Socially responsible market release of GMO medicines

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(UK condensed version)

COGEM
The Commission on Genetic Modification (COGEM) advises the government on the potential risks of genetic modification to human health and the environment. Furthermore, the COGEM brings ethical and social issues linked to genetic modification to the attention of the ministers involved.

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Summary

The Commission on Genetic Modification (COGEM) questions the European procedure of granting marketing authorisation for medicines consisting of or containing genetically modified organisms (GMOs). COGEM has reservation whether the European Agency for the Evaluation of Medicinal Products (EMEA) is competent to ensure that all appropriate measures are being taken to avoid adverse effects on the environment that might arise from GMO medicines placed on the market. COGEM therefore recommends a number of improvements to this authorisation procedure.

EMEA was established in the interest of public health, and to ensure the smooth functioning of the internal market in the pharmaceutical sector. To accomplish this a centralised procedure was introduced. However, the economic interest has resulted in a procedure that does not appear to correspond with mondial and European environmental policies. The centralised procedure does not seem to be in line with the intention of the 'precautionary' and 'participation' principles.

COGEM has the following reservations about the centralised procedure.

- Limited access to the technical dossier and the risk assessment report written by EMEA means that the national competent authorities of the EU Member States are not able to verify EMEA's decision concerning the environmental risks.
- Although the national competent authorities are consulted, EMEA is not obliged to take their comments into account.
- Experts with knowledge and experience of environmental risk assessments appear to be absent within EMEA, probably due to their selection criteria. This raises the question as to whether EMEA is capable of making the right decisions on environmental risk assessments, and interpreting these according to national environments.
- The procedure has no public consultation process. Only after the marketing procedure for a medicine has been finalised is the general public informed about the product via publication on the EMEA website. Furthermore, there is no opportunity for the general public to verify the procedure.
- It is not clear whether the licences granted by EMEA also include the production process.

COGEM makes the following recommendations for improving the quality of the centralised procedure:

COGEM advises the Netherlands Ministry of Housing, Spatial Planning and the Environment (VROM):

- To notify EMEA and the European Commission of the remarks and recommendations defined in this report.

COGEM advises EMEA:

- To provide a very detailed description of the centralised procedure on the EMEA website, including a clear statement of the authorities involved (and their powers), and the role that the general public plays in this procedure.
- To give the national competent authorities specialising in environmental risk assessments full access to the technical dossier submitted by the applicant, as well as to the scientific assessment reports provided by EMEA. This increased access would give the national competent authorities the opportunity to evaluate the committee's considerations and to make their own judgements on the risks for their particular national environment.
- To ensure that all remarks and objections by the national competent authorities regarding the dossier or the assessment report are presented to all members of the committee.
- To extend the list of external experts to include scientists with experience in environmental risk assessment.
- To give the general public partial access to the technical dossier, thereby increasing their involvement in this process.

COGEM advises the European Commission:

- To create the opportunity, where enduring differences of opinion exist between EMEA and the national competent authorities, to submit this disagreement to a second independent advisory committee (i.e. arbitrator).
- To inform and consult the general public prior to taking authorisation decisions concerning GMO medicines. COGEM feels that implementing a consultation procedure, combined with better access, would result in uniform procedures for marketing GMOs.
- To clarify the uncertainties regarding the extent of the authorisation and its relevance to the production process.

Socially responsible market release of GMO medicines

1. Introduction

Two European procedures are of particular interest with respect to authorising products consisting of or containing GMOs. The majority of the products follow the authorisation procedure as defined in Directive 2001/18/EC[1]. However, for medicines consisting of or containing genetically modified organisms (GMO medicines) for both human and veterinary use, the centralised authorisation procedure as defined in Regulation 2309/93[2] must be followed. The safety of human beings and the environment is very important in both procedures. Both procedures include an extensive environmental risk assessment in order to establish a high level of environmental protection. Since both procedures concern the marketing of a GMO, comparable environmental risk assessments could be expected. However, contrary to the procedure for GMO products, the centralised procedure for GMO medicines, as co-ordinated by EMEA, does not appear to be in line with the precautionary and participation principles.

Background information

The Rio de Janeiro Declaration[3] established a worldwide collaboration for sustainable development, with environmental protection for future generations as a basic element. The Declaration lists 27 principles of sustainable development, such as the precautionary and participation principles (respectively principle 15 and 10). The precautionary principle stipulates that, when potentially dangerous effects to the environment or public health exist, and scientific evaluation does not allow this risk to be determined with sufficient certainty, then measures must be taken to avoid these unacceptable effects. A scientific evaluation should be made prior to taking such decisions. This should be as complete as possible and, where possible, identify the degree of uncertainty at each stage. The decision-making procedure should be transparent and should involve all interested parties. The measures based on the precautionary principle should be consistent with similar measures already taken, as well as being proportionate to the chosen level of protection and non-discriminating.

The participation principle confirms the importance of participation by the general public with regard to environmental matters. The public should have access to environmental information and be involved in environmental decisions. Facilitating participation by the general public, by making information available, will achieve a greater environmental awareness. Public access to rectify the procedure should also be provided.

The Charter of Fundamental Rights of the European Union[4] confirms that, in accordance with sustainable development principles, a high level of environmental protection must be integrated into EU policies. Article 174 of the founding EU Treaty[5] confirms that European policies on environmental matters are based on this precautionary principle. The participation principle is enforced within European law under the Convention of Aarhus[6].

1.1 Procedure for marketing GMO products (other than medicines)

When placing GMO products other than medicines on the market, the request for European authorisation should be submitted to the competent environmental risk assessment authorities in one of the EU Member States. The individual Member State is then responsible for preparing the environmental risk assessment report and proposing the marketing measures to be taken. In view of various local differences in the environment and the implications to the risk assessment, Member States are closely involved in this procedure. They are able to evaluate the assessment according to their national situation and to raise objections to the proposed measures. If conflicts occur between Member States, the disagreement is submitted to one of the independent EU advisory committees. After considering their advice, the European Commission then decides whether or not to grant the authorisation. The general public is informed about the proposed measurements and consulted prior to the decision-making process.

1.2 Procedure for marketing GMO medicines

Contrary to the procedure for GMO products, assessment of GMO medicines is not the responsibility of any single Member State, but is co-ordinated by the European Agency for the Evaluation of Medicinal Products (EMEA). Applications are made directly to EMEA and are evaluated by one of the scientific committees considering the quality, safety and efficacy of the medicines. One of the committee members, the ‘rapporteur’ assesses the risk assessment submitted with the application. Only that part of the assessment report dealing with the environmental risks will be made available to the competent national authorities in the field of environmental risk assessment. The rest of the assessment report, and even the complete environmental risk assessment submitted by the applicant (part V of the dossier), remain confidential. Access by the national authorities is therefore limited to the summary of the assessment (part II.H of the dossier). The national competent

authorities have an opportunity to comment on the assessment report or raise objections to the proposed measures, but their remarks are not necessarily taken into account. It is up to the rapporteur whether comments by competent authorities are forwarded to the other members of the committee. The European Commission makes its decision regarding marketing authorisation based on the committee's opinion.

The centralised procedure is not open to participation by the general public. The public has no access to the dossier and is not consulted prior to the decision-making process. Only at the final stage of authorisation is the public informed via publication on the EMEA website.

2. Remarks on the centralised procedure

EMEA was established in the interest of public health, to ensure the smooth functioning of the internal market in the pharmaceutical sector. To accomplish this a centralised procedure was introduced. However, this procedure looks as if it puts the interests of the pharmaceutical industry first, resulting in a procedure that is in conflict with other European policies on environmental issues.

The first principle of the Rio de Janeiro Declaration states that human beings are at the centre of sustainable development concerns, and that they are entitled to a healthy and productive life, in harmony with nature. This basic principle states that economic progress is inextricably bound up with protecting the environment. Pursuing a good environmental policy not only protects the environment, but also improves the economy.

This section defines the possible shortcomings of the centralised procedure and takes into account the possible distrust that might arise as a result of these shortcomings.

2.1 Communication with Member States

Living organisms, whether released into the environment for experimental purposes or as commercial products, may spread throughout the environment, depending on the characteristics of the organism and the environmental conditions. Due to local differences, such as population density, flora and fauna, and local climate, releasing GMOs may lead to different environmental effects. It is therefore essential that attention is focused on the differences between national environments for controlling risks arising from releasing GMOs into the environment. Regulation 2309/93 included this statement, but EMEA seems to be neglecting its importance. The regulation states that ‘necessary’ consultations will be held between the committee rapporteur and the national authorities, but does not include the powers of the national authorities. EMEA has converted this into a procedure in which the national authorities are consulted, but their remarks and recommendations are not necessarily taken into account in the evaluation.

2.2 The rapporteur decides to submit Member State comments

The consideration as to whether comments by the national competent authorities are relevant, and the decision whether or not to submit these comments to the other members of the scientific committee, is the sole responsibility of the Rapporteur. The possibility of the rapporteur acting according to his/her own views does not correspond with the Dutch legislation of 'being informed'. The ability to withhold possibly relevant information from the other members of the committee and, indirectly the European Commission means that decision makers cannot confirm, with complete certainty, that their decision is based on all the relevant information. This brings the legitimacy of their decision into question. The possibility that the rapporteur could act according to his/her own view counteracts the essence of feedback to rectify decisions taken by a single individual. Appointing several rapporteurs would lead to unsystematic governmental decisions, leading in turn to legal insecurity.

The centralised procedure offers applicants the opportunity to express their preferences regarding the appointment of a rapporteur. This contradicts the normal scientific advice procedure. EMEA implies that rapporteur selection is based partly on applicant preferences. As the rapporteur is in a particularly vital position, this creates a situation that may lead to distrust by the national competent authorities and the general public.

2.3 Limited access to the dossier by competent authorities

As a result of their limited access to the technical dossier and the risk assessment report written by the rapporteur, the national competent authorities in the Member States are not able to verify EMEA's decision with regard to the environmental risks.

In the case of GMO medicines, requests submitted by applicants are accompanied by a complete technical dossier that includes the environmental risk assessment (part V of the dossier). This remains confidential, as access by the national authorities is limited to the summary of the assessment (part II.H of the dossier). Only that part of the assessment report dealing with the environmental risks is made available to the national competent authorities. The authorities are therefore not able to ensure that all possible effects, such as indirect effects, are taken into account and that the proposed measures are consistent with similar measures already taken, that they are proportionate to the chosen level of protection and non-discriminating.

2.4 The expertise of the experts

The manner in which EMEA deals with the national competent authorities is possibly due to its belief that internal expertise safeguards are sufficient to assess whether placing GMO medicines on the market poses a hazard to the environment. However, the medicine evaluation experts representing the national competent authorities cover all the various scientific fields necessary for evaluating medicinal products, including inspection and pharmacovigilance activities for both human and veterinary use. Environmental risk assessment experts are rarely represented within EMEA, probably due to their selection criteria. This raises questions as to whether EMEA is competent enough to ensure that all appropriate measures are taken to avoid adverse effects on the environment and to interpret these according to the national situations.

2.5 Participation by the general public

In its 2002 work programme EMEA[7] announces that developing improved transparency and a communication policy is an important objective. Supplying sufficient information prior to taking decisions is one of the conditions for ensuring a transparent procedure. However, with regard to the centralised procedure, EMEA does not inform the general public before decisions are made. The public receives no information until EMEA has received the decision granting marketing authorisation from the European Commission[11]. In addition to the fact that the general public has no access to the dossier and the assessment reports, there is also no opportunity to raise objections or even submit remarks. EMEA's policy regarding the general public therefore does not conform to the principle of participation. Participation is the key to democracy. Decisions taken by the government are only legitimate when the public supports these decisions. EMEA does not foresee that applications should be made public if, according to Dutch law, these infringe on the public interest. The idea behind these laws is that the government should be held accountable for its actions.

As agreed when it was originally set up[2], EMEA protects both the interests of the public and the pharmaceutical sector. However, the confidentiality within the centralised procedure suggests that the interests of the pharmaceutical sector are being favoured. Protecting public interest seems to be restricted to evaluating the efficacy and safety of the medicine as it concerns the patient. The wider interest of the public in general, by providing a well-founded environmental policy, seems of lesser importance.

To withhold public access to this information before taking such decisions will result in problems, such as acceptance and perception. Procedures and decision-making processes that are not transparent mean that such decisions are generally not accepted without comment, particularly by the more organised sections of the general public. It is possible that such lack of transparency could lead to social unrest.

2.6 Uncertainties concerning authorisation

Marketing authorisation for GMO medicines granted by the European Commission is valid throughout the entire European Union[2]. However, there are some uncertainties about the extent of this authorisation with regard to the production process. This lack of clarity has led to confusion, not only within the competent environmental risk assessment authorities, but also for the applicant. If the marketing authorisation does not include the production process, it is unclear as to how and where production authorisation should be obtained. This seems to be an omission in the legislation.

If marketing authorisation does include the production process it is unclear whether this process is assessed within the EMEA evaluation. Part II.H of the technical dossier, which is accessible by the national authorities, gives no clarification of this point.

3. Recommendations

COGEM makes the following recommendations to improve the quality of the centralised procedure.

3.1 Recommendations to the Ministry of VROM

To ensure a well-considered authorisation procedure, COGEM advises the Ministry of VROM:

- To bring the remarks concerning the centralised procedure and the recommendations defined in this report to the attention of the European Commission and EMEA.

3.2 Recommendations to EMEA

A more transparent procedure

Transparency is a form of social acceptance of governmental proceedings, with the assumption that the government is approachable. Attempts must be made to increase the transparency of the centralised procedure, where possible.

COGEM therefore advises EMEA:

- To publish a very detailed description of the centralised procedure on the EMEA website. This is an easy, but effective, way to remove uncertainties about the centralised procedure for a third party. The description should include a clear overview of the authorities involved, and their powers, as well as the role played by the general public in the procedure.

Consulting the national authorities

COGEM supports the importance of a European procedure but considers the involvement of the national competent authorities to be essential. Local differences in environmental conditions should be included in the evaluation of the risk assessment.

COGEM therefore advises EMEA:

- To give the national authorities specialising in environmental risk assessments full access to the technical dossier submitted by the applicant, as well as to the scientific assessment reports provided by EMEA. This increased access would give the national competent authorities the opportunity to evaluate the committee's considerations and to make their own judgements on the risks regarding their own national environment. The confidentially of the technical dossier should be guaranteed.

- To ensure that all remarks and objections by the national competent authorities regarding the dossier or the assessment are presented to all members of the committee.
- To ensure the independence of the rapporteur by appointing by rotating scheme.
- To extend the list of external experts to include scientists with experience in environmental risk assessment. The national competent authorities can assist in selecting these experts. Including these experts and guaranteeing that comments by the national authorities are taken into account would, in COGEM's opinion, provide sufficient knowledge within EMEA to provide a complete assessment of the environmental risks.

Informing the general public

Facilitating participation by the general public, by making information available, will produce a greater awareness of environmental matters. COGEM is also of the opinion that a procedure that is accessible to the general public will be more precise and trustworthy.

COGEM therefore advises EMEA:

- To facilitate participation by the general public by allowing partial access to the technical dossier. This will still protect the commercial interests of the manufacturer.

  COGEM feels that the following information should be made public: name and address of the manufacturer, a description of the GMO minus any commercially important details, the application and the environmental risk assessment report with the proposed measures. The public is thus able to assess the proposed measures on the basis of this information. Publishing this information on the EMEA website seems a suitable publication medium.

3.3 Recommendations to the European Commission

Consulting the national authorities

Decisions should be based on a full evaluation of all possible risks. In COGEM's opinion the European Commission should do everything in its power to ensure that this evaluation is as complete as possible.

COGEM therefore advises the European Commission:

- To create the opportunity, where enduring differences of opinion exist between EMEA and the national competent authorities, to submit this disagreement to a second independent advisory committee (i.e. arbitrator). The procedure for granting authorisation for GMO products is different to that for

medicines, and provides the possibility for a second opinion. Existing problems between EMEA and national authorities should be considered by one of the authorised committees within the European Commission. The European Com-mission should make its decision based on this committee's advice. COGEM believes that adding the opportunity to ask for a second opinion will improve the quality of the procedure and the credibility of the decision-making process.

Participation by the general public

Participation is required within a democratic society, and consulting the general public is therefore an essential element. Leaving the evaluation and handling methods regarding environmental risks to the decision-makers and experts does not concur with the principles of participation.

COGEM therefore advises the European Commission:

- To inform and consult the general public prior to taking authorisation decisions regarding GMO medicines. The way, in which the general public is consulted, before authorisation for products other than medicines is granted, seems to be reasonable. The European Commission informs the general public by publishing the information on the Joint Research Centre website, e.g. a short summary including details of the GMO, the environment and the assessment. The general public can then submit comments, via e-mail, up to four weeks after publication. Implementing this consultation procedure, combined with additional access opportunities would result in equivalent procedures for market release of GMOs.

Authorisation for the production process

A number of uncertainties exist regarding the extent of the authorisation in respect to the production process. This lack of clarity has led to confusion, both within the competent environmental risk assessment authorities as well as for the applicant. This seems to be an omission in the legislation.

COGEM therefore advises the European Commission:

- To clarify the uncertainties regarding the extent of the authorisation and its relevance to the production process.

  When assessing the risks, the production circumstances vary widely from those for market release of GMOs. These variations make an assessment specific to the production process absolutely essential. As this is not a matter of introducing GMOs into the environment, but of limited use, COGEM considers a national approval procedure to be sufficient.

References

Declarations and Legislations

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2. **Council Regulation 2309/93;** Council regulation (EEC) No 2309/93 of 22 july 1993 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use ad establishing a European Agency for the Evaluation of Medicinal Products.
3. **The Rio de Janeiro Declaration**; The Rio de Janeiro Declaration on Environment and Development. The United Nations Conference on Environment and Development, Rio de Janeiro from 3 to 14 June 1992.
4. **The charter of the fundamental rights of the European Union** (2000/C 364/01) of 18 December 2000
5. **Consolidated version of the Treaty establishing the European Community**; 24 December 2001
6. **Convention of Aarhus**; Convention on access to information, public participation in decision-making an access to justice in environmental matters. Aarhus, 25 June 1998.

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7. Work programme for the European Agency for the Evaluation of Medicinal Products 2002.
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9. The European Agency for the Evaluation of Medicinal Products. Eighth annual report 2002.
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11. SOP/005/96: Centralised procedure: from assessment reports to European Public Assessment Report (EPAR).
12. CVMP/037/97: Compliance with article 28(4) of council regulation (EEC) No 2309/93.
13. EMEA/SOP/2072/99: Scientific advice to be given by the CPMP for innovative medicinal products.