The Dutch *GMO Application Process* in short

The GMO office

The GMO Office performs a number of legal duties within the framework of national and European legislation and international conventions in the field of genetically modified organisms (GMOs). These tasks are executed under commission of the Ministry of Infrastructure and Water Management (IenW). The GMO Office oversees the contained use, deliberate release and marketing authorization applications of GMOs. For the contained use of GMOs the GMO Office assesses notifications and grants permits. For both deliberate release and marketing authorization applications of GMOs the GMO Office handles content-related preparations, including the risk analysis. In addition, the GMO office is the primary contact person for all parties involved in working with GMOs, as well as a policy adviser to the Ministry of IenW. The GMO Office facilitates communication between policy makers and the scientific field, and provides training courses on working with GMOs.

For more information regarding other government instances see infographic "National Collaborations".

For more information regarding what areas the GMO office overseas see infographic "Areas of Responsibility".

Activities under Contained Use

What is a risk assessment and why is it necessary?

Contained use is meant to ensure that GMOs cannot escape the facility in which they are handled.
A GMO is generally composed of a host, a vector and an introduced donor sequence. When conducting the risk assessment, first you assess all characteristics of the host, vector and donor sequences independently and subsequently in the context of the GMO. Second, you consider the activities involving the GMOs, for example, large scale production or use of a FACs. You then need to determine how the planned activities can be carried out safely, so that the risks to human health and the environment are negligible.
The risk assessment determines which level of containment (I, II, III or IV) and which category of physical containment (e.g. laboratory or green house) applies to your activities. The containment level also determines which procedure you must follow to apply for your GMO activities. Levels I and II are subject to the notification procedure and levels III and IV are subject to the permit procedure.

Table 1: Different biosafety levels

Level	Pathogenicity	Prophylaxis or treatment	Example
I	Non-pathogenic	Not necessary	*E. coli* K12
II	Mild disease	Available	*E. coli* wildtype, Adenovirus
III	Severe disease	Available	*Mycobacterium tuberculosis*, HIV
IV	Severe disease	Not available	Lassa virus

For more information regarding the internal oversight when working with GMOs see infographic "Internal Organization IG".

Performing a risk assessment using annex 5

Part I

Annex 5 part I of the Ministerial Regulation on GMOs is a classification scheme for you to follow when conducting a risk assessment. It consists of a set predefined outcomes of risk assessments related to different clearly defined groups of GMOs with a similar risk profile. Annex 5 is split into sections 5.0 to 5.6., that are further subdivided, denoted by the letters a., b., c., etc, which represent the predefined outcomes of the risk assessment. When conducting a risk assessment, you must carefully follow the classification scheme of annex 5 taking into account the properties of your host organism, vector and donor sequence in order to determine the correct predefined outcome. This predefined outcome is linked to a level of containment (I, II, III or IV) and category of physical containment. While performing the risk assessment according to annex 5, it's important to check if the host organism you are intending to use is included in one of the following lists: annex 2 (list of apathogenic microorganisms), annex 4 (list of pathogenic microorganisms and viruses) or annex 7 (list of plants).

Part II
For each category of physical containment standard facility and work regulations are defined in annex 9, however these do not always provide sufficient protection. For this reason additional standard containment and protective measures for specific GMOs or activities with GMOs have been included in annex 5, part II. These predefined additional containment and protective measures only exist for the level I and II notification process. For level III and IV containment and protective measures are reviewed and assessed on a case-by-case basis. After you have completed your risk assessment following annex 5, part I and determined the appropriate containment level and category of physical containment, you will need to determine in part II whether additional standard containment and protective measures are required for adequate protection. Examples where such additional protective measures are required include GMOs that can spread via the oral-fecal route or small-scale production in a bioreactor. Each additional containment and protective measures of annex 5 part II corresponds to a set of measures within annex 9, where more details are noted.

Performing a risk assessment according to annex 8

It's possible that the risk assessment of your GMO or intended activities involving GMOs does not follow the classification scheme of annex 5. This may be the case if:

- Annex 5 is not applicable, e.g. your host / donor are not listed in the annexes 2, 4 and 7 or you want to conduct experiments for which the standard equipment and work instructions do not provide adequate protection.
- Your outcome of the risk assessment according to annex 5 is unclear, and you are doubting between two levels of containment.
- You wish to deviate from the risk assessment according to annex 5, for example because you believe that the GMO experiments can be performed safely within lower containment level.

In these cases you perform a risk assessment in accordance with the general principles as described in annex 8, which lists step by step instructions. First you ascertain the harmful properties of the GMO and you consider the intended activities, which lets you determine the appropriate category of physical containment. Second, you check whether the chosen category of physical containment offers appropriate protection for the intended GMO work. Third, you determine if any additional measures are required for the risk to human health and the environment to be negligible. The fourth and final step is to double check the entire risk assessment. The risk assessment and outcome according to annex 8 needs to be submitted to the GMO Office for assessment by means of a 2.8 permit request.

For more information regarding the procedures see infographic "Procedures IG".

Deliberate release activities

Risk assessment IM (ERA and 9 areas of concern)

Deliberate release is the intentional introduction in the environment of a GMO outside of a contained use facility, for example during field trials with GM plants or gene therapy treatments for patients. All activities with GMOs (for research purposes) under deliberate release (i.e. introduction into the environment) (I) require a permit, meaning you must submit a permit application before you are allowed to start your activities. The risks to human health and the environment will be assessed on the basis of your application for each GMO and planned activities by the GMO Office.
Potential adverse effects of the GMO when introduced deliberately into the environment are identified and evaluated in the environmental risk assessment (ERA). Conclusions on the potential environmental impact from the release focusses on the following 9 areas of concern: persistence/invasiveness, selective advantages or disadvantages conferred to the GMO, potential for gene transfer, and impacts on target organisms, non-target organisms, biogeochemical processes, human health, animal health and (agricultural) management practices.
The ERA follows a comparative approach in which potential risks are evaluated compared to a non-modified comparator, thus focusing only on the potential adverse effects resulting from the new trait.
The ERA may identify risks that require risk management. If applicable, specific provisions will be included in the permit which the permit holder needs to adhere to during and after the activities with GMOs. Furthermore the permit holder needs to submit mandatory reports of the conducted activities at specified timepoints. In advance of the actual start of the (annual) activities under a permit a description of the proposed work must be submitted to the GMO Office. All procedures and requirements regarding the deliberate release of GMOs are laid down in Directive 2001/18/EC.

For more information regarding the procedures see infographic "Procedures IM".

Table 2: Terms regarding relevant actors

English	Dutch	Dutch abbreviation	Additional Information
Genetically modified organism	Genetisch gemodificeerd organisme	ggo	
GMO Office	Bureau GGO	BGGO	Grants permits for activities involving GMOs
Human Environment and Transport Inspectorate	Inspectie Leefomgeving en Transport	ILT	Monitors compliance regarding the safe use of GMOs in laboratories, field trials and gene therapy research
Ministry of Infrastructure and Water Management	Ministerie van Infrastructuur en Waterstaat	IenW	Develops policies to ensure activities involving GMOs are safe
The Netherlands Commission on Genetic Modification	Commissie Genetische Modificatie	COGEM	Advises on the risks to human health and the environment related to the production and use of GMOs
Biological Safety Officer	Biologischeveiligheids functionaris	BVF	Supervises the safety of all GMO activities under contained use
Legal entity	Rechtspersonen	RP	Is ultimately responsible for the safety of all activities involving GMOs inside the organization
Responsible employee	Onderzoeksleider	OL	Is responsible for the day-to day operation of GMO activities at level I and level II
Responsible employee	Verantwoordelijk medewerker	VM	Is responsible for the day-to day operation of GMO activities at level III
Environmental Safety Officer	Milieuveiligheids-functionaris	MVF	Supervises the safety of all GMO activities under deliberate release

Table 3: Terms regarding contained use

English	Dutch	Dutch abbreviation	Additional Information
Contained use	Ingeperkt gebruik	IG	Construction, use or storage of GMOs within a facility with specific containment measures
Category of physical containment	Categorie van Fysische Inperking	CFI	Contained use area eg a laboratory, a greenhouse or an animal facility
Notification procedure	Kennisgeving		Applicable in contained use for containment levels I and II
Permit procedure	Vergunning aanvragen		Applicable in contained use for containment levels III and IV
Ministerial Regulation on GMOs	Regeling ggo		Dutch legal regulations regarding use of GMOs
Annex 5	Bijlage 5		Classification scheme to follow when conducting a risk assessment
Predefined outcomes of the risk assessment	Inschalingsartikelen		Outcome of the risk assessment following annex 5
Annex 2	Bijlage 2		List of apathogenic microorganisms
Annex 4	Bijlage 4		List of pathogenic microorganisms and viruses
Annex 7	Bijlage 7		List of plants
Annex 8	Bijlage 8		General guidelines to perform a risk assessment if annex 5 is not applicable
Annex 9	Bijlage 9		Standard facility and work regulations
Environmental permit	Omgevingsvergunning		Permit for contained use facilities

Table 4: Terms regarding deliberate release

English	Dutch	Dutch abbreviation	Additional Information
Deliberate release	Introductie in het milieu	IM	The intentional introduction in the environment of a GMO outside of a contained use facility
Clinical / veterinary	Medisch veterinair	IM-MV	Research activities with genetically modified organisms involving human subjects in a clinical study or veterinary applications
Agriculture	Landbouw	IM-L	Activities with genetically modified plants whether or not they are in association with other GMOs
Environmental risk assessment	Milieurisicobeoordeling	MRB	Process of evaluating the potential harm of the planned activities on the environment and living organisms
Gene Therapy Office	Loket gentherapie	LG	Streamlines the licensing and permit granting procedures for clinical gene therapy studies
Annual report	Verslag van verrichte werkzaamheden	VVW	Needs to be submitted by the user at specified time points
Description of proposed work	Beschrijving van voorgenomen werkzaamheden	BVW	Description of the planned activities of the study, that has to be handed in 15 days prior to starting the study
Permit under fixed conditions	Vergunning onder vaste voorwaarden	VOV	A specific, shorter procedure for certain crops, vectors and cells
Amendment	Wijziging		An amendment is for changes that have no significant consequences for the environmental risk assessment
Notification	Melding		A notification is for changes that have no consequences for the environmental risk assessment
Differentiated procedure	Gedifferentieerde procedure		A specific procedure applicable for certain crops
Marketing authorisation applications	Marktaanvragen	MA	Applicable procedure for the commercial release of a GMO

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