

Part I

Part II

Workability Practices

Executive Summary

Schenkelaars Biotechnology Consultancy
BioCollectief

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**Schenkelaars Biotechnology Consultancy
BioCollectief**

**Study in order of:
Ministry of Economic Affairs**

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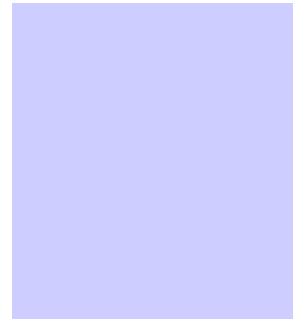
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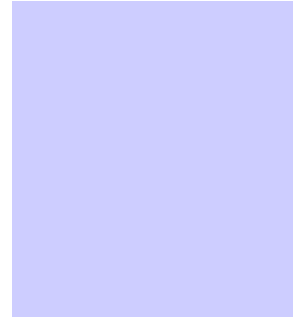
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Foreword

In order to draw conclusions about the ‘workability’ for applicants of the implementation practice of legislation for biotechnology in the Netherlands as well as to develop recommendations to improve this workability, this survey has been commissioned by the Dutch Ministry of Economic Affairs to Schenkelaars Biotechnology Consultancy and BioCollectief. The 1st phase of this survey was focussed on the implementation practices of legislation for biotechnology *research* in the Netherlands. Based on findings from the 1st phase survey, this 2nd phase survey aimed at an international comparison of the ‘workability’ of existing legislation and regulations for biotechnological research (Part I). In addition, the 2nd phase survey also aimed at identifying potential bottlenecks for notifiers and operators of new and proposed EU legislation for biotechnology products in the agro-food chain and at developing recommendations for authorities to address these potential bottlenecks (Part II).

This document contains an executive summary of the 2nd phase survey report, which is divided in two parts: Part I “International comparison of the ‘workability’ of existing legislation for biotechnological research and recommendations to Dutch authorities” and Part II “New and proposed EU legislation for GMOs from farm to fork: Bottlenecks for notifiers and operators, and recommendations to authorities”.

Part I offers insight into the current bottlenecks of the Dutch application procedures for field trials with GMOs, gene therapy and the genetic modification of animals, as experienced by several Dutch applicants. The conclusions from the comparison contribute to effective solutions that will improve the ‘workability practice’ for applicants.

Part II formulates recommendations to authorities and aims at improving the 'workability' for notifiers and operators of new and proposed EU legislation for GMOs from farm to fork.

During the survey the research team has been accompanied by an Advisory Committee consisting of representatives of the Ministry of Economic Affairs, the Ministry of Education, Culture and Science, the Ministry of Public Health, Welfare and Sports, the Ministry of Housing, Spatial Planning and the Environment, the Ministry of Agriculture, Nature and Fisheries, the Royal Netherlands Academy of Arts and Sciences, and the Netherlands' Biotech Industry Association Niaba. The members of the Advisory Committee have provided many additional insights and helpful comments on a draft version of this report, but the final analysis of bottlenecks and the recommendations are the sole responsibility of the authors of this report.

We think this report contains valuable information for the Dutch government on how to apply best practices for applicants for current application procedures and for new and proposed legislation. Good communication between competent authorities and applicants or notifiers seems crucial in effectively carrying out transparent and predictable procedures with low manageability burdens.

Finally, we would like to thank all contacted authorities and organisations, interviewees, and members of the Advisory Committee for their participation and hope this report is a useful resource.

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Introduction

1.1 Background

The Dutch government's White Paper on an Integral Biotechnology Policy of 28 September 2000 (INB) announced to investigate "the transparency and the manageability burden of legislation regulating biotechnological research for research institutes and industry". As a consequence, the Ministries of Economic Affairs and Education, Culture and Science, in consultation of the Ministry of Public Health, Welfare and Sports, the Ministry of Housing, Spatial Planning and the Environment, and the Ministry of Agriculture, Nature and Fisheries, commissioned a "1st phase survey of bottlenecks as experienced by applicants in the implementation practices of legislation for biotechnological research in the Netherlands" to a joint research team of BioCollectief (Amsterdam) and Schenkelaars Biotechnology Consultancy (Leiden). In April 2002, the research team reported its findings to the Advisory Committee, consisting of representatives of the aforementioned ministries as well as the Royal Netherlands Academy of Arts and Sciences and the Netherlands' Biotech Industry Association Niaba.

In the 1st phase it was impossible to cover all categories of regulated biotechnology activities. Therefore the focus was on those categories of regulated activities where Dutch applicants experienced most bottlenecks in the workability. After explorative interviews with two professional societies and in close collaboration with the Advisory Committee the 1st phase survey was limited to four different Dutch categories of regulated activities:

- Category 1: Contained use of GMOs.
- Category 2: Field trials with GMOs.
- Category 3: Gene therapy.
- Category 4: Genetic modification of animals.

According to the findings of the 1st phase, interviewees of research institutes and companies indicated to experience hardly any serious bottlenecks in the implementation practice of legislation for Category 1 activities, whereas various, serious bottlenecks were experienced for implementation of legislation for activities of Categories 2, 3 and 4. Common elements in the experienced bottlenecks were that regulatory decision-making procedures lasted long, the manageability burden was high and the transparency could be improved. The findings of the 1st phase survey further indicated a large heterogeneity in the bottlenecks experienced by research institutes and companies.

1.2 Objectives

Based on findings from the 1st phase survey, this 2nd phase survey had a twofold aim.

1. The objective of the Part I survey was to draw conclusions about the 'workability' of the implementation practice of legislation for biotechnology in the Netherlands as well as to develop recommendations to improve this workability for Dutch applicants. The international comparison therefore aimed at comparing the implementation practices of legislation for biotechnology *research* in the Netherlands to those in Germany, the United Kingdom (UK), France, and the United States (US), with a particular view to learn from "best practices" on the workability for applicants.
2. In addition, the Part II survey aimed at identifying potential bottlenecks for notifiers and operators of new and proposed EU legislation for biotechnology *products* in the agro-food chain and at developing recommendations for authorities to address these potential bottlenecks.

1.3 Reader

This document contains the conclusions and recommendations of the Part I and Part II survey. Chapter 2 starts with a general conclusion on workability practices for the application procedures followed by the specific workability practices and recommendations for each case. Chapter 3 summarises potential bottlenecks of new and proposed EU legislation for biotechnology *products* in the agro-food chain and summarises recommendations for authorities to address these potential bottlenecks. Chapter 4 outlines the research team and the Advisory Committee.

Summary international comparison

2.1 General conclusions and recommendations of the international comparison

During the past year Dutch competent authorities (CAs) have initiated various activities to improve the workability of their application procedures for applicants. However, by comparing the Netherlands with the other investigated countries, it can be concluded that the Dutch application procedures could be further improved by increasing the predictability and transparency. To do so CAs should increase their communication and education activities. In parallel to these activities a co-operative attitude of CAs and applicants is essential. The following general best practices could contribute to the improvement of an application procedure in general:

1. To decrease unclearness for applicants and to lower burdens for a CA and an applicant during the evaluation it is preferable that the CA improves its provision for a **formal preliminary consultation**, in which a draft application is discussed prior to official submission. Applicants should be informed about this possibility for a preliminary consultation. The main goal is to clarify questions and problems of the applicant in filing the application. This will decrease the number of formal requests for additional information during the evaluation procedure, which delays the total time taken for decision-making. Considering the possibility for an appeal, a preliminary consultation should be executed as transparent and juridical correct as possible to prevent for procedural mistakes.
-

Therefore the consultation has to be registered and official minutes of the meeting should be made. The proceedings and intentions of such a preliminary consultation should be laid down in Standard Operating Procedures (SOPs) to ensure good compliance.

2. To lower burdens for applicants and a CA during the evaluation procedure contacts between the CA and the applicant can be further intensified by designation of one **contact person** from the CA to a specific application. This primary contact person, who should be a field-expert, can be consulted preliminary to the application, actively assist the applicant, mediate between an Advisory Committee and the applicant in case of additional questions, and act as a general source of information on all further relevant matters. Improved communication will enhance the transparency and predictability of the procedure. The basic principle of this system is co-operation from both sides during processing the application and ensuring a proper evaluation.
3. Applicants should be invited to **orally clarify** the application during a committee meeting. This approach provides an opportunity to correct misunderstandings and to supply additional information, on which the decision is based. The oral clarification prevents delays caused by written requests for additional information.
4. In general CAs should provide detailed **up to date information** to applicants and the public. The Internet seems the best option to provide specific information on law and regulations in the Netherlands and EU (and optionally other countries as well). Detailed information on a specific regulation should include the application procedure, up-to-date guidelines and criteria, legislative issues, links to other relevant websites, news on the latest developments and changes (for example by an online e-mail newsletter that also provides general news, articles and publications of the CA or other relevant organisations). Furthermore, for each application the website should provide the on-line application form and guidance documents.
5. **Changed evaluation criteria** in the Netherlands should be discussed with the applicant, and preferable other stakeholders as well, before criteria are performed and utilized. Applicants have to be notified in a timely manner and the new criteria should be as transparent as possible on whether an application will be approved and under which additional conditions.
6. CAs should initiate **annual meetings** with applicants to evaluate the 'workability' of the application procedure, to address problems, and to discuss emerging issues on for example political, legislative, and procedural aspects.
7. CAs should actively **inform and educate** applicants on how to properly submit an application, for example by organising a training, workshop or seminar.
8. Dutch CAs should increase **contacts** on issues concerning shared application procedures, to smoothen the procedure and decrease burdens to a minimum. In general CAs could also initiate more contacts with their foreign counterparts to learn from each other.

2.2 Field Trials with GMOs

Comparing the Netherlands and the investigated countries

In general the Dutch Part B approval procedure does not seem to differ much from the other three EU countries in terms of transparency, overall effects and manageability burden. Due to the national implementation of the Directive 90/220/EC and the new Directive 2001/18/EC, Germany, the UK, France, and the Netherlands appear to process applications in a very similar manner. France, Germany, and the Netherlands have not yet fully implemented the new Directive but they are expected to do so somewhere mid 2003.

The UK, Germany, and France seem to be confronted with the same bottlenecks as the Dutch approval procedure concerning delays due to political interference, burdens as a result of public input, and sometimes vagueness of the application forms.

Differences appear at the number of involved authorities, the average time taken for decision-making, the contact with the competent authority, the public input process, and the information supply towards applicants.

The EU basic attitude towards GMOs differs fundamentally from the US, which is reflected in the regulatory approach towards field trials with GMOs. Both systems evaluate biosafety risks of the product, but depending on the production method different kinds of legislation apply. In comparing both types of legislation good account has to be taken of these differences. However, applicants in Germany, the UK, and France refer to the US system, which seems to suffer less political interference than the EU system and is regarded more transparent and predictable than the EU procedure. US applicants seem content with the US procedure on this issue and do not seem to suffer delays or non-transparent procedures as a result of political interference.

Results 1st phase survey

During the 1st phase survey five Dutch applicants were interviewed on their experiences with the application procedure of Bureau GGO (which is part of the Ministry of Housing, Spatial Planning, and the Environment (VROM)). The results of the Phase 1 study represent the experiences of the interviewed applicants and are:

1. In general the contacts with Bureau-GGO are considered helpful. Applicants can contact Bureau-GGO by email or telephone and questions tend to be answered to the applicant's satisfaction.
2. The application forms are generally clear. However, applicants experience a lack of transparency concerning the degree of details that they have to submit with their application.
3. The last few years the time taken for decision making has increased considerably, compared to the situation before 1998.
4. Many applicants experience a high burden during the procedure, due to appeal of interest groups.

5. In several applications of 1999 delay occurred, due to the denial of the Minister to grant the permit after positive advise of the COGEM.
6. The Ministry of VROM has applied changed evaluation criteria on previously submitted applications. This resulted in denial of permits, without a possibility for the applicants to submit additional relevant data in response to the new criteria
7. Applicants were not adequately informed by the Ministry of VROM about the changed criteria.

Recommendations

Based on the findings in the other countries and the experienced bottlenecks in the Dutch application procedure several recommendations can be formulated to further improve the Dutch situation. The recommendations aim at improving transparency and predictability of the procedure to lower manageability burdens. The recommendations are:

1. To improve transparency and predictability of the application procedure the contact person of Bureau GGO could further increase his pro-active role. Improved communication should apply when the contact person is consulted preliminary to the application, actively assists by submitting the application, mediates between COGEM and the applicant in case of additional questions, and by acting as a general source of information on all further relevant matters. The basic principle of this system is co-operation from both sides during processing the application and ensuring a proper environmental safety evaluation. To create a workable system, co-operation of the applicants is necessary as well.
2. The Ministry of VROM/Bureau-GGO and COGEM should evaluate and improve the regulation practicability and the application forms regularly. Regular consultations with applicants to address problems will lower the manageability burden for the applicant and the Ministry of VROM/Bureau-GGO.
3. The Dutch government should initiate the development of a framework of decision-making criteria for 'unacceptable risks', because applicants experience a lack of clarity about data requirements while public groups contest the approach to the risk assessment. It is highly recommended that the Dutch government initiates a fair wider-scale debate with input from all stakeholders. The aim of this debate should be to determine decision-making criteria for 'unacceptable risks' and to identify those issues that need further scientific research and normative discussions. Due to increasing scientific knowledge and changing public insights the framework needs to be revisited regularly.
4. The Ministry of VROM/Bureau GGO should approach public groups more actively to take notice of their comments during the public consultation period. The assignment of a contact person at the Ministry of VROM is preferable in gaining more mutual understanding. In parallel to the wider scale debate, in which public groups co-operate in formulating the framework, manageability burdens of the public consultation procedure could decrease, as well as the amount of appeals.

5. Changed evaluation criteria should be discussed with the applicant, and preferably with other stakeholders as well, before criteria are performed and utilized. Applicants have to be notified in a timely manner and the new criteria should be as transparent as possible on whether an application will be approved and under which additional conditions.
6. Bureau-GGO could improve information supply to the applicants on the Internet homepage by providing detailed up-to-date information about the general application procedure on matters of when, how, and by whom a decision will be taken.

2.3 Gene Therapy

Comparing the Netherlands and the investigated countries

In the Netherlands and the other investigated European countries two different regulatory frameworks cover gene therapy clinical trials. The first framework consists of three directives that regulate the use of GMOs: 1) Directive 98/81/EC on containment of GMOs to protect workers and the environment during the production process; 2) Directive 2001/18/EC on the deliberate release of GMOs into the environment; 3) Directive 2000/54/EC on the protection of workers from the risks related to exposure to biological agents. While some member states regulate gene therapy clinical trials under the contained use directive, others regulate it under the deliberate release directive. In addition there are differences in public consultation among countries under the deliberate release directive.

The second framework covers the evaluation of the design and conduct of clinical trials, which is regulated at two distinct levels in the European Union. The evaluation procedures are not standardized among member states. In each member state several CAs (including an independent ethical committee) evaluate early phases of clinical trials, but the evaluation procedures and the level where the evaluation takes place differs considerably. By contrast late phase clinical trials leading to market authorisation are covered by the centralised procedure through the European Medicines Evaluation Agency (EMA).

As a result of these two different regulatory frameworks there is a considerable heterogeneity in the national evaluation procedures and the requirements for gene therapy clinical trials throughout the EU. Applications for European wide multi-centre gene therapy clinical trials are therefore difficult and complex. The new European Directive of 2001 on Good Clinical Practices (GCP) is the first attempt to streamline and harmonise the clinical trial evaluation procedures among the member states. However, in case of gene therapy clinical trials the Directive does not incorporate the three Directives on GMOs, which means the European Union still lacks an integrated model for the regulation of gene therapy clinical trials. As a result the differences between the national regulatory frameworks will persist, even if every member state has fully implemented this new Directive on GCP, because of the differences in the implementation of the GMO directives.

By contrast in the US the evaluation criteria, requirements, and evaluation procedures are set at the federal level, while the implementation is both at the federal and the institutional level. The Food and Drug Agency (FDA) must approve all phases of clinical trials and market authorisation. In addition the Recombinant Advisory Committee (RAC) at the National Institute of Health (NIH) performs an evaluation of all gene therapy applications that is open to the public. Furthermore at the level of each institution two independent committees evaluate the biosafety and ethical aspects of a gene therapy application, according to strict national regulations. These two committees are under stringent oversight by federal agencies.

Results 1st phase survey

The 1st phase survey analysed existing bottlenecks in the evaluation procedures for gene therapy clinical trials by in-depth interviews with three applicants, who were closely involved with nine applications of the total of fifteen applications until now. The results of this 1st phase survey are:

- 1 Three CAs, each with different goals and serving different purposes, have to give their approval to a gene therapy application, but they do not (yet) seem to act in a co-ordinated manner. A one door-one key procedure and a single integrated application form are lacking. Instead there are three different procedures with different time frames. Moreover, in the evaluation procedures the separation of tasks of the CAs is insufficiently observed, leading to an overlap between both procedures, which confuses applicants.
- 2 The evaluation procedures, the information requirements and the evaluation criteria used by the CCMO were considered unclear, which caused in several cases a delayed approval. The interviewees considered the information they had to provide to the CCMO in their application, and in case of a request for additional information, unclear. In their view a clear and transparent evaluation-scheme accompanied by adequate guidance documents was missing. Moreover, The CCMO often made subsequent requests for additional information during an evaluation procedure and applicants argued that the requirements appeared to change during the evaluation procedure. Some interviewees were not aware of the possibility to have an informal preliminary consultation with the CAs; others doubted these meetings would be helpful.
- 3 The interviewees considered the general attitude of the CCMO as not sufficiently cooperative, because the CCMO often adapted a formal and meticulous attitude towards the evaluation of gene therapy applications. However, due to the small number of applications it has to be noted that both applicants and CAs had little chance to gain experience in submitting and evaluating gene therapy applications. By contrast interviewees found the Ministry of VROM/Cogem helpful during their evaluation of gene therapy applications.

Recommendations

The past two years the Dutch CAs, especially the CCMO, made considerable efforts to improve their communication towards applicants. However, based on the findings in the

other countries several best practices can be formulated to further improve the Dutch situation:

1. It is essential that applicants know the requirements for a gene therapy clinical trial in detail; otherwise an applicant is not able to provide the CAs with the necessary information and to protect patient safety. Therefore, the Dutch CAs should acknowledge that their outreach activities are of critical importance for applicants and a requirement for outreach activities should be adopted in the Dutch laws. Sufficient funds should be allocated to develop the following initiatives:
 - a. Extend the information provided on the Dutch CAs Internet sites, by publishing an extensive explanation of the various applicable laws and requirements.
 - b. Organise annual meetings to foster discussion on emerging issues or new policy initiatives. Once a year the Dutch CAs should get together with the Dutch professional societies and trade organisations to evaluate all aspects of the application procedures.
 - c. Set up training courses in collaboration with professional societies to educate applicants on all aspects of clinical gene therapy studies and how to properly submit a gene therapy clinical trial application.
 - d. Develop in close collaboration with experts from the field a gene therapy handbook, which provides applicants with a clear and elaborate explanation of their standard practices, procedures and requirements.
2. The Dutch CAs should further improve their communication and basic attitude towards applicants in an attempt to lower the number of requests for additional information. The Dutch CAs should take the lead to ensure good contacts with their applicants; change from a passive to an active role and from a formal standpoint to a more co-operative standpoint and improve communication and contacts with applicants. This change of culture should not only rely on good intentions of the CAs, but should be incorporated in the underlying laws and regulations. The CAs should therefore develop Standard Operating Procedures (SOPs), which incorporate the following communication strategies:
 - a. Designate one member of the CA to a specific application. This central contact person can be consulted prior to submission of the application. He or she should actively assist in submitting the application, mediate between CAs and the applicant in case of additional questions, and act as a general source of information on all further relevant matters. This pro-active contact person should focus on co-operation with the applicant by processing the application.
 - b. Strengthen the information exchange at a preliminary consultation. The applicant should be allowed to have a formal preliminary consultation based on a draft application. Official minutes should be made and sent to the applicant. Not only the principle investigator should attend this meeting, but also the research coordinator, the hospital pharmacist, the biosafety officer, and an expert from the vector manufacturer.
 - c. The applicant should be invited to orally clarify the application and to answer possible questions of the CAs during the decision-making process.

This interaction should solve any remaining misunderstandings or indistinctness.

3. The Dutch CAs should consider implementing a one door-one key procedure accompanied by a single integrated application form in an effort to streamline the evaluation procedures and to ensure an efficient and transparent evaluation of a gene therapy application. One of the CAs should be made responsible for the coordination of the national evaluation procedures. The designated CA should assure that the task separation between the evaluation bodies is sufficiently observed and prevent communication problems between applicants and the evaluation bodies. The research team recognises the need for the three separate evaluation procedures currently in place. Therefore the proposed one door-one key procedure keeps the three separate evaluation procedures along with their legal requirements and time frames in place, but calls for the coordination of the national evaluation procedures via a single, clearly identified point of contact located at one of the CAs involved.

2.4 Genetic Modification of Animals

Comparing the Netherlands and the investigated countries

For all EU Member States the requirements on animal welfare are covered by Directive 86/609/EEG, which will be revised this year. The Directive requires personal and institutional licences. Except for France, prior to the start of the animal experiment all investigated countries, including the Netherlands, perform at the institutional level an obligatory animal welfare evaluation by an institutional committee (IC). In the Netherlands the institutional evaluation is done by the Dutch Animal Experimental Commissions (DECs) and this procedure differs from the other investigated countries, since it additionally includes an ethical evaluation, in which the animal's harm is weight to the likely benefits for society.

Furthermore the Netherlands differs for its additional evaluation at national level by the Commission for Biotechnology with Animals (CBD) of the Ministry of Agriculture, Nature, and Fisheries (LNV), as required by the Dutch Decree on Biotechnology with Animals 1997 (BBD). This Decree was adopted to address public concerns about the genetic modification of animals in the Netherlands. The CBD handles a unique framework of evaluation criteria establishing the basic principle that the genetic modification of animals is forbidden, because this conflicts with the "intrinsic value" of the animal. After evaluation by the CBD, only experiments of substantial social benefit, for which no alternatives are available and for which the likely benefit for society adds up to the impact on animal welfare, health and "intrinsic value", are permitted. This basic principle is known as the "no-unless" principle. None of the investigated countries perform such an evaluation. However in Germany and the UK an additional animal welfare evaluation is performed at the national (local in Germany) level as well, but this evaluation does not evaluates the specific impact of the genetic modification on the animal's "intrinsic value".

Other differences between the Dutch procedure and investigated countries are that the time taken for decision making by the CBD seems much longer than any evaluation in the other countries. Only the Netherlands provide in the possibility for public consultation during the evaluation procedure. Furthermore, Dutch applicants seem to consider colleagues as primary source of information for submitting an application to the CBD, while applicants in Germany and the UK mark the CA as primary source of information.

Results 1st phase survey

During the 1st phase survey four Dutch applicants were interviewed on their experiences with the application procedure for the genetic modification of animals. The results of the 1st phase survey represent the experiences of the interviewed applicants and are:

1. Applicants consider the legal time and time taken for decision making of the CBD as a heavy burden, since the whole procedure generally lasts more than six months resulting in delayed research projects.
2. The formal application procedure is clear and applicants are informed during the process but the commission's considerations, on which the final decision is based, do not seem clear.
3. Discussion between applicants and the CBD concerning the definition of "evaluation units" (toetsbare eenheid) occurs.
4. Overlap seems to occur between the DEC procedure and the CBD procedure, since applicants experience in practice that both evaluations apply a cost/benefit assessment (social concern weight versus animal harm).
5. Improvement of the application form and guidance document is preferable on issues concerning ethical considerations.

Interestingly the Dutch applicants mainly experience bottlenecks during the Ministry of LNV/CBD procedure on the practices for which the Netherlands is unique among the investigated countries. This concerns the legal time, the time taken for decision-making and the CBD's unique framework of evaluation criteria.

Recommendations

Based on the findings in the other countries and the experienced bottlenecks in the Dutch application procedure several recommendations can be formulated to improve the Dutch situation. This study has focussed on workability solutions within the current legislation framework. From this perspective the Ministry of LNV/CBD should improve two main aspects: The framework of evaluation criteria and the time taken for decision-making. To improve these issues the following recommendations are:

1. If the Dutch government wants to stick to an independent commission to review the impact on the animal's "intrinsic value" a clear interpretation of the "evaluation unit" has to be obtained and communicated. Otherwise the procedure does not seem workable for applicants and research projects will suffer high application burdens. Therefore improved communication between

applicants and Ministry of LNV/CBD is recommended to define a clear interpretation of the “evaluation unit”.

2. The Ministry of LNV/CBD and DEC's should be more closely involved to streamline both evaluations and prevent for overlapping evaluation criteria. Information sharing seems crucial on this aspect and therefore the Ministry of LNV should assign members to act as an information shortcut to the DEC's.
3. With regard to public concerns and the need for clear application requirements for the applicants, the Netherlands must improve the framework of decision-making criteria for the CBD. A more concrete framework should be formulated to smoothen the application procedure and to address public concerns. The creation of this framework should be initiated by a debate in which all stakeholders are heard. Subsequent regular meetings are recommended to improve the framework as a result of new scientific insights and changed social-ethical considerations.
4. To decrease unclearness for applicants and to lower burdens for Ministry of LNV/CBD and applicant during the evaluation it is preferable that the Ministry of LNV improves its provision for a preliminary consultation, in which a draft application is discussed prior to official submission. Considering the possibility for an appeal, a preliminary consultation should be executed as transparent and juridical correct as possible to prevent for procedural mistakes
5. To lower the time taken for decision-making it is recommended to have more regular CBD meetings and to implement an electronic application procedure to improve information exchange. The electronic procedure will decrease the manageability burden for applicants and Ministry of LNV/CBD.
6. To improve communication between applicants and Ministry of LNV/CBD it is recommended that Ministry of LNV assigns one primary contact person to an application and to prepare the evaluation for the next meeting. This person should also conduct the preliminary consultation and act as a primary information source for the applicant on all issues concerning the application. This contact person should preferably be the same person who is associated with the DEC of the applying organisation as well.

Summary new and proposed EU legislation for GMOs from farm to fork

Since the *de facto* moratorium on market-approvals of GM crops under the deliberate release Directive 90/220 the European Commission, the Parliament and the Council of Ministers have sought to improve the EU's regulatory framework for use of GMOs from farm to fork. Until now the existing regulatory framework further consists of the Novel Food Regulation for GM food and labelling rules for GM food based on the detectable presence of 'modified' DNA or protein. So far, only Directive 2001/18 for the deliberate release of GMOs, which repeals the 'old' Directive 90/220, has entered into force on 17 October 2002. By this date it should have been implemented in national legislation of EU member states.

Besides Directive 2001/18, the new regulatory framework consists of (proposals for) amendments of the seed Directives, a Regulation on GM food and feed, a Regulation on traceability and labelling, a Directive on environmental liability and a Regulation on transboundary movement of GMOs. These proposals have not yet been (fully) adopted and are therefore still open to political debate between the European Council of Ministers and the European Parliament. However, most proposals have already reached the stage of a 2nd reading by the European Parliament. Generally, in its 1st reading, the European Parliament wished more strict regulations than European Council of Ministers. As a consequence, there is hardly any space left for political negotiations on these proposals.

In essence, the new regulatory framework has a twofold aim. First, harmonisation of environmental, food and feed safety assessments of GMOs, GM seeds and GM food and feed within centralised authorisation procedures. And second, consumer choice through mandatory traceability and labelling of GMOs, GM seeds and GM food and feed through establishment of thresholds for the presence of GM material in non-GM seeds and non-GM food and feed. When the proposed Regulations for GM food and feed and their traceability and labelling are adopted, present *de facto* moratorium on market-approvals under the deliberate release directive, should be lifted. However, it cannot be excluded that some EU member states will still support the *de facto* moratorium until the proposed Directive on environmental liability has also been adopted.

Against this background, Part 2 of the 2nd phase survey on the ‘workability’ of biotechnology legislation aimed at identifying potential bottlenecks for notifiers and operators of new and proposed EU legislation for GM *products* from farm to fork and at developing recommendations for authorities to address these potential bottlenecks. For each new or proposed Directive or Regulation a series of bottlenecks for notifiers and operators have been identified. Some of these bottlenecks are specific for a (proposed) Directive or Regulation, while others result from a complicated or unclear interface between one or more (proposed) Directives or Regulations. Moreover, some recommendations to authorities will require political negotiations between stakeholders within a (proposed) Directive or Regulation to gain societal consent, whereas other recommendations will require authorities to consult stakeholders in due time with a view to (fundamentally) revise a (proposed) Directive or Regulation.

In general, operators downstream, such as biotechnology industry, seed industry, and food industry, and operators upstream, such as retailers, welcome a harmonisation and centralisation of environmental, food and feed safety assessments of GMOs, GM seeds and GM food and feed. Yet the scope and objectives thereof are not yet fully transparent. As a consequence, notifiers do not consider the outcome of an authorisation procedure and the time taken for decision-making as predictable. There is therefore a need for authorities, notifiers and other stakeholders in the agro-food chain to negotiate ‘temporary’ decision-making criteria for ‘unacceptable risks’ in national, European and international forums. This could help to increase the predictability of the outcome of the authorisation procedures and to decrease the actual time taken for decision-making. Further, given that other continents consider most of the commonly used antibiotic-resistance markers (ARMs) in GM plant breeding as safe, notifiers argued for establishing a positive list with one or two ARMs for monocots, respectively one or two ARMs for dicots. Otherwise imports of GMOs and GM food and feed with ‘non-EU-authorized’ ARMs from non-EU countries should be forbidden, as well as exchange of experimental GM plant material with such ARMs. In addition, the biotechnology industry and the seed industry would like authorities to streamline and harmonise ‘event-approval trials’ under Directive 2001/18 and ‘GM variety-approval trials’ for placing on the Common Catalogue, so as to increase the time left for commercialisation of an ‘event’.

As regards the proposed Regulation on traceability and labelling, operators downstream strongly differ of opinion with operators upstream. Downstream operators, in particular grain traders, crushers and food and feed manufacturers, mostly consider the switch from labelling on the basis of the detectable presence of 'modified' DNA or protein to 'origin-labelling' as unworkable and unenforceable, in particular for imports of GM and non-GM food or feed with 'non-detectable' ingredients from non-EU countries. However, retailers, consumer co-operatives, and consumer organisations view 'origin-labelling' as desirable. Despite these differences in views operators downstream and upstream agree that authorities should establish an internationally operating accreditation body for verification of documentation on the GM origin, respectively non-GM origin, which operators must pass on along the chain. As long as such an international accreditation body is not available, authorities should assume that a food or feed (ingredient) originates from GMOs and should be labelled accordingly. Only if operators can demonstrate that they have taken (Identity Preservation) measures along the chain to avoid the presence of GMOs in a food or feed below the labelling-threshold, a food or feed (ingredient) does not need to be labelled.

Moreover, operators downstream have different views than operators upstream on the thresholds proposed for the adventitious presence of GM seeds in lots of conventional non-GM seeds, respectively for the adventitious presence of GMOs in non-GM food and feed. The lower these thresholds are set, the higher the costs will be for meeting them. Since these costs are mainly made downstream and it is not certain whether these costs can be (fully) recouped upstream, downstream operators generally argue for much higher thresholds than upstream operators do. Further, because of the rapidly growing acreage for commercial cultivation of 'non-EU-authorized' GM crops and GM seed multiplication in other continents, globally operating seed companies are facing increasing difficulties to avoid the presence of 'non-EU-authorized' GM seeds in conventional seed lots. In a few instances sales of conventional seeds of certain crop species and conventional breeding programs have already come to a stop in Europe out of liability considerations. Authorities should therefore introduce a fast-track EU procedure for approval of the adventitious presence of 'non-EU-authorized' GM seeds in (imports of) lots of non-GM seeds. But such a fast-track procedure needs to be negotiated at the political level, in order to obtain societal consent.

Further, operators downstream hinted that the EU's (proposed) regulatory framework for GMOs would probably be in conflict with WTO agreements on Sanitary and Phytosanitary measures (SPS) and on Technical Barriers to Trade (TBT). Major trading partners have expressed concerns about the EU's approach to risk assessment and authorisation procedures, the time frames for decision-making, the basis for labelling, the adventitious presence thresholds for 'EU-authorized' and 'non-EU-authorized' GM materials, and the difficulties to implement, control and enforce traceability. Remarkably, the EU Commissioner for Health and Consumer Protection admitted that if the US complains to the WTO, the legal defences available to the EU would be 'very narrow'.

Finally, since the EU's regulatory framework for GMOs from farm to fork has not yet fully adopted, it is difficult to fully assess all potential consequences for notifiers and operators at different stages of the agro-food chain. However, given that the manageability burden and regulatory costs for notifiers and operators are likely to increase, a consequence could be that small and medium size enterprises might have greater difficulties to comply with the EU's regulatory framework for GMOs than large enterprises. In addition, the lower the thresholds are set for the adventitious presence of GM material in non-GM seeds, respectively in non-GM food and feed, the higher the added costs will be for operators. Again, structural impacts on the biotechnology industry, seed industry, grain trade and food and feed industry are possible and likely, as the added costs seem to be characterised by a (strong) size bias.

Research team and Advisory Committee

This study is a result of a close collaboration of the research team and an advisory committee. The members of both groups are listed below.

4.1 Research team

The joint research team of Schenkelaars Biotechnology Consultancy (Leiden) and BioCollectief (Amsterdam) consisted of the following people:

- Ir. J.P.M. Schenkelaars, project leader and author of part 2;
- J. Kampmeijer M.Sc., author of part 1;
- R. van der Zanden M.Sc., author of part 1;

4.2 Advisory Committee

At several meetings and occasions during this study the Advisory Committee provided feedback on the objectives, the methodology, the selection of the benchmark partners and the preliminary findings. Members of the Advisory Committee further assisted the research team in contacting their foreign counterparts. Many additional insights and helpful comments on a draft version of this report has been provided by the Advisory

Committee, but the final analysis of bottlenecks and the recommendations are the sole responsibility of the author of this report.

The members of the Advisory Committee were:

- Ir. M.W. Horning (chairman); Ministry of Economic Affairs; Department of Market and Innovation.
- J.H.A.A. Uitzetter Ph.D. M. L.; Ministry of Economic Affairs; Department of Market and Innovation.
- Ir. J.B.F.C. van den Assum; Ministry of Agriculture, Nature Management and Fisheries; Department of Veterinary and Food Policy and General Environmental Affairs.
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