Advice Categories of genetically modified organisms exempted from an environmental risk assessment in the Biotech Act I

COGEM-advice CGM/260105-02

1. Introduction

The Ministry of Infrastructure and Water Management (I&W) has requested advice from COGEM on Biotech Act I, the first part of the legislation published by the European Commission on 16 December 2025. Biotech Act I categorises genetically modified organisms (GMOs) into four groups that are exempt from GMO regulations and environmental risk assessment in clinical trials. I&W has asked COGEM whether the risks to human health and the environment are negligible if no environmental risk assessment is carried out for these GMOs.

2. Background information

On 16 December 2025, the European Commission (EC) published the first part of the Biotech Act (Biotech Act I).[1] Through the Biotech Act, the EC aims to "position the EU as a leader in biotechnology by advancing R&D, fostering an ecosystem where biotech innovation can thrive and boosting the growth potential of biotech companies in the EU".[2] The first part of the Biotech Act focuses on accelerating and simplifying the regulation of health-related biotechnology products, with the aim of bringing these products to market more quickly after their development in the laboratory. The second part of the Biotech Act, which will contain measures for other areas of biotechnology, is expected to be published in 2026.

Biotech Act I is part of a larger package of measures to stimulate the biotechnology sector in the EU. Alongside the publication of this proposal, the EC has also put forward a proposal to amend Directive 2001/18/EC (and Directive 2010/53/EU) on genetically modified micro-organisms and human organs,[3] and a proposal to simplify and strengthen food and feed safety rules.[4]

One of the proposed relaxations of the regulations is to exempt certain groups of GMOs considered safe from environmental risk assessment in clinical trials. This is stated in Article 57(2) of the Biotech Act I. The exact wording of the article is shown in text box 1. COGEM has been asked for advice on the implications of this specific article for the safety of human health and the environment.

Text Box 1. Article 57(2) from the Biotech Act I

Advanced therapy investigational medicinal products containing or consisting of genetically modified organisms presenting no or negligible risks

By way of exemption from Article 5a of Regulation (EU) No 536/2014 [as added by the revised Regulation No (EC) 726/2004], sponsors of clinical trials that concern advanced therapy investigational medicinal products as defined in Article 2(7) of that Regulation, consisting or containing GMOs, are notrequired to submit an environmental risk assessment, if those products belong to at least one of the following categories:

(a) non-viable or replication deficient viral vector that is used to deliver a genetic sequence of human origin, and the vector does not carry an antimicrobial resistance gene;
(b) genetically modified somatic cells, that cannot secrete or produce infectious agents due to the genetic modification;
(c) genetically modified bacteria that do not carry an antimicrobial resistance gene;
(d) genetic material altered using genome editing techniques (ex vivo or in vivo), provided that it has generally negligible adverse effects on human health and the environment.

3. Considerations

The EC aims to simplify the regulations governing biotechnological products for health in order to strengthen the EU's position in the field of biotechnology. It states that it wishes to safeguard health and the environment at the same time. To streamline the authorisation process for conducting clinical trials with GMOs, the EC proposes in Article 57(2) of the Biotech Act I to exempt four categories of GMOs from GMO regulations for clinical trials. The Ministry of Infrastructure and Water Management has asked COGEM whether this exemption would still guarantee the safety to human health and the environment.

3.1 General

COGEM notes that Biotech Act I proposes several major changes to the GMO regulations. In addition to the proposal to exempt four categories of GMOs from the environmental risk assessment for deliberate release into the environment during clinical trials, it is also proposed to exempt the import and manufacture of these GMOs from GMO-related requirements of Regulation (EU) 536/2014 ('Clinical Trials Regulation'). Furthermore, it is proposed that the environmental risk assessment of veterinary medicinal products containing GMOs should henceforth only be carried out under Regulation (EU) 2019/6 for veterinary products, and no longer under Directive 2001/18.

3.2 Four categories GMOs exempted from environmental risk assessment

COGEM notes that the four categories of GMOs in the proposal are broadly and ambiguously defined, leaving them open to multiple interpretations. Consequently, a wide range of GMOs could be exempted from an environmental risk assessment in clinical trials, without it being clear whether this is the legislator's intention. Furthermore, the defined categories also include GMOs that pose a potential risk to human health and the environment, which contradicts the premise that only 'safe' GMOs are exempted.

COGEM is therefore of the opinion that the safety of human health and the environment cannot be guaranteed if these four categories of GMOs are exempted from an environmental risk assessment in clinical trials.

The implications for risks to human health and the environment when these GMOs are exempted from an environmental risk assessment are specified below for each category.

3.2.1 Category a: 'non-viable or replication deficient viral vector'

The description of 'category A GMOs' in the proposal does not define what is meant by 'non-viable or replication-deficient viral vector', nor the criteria that such vectors must meet.

The scope of the description is broad and seems to cover all viral vectors that are no longer able to replicate and spread, as long as they carry genetic sequences of human origin and do not contain antibiotic resistance genes.

A non-spreading phenotype is created through genetic modifications in the viral genome, whereby one or more genes essential for genome replication and/or virus spread are disrupted or removed. There is a wide range of highly diverse viral vectors with varying risk profiles, all of which appear to meet the criteria for this category. Most of these vectors have not yet been used in clinical trials. Furthermore, scientific developments are progressing rapidly, and new types of vectors are constantly being developed.

COGEM notes that it is unclear in how "non-viable" vectors differ from "replication-deficient" vectors.[a] Possibly, this refers to replication-deficient and replication-incompetent vectors. Replication-deficient means that essential genes for genome replication are partially or completely lacking, thereby blocking the multiplication and spread of the GMO. Replication-incompetent means that replication of the genome is still possible, but other obstacles prevent the formation of new GMOs. For example, in replication-incompetent viruses, the structural genes may be partially or completely removed, preventing the formation of new viral particles and further spread from the infected cell.

COGEM points out that, in some cases, when the above-mentioned vectors are used in clinical trials, their spreading properties can be restored. This can occur, for example, through the acquisition of compensatory or restorative mutations in the genome, by recombination with a wild-type virus or a related organism present in the patient, or by complementation. Recombination can result in a new replication-competent variant of the GMO with properties different from those of the parental organism. The risks of recombination or complementation depend on the pathogenicity and biological properties of the parental organism, the mutations that are introduced, the method of production of the GMO, and the possibility of exchanging genetic information with related organisms.[5] COGEM has previously concluded that it is not possible to determine beforehand that the environmental risks of all replication-deficient and replication-incompetent GMOs are negligible.[5]

In addition, COGEM notes that whether viral vectors are replication-incompetent and unable to spread may depend in part on the host. As a result, a vector may be replication-incompetent in humans but replication-competent in, for example, (farm) animals. Animal viruses and vectors derived from those viruses are currently being tested in clinical trials.

Based on the above considerations, a generic exemption for "non-viable or replication-deficient viral vectors" is undesirable. COGEM is of the opinion that the safety to human health and the environment cannot be guaranteed if all possible replication-deficient and replication-incompetent viral vectors are exempted from an environmental risk assessment in clinical trials.

[a] 'Viral vector' is defined in de Biotech Act I as "a genetically modified virus that is used to deliver genetic material into cells."

3.2.2 Category b: 'genetically modified somatic cells'

The proposal exempts genetically modified (GM) somatic cells. These GM cells themselves do not pose a risk to human health and the environment because they cannot spread to third parties or into the environment. However, the proposal not only exempts the use of these cells, but also their production from an environmental risk assessment.

COGEM notes that although the proposal takes into account the possible secretion and production of infectious particles by GM cells in the medical product, other important aspects for human and environmental safety are not considered. This is because the production process is also exempted from an environmental risk assessment. Somatic cells can be genetically modified in various ways. Replication-deficient lentiviruses or retroviruses are often used for this purpose, but modifications can also be made using AAV vectors or CRISPR/Cas.

Depending on the method used to genetically modify the cells, unintended replication-competent viruses may be formed during the production of the viral vector, free infectious vector particles may remain present in the medicinal product, or possible recombination or complementation of the vector may occur in the final product (the GM cells). A built-in viral vector in the cells may also be reactivated or recombine with a wild-type virus, as is the case with the use of non-SIN lentiviral vectors.

Based on the above considerations, COGEM is of the opinion that the safety of human health and the environment cannot be guaranteed as a result of the overly broad exemption from an environmental risk assessment for clinical studies with genetically modified somatic cells, particularly with regard to the production of the cells.

3.2.3 Category c: 'genetically modified bacteria'

COGEM points out that experience of using GM bacteria in clinical studies is limited. For instance, COGEM has only issued advice on a few occasions in recent years concerning clinical studies involving GM bacteria.[6,7,8] Nevertheless, the proposal for the Biotech Act generically exempts GM bacteria from an environmental risk assessment when used in clinical studies. The only condition is that these GM bacteria may not express antimicrobial resistance genes. This means that all future applications with currently unknown risk profiles would also fall under this exemption.

COGEM notes that GM bacteria expressing harmful genes are also exempt from the environmental risk assessment under the conditions of the proposal for the Biotech Act I. Examples include sequences that lead to increased virulence, altered host tropism, or toxin production. COGEM points out that clinical studies have been conducted in the past with GM bacteria in which genes thought to have a beneficial effect on patients were introduced, but the expression of which could potentially have an adverse effect on healthy individuals.[7,8] In the aforementioned advices, COGEM therefore prescribed additional measures because, without these, harmful effects on third parties or the environment could not be ruled out.[6,7,8]

Taking everything into consideration, COGEM is of the opinion that the safety of human health and the environment is not guaranteed under the proposed exemption from the environmental risk assessment for GM bacteria in clinical studies.

3.2.4 Category d: 'genetic material altered using genome editing techniques'

It is unclear to COGEM exactly which medical products fall under this category. Due to the broad and ambiguous description, it appears that all plasmids, mRNAs, self-amplifying mRNAs and other nucleotide-based applications are exempt from an environmental risk assessment for clinical trials. The only condition imposed is that these applications must have a negligible adverse effect on human health and the environment, without this being defined or delineated.

COGEM points out that this condition leads to circular reasoning. In order to determine whether a product has a negligible adverse effect, an environmental risk assessment is necessary. If this assessment is omitted for medicinal products that fall under this category, there is no objective justification for the exemption.

Taking the above into consideration, COGEM is of the opinion that the safety of humans and the environment is not guaranteed under the proposed exemption from the environmental risk assessment for this category in clinical trials.

4. Advice

COGEM is of the opinion that exempting the four categories of GMOs mentioned above from environmental risk assessment in clinical trials, as proposed in the Biotech Act, would no longer guarantee safety of human health and the environment.

COGEM notes that it is possible to exempt the use of more strictly defined groups of GMOs in clinical trials from the obligations of GMO regulations. These could include, for instance, GMOs that fall under the Dutch simplified authorisation procedures with a set of standard licence conditions ('vergunning onder vaste voorwaarden' – VoV), or GMOs for which COGEM has drawn up a generic environmental risk assessment. This includes clinical trials involving viral vectors derived from adeno-associated virus (AAV) [9,10,11], replication-deficient adenoviral vectors[12], the vaccinia virus MVA[13], and clinical studies in which GM cells are modified ex vivo with replication-deficient retro- or lentiviral vectors and then returned to the patient. [14,15,16,17,18]

Other groups of GMOs could be added to this list after they have undergone a generic environmental risk assessment based on accumulated knowledge, which has established that their use in clinical studies does not pose a risk to human health or the environment.

5. General remark

COGEM has previously remarked that GMO regulations are no longer in line with current scientific developments and considers it necessary to amend and streamline the regulations and authorisation procedures.[5,19,20,21] However, with the current proposal, the EC is wrongly seeking to address the problem of excessive regulatory pressure by abolishing parts of the risk assessment based on overly generic criteria, thereby compromising the safety of human health and the environment.

The proposal to amend the regulations (Biotech Act I) is extensive and far-reaching. In addition to the proposal to exclude categories of GMOs from environmental risk assessment, it is also proposed, for example, that veterinary products and studies should no longer be assessed under GMO regulations but instead under the Regulation on veterinary medicinal products.[22] As the EC published the proposal

just before Christmas and the holiday period, there have been limited opportunities to thoroughly study all aspects of the proposal and assess them on their merits. Given the wide scope of the proposal and its potential consequences, this is regrettable and does not contribute to democratic legitimacy.

COGEM is currently studying the further content of the Biotech Act I in more detail and will issue additional advice if necessary.

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