operators and the authorities have sometimes doubts on whether a notification is actually required or not.

In addition to this, Finland pointed out difficulties in classifying uses of viruses and cell cultures, particularly in cases where their pathogenicity has been reduced , and reported on the existence of different views about the legal status of micro-organisms when nucleic acids are transiently introduced in the host cell but these are not inherited by the progeny and when the organism resulting from the genetic modification is genetically identical to a wild-type organism. In that regard, it asked for the development of Commission guidance clarifying these questions.

[15] Denmark, Estonia, Greece, Cyprus, Latvia, Lithuania, Poland, Portugal, Slovakia and Slovenia.
[16] The Czech Republic, Germany, Luxembourg, the Netherlands and Finland.

Finally, in view of the frequently changing premises of individual research groups and organisations as well as SMEs, Finland asked for a reconsideration of the notification requirements in Article 6 of the Directive, at least as regards class 1 uses, in order to lower the administrative burden.

The Czech Republic raised questions on the legal status of certain products (e.g. whether cell lines, tissue samples or sub-cellular elements fall under the Directive).

The Netherlands reported difficulties with the interpretation of the definition of GMOs, e.g. in relation to viral replicons[17], and stressed that the general principles and specific measures required in Annex IV of Directive could not be appropriately applied for some notified activities, e.g. in relation to the production of advanced therapy medicinal products (ATMPs)[18] and vaccines.

Some Member States (Czech Republic, Netherlands and Finland) highlighted that the GMO/GMM definitions should be updated in light of the application of new molecular biology techniques. Finland also suggested to evaluate the pros and cons of a technology-based regulation versus a trait-based regulation when dealing with rapidly developing techniques. The Netherlands saw a need for a discussion on the interpretation of the GMO definition at the EU level.

France highlighted difficulties applying the Directive as regards *in vitro* random mutagenesis following the decision of the French Council of State of 7.2.2020[19]. France also asked whether the techniques and organisms that fall within the scope of Directive 2009/41/EC are to be considered identical to those falling under Directive 2001/18/EC.

Germany noted that several competent authorities of the Federal States pointed to a lack of clarity regarding the application to GMMs of the Court of Justice of the EU (CJEU) judgment in Case C-528/16[20] concerning organisms obtained by new techniques/methods of mutagenesis. It reported discussions with operators, where the definition of GMO was no longer clear for newly developed techniques (such as CRISPR/Cas) and raised questions on the classification of activities for the production of organisms with a low risk, created in a closed system, using the new genomic techniques.

Bulgaria, Italy and Sweden noted the complexity in distinguishing between contained use and deliberate release as regards clinical trials with GMOs/GMMs, and Spain highlighted that the fact that Member States have different interpretations and approaches creates difficulties for the competent authorities, companies and users.

Sweden reported on ongoing work to clarify the national requirements concerning clinical trials with GMMs as regards their transportation, storage and preparation before medicinal product are administered to patients (i.e., clinical trial subjects).

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[17] A viral replicon is a genetic material originated from a viral genome and which can self-replicate (construct an identical copy of itself).

[18] *ATMPs* are medicines for human use that are based on genes, tissues or cells.

[19] https://www.conseil-etat.fr/decisions-de-justice/dernieres-decisions/conseil-d-etat-7-fevrier-2020-organismes-obtenus-par-mutagenese

[20] Judgment of 25.7.2018, Case C-528/16, *Confédération paysanne and Others* (ECLI:EU:C:2018:583)

Ireland suggested to align the requirements for class 1 uses with Directive 2000/54/EC on the protection of workers from risks related to exposure to biological agents at work[21], because class 1 uses involve usually strains with a long history of safe use, which present no or negligible risk. It noted that Directive 2000/54/EC does not require the notification of activities involving risk group 1 biological agents but requires compliance with the principles of Good Occupational Safety and Hygiene.

Norway asked which regulatory framework to apply when it comes to uses involving GM animals at different animal developmental stages, as national requirements on GM-animals are not properly adapted to this, and the Directive's requirements (including on cells in culture) are often better suited.

7. Overview of contained uses and premises

Information on the number of notifications and amendments submitted for contained uses of GMMs, number of premises and number of contained uses of GMMs reported by each Member State are provided in the national Member States reports.

For those Member States that have extended the scope of their national legislation to the contained use of GM animals and GM plants[22], information on the number of notifications for contained uses of GMOs other than GMMs submitted is also provided in the national Member States reports.

There are no major changes in the number or the type of notifications received.

The number of notifications varies yearly for some Member States. An overall tendency is a slowly decreasing number of notifications regarding plant research and an increasing number of research related to pharmaceutical/therapeutic applications (Spain and Finland).

Finland noted that core facilities providing GMO services to other operators (research groups or companies) are becoming more widespread. The number of notifications from the commercial sector has remained low in comparison with the basic research sector. The vast majority of notifications concern biomedical research and relate to research activities under class 2.

However, notifications of class 3 uses have increased, some of them (during the year 2020) related to the SARS-CoV-2 virus (Spain and Germany). Germany reported around 30% of class 3 activities concerning research on SARS-CoV-2. Slovenia and France noted that the number of notifications almost doubled in the reporting period, particularly in class 2 uses due to the COVID-19 pandemic, since many research institutions started research on the SARS-CoV-2 virus. France highlighted that in 2020, during the pandemic, the number of notifications increased by 27.5% compared to the previous year.

Norway reported an increase in notifications of class 2 uses of GMMs, alone or in combination with GM animals, and noted a stable number of notifications from large scale production of GMOs, clinical trials with GMO medicines, GMOs used in education and from the use of GM animals and GM plants.

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[21] Directive 2000/54/EC of the European Parliament and of the Council of 18 September 2000 on the protection of workers from risks related to exposure to biological agents at work (seventh individual directive within the meaning of Article 16(1) of Directive 89/391/EEC) **(***OJ L 262 , 17/10/2000, p.21).*

[22] All, except Estonia, Greece, Italy, Cyprus, Latvia, Luxembourg and Romania.

Some Member States observed an increase in the overall number of notifications, in particular in 2021, and noted an increase in the number of GM lines in animal testing.

Table 1: Overview of authorised classes of contained uses in the Member States

Class of use	**Number of MS**	
No notifications	1	Greece
Class 1 only	3	Bulgaria, Latvia, Romania
Up to class 2	7	Cyprus (only class 2), Croatia, Lithuania, Norway, Slovenia, Slovakia and Iceland
Up to class 3	12	Austria, Belgium, the Czech Republic, Denmark, Estonia, Spain, Ireland, Italy, Luxembourg, the Netherlands, Portugal and Finland
Up to class 4	4	Germany, France, Sweden, Hungary

The majority of the Member States that received notifications for GM plants or GM animals[23] did not encounter specific challenges related to those.

PART II: INVESTIGATIONAL MEDICINAL PRODUCTS THAT CONTAIN OR CONSIST OF GMOs

All Member States, except Lithuania and Croatia, reported no changes in the manufacturing and administration of investigational medicinal products (IMPs) for human and veterinary use (table 2).

Lithuania amended the national legislation and procedures for authorisation of clinical trials under Regulation 536/2014[24].

Croatia issued a guidance for clinical research.

Table 2: Authorisation of IMPs under the Directive and total number of authorisations

	Human use		**Veterinary use**	
	Manufacturing	**Administration**	**Manufacturing**	**Administration**
AT	Yes / 0	Yes / 0	Yes / N.D	Yes / N.D
BE	Yes / 11	Yes / 94	Yes / 0	Yes / 0

[23] Belgium, the Czech Republic, Denmark, Ireland, France, Croatia, Hungary, the Netherlands, Austria, Portugal, Slovenia and Slovakia.

[24] Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.

BG	Yes / 0	N.A	N.A	N.A
CY	N.A	N.A	No	N.A
CZ	Yes / 1	N.A	Yes/ 0	N.A
DE	Yes / N.D	N.A	Yes / N.D	N.A
DK	Yes / 0	Yes / 15	Yes/0	Yes/ N.D
EE	N.A	N.A	N.A	N.A
EL	N.A	N.A	N.A	N.A
ES	Yes / 11	Yes/ 8	Yes/ N.D	N.A
FI	Yes / 6	Yes / 5	Yes / 0	Yes / 0
FR	Yes / 5	Yes / 0	Yes / N.D	Yes / N.D
HR	Yes / 2	Yes / 2	No	No
HU	N.A	N.A	N.A	N.A
IE	Yes /58	No	Yes /0	No
IT	Yes / 72	Yes / 68	Yes / 0	Yes / 0
LT	N.A	Yes/3	N.A	N.A
LU	N.A	N.A	N.A	N.A
LV	N.A	N.A	N.A	N.A
MT	No report submitted			
NL	Yes /N.D	N.A	Yes /N.D	N.A
PL	N.A	N.A	N.A	N.A
PT	Yes /2	N.A	N.A	N.A
RO	Yes / 0	N.A	Yes / 0	N.A
SE	N.A	N.A	N.A	N.A
SI	N.A	N.A	N.A	N.A
SK	Yes / 0	N.A	Yes /0	N.A

N.D: not determined

N.A: Clinical trials with IMP containing GMOs are not regulated under the Directive.

France and Slovakia reported applying fast-track procedures to process applications related to the COVID-19 pandemic, in accordance with the derogation provided in Regulation (EU) No. 2020/1043[25], which applied to the environmental risk assessment of IMP (prior environmental risk assessment for clinical trials not required as long as COVID-19 is considered a pandemic by the WHO) and the consent under the Directive.

Spain acknowledged that significant progress has been done on the interplay between the GMO and the medicinal products legislation, and that it would be desirable to continue work to harmonise and clarify the legal framework for clinical trials with GMOs/GMMs at EU level. France stressed that, since the implementation of the common application forms for IMPs, the environmental risk assessment has greatly improved as only relevant information was required by the competent authorities.

Italy reported difficulties by sponsors, authorisation holders and users to cooperate in order to prepare the notification to the competent authorities, particularly in a case of multicentre clinical trials, and highlighted that a better cooperation with the other national competent authorities would allow to get more data and to improve the monitoring system. Italy stressed the importance of having a harmonised approach among the competent authorities.

Belgium developed a practical guidance in order to help clinical trial sponsors and investigators of IMPs to determine the procedural requirements to be followed for their clinical trial with GMO-medicinal products and noted that the Federal Agency for Medicines and Health Products also provided a preliminary advice on which legislative procedures on biosafety should be followed.

A few Member States (Spain, France and Italy) called for a European consensus on regulatory aspects of clinical trials and early access to new medicinal products containing or consisting of GMOs.

PART III: GENE DRIVE MODIFIED ORGANISMS

Gene drive[26] modified organisms (GDOs) are not covered by the Directive if they do not involve the use of microorganisms as defined in the Directive**.** Nevertheless, Member States were invited to provide information, if any, on their experience with regulating the contained use of GDOs and how the national legislation, if any, is applied in this respect.

Only Germany reported a change in national legislation since the last reporting period and noted that the provisions on GDOs have been included in the newly amended genetic engineering safety regulation (‘Gentechnik-Sicherheitsverordnung’). Activities with GDOs are initially assigned a safety level of class 3, which requires an approval (prior consent) by the competent authority before they can proceed (Article 9(2) Directive 2009/41/EC). An advisory board is involved in a case-by-case assessment and the recommendation of specific safety measures are issued on this basis. The competent authority can assign another safety level to the activities on the basis of a risk evaluation as well. Individual safety measures are specifically tailored to the organism in question.

[25] Regulation (EU) 2020/1043 of the European Parliament and of the Council of 15 July 2020 on the conduct of clinical trials with and supply of medicinal products for human use containing or consisting of genetically modified organisms intended to treat or prevent coronavirus disease (COVID-19), OJ L 231, 17.7.2020, p. 12.
[26] For the purpose of this report, "gene drive" is a system of biased inheritance in which the ability of a genetic element to pass from a parent to its offspring through sexual reproduction is enhanced.

Two Member States (Italy and the Netherlands) reported new notifications for GDOs received under their contained use legislation:

- on *Anopheles gambia* for the development of GM mosquitoes for malaria control, and *Aedes aegypti* mosquitoes and *Drosophila suzukii* genetically modified with reduced reproductive capacity of offspring (2 notifications of class 2 – Italy);

- on nematode *Caenorhabditis elegans* to study the spread of a gene drive and the possibility of resistance development against it (one notification of class 2 – Netherlands).

These Member States shared their practical experience[27] applying containment and protective measures for activities involving GDOs.

Some Member States[28] provided their views on risk assessment and risk management of GDOs and noted that the risk classification system applied at national level to GDOs and the containment measures would be the same as the ones the Directive provides for GMMs. However, the specific characteristics of the GDOs should be taken into account on a case-by-case basis[29].

Belgium noted that the risk assessment and risk classification principles provided by the Directive for GMMs in contained use remain appropriate for activities with GDOs. However, Belgium highlighted that in the processes of risk assessment and risk management, specific characteristics of the GDO (the rapid spread of the GDO-carried modification through several generations of target or non-target organisms) should be considered. Some other aspects would also merit further attention, depending on the particular GDO manipulated, for example if it is an arthropod. In this context, the SBB has contributed to the elaboration of guidelines to help users and competent authorities in the classification and management of activities with GDOs[30].

Some Member States[31] have adopted emergency plans for contained uses with GDOs.

Bulgaria indicated that it would be appropriate to consider initially that any GDO will pose a high risk for the environment and to apply stringent containment measures. Less stringent containment measures could be set on a case-by-case basis if it is demonstrated that the risks are lower.

Sweden noted that if a GMM was modified with a gene drive mechanism, it should be subject to contained use of at least class 2.

Some Member States[32] stressed that their experience with GDOs is still very limited and expertise is needed in this field. Those Member States highlighted that the rapid development of the technology and the containment adaptation to it, as well as uncertainties on environmental risk assessment are important elements to be considered for activities with GDOs.

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[27] The detailed information is available in national reports.
[28] Belgium, Bulgaria, the Czech Republic, Germany, Ireland, Spain, Italy, Luxembourg, Lithuania, the Netherlands, Finland and Sweden.
[29] the Czech Republic, Spain, Luxembourg and Finland
[30] CJB van der Vlugt, DD Brown, K Lehmann, A Leunda, N Willemarck (2018).
[31] Belgium, the Czech Republic and the Netherlands.
[32] Bulgaria, the Czech Republic, Ireland, Lithuania and Finland.

Ireland requested guidelines or regulatory information specifically addressing biosafety and gene drive use.

CONCLUSIONS

Member States reported their experience with the Directive for the period 2019-2021 to the Commission. This report summarises their contributions on various aspects of the implementation of the Directive and their experience with IMPs and GDOs. Some clarifications from the Commission are also added in this section, to address Member States' comments.

In a few Member States national legislation was adapted in order to reflect the current state of science and technology development and the need to keep up to date the level of knowledge and expertise for the assessment of contained uses of GMOs/GMMs.

In general, the national reports show that Member States cope well with the implementation of the Directive and ensure that all measures are taken to avoid adverse effects on human health and the environment which might arise from the contained use of GMMs. However, some Member States considered the GMO/GMM definitions do not reflect the current state of development of science and technology and a few Member States considered that there is a lack of legal clarity as regards organisms obtained by new genomic techniques, following the Court of Justice of ruling in Case C-528/16 concerning mutagenesis.

In this regard, the Commission recalls that, in its 2015-2018 report[33], it referred to the applicability of the interpretation made by the Court of Justice of the mutagenesis exemption set out in Directive 2001/18/EC (Article 3(1) of that Directive read in conjunction with point 1 of Annex IB) and confirmed that it also applies to the exemption of mutagenesis techniques in point 1 of Part A of Annex II to Directive 2009/41/EC. Some clarifications on the scope of the Directive were also given in the Commission Staff Working Document "Study on the status of new genomic techniques under Union law and in light of the Court of Justice ruling in Case C-528/16" ("Commission study on new genomic techniques") published in April 2021[34].

Some Member States reported difficulties in the notification and approval process. Those were related to the time limits for processing notifications and following the administrative procedures as well as to requests for additional information needed for risk assessment due to the complexity of notifications.

In order to reduce administrative burden, one Member State suggested aligning the requirements for contained use of class 1 with the requirements in Directive 2000/54/EC on the protection of workers from risks related to exposure to biological agents at work.

It should be noted that both Directives share the common goal to protect human health against risks arising or likely to arise from exposure to biological agents. However, in addition to this, Directive 2009/41/EC has the objective to protect the environment and lays down the measures to this effect.

The national reports highlighted once again the complexity of completing notification and authorisation procedures under different regulatory frameworks for IMPs i.e. under Directive

[33] COM(2021) 266 final
[34] SWD(2021) 92 final

2009/41/EC and Regulation (EU) No 536/2014 respectively, differences in Member States' approaches as regards the environmental risk assessment of clinical trials with IMPs and the need to continue working to harmonise this field. This issue was particularly highlighted in the context of the COVID-19 pandemic and access to medicinal products that were urgently needed to overcome/prevent emerging public health issues.

The Commission's Communication on a Pharmaceutical Strategy for Europe[35] recognized that the regulatory requirements for the authorisation of medicines for human use that contain or consist of GMOs should be fit for purpose when it comes to addressing the specificities of medicines and the conduct of clinical trials with those products in the EU. It furthermore indicated that solutions would be explored during the evaluation of the pharmaceutical legislation considering the mechanisms for the continuous and timely adaptation of its technical requirements in light of emerging science and technologies with a view to enhance effectiveness and protect human health while minimising harmful impacts on the environment.

In terms of enforcement, no serious cases of non-compliance have been reported as regards safety for human health and the environment.

The COVID-19 pandemic has forced enforcement authorities to swiftly adjust their practices, dealing with specific challenges and limitations on the possibility to conduct on-site inspections, and requiring changes in work patterns imposed by lockdowns, while at the same time ensuring that biotechnology research is conducted under safety conditions.

In general, competent authorities responded to the COVID-19 pandemic using different tools, and a number of measures were introduced following a risk-based approach that prioritised inspections and enforcement in areas where critical risks were identified, and temporarily suspending inspections of low-risk contained-use activities. The use of digital tools was also highlighted as a way to increase knowledge and skills for the prevention of risks and protection of health and the environment in the case of contained use of GMMs between research institutions, in order to share knowledge and gather new evidence.

As regards GDOs, the national reports show that experience in this field is still limited. Reporting Member States indicated that there would be no particular challenges in applying the same measures for GDOs as the ones the Directive provides for GMMs, and that the risk assessment and risk classification principles provided in the Directive would be appropriate for activities with GDOs, while considering their specific characteristics on a case-by-case basis.

Some Member States have requested guidance addressing biosafety issues in relation to the contained use of GMMs, particularly in the context of biotechnology developments and new genomic techniques.

The Commission study on new genomic techniques published in 2021 concluded that the necessary scientific knowledge on the application of these techniques in GMMs is still limited or lacking, especially on safety aspects. The report, explained that, as regards the use of new genomic techniques in microorganisms, the Commission intended to continue to build up the required scientific knowledge, in view of possible further policy actions[36]. To this end, the

[35] COM(2020) 761 final

[36] Based on the findings of the study, the Commission is working on an initiative to propose a legal framework for plants obtained by targeted mutagenesis and cisgenesis and for their food and feed products:

European Food Safety Authority has been mandated to gather information and provide an opinion on new developments in biotechnology applied to microorganisms, in order to get an up-to-date and deeper understanding of the use of the technologies in this area and of possible risks associated to them[37]. In addition, the European Network of GMO Laboratories, assisted by the European Union Reference Laboratory on GM food and Feed, is developing a report on the detection of GMMs, including those obtained by new mutagenesis techniques[38].

The Commission organises regular meetings of the national competent authorities responsible for the Directive, where it will continue to discuss with these authorities relevant issues concerning the implementation of the Directive.

https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/13119-Legislation-for-plants-produced-by-certain-new-genomic-techniques_en

[37] https://open.efsa.europa.eu/questions/EFSA-Q-2022-00508

[38] https://gmo-crl.jrc.ec.europa.eu/ENGL/docs/MandateENGL_WG_GMM.pdf