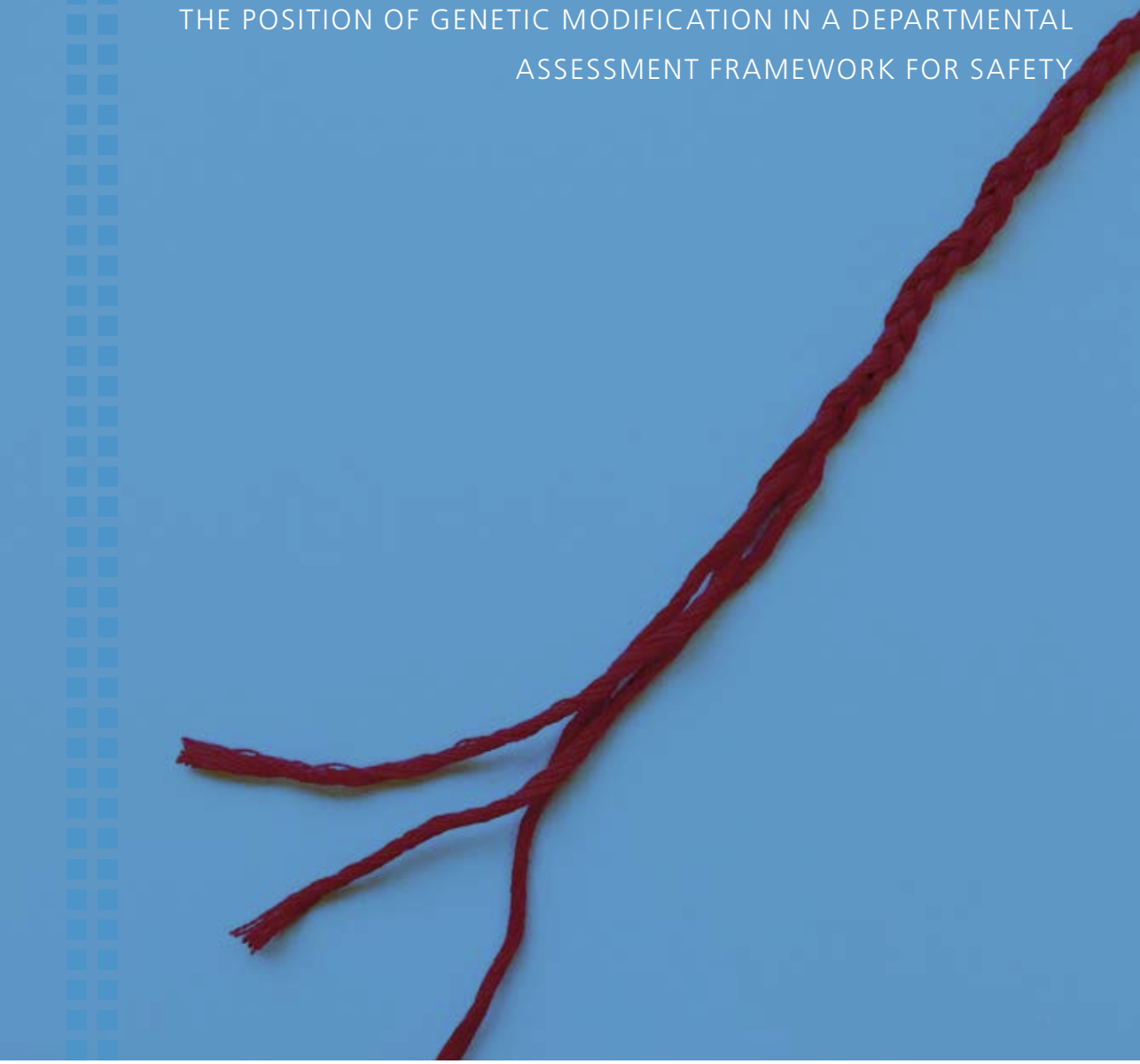
COMMISSIE
COGEM
GENETISCHE
MODIFICATIE

TOPIC REPORT
CGM/151215-02

RECURRENT THEMES IN GMO AUTHORISATION:

THE POSITION OF GENETIC MODIFICATION IN A DEPARTMENTAL ASSESSMENT FRAMEWORK FOR SAFETY



Colofon
Design: Avant la lettre, Utrecht

COGEM provides scientific advice to the government on the risks to human health and the environment of the production and use of GMO's and informs the government of ethical and societal issues linked to genetic modification. (Environmental Management Act §2.3).

SUMMARY

The Ministry of Infrastructure and the Environment wants to develop a comprehensive assessment framework for use in all its policy areas that involve risk and safety issues. In 2014, as part of this process the ministry published a policy paper called 'A Considered Approach to Safety: Recurrent Themes' [Bewust omgaan met veiligheid: rode draden]. As genetically modified organisms (GMOs) are one of the topics in the ministry's 'safety domain', COGEM has investigated how the policy for GMO authorisation matches up to the ten principles set out in the policy paper.

COGEM concludes that the GMO authorisation procedures are fully or partially in line with some of the principles for a considered approach to safety (transparency, responsibility, precaution and future-proofing). However, they do not align, both in terms of policy and (logically) the implementation of that policy, with the principles of appraisal, security and safety, and integrating innovation with safety.

GMO policy leaves little or no room for political judgement on the balance between costs and benefits, because GMOs are only permitted if the risks are negligible. As a result, some potential gains for society may be missed and innovation frustrated.

In addition, GMO policy does not perform well against the principles of transparency and involvement. Some authorisation procedures are hardly transparent to third parties (for example, for contained use and marketing authorisation for GM medicines). The possibilities for involving citizens in the decision-making process are for practical purposes limited by the conditions on submitting representations.

CONTENTS

1

INTRODUCTION

In 2014 the Ministry of Infrastructure and the Environment published the policy paper 'A Considered Approach to Safety: Recurrent Themes' [*Bewust omgaan met veiligheid: rode draden*] (hereafter referred to as CAS). The document is part of a wider project to develop a comprehensive assessment framework for all the risk and safety issues within the ministry's policy remit. Biotechnology and genetically modified organisms (GMOs) are one of the topics in the ministry's environmental safety domain, which means that GMO policy should also as far as possible be compatible with this assessment framework.
With this in mind, COGEM investigated, for the areas covered by its remit, how the GMO authorisation policy matches up to the ten principles set out in the ministry's policy paper. This report examines how the ten principles for a considered approach to safety are reflected in the GMO authorisation procedures.

1.1 'A CONSIDERED APPROACH TO SAFETY: RECURRENT THEMES'

The different safety domains, such as environmental policy, drinking water quality, flood protection, environmental safety, rail safety, air traffic safety, etc., each have their own context. As a consequence of the differences between these fields, a range of specific measures are needed to ensure human and environmental safety in each case. The considerations that must be weighed up in safety policy form a complex network with a diversity of stakeholders and interested parties in parliament and society. However, these tailored solutions are in danger of obscuring the goal of creating a single broad assessment framework.[1]
In its CAS policy paper the ministry describes the components of the network in the field covered by its safety policy and then identifies the recurrent themes in the network of the various safety domains. Overarching aspects are obviously the promotion of safety and the management and reduction of unacceptable risks. Other important aims are preventing social problems in the physical environment. The 'solvability' of the last point is complicated by the differences of opinion about the public interest, the distribution of costs and benefits and the underlying comparability of risks. Scientific insights make an important input to the appraisal of policy options and political decision-making. However, the document recognises that this decision-making process should also take account of other, less quantifiable factors, such as perception, emotion, justice, economic interests, and the national and international legal context. The

document identifies ten principles for a considered approach to safety that can help to bring these factors within the orbit of the decision-making process.

1.2 TEN PRINCIPLES FOR A CONSIDERED APPROACH TO SAFETY

The principles form the building blocks of an assessment framework for use in the policy processes within the ministry's risk and safety domain. The principles came originally from the government's 2006 vision document 'Coping Rationally with Risks' [*Nuchter omgaan met risico's*].[2] A few additional points were added to this list in 2009 and 2013.[3,4]

Principles for a considered approach to safety

1. Ensure a transparent political decision-making process in which choices are supported by arguments.
2. Decisions must explicitly state the responsibilities of government, businesses and citizens.
3. Weigh up the dangers and risks of activities, and as far as possible balance them against the costs and benefits to society of those activities.
4. Involve the public at an early stage of the policymaking process, tailoring the type and degree of public engagement to the nature of the issue.
5. Where possible, take account of cumulative risks arising from different sources.
6. Apply the precautionary principle to new or uncertain risks.
7. When new risks are involved it is especially important to consult the public throughout the whole policymaking process and talk about interests, emotions, risk perception and ethical considerations.
8. Make use of the existing knowledge available in society to identify new risks early on.
9. Link security and safety: do not lose sight of one when policy focuses on the other, and investigate possibilities for combining them.
10. Ensure that innovation and safety reinforce each other, that safety requirements do not frustrate innovation, and that innovation goes hand in hand with safety.

1.3 POLICY MUST TAKE ACCOUNT OF CONTEXT

The policy paper states that the policy process should take account of different contexts, each of which should be represented in the final assessment. These are the physical environment (material world or actual situation), the legislative framework and national and international agreements (system world), and the social and psychological context of norms, values, emotions and perceptions. COGEM notes that in addition to these, the economic context also plays a part.

The ten principles are not all relevant for each and every step in the policy process.[a] Several principles are important at the beginning of the process (principle 10), while others are most relevant when identifying policy options (principles 7, 8 and 9), weighing up these options (principles 3, 4, 5 and 6) or during the final political decision-making (principles 1 and 2).

a. Section 2.3 of the policy paper 'A Considered Approach to Safety: Recurrent Themes'.

2

A CONSIDERED APPROACH TO SAFETY IN THE GMO REGULATORY PROCEDURES

In this chapter the ten principles for dealing with safety and risks are discussed in the light of the practical implementation of GMO policy: the authorisation procedures. These are examined from the perspective of three main stakeholders: the applicant, the government and the citizen. The policy paper states that the ten principles relate to the policy process which consists of the situation, the possibilities for intervention, the appraisal of policy options and the decision-making process. The implementation of policy, monitoring, enforcement and evaluation are outside the scope of the policy paper:

The appraisal of policy options ends with an advice or proposal for a (political) decision. This decision is supported by the outcome of the appraisal of policy options, but in the final phase always contains a political element as well. The decision does not follow automatically from the appraisal process. The scientific community, stakeholders and the public therefore have a limited influence on the final decision, which is confined to the democratic political process. This policy paper, the assessment framework, is not about the 'sharp end' of risks: dealing with incidents, the local consequences of implementation and the enforcement of political decisions. However, if these consequences and developments do at any time give reason for the national government to take new decisions, this assessment framework will be revisited.
(Section 2.1 of 'A Considered Approach to Safety: Recurrent Themes')

COGEM has some reservations about this. First, the implied dividing line between policymaking and implementation is not always at all clear in practice. In addition, stakeholders are directly confronted with implementation policy, enforcement and all its consequences. The paper correctly points out that the 'sharp end' of the risks – the public response to incidents or the practical outcomes of policy they are confronted with – can give rise to the need to take new decisions. COGEM observes that the principles for safety policy should also work through in the practical implementation of that policy. If the principles are not or are inadequately applied to the practical implementation of policy, that should be reason enough to re-examine the assessment framework. To investigate the link between policymaking and implementation, this report links, wherever possible, the various steps in the GMO authorisation procedures (**see Box 1**) to the principles of GMO policy on which they are based.

1. GMO authorisation procedures in brief

The principle behind EU and therefore also Dutch policy for GMOs is that all appropriate measures should be taken to prevent any possible damage or adverse consequences for human health and the environment. These measures are drawn up on the basis of an environmental risk assessment and imposed as conditions in a consent for the relevant activities involving GMOs.

Three distinct types of consent are given for activities involving GMOs: Contained Use (CU), Deliberate Release to the Environment (DR) and Marketing Authorisation (MA). CU consents are for activities in laboratories, animal houses, greenhouses, etc., where the environment and containment measures can be reliably controlled and managed. The procedures for CU consents are generally shorter than the procedures for DR and MA consents. This is partly because deliberate release and market introductions cannot be controlled to the same extent and are subject to a much greater number of variables that have to be taken into consideration in the risk analysis. DR consents are for experiments carried out outside the laboratory or other contained areas and include field trials with GM crops and veterinary and clinical studies.

CU and DR consents are the responsibility of the national authorities and in the Netherlands fall under the responsibility of the Ministry of Infrastructure and the Environment. Marketing authorisations are European consents issued by the European Commission in a centralised procedure in which all EU Member States are given the opportunity to comment on and evaluate applications. There are two kinds of marketing authorisations: for importing or cultivating GM crops and for GM medicines. The authorisation procedures for GM crops are the responsibility of the European Food Safety Authority (EFSA). The responsibility for assessing applications for GM medicines lies with the European Medicines Agency (EMA).

The rules on issuing GMO consents in the Netherlands are set down in the GMO Decree and the GMO Regulation.[b,c] The day-to-day administrative and information provision tasks are handled by the GMO Office at the National Institute for Public Health and the Environment (RIVM). Depending on the type of application, advice is obtained from COGEM (on environmental risks for some CU applications and for all DR and MA applications), the RIKILT Institute of Food Safety (on food safety for European applications for food/feed GM crops) or the Central Committee on Research Involving Human Subjects (CCMO) (for medical/ethical evaluation of clinical studies). For laboratory experiments, in addition to a CU consent for the experiments a consent is also needed for the facilities (laboratory, animal house, greenhouse, etc.) where the experiments are to be carried out. Consents for contained use facilities are issued under the Environmental Licensing (General Provisions) Act by the municipal authority where the facility is located.

b. Genetically Modified Organisms Decree 2013

c. Ministerial Regulation on Genetically Modified Organisms 2013 >>>

A detailed overview of the GMO authorisation procedures can be found on the websites of the Ministry of Infrastructure and the Environment, the GMO Office, the European Commission, the EFSA and the EMA.[5,6,7,8,9]

2.1 TRANSPARENCY

PRINCIPLE 1: Ensure a transparent political decision-making process in which choices are supported by arguments.

The transparency of decision-making on GMOs depends on 1) whether and how a consent application and any draft and final decisions on the application are publicised, and 2) to what extent the grounds on which the decision is based are explained.

A consent to create and use GMOs can be granted if the activities do not put human, animal and environmental safety at risk.[10] Consents can therefore only be refused in the interests of protecting human and environmental health.d The GMO authorisation procedure does not include a benefit-risk appraisal. This decision-making rationale is a standard part of the draft/final decision on CU and DR applications: if the risks are negligible, a consent is issued. Applications for marketing authorisations follow a European procedure which ends with a draft decision by the European Commission. The grounds for the decision are also included in draft decisions on marketing authorisation and are based on the environmental risk assessment.

The government uses various instruments to facilitate a transparent decision-making process on applications for GMO consents. The website of the GMO Office contains details on the supporting information required for the various types of applications (CU, DR and MA) and the risk assessment procedures. The 'biotechnology consent database' contains information on all applications pending and consents issued.[11] Interested parties are notified of draft and final decisions on new applications either directly or via the national newspapers. The degree of transparency provided on consents depends on the type of consent:

- For CU, applications and draft decisions are not made public. The decisions are sent to the interested parties[e] (the applicant and the local authorities). The public

d. Article 9.2.2.3, paragraph 2 of the Environmental Management Act

e. Article 1.2, paragraph 1 of the Administrative Law Act

and local residents are not deemed to be interested parties for these consents. The consent database contains all CU consents that are still valid. However, the information is limited to the title, the name of the consent holder and a list of organisms subject to genetic modification. The risk analyses may not be consulted, except in cases in which COGEM was asked to advise on the CU consent. These advisory reports are publicly available on the website. However, to obtain all the relevant information, any interested parties must make the connection between the information in the database and the publications on the website.

- For DR, the draft decisions are published in national newspapers and the Government Gazette (*Staatscourant*) and entered into the database.[f] The risk analysis is part of the draft and final decisions. Draft decisions are put on public display for six weeks to give interested parties an opportunity to submit representations if they so wish. For DR applications the group of interested parties is much broader than for CU applications, and include not only the applicant and the local authorities, but also local residents and legal persons such as local societies.[g] The final decision mentions all the representations received and states whether and why these did or did not lead to any alterations to the draft decision.[12] Once a decision has been taken on the application, interested parties may appeal against the decision to the Council of State.
- Applications for placing on the market of GM crops (import and cultivation) and GM medicines for humans and animals are both centralised EU procedures, but the transparency of the procedures differs. Applications for marketing authorisation for GM crops are made public on two occasions. The first is the publication of a summary of the application and the second is the publication of the assessment report. These are published on the website of the European Commission and the public (everyone) is free to submit observations and opinions.[13] The submitted comments are also published. The political decision-making on European authorisations for placing on the market takes place in various steps and voting rounds by the Member States according to EU comitology procedures.[h] The transparency of this process for assessing applications for GM crops stands in contrast to the application procedure for GM medicines and GM vaccines via the EMA.[14] Those applications and the whole assessment and authorisation procedure are strictly confidential and the advice given by COGEM on the applications must not be made public. Even the fact that an application has been made is confidential information.
- Like all environmental permits, consents for establishing CU facilities under the Environmental Licensing (General Provisions) Act are published in a local authority

f. Genetically Modified Organisms Decree. Explanatory memorandum, par. 10. Publication of decisions and legal recourse

g. Article 1.2, paragraph 1 of the Administrative Law Act

h. Procedures in which the European Commission exercises the implementing powers delegated to it by the EU legislator under the review of committees consisting of representatives from the EU Member States

paper, newspaper or local freesheet, or on the internet. Interested parties, including local residents, can make representations.

Subconclusion: The decision-making procedures on GMO applications are open to those directly involved and to third parties. The transparency of the procedures and the decision-making process depends on the type of consent. For CU consents, this appears to be a deliberate choice by the Dutch government relating to who are considered to be the interested parties (**see section 2.4**). DR consents and the grounds for the decision taken are open to third parties. For GM medicines it has been decided at the EU level that transparency in relation to the decision-making and underlying reasoning is not necessary or desirable.

2.2 RESPONSIBILITY

PRINCIPLE 2: Decisions must explicitly state the responsibilities of government, businesses and citizens.

Various parties are involved in the decisions and oversight of the authorisation procedures for GMOs (see Table 1).

TABLE 1: ORGANISATIONS INVOLVED IN GMO AUTHORISATION PROCEDURES

Name	Responsibility
Local authority	Environmental permits (Environmental Licensing (General Provisions) Act) for CU facilities
Environment ministry	Policy on and authorisation of GMO activities
GMO Office	Implementation of Genetically Modified Organisms Decree and information provision
ILT	Enforcement of GMO consents (CU and DR)
NVWA*	Enforcement of GMO consents (MA)
COGEM**	Advice on environmental risks (authorisation) Monitoring of ethical and social aspects of GMOs
RIKILT	Advice on food safety for marketing authorisation of GM crops
CCMO	Advice on protecting test subjects in medical academic research
EFSA	Advice to the European Commission on food and environmental safety of GM crops
EMA	Scientific evaluation of medicines (including GM medicines)
Applicant	Submission of data and compliance with consent conditions
BSO/ESO	Advice and support on applications Surveillance of compliance with consent conditions
Responsible officer	Providing application information
EC***	Decisions on European applications for placing on the market

* Netherlands Food and Consumer Product Safety Authority

** COGEM is only involved in CU application procedures for activities with new GMOs that have not already been classified and applications for a lower level of containment than required by the regulations.

*** Decisions on European authorisations for placing on the market are made in various stages and voting rounds according to EU comitology procedures. These are not explained further in this report.

The safety of genetic modification has always been a government responsibility. Under the GMO Decree, the Ministry of Infrastructure and the Environment is responsible for issuing consents for activities with GMOs. The ministry draws up the rules for experiments and applications and the day-to-day administration is handled by the GMO Office at RIVM, which in specific cases is assisted by advisory bodies such as COGEM and RIKILT.[10] This ensures that the required measures and consents are based on sound scientific evidence and/or expert judgement. For clinical studies the Central Committee on Research Involving Human Subjects (CCMO) is involved.

Applicants (legal persons) are assisted by the biological safety officers (BSOs) and environmental safety officers (ESOs) in their institute, company or organisation. These officers are responsible for ensuring the application is made correctly. Applications are drawn up with the responsible officer (RO). The safety officers check whether everything is done according to the rules and are the first point of contact for inspections by the Human Environment and Transport Inspectorate (ILT). In this capacity they have a liaison function between the government and their own organisation. To a certain extent they are an arm of government to guarantee safe practices and ensure the rules are observed. Through their professional association, the BSOs Platform (BVF Platform), they can inform the government of developments relevant to safety.[15]

Until recently a consent was needed for all activities involving GMOs. Under the new GMO Decree, which came into force on 1 March 2015, some of the responsibility for working with GMOs has been transferred to the institutes and companies concerned. For experiments in the lowest safety classes of CU activities (Classes 1 and 2k) the applicant is only required to notify the relevant authority. Individual citizens have no active responsibility in the GMO authorisation procedure. Local authorities are responsible for issuing the environmental permit (Environmental Licensing (General Provisions) Act) for premises where research with GMOs is done (laboratories, animal houses, greenhouses, etc.). As interested parties they are also informed about the CU consents issued for activities in these facilities.

Subconclusion: Various parties are involved in the GMO authorisation process, depending on the type of consent. The main responsibilities lie with the Ministry of Infrastructure and the Environment, which has transferred some of its tasks to the GMO Office and advisory bodies such as COGEM and RIKILT. Consents state who the applicant is, the issuing authority and the parties which have made an input to the decision on the application, so that it is clear exactly what role the various parties have had in the decision-making process.

2.3 APPRAISAL

PRINCIPLE 3: Weigh up the dangers and risks of activities, and as far as possible balance them against the costs and benefits to society.

The principle behind the EU GMO legislation, and therefore also the Dutch GMO legislation, is that a consent for GMOs is issued if all appropriate measures have been taken to prevent any possible damage or adverse consequences for human health and the environment. The risks must be negligible (**see Box 2**).[i] The decision-making process does not include the weighing of hazards and risks against social costs and benefits, neither is consideration given to whether or not the conventional alternative would incur greater adverse effects. Insect resistant GM crops are only authorised if it can be shown that non-target insects are not adversely affected, whereas the existing alternative (insecticides) do have adverse effects on other organisms in the environment.
The government leaves judgement on the desirability of genetically modified foods to consumers and producers.[j] The labelling of GM foodstuffs allows consumers to decide for themselves whether they want to buy the products. In addition, coexistence rules (such as isolation distances) are applied to prevent the cultivation of GM crops leading to unacceptable damage to other producers.[k]

2. Negligible?

In general, risks are described in terms of the probability that something will happen in relation to the size of the effect, expressed by the formula: risk = probability x effect (impact). Risk analyses may be either quantitative or qualitative. Various methods of analysis have been developed.[16]

Environmental risk assessments generally consider not one but several possible adverse events at various levels. Some of the risks of these elements of the environmental risk assessment can only be expressed in different variables or units. Moreover, it is usually not possible to calculate risks quantitatively in biological research. This means that environmental risk assessments of GMOs are mostly qualitative in nature and based on specific national and international methods for appraising effects and setting baselines. The choice of these methods is determined, among

>>>

i. Under article 9.2.2.3, paragraph 2 of the Environmental Management Act, consent may only be denied in the interests of protecting human health and the environment.

j. Regulation (EC) No. 1830/2003.

k. Seeds and Planting Materials Act 2005. Cultivation Regulation, Chapter 2, Article 6.

other things, by what is considered to be worth protecting and what is considered to be conventional (as opposed to genetically modified). When used in consents, the term 'negligible' is a qualitative description of a risk, like 'small', 'large' and 'very large'.

In most dictionaries and encyclopaedias negligible is defined as 'so small or unimportant as to be not worth considering; insignificant'. This qualification is applied to events that are very unlikely to happen, but of which it can be assumed that they will at some time occur (possibly tomorrow, or not for a very long time). An example is the probability of a meteorite hitting the earth or an airplane crashing. The probability of these events happening is numerically negligible, although their impact if they do occur can be very big indeed, which can alter people's perception of the risks. An airplane crash can easily cause 200 deaths, but this does not stop most people from flying, because they consider the risk of a crash to be acceptable. In comparison, a similar number of casualties in an incident involving a GMO would be considered to be an extremely large and unacceptable risk. This difference is all about risk acceptance. The degree of risk acceptance can vary from individual to individual and depends to a certain extent on the perceived benefit in relation to the risk, how voluntary the situation is and the available alternatives.[17]

In the context of risk assessments of GMOs, the term 'negligible' is interpreted in a different way. The underlying principle is that activities with GMOs should involve 'no risk' at all. If a risk is identified, management measures are imposed to exclude the risk, such as working in a GMO laboratory with a higher containment level or applying specific safety rules. Each consent states the conditions applying to the authorised activities. When the consent holder meets these conditions for working with the GMO, the identified risks associated with that GMO and the activities concerned are negligible. The assessment is based on an expert opinion of the various risks and the cumulative risks, which is always based on the knowledge available at that time. New insights may lead to an amended expert opinion, possibly resulting in a relaxation or tightening up of the consent conditions.

It is not scientifically possible to demonstrate the absence of a possible effect and so it is impossible to claim that there is a 0% risk and that therefore the activity is 100% safe. In view of this, in its advisory reports COGEM includes the statement that if the activities are carried out under the recommended containment level and measures, the risks will be negligible.

At the beginning of 2015 an exception was created to the rule that when considering applications for the cultivation of GM crops only the safety of the GMO can be taken into account. The basic principle remains that risks to human health and the environment must be negligible, but with the introduction of Directive 2015/412 Member States may take account of other safety considerations in addition to the environmental risk assessment when taking decisions on the cultivation of GM crops.[l] This step opens up the possibility of making partially more wide-ranging assessments of GM

l. Directive (EU) 2015/412

crops; partially because only additional reasons can be put forward in order to reject a GM crop that has previously been found to be safe. The positive effects of a GM crop cannot be considered in the decision-making process.

Although weighing up the possible risks against the benefits to society, as is usual in other safety domains, is still not possible **(see Box 3**), the new directive does open up the possibility of bringing associated side-effects more into the equation.

3. Cost-benefit appraisals in other safety domains

In many safety domains it is standard practice to weigh up the risks against the potential benefits and to accept a certain amount of risk. A few examples from the CAS policy paper:

- **Drinking water quality: The quality of drinking water in the Netherlands is high, but it is not possible to continually measure the levels of contaminants and microorganisms. This makes it crucial to have a good risk assessment and risk management, such as a preventive policy, good manufacturing practice and quality control.**
- **Environmental safety: Safety and risk policies are designed to protect human and environmental health against health and environmental risks considered unacceptable to society.**
- **Pipelines: Policy relating to pipelines is characterised by clear standards (limit values) based on the most recent scientific and technical insights as well as flexibility for local interpretation…. Moreover, a transparent balancing of economic interests, safety and planning considerations is made.**
- **Rail safety: Each year railway accidents happen in which people are killed and injured. Absolute safety cannot be guaranteed: it is simply not realistic to expect to be able to exclude all possibility of accidents occurring. For this reason the costs and benefits of measures are weighed up in various different scenarios, which increases the transparency of the process.[18]**

Two examples from other policy areas:

- **Vaccines: Human vaccinations usually involve the acceptance of a certain level of risk, whereby a very small number of those vaccinated may suffer serious side-effects. A balance is struck between the benefits of the vaccine and the possible side-effects.[19]**
- **Food safety: Food must be reliably safe. The Dutch government sees to it that food companies observe the rules. But despite the extensive regulations and monitoring of food quality, things regularly go wrong and products end up in the food chain that can present a risk to consumers.[20]**

Subconclusion: As the GMO assessment framework is based entirely on the condition that any risks must be negligible, the political decision-making process cannot involve the weighing up of hazards and risks against social costs and benefits. The GMO policy therefore seems to be diametrically opposed to the policies in other safety domains

and the ministerial policy paper. Prohibiting experiments with GMOs when it cannot be ascertained in advance that any risks will be negligible and not considering the possible benefits restricts the potential and opportunities this technology has to offer. For example, the strict observance of this rule makes it difficult to conduct clinical experiments with gene therapies and similar treatments in the Netherlands and Europe.[21] A condition for weighing up risks and benefits is that both must be quantifiable, which requires a refinement of the two categories of negligible and non-negligible risks.[m]

m. In 2015 COGEM established a working group to investigate the possibility of further quantifying risks

2.4 INVOLVEMENT

PRINCIPLE 4: Involve the public at an early stage of the policymaking process, tailoring the type and degree of public engagement to the nature of the issue.

If they wish, citizens can contribute to the drafting and revision of legislation. Before the revised GMO Decree and GMO Regulation were adopted, interested parties were given the opportunity to make representations during the preliminary scrutiny procedure.[n,22] The ability of individuals to participate in the decision-making on applications for GMO consents depends on whether or not they are deemed to be an interested party. According to the website of the GMO Office an interested party is someone who has a direct interest in the decision, for example because they live close to the site in question. A legal person, such as a society or foundation, may also make objections, as long as its charter or constitution states that its purpose is to act in the interests of the environment.[23] To be able to participate in the decision-making process, citizens must know about the GMO regulations, the procedures, the applications for consent and proposed decisions (**see section 2.1**), and the degree of involvement depends on the type of consent and the proposed activities. The effectiveness of this involvement is limited by the conditions that representations must satisfy before they can be taken into consideration. Only arguments relating to environmental risks are accepted.

CONTAINED USE

For CU applications the public are not considered to be interested parties (in the legal sense) when the activities concerned are experiments. The interested parties in these cases are local authorities and applicants. They are sent the draft decision. Since the introduction of the new GMO Decree, for activities in the lowest safety levels it is sufficient to give notice of the activities. As no consent is issued, these activities are not open to objection and appeal.

n. A preliminary scrutiny procedure (*voorhangprocedure*) precedes the adoption procedure. The decree goes to the House of Representatives and/or the Senate once it has been drawn up and approved by the Council of Ministers (the cabinet), but before the Council of State issues its advice. The preliminary scrutiny procedure does not always involve parliament as a whole. Sometimes the draft legislation only goes before the House of Representatives and sometimes also, via publication in the Government Gazette, before the population as a whole. In this period individuals and organisations can submit comments, which can be taken into account in the legislation because the text only goes to the Council of State after these reactions have been received and then – with the advice of the Council of State – to the Crown for adoption. Source: https://nl.wikipedia.org/wiki/Voorhangprocedure.

The involvement of individual citizens in CU procedures is limited to applications relating to facilities (or 'premises') where the experiments are to be carried out. Anyone may make representations on draft decisions on contained use premises[12] and these are considered when the decision is made on the application. Under the general provisions of the General Administrative Law Act, the decision is then open to appeal. The reason for deeming individuals not to be interested parties is that consents issued under the GMO Decree are so complex that only experts can fully understand them.[o] Moreover, the number of consents issued under the GMO Decree will be many times more than the number of environmental permits. For these reasons the timing of public consultation on GMO activities is considered to be most effective at the stage when an environmental permit needs to be obtained. However, applications for certain types of laboratory are rather abstract because they give only a global indication of the types of experiments which will be carried out. Moreover, an environmental permit may have been issued a long time ago, when the technical and scientific possibilities were more limited. It can also be questioned whether ordinary citizens have the necessary expertise to object to an environmental permit for a GMO facility if CU consents are too complex to be understood.

DELIBERATE RELEASE INTO THE ENVIRONMENT

For deliberate release into the environment (field trials and clinical studies), draft and final decisions are published in the Government Gazette and national newspapers, and anyone may make representations.[p] Appeal against the final decision at the Administrative Law Judicial Division of the Council of State is only open to interested parties.[q] Field trials must be notified to the EU Member States. They are informed by the European Commission and may submit comments or reservations if they so wish.[24,25]

MARKETING AUTHORISATION

Applications for placing on the market of GMO crops are EU procedures which include two rounds of public consultation.[r] The first round of public consultation is the putting on public display of a summary of the application and the second round is the putting on public display of the assessment report on the application. In both cases the public may make representations. In addition, the environment minister has decided to make closed case files on applications for placing on the market publicly available for inspec-

o. See explanatory memorandum to the Genetically Modified Organisms Decree

p. GMO Decree, explanatory memorandum, 10.3 legal recourse on deliberate release into the environment

q. https://www.rechtspraak.nl/Naar-de-rechter/Uw-situatie/Onderwerpen/Pages/Omgevingsvergunning.aspx

r. GMO Decree, explanatory memorandum, 10.4 legal recourse on marketing authorisations

tion. Comments by members of the public must be submitted to the European Commission within 30 days. As for other consent applications for GMOs, only comments regarding environmental risks can be taken into consideration.

Depending on the directive under which the consent is being applied for, either the European Commission or one of the Member States issues the consent. These decisions are open to objection and appeal and in the final instance interested parties may appeal to the courts. This has happened on a few occasions when no decision was forthcoming. In 2008 BASF appealed to the European courts to force a decision on the GM potato Amflora,[26] and in 2013 Du Pont & Pioneer went to the courts to force the Commission to take a decision on maize 1507.[s]

In recent years individuals and political parties have taken various initiatives to make municipalities or provinces 'GMO-free zones'. In the past, the ministry has said initiatives like 'gene-tech-free Nijmegen'[t] were 'unnecessary' because the safety assessment and coexistence rules provide sufficient guarantees for the safe cultivation of GM crops.[27]

Subconclusion: In some but not all cases individuals have opportunities to contribute to the decision-making procedures on applications for GMO consents. As stated in the CAS policy paper, the degree of public consultation and involvement has its limitations. Moreover, it is subject to criteria such as the relevance of the representation or objection under the laws and regulations in force. GMO authorisation is based on an assessment of the risks to human health and the environment. Arguments that lie outside the scope of the environmental risk assessment cannot therefore be considered in the decision-making process, but neither is thought given to where these argument could play a part in the process. There would appear to be no question of engaging in a dialogue (**see section 2.7**).

s. Pioneer v. Commission (Case T-164/10)

t. In 2012 the Municipality of Nijmegen declared itself a 'gene-tech-free zone' and adopted this resolution in its local plan. This means that no genetically modified agricultural crops may be cultivated in the municipality. The declaration does not affect products sold in supermarkets or research carried out in Nijmegen.

2.5 BROADER PERSPECTIVE

PRINCIPLE 5: Consider the possibility of an accumulation of risks from different sources in the decision-making process

The Dutch GMO legislation addresses the direct risks of GMOs. Indirect risks or cumulative risks from other areas of activity are hardly taken into account, if at all. Side-effects also play little or no role in the final decision-making process (**see section 2.3**), mainly because these other risks and the relevant safety measures fall under other regulations. There is a strong and understandable tendency not to assess overlapping risks. For example, the Dutch standpoint on herbicide tolerant GM crops is that the assessment of the herbicides has already been made under the legislation on plant protection products and that the development of resistance by weeds is an agronomical risk and not a GMO risk. In specific cases of contained use, consideration is given to possible interactions between the GMO and other organisms present, but the risks of activities with wild-type organisms is not covered by the GMO regulations. Neither do the risks of the activities for the laboratory technician fall under the GMO regulations, but they are covered by the occupational safety, health and welfare regulations. However, if contamination of laboratory workers could lead to a GMO escaping from the laboratory, this risk is taken into account.

The ideal of a strict separation of risk assessments can be complicated by the increasing integration of different technologies, such as biotechnology with nanotechnology or with 3D printing. These new technological applications cannot always be defined within the realms of a single technology or type of application[28] and as a result it is not always clear which regulations they are covered by, if any. Moreover, new applications that make use of a combination of several technologies may also involve new risks that are not caused by any of the technologies on their own.

Subconclusion: The existing GMO authorisation procedures leave little room for taking account of cumulative risks. The integration of biotechnology with other technologies raises the important issue of acknowledging and identifying cumulative risks. Taking more explicit account of the possibility of an accumulation of risks of different origins raises the question of whether and how this should be done in practice. What measures are necessary or desirable and under which regulations should they be included?

2.6 PRECAUTION

PRINCIPLE 6: Apply the precautionary principle to new or uncertain risks.

The precautionary principle is frequently used without always specifying exactly what is meant by it. There are in fact various different interpretations and versions of the precautionary principle.[29] The GMO regulations refer to the explanation given by the European Commission:

The precautionary principle enables rapid response in the face of a possible danger to human, animal or plant health, or to protect the environment. In particular, where scientific data do not permit a complete evaluation of the risk, recourse to this principle may, for example, be used to stop distribution or order withdrawal from the market of products likely to be hazardous.[30]

The policy on GMOs and genetic modification is that they present uncertain risks that should be assessed separately. The precautionary principle is therefore the cornerstone of the GMO regulations for contained use, deliberate release into the environment and placing on the market. A consent for GMOs is issued if all appropriate measures have been taken to prevent any possible damage or adverse consequences for human health and the environment. If the risks cannot be reduced to a level at which they are considered to be negligible, for example by requiring an appropriate containment level or by taking specific safety measures, no consent can be issued.

Subconclusion: The precautionary principle is the cornerstone of the GMO regulations. As such, the GMO policy fully satisfies principle 6 of the policy paper on a considered approach to safety.

2.7 DIALOGUE

PRINCIPLE 7: When new risks are involved it is important to consult the public throughout the whole policymaking process and talk about interests, emotions, risk perception and ethical considerations.

Authorisation procedures are by definition legal processes. Some of these processes include opportunities to involve the public. The CU procedures themselves do not include these opportunities, but the licensing procedure under the Environmental Licensing (General Provisions) Act for the laboratory where the experiments are to take place do (**see section 2.4**). The DR procedures include a six week period in which the public has the opportunity to make representations on the proposals.

In all cases the public consultation provisions involve the opportunity to make representations, to present arguments and objections for consideration by the government authority when coming to its decision. In its decision, the authority states how it has responded to each of the representations made. Objections to the authority's decision may be made by appealing to the courts. Only objections relating to environmental risks are taken into account in the decision-making process. As yet there is no opportunity to have arguments other than those relating to environmental risks taken into account. Such arguments are generally rebutted with reference to the consumer's freedom of choice, which is guaranteed among other things by the labelling of GM products.

Subconclusion: As mentioned above, in the decision-making process on GMO consents there is no room for consideration of interests, emotions, risk perceptions or ethical arguments (**see section 2.3**), which means that in the policymaking process there is also no room for dialogue between the government and society on these aspects. The government may listen to the opinions of individuals and stakeholders on these issues, but will not give any weight to these arguments when coming to a decision. In specific cases the public is given an opportunity to become involved in the authorisation procedure, but this is limited to making representations and does not include entering into a dialogue. A dialogue requires, among other things, a clear set of discussion rules, expectation management, the possibility of expressing opinions based on different sets of values and clear justification of positions.

2.8 FUTURE-PROOF

PRINCIPLE 8: Make best use of the knowledge available in society to identify potential new risks.

This principle is about the importance of identifying new risks at an early stage. Globalisation, social networks, the internet, the growth in the literature and a broad national and international network ensure the rapid spread of new information and knowledge, including research on GMOs. New developments get passed on quickly and are discussed on internet forums and social networks, and at workshops and conferences. Moreover, various Dutch and European stakeholders active in the field of GMOs give the government and its advisory bodies their own views on technical and scientific developments and their potential policy implications.

Government policy on genetic modification is designed to take this into account. Under its statutory duties, COGEM informs the ministry about scientific developments, draws attention to new risks and social and ethical issues concerning applications of genetic modification, and gives advice on applications for new types of experiments and activities involving organisms that have not yet been classified. Applications for consent are handled by the GMO Office at RIVM, where the necessary expertise is available in house.

Within the relevant central government departments there seems to be a policy of disposing of in-house subject-matter expertise and outsourcing the required expertise whenever necessary. This is creating a separation between scientific knowledge and policy knowledge, making the government increasingly dependent on semi-governmental organisations such as COGEM, RIVM and other advisory bodies for scientific knowledge. For the departments concerned this raises the important question of how they know when they lack a specific piece of knowledge or expertise.

Subconclusion: In the GMO authorisation process existing knowledge is obtained from the literature, meetings, and networks maintained through formal channels, such as semi-governmental agencies and advisory bodies. Other bodies are generally not actively consulted.

2.9 SECURITY AND SAFETY

PRINCIPLE 9: Link security and safety: do not lose sight of one when policy focuses on the other, and investigate possibilities for linking them together.

Biosafety is about protecting humans and the environment against the possible adverse effects of biological agents. Biosecurity is about securing biological agents and knowledge in order to prevent their misuse. GMO authorisation is based on environmental risks (biosafety) and takes no account of biosecurity aspects. At least for the time being, biosecurity is considered to be a separate subsection of the life sciences that involves a different set of expertise and issues from biosafety. Despite this, though, both fields are closely related and the arguments and outcomes of the environmental risk assessment can be relevant for biosecurity. Some containment and control measures imposed in the interests of biosafety, such as restricted access to laboratories, can also (to a limited degree) help to increase biosecurity. However, there are also situations in which biosafety and biosecurity are at odds with each other, such as the visible transport of potentially hazardous organisms (e.g. due to labelling or listing on a bill of lading or other forms), which may be undesirable from a biosecurity point of view.

The government wants laboratories to address biosecurity as well as biosafety issues and is developing policies to this end.[31] In the Netherlands the Biosecurity Office has been established at RIVM with the aim of disseminating the government's new policy on biosecurity, for example by holding workshops and providing information.

Subconclusion: Biosafety and biosecurity are strictly separate under current policy, whereas the policy paper states that it is desirable to link the two together. There are close links between biosecurity and biosafety and scientific developments. An extensive analysis of the advantages and disadvantages of combining the two is necessary in order to determine whether linking the two is possible and desirable.

2.10 INNOVATION AND SAFETY

PRINCIPLE 10: Ensure that innovation and safety reinforce each other, that safety requirements do not frustrate innovation, and that innovation goes hand in hand with safety.

The GMO regulations can be described as complicated and strict, which is due in part to the exceptional status of GMOs and the precautionary principle. The fundamental position of Dutch and European GMO legislation is that activities involving GMOs or uses of GMOs can be permitted only if the risks are negligible. This legislative aim of zero risk is an obstacle to innovation. To demonstrate the absence of any risk associated with a commercial application, an exhaustive file of evidence has to be compiled and for GM crops the cost of compiling such a file can run into tens of millions of euros.[32] Just a few large multinational companies can afford to make such an investment and these costs can only be recovered when the crop is cultivated worldwide on a large scale. The GMO regulations therefore form a barrier to smaller companies and more restricted applications.[33]

Another example of the inhibitory impact on the innovativeness of Dutch companies and institutions is the debate about whether or not new biotechnological techniques fall under the GMO legislation.[34,35,36] If the EU decides that these new techniques and their products do fall under the GMO legislation, it may no longer be profitable for companies in the Netherlands (and other EU Member States) to continue with such developments. This is one of the reasons why biotechnology companies are moving their activities outside the EU.

Over the past few years the Dutch environment ministry has been working on a simplification of the Dutch regulations on CU in a revision of the Genetically Modified Organisms Decree.[n] By making the regulations more transparent and simplifying the authorisation procedure the ministry aims to reduce the administrative costs for applicants and authorising authorities. This process resulted in the introduction of the new Genetically Modified Organisms Decree in 2014 and the new Ministerial Regulation on Genetically Modified Organisms came into force in 2015.

The ministry's primary task is to guarantee a safe and healthy environment, which includes safe working with GMOs. Stimulating innovation is not a primary task. In the 'genetic modification' safety domain the government (the environment ministry and the GMO Office) has an inherently dominant position as the authorising authority. This makes the position of the applicant, for whom innovation is of great importance, a weak one, because the possibilities for appeal are limited. If an institution or company disagrees with a decision on their application for consent, it can go to court. For deliberate release into the environment and applications for placing on the market there

are just a few examples when such actions have been brought. As far as we know no such action has ever been taken for applications for contained use, despite the fact that hundreds of consents and amended consents are issued each year. However, it seems unlikely that there has never been a difference of opinion between the applicant and the licensing authority about the containment level of the laboratory and additional conditions attached to the consent, given that COGEM has in the past issued advice on many applications for reclassification at a lower level of containment.

Subconclusion: The pursuit of both innovation and safety are hard to combine in GMO authorisation practice. The use of the precautionary principle, the slow decision-making process at the EU level and the considerable burden of proof and costs to the applicant restrict the room for innovation.

3

A CONSIDERED APPROACH TO SAFETY IN COGEM ADVICE AND TREND MONITORING

COGEM has an input to both the authorisation process, by providing technical and scientific advice, and the policymaking process, by informing the government about scientific developments and the ethical and social aspects of genetic modification. In this chapter we reflect on how COGEM's working methods align with the principles set out in the environment ministry's policy paper on a considered approach to safety.

PRINCIPLE 1: Transparent political decision-making process

Strictly speaking, this principle is not relevant to COGEM because the Commission has an advisory role and does not take decisions on applications. On the other hand, COGEM's advice makes an important contribution to the decision-making process and must be transparent and well argued if it is to inform and support the final political decision.

COGEM's advisory reports set out as clearly as possible how and why the advice has been prepared on the consent application. These reports always discuss the key facts of the application, recent and relevant literature, and the considerations and arguments leading to the positive or negative advice. For some applications, COGEM indicates which elements are included in its environmental risk assessment. Classifications of microorganisms are accompanied by an explanation of the classification scheme and criteria used. COGEM has published various advisory and topic reports on the information that should be required for the environmental risk assessment for contained use, field experiments, clinical experiments, etc. These reports are intended to contribute to the transparency of the decision-making process.

Communications between the members of COGEM, the secretariat and the chair or executive board are not made public. Advice given by COGEM reflects the decision-making process among the members, including any uncertainties and discussions that have played a part in the formulation of the advice. If the members cannot agree, a minority opinion is included in the advice. Should any members be excluded from

contributing to the advice because of possible conflicts of interest, the names of the members concerned are also stated in the advice. The declarations of members' interests and additional activities can be found on the COGEM website. COGEM's advisory reports are publicly available on the website, including all those for CU and DR and some reports on applications for placing on the market. Applications and decisions on marketing authorisation for GM medicines are not made public, including COGEM's advice and argumentation. This does not contribute to the transparency of decision-making.

PRINCIPLE 2: Clarity of decision-making responsibilities

In its advice COGEM states as clearly as possible which risks it has examined and what aspects have been considered. In some cases COGEM also explicitly states what risks or aspects it has not examined. COGEM's advice on applications for the importation and cultivation of GM crops explicitly state that it advises on environmental risks and that other bodies (EFSA and RIKILT) are responsible for the food safety assessment. In its advice on clinical studies COGEM does not explicitly state that it only examines the environmental risks and not patient safety. COGEM does not advise on occupational safety, health and welfare aspects, activities with pathogenic wild-type organisms or the effects of pesticides. COGEM's advice draws a distinction between the information and argumentation of the applicant and the considerations and argumentation of the COGEM members. COGEM's task and role in the process are not stated in all its advisory reports, but can be found on the website. In some of its topic reports COGEM explains its trend monitoring task and, in this capacity, what it does and does not comment upon.[37]

PRINCIPLE 3: Weighing up dangers and risks against the costs and benefits to society

Weighing up risks and benefits is a political task. COGEM supports this process by producing solicited and unsolicited topic reports in which it describes the broader social considerations that can play a part in new developments in the field of genetic modification. If balancing the dangers and risks of certain developments against social benefits and costs is to play a part in the GMO authorisation process, a certain amount of risk may have to be considered acceptable as long as the benefits are sufficient. However, this would require a different classification and description of the risks of GMOs. For example, what is meant exactly by a very small risk, a small risk, a large risk and a very large risk? In anticipation of this discussion, COGEM established a working group in 2015 to investigate the possibility of producing descriptions of various groups of risks.

PRINCIPLE 4: Involve the public

COGEM is an expert commission and does not involve the public in its advisory process, although its publications are announced on the website for anyone who is interested. Neither is the public involved in COGEM's trend monitoring task. Informing the public and organising debates are not part of COGEM's remit. However, clearly describing and explaining the various perspectives, interests, emotions, risk perceptions and ethical considerations in the debate about GMOs can help the government to bring the public into the discussion. Topic reports attempt to cover as many different viewpoints as possible on the topic under discussion to facilitate the policy debate and political decision-making.

PRINCIPLE 5: Accumulation of risks from different sources

COGEM's task is to investigate and estimate the environmental risks associated with GMOs. In its advice the Commission does not take account of risks outside its own field of competence, in accordance with Dutch policy. This includes risks associated with things like the use of pesticides, the development of resistance in weed plants and the risks related to patient safety. COGEM can raise these issues, and has indeed done so several times over the years.[38,39,40,41] When considering laboratory experiments with GMOs, for example, COGEM implicitly includes the risks of working with wild-type pathogens in its considerations. Its advice also takes account of vulnerable groups in society, such as children, immunocompromised persons, pregnant women and old people. Whether this falls under cumulative risks or worst-case scenarios in the risk assessment is difficult to say. The boundary between a worst-case scenario and cumulative risks is not altogether clear.

PRINCIPLE 6: Precautionary principle

COGEM adheres to the precautionary principle and bases its technical and scientific advice on worst-case scenarios. If there are scientific grounds to doubt the absence of risks to human health and the environment, the Commission advises the use of additional safety measures. If it is not possible to reduce the risk to a negligible level by taking additional safety measures, COGEM will give a negative advice on the application and proposed activities.

PRINCIPLE 7: Dialogue on interests, emotions, risk perception and ethical considerations

COGEM has a statutory duty to inform the government about the ethical and social aspects (in the broadest sense) of genetic modification. This is important information for the government when entering into a dialogue with the public and specific stakeholders. How the government conducts its dialogue with society and how it uses the results in its policymaking are political decisions.

PRINCIPLE 8: Make best use of existing knowledge to identify new risks

COGEM reports on new developments relating to genetic modification that may require a response from government in the future. These do not necessarily have to be new risks. In the past, COGEM has produced various topic reports on new developments that could have consequences for GMO policy: gene therapy in China, synthetic biology, off-label use and new techniques such as genome editing with Zinc fingers and CRISPR/Cas.[40,42,43,44,38,45,46]

The broad experience of COGEM's members and their national and international networks within their own fields ensure that the Commission remains up to date on the latest international developments and potential new risks. The documents provided at the meetings for information only form an additional input to this process, as does the attendance by the COGEM secretariat at conferences, where information is obtained on new developments and investigated further with the help of the expertise of the members.

PRINCIPLE 9: Link security and safety

COGEM's advice does not cover biosecurity issues, in line with its statutory duty to advise specifically on biosafety issues. However, in recent years biosecurity has attracted growing attention and COGEM's interest in the topic has increased accordingly. Some of the issues COGEM considers when preparing advice (e.g. pathogenicity, probability of dispersal) are important for both biosafety and biosecurity, but within its current statutory duty COGEM does not have the necessary expertise (such as knowledge of bioterrorism and trends and activities in this area) to be able to make biosecurity assessments. COGEM's position is that it does not have a role to play in the assessment of biosecurity issues, but should the results of investigations relating to applications for consent prove to be useful for other purposes, such as biowarfare or bioterrorism, COGEM will draw attention to this dual use.

PRINCIPLE 10: Integrate innovation and safety

COGEM has a research budget for projects that support its tasks. Some research projects identify new developments, while others investigate specific questions relating to environmental risks on which no research has yet been done. COGEM's research programme ensures that it is kept up to date on new developments in biotechnology and if necessary can adapt its working methods (environmental risk assessment) to take these into account.

If COGEM comes to the conclusion that the safety requirements and regulations are no longer in line with scientific developments, or if they form an unnecessary obstacle to innovation and the further development of biotechnology, it informs the government. These aspects are raised in COGEM's topic reports and in the biotechnology trend analysis.

4

CONCLUSIONS

The policy paper 'A Considered Approach to Safety: Recurrent Themes' (CAS) is part of a project of the Ministry of Infrastructure and the Environment to develop an integrated risk and safety assessment that will cover topics such as environmental policy, drinking water quality, flood protection, environmental security, rail safety, air traffic safety, etc. Biotechnology and GMOs are part of the safety domain of environmental policy. The document identifies ten key principles for a considered approach to safety. In this report COGEM has investigated, in the areas covered by its remit, how the GMO authorisation policy matches up to the principles set out in the ministry's policy paper.

COGEM concludes that the GMO authorisation procedures are fully or partially in line with some of the principles for a considered approach to safety (transparency, responsibility, precaution and future-proofing), but do not align, both in terms of policy and (logically) the implementation of policy, with the principles of appraisal, security and safety, and integrating innovation with safety.

The GMO policy diverges in important respects from principle 3 in the ministry report (weigh up the dangers and risks of activities, and as far as possible balance them against the costs and benefits to society):

- The principle underlying the GMO implementation policy is that genetic modification and GMOs may only be permitted if the risks are negligible (the term 'negligible' does not mean that there is no risk at all, but that the risks do not exceed those associated with established practices).
- This means that the costs and benefits of proposed GMO research and applications are not weighed up, whereas they are in other safety domains within the ministry's policy areas.
- Within the current assessment framework there is little or no room for political decision-making on the balance of the costs and benefits.

The decision to only permit GMO activities if the risks involved are negligible has a number of consequences:

- The costs of testing and authorising a GMO are high, because any risks have to be almost entirely eliminated.
- Innovation and potential gains for society are frustrated. The high safety standards and the associated burden of proof make it very costly to carry out experiments and studies, such as gene therapy studies, or to obtain authorisation to market gene therapies and other GMOs.

- The public debate about GMOs focuses on the safety or alleged danger of GMOs. There is no place in the policy for arguments about the desirability or possible costs and benefits to society of GMOs.

GMO policy also largely fails to meet the principles on the following points:

- Some authorisation procedures are hard to follow and understand for third parties, particularly for contained use and marketing authorisation for GM medicines.
- On paper there are possibilities for involving the public in the decision-making process on consent applications, but these are limited in practice by the conditions that have to be met by representations and letters of objection before they can be taken into consideration (definition of who is an interested party, only representations regarding environmental risk are valid).
- For some types of consent there are opportunities to make representations and objections, but no arrangements for broader involvement or dialogue. Offering opportunities for public consultation and lodging objections while in practice little is done (or can be done) with them can lead to discontent among those concerned.

Biotechnology and GMOs are one of the safety domains within environmental policy in which the ministry is active. COGEM's purpose in preparing this topic report is to make a contribution to the development of an integrated assessment framework for the various safety domains.

REFERENCES

1. Ministerie van Infrastructuur en Milieu (2014). Bewust omgaan met veiligheid: rode draden. Een proeve van een IenM-breed afwegingskader veiligheid
2. Kabinetsvisie nuchter omgaan met risico's. Kamerstuk 28 089, Nr. 15, 29 mei 2006
3. Kabinetsreactie op advies WRR en GR, Kamerstuk 28 089, Nr. 23, 2 april 2009
4. Brief Tweede Kamer. Omgaan met nieuwe risico's .c. nanomaterialen, Kamerstuk 29 338, Nr. 124, 5 september 2013
5. Rijksoverheid. Wetten en regels biotechnologie. https://www.rijksoverheid.nl/onderwerpen/biotechnologie/inhoud/wetten-en-regels-biotechnologie (Bezocht 13-12-2015)
6. Ggo-vergunningverlening. Wet- en regelgeving ggo's. http://www.ggo-vergunningverlening.nl/Wet_en_regelgeving_genetisch_gemodificeerde_organismen (Bezocht 13-12-2015)
7. Europese Commissie. GMO legislation. http://ec.europa.eu/food/plant/gmo/legislation/index_en.htm (Bezocht 13-12-2015)
8. European Food Safety Authority. GMO regulatory framework. http://www.efsa.europa.eu/en/topics/topic/gmo (Bezocht 13-12-2015)
9. European Medicines Agency. http://www.ema.europa.eu (Bezocht 13-12-2015)
10. Rijksoverheid. Beleid genetisch gemodificeerde organismen. http://www.rijksoverheid.nl/onderwerpen/biotechnologie/beleid-genetisch-gemodificeerde-organismen (Bezocht 13-12-2015)
11. Bureau GGO vergunningendatabase. http://www.ggo-vergunningverlening.nl/Vergunningendatabase (Bezocht 13-12-2015)
12. Ggo-vergunningverlening. Veel gestelde vragen, zienswijzen. http://www.ggo-vergunningverlening.nl/Veel_gestelde_vragen/Veel_gestelde_vragen_Introductie_in_het_milieu/Zienswijzen (Bezocht 13-12-2015)
13. Europese Commissie. GMOS; public consultations. http://ec.europa.eu/food/plant/gmo/public_consultations/index_en.htm (Bezocht 13-12-2015)
14. European Medicines Agency; advances medicinal products. http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000294.jsp&mid=WC0b01ac05800241e0 (Bezocht 13-12-2015)
15. Platform biologische veiligheidsfunctionarissen. http://www.en.bvfplatform.nl/ (Bezocht 13-12-2015)
16. Linkova L. et al. (2009). Weight-of-evidence evaluation in environmental assessment: Review of qualitative and quantitative approaches. Science of the total Environment 407: 5199–5205
17. Slovic P. (2000). The perception of Risk. Earthscan publications Ltd, London. UK
18. Ministerie van Verkeer en Waterstaat (2010). Veilig vervoeren, veilig werken, veilig leven met spoor. Derde kadernota railveiligheid
19. Rijksvaccinatieprogramma; Bijwerkingen. http://rijksvaccinatieprogramma.nl/Bijwerkingen (Bezocht 13-12-2015)
20. Ministerie van Landbouw, Natuur en Voedselkwaliteit (2004). LNV consumentenplatform. Voedsel zonder risico: wensen en grenzen
21. Actal (2015). Advies inzake onderzoek regeldruk nieuwe geneesmiddelen. Kenmerk: JtH/RvZ/MK/2015/088 12 augustus 2015

22. Ggo-vergunningverlening; nieuwe besluit en regeling. http://www.ggo-vergunningverlening.nl/Nieuwe_Besluit_en_Regeling_ggo (Bezocht 13-12-2015)
23. Ggo-vergunningverlening; bezwaren. http://www.ggo-vergunningverlening.nl/Veel_gestelde_vragen/Veel_gestelde_vragen_Introductie_in_het_milieu/Bezwaren (Bezocht 13-12-2015)
24. 2004/204/EG: Beschikking van de Commissie van 23 februari 2004 tot vaststelling van nadere voorschriften voor het functioneren van de in Richtlijn 2001/18/EG van het Europees Parlement en de Raad bedoelde registers voor de vastlegging van informatie betreffende genetische modificaties in GGO's (Voor de EER relevante tekst) (kennisgeving geschied onder nummer C(2004) 540)
25. European Commission Joint Research Centre. Database on the notification for GMO releases (GMOINFO) - GMO Register. https://ec.europa.eu/jrc/en/scientific-tool/database-notification-gmo-releases-gmoinfo-gmo-register (Bezocht 13-12-2015)
26. BASF Amflora facts, 29 October 2009. http://fundacion-antama.org/wp-content/uploads/2010/03/2009.10.29.Amflora_Starch_Facts.pdf (Bezocht 13-12-2015)
27. IenM (2012). Brief aan het college van B&W van de gemeente Nijmegen: reactie brief "Nijmegen Gentechvrije stad". Datum: 24 februari 2012. IenM/BSK-2012/14755
28. COGEM (2015). Signalerende aanbiedingsbrief economische analyse Nederlandse biotechnologiesector. CGM/150305-02
29. Ahteensuu M & Sandin P (2012). The Precautionary Principle. In Handbook of Risk Theory, pp 961-978
30. Commission of the European Communities. February 2, 2000 Communication From The Commission on the Precautionary Principle
31. Bureau Biosecurity. http://www.bureaubiosecurity.nl/Beleid (Bezocht 13-12-2015)
32. Schenkelaars Biotechnology Consultancy (2008). Dossierkosten markttoelating gg-gewassen in de VS en de EU. COGEM onderzoeksrapport CGM 2008-05
33. COGEM (2008). Signalerende aanbiedingsbrief bij onderzoeksrapport dossierkosten. CGM/20090312-01
34. COGEM (2006). Nieuwe technieken in de plantenbiotechnologie. Signalering CGM/061024-02)
35. Europese Commissie. (2008). Working group on the establishment of a list of techniques falling under the scope of directive 2001/18/EC on the deliberate release of genetically modified organisms into the environment and directive 90/219/EEC on the contained use of genetically modified micro-organisms
36. Lusser M. et al (2012). Deployment of new biotechnologies in plant breeding. Nature Biotechnology 30: 231–239
37. COGEM (2014). Ggo's te kijk gezet: Het gebruik van genetisch gemodificeerde organismen in tentoonstellingen. Signalering CGM/141219-01
38. COGEM (2009). Off-label gebruik van ggo-geneesmiddelen: zegen of zorg? Signalering CGM/091214-01
39. Riemens *et al*. (2012). Inventory of possible crop cultivation changes as a result of the introduction of GM crops in the Maritime Zone of Europe. COGEM onderzoeksrapport CGM 2012-09
40. COGEM (2006). Ontwikkelingen gentherapie in China. Signalering CGM/060502-01
41. Van de Wiel et al. (2011). Crop volunteers and climate change. Effects of future climate change on the occurrence of maize, sugar beet and potato volunteers in the Netherlands. COGEM onderzoeksrapport CGM 2011-11
42. COGEM (2006). Synthetische biologie; een onderzoeksveld met voortschrijdende gevolgen. Signalering CGM/060228-03
43. COGEM (2008). Biologische Machines? Signalering CGM/080925-01

44. COGEM (2013). Synthetische Biologie – update 2013. Signalering CGM/130117-01
45. COGEM (2009). Zincvinger aan de pols; ontwikkelingen en implicaties van de zinkvingertechnologie. Signalering CGM/090616-02
46. COGEM (2014). CRISPR-Cas: revolutie uit het lab. Signalering CGM/141030-01