TESTBIOTECH Background 8 - 12 - 2016

Testbiotech comment on draft EU Commission Directive amending Directive 2001/18/EC of the European Parliament and of the Council as regards the environmental risk assessment of genetically modified organisms

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Content

Summary

This briefing provides an overview with tables, of the changes to the Annexes to EU Directive 2001/18 as proposed by the EU Commission, and also includes Testbiotech comments. We have further outlined some of the basic elements and principles of environmental risk assessment for genetically engineered plants.

Based on detailed analysis, we reject the current proposal of the EU Commission in most of its elements and instead make the following recommendations for future environmental risk assessment:

- **Avoid oversimplification:** It has to be acknowledged that the absence of observable effects cannot be interpreted as evidence for the safety of the plants. Risk assessment has to be based on a broad range of empirical data and mandatory investigations that can cast a 'wide but finely meshed net' at each level of risk assessment, and not be organised in a linear model. In general, risk assessment has to deal with non-knowledge and unexpected effects as well as new areas of knowledge. The assessment has to include worst case scenarios.
- **Make empirical testing mandatory:** Clear mandatory criteria must be defined for each step

of risk assessment (laboratory, greenhouse, small-scale experiments, non-target organisms, pollinators, wildlife species etc.).

- **Define a proper step-by-step process:** The impact of climate and specific regional conditions on the plants as well as interference with other biotic or abiotic stressors should be investigated under controlled conditions before genetically engineered plants are released.
- **Assess combinatorial effects:** Special attention must be paid to synergistic and cumulative effects, such as those stemming from mixtures of herbicide residues, the stacking of Bt toxins or interactions between Bt toxins and herbicide residues.
- **Take on board new scientific insights:** Some of the most dynamic new scientific findings are in epigenetics, the concept of the hologenome (looking at the organism and its microbiome as a unit) and RNAi effects. There have been significant advances made in understanding signalling pathways and related implications for e.g. plant defence mechanisms. All these areas are relevant for the risk assessment of genetically engineered organisms and should be included in Annex II of the Directive.
- **Apply new methods:** A much broader set of empirical data is required to assess the technical properties and genetic stability (including metabolic profiles) of genetically engineered organisms, their reaction to environmental conditions and their interactivity with the environment. It is, moreover, essential to develop a 'stress-test' in order to expose the genetically engineered plants to defined stressors.
- **Define cut-off criteria:** Criteria for the rejection of applications must be integrated into the overall concept. It must be made sufficiently clear to applicants at an early stage that invasive plants that are and/or persistent will be rejected as will plants that foster unsustainable agricultural practices.
- **Establish improved data requirements:** Fully validated methods for measuring new gene products, such as new proteins, have to be made available to enable independent controls. In addition, independent controls have to be integrated at each step of data generation.
- **Make all data available:** It must be made mandatory for the companies to make all risk relevant data available, including data from investigations that do not show results that the companies might have expected.
- **Make material for research available:** As soon as applications are filed, the company must make sure that access to relevant material is available for independent research.

1. Avoidance of overly simplistic approaches

Deliberate release and cultivation of genetically engineered organisms exposes the environment and the chain of food production to new, large-scale biological functions and compounds, which were not evolved and adapted to in evolutionary processes. The delicate balance between plants and the environment is governed by the totality of the plants’ regulatory processes, taking into account associated microbiomes and their interaction with the environment.

Modern molecular biology shows that the function of a gene, the processes of gene regulation and the interaction between genes and environment are not organised in a linear cause-effect relationship, but often follow non-linear patterns while emerging. These risks or hazards might only be identified by a concept that follows a different principle of 'expect the unexpected' at each level of the process.

Outside the laboratory, living organisms do not interact with single stressors in defined dosages. In

the real world, they face a combination of physical, chemical and biological environmental stressors that vary in space and time.

- For example, in the context of Bt toxins, combinatorial effects in non-target organisms are evident from peer reviewed publications. Thus, risk assessment of Bt plants cannot simply be reduced to hazard and exposure analyses, but has to take into account interaction with the recipient environment.

- Non-linear effects can also be triggered by stacking events or by the parallel cultivation of genetically engineered plants with different traits.

- Considerable attention must also be paid to effects that only occur under certain environmental conditions, such as climatic change. Genetically engineered plants inherit technically derived features that are not controlled by the plant's gene regulation. Technical failures, such as genetic instabilities and the rise of undesired components can be triggered by specific environmental conditions.

In general, the absence of observable effects should not be interpreted as evidence of the safety of any particular effect. Faced with these huge challenges, companies and risk assessment authorities often tend to react with an overly simplistic approach; and if very limited testing does not provide evidence for potential hazards no further detailed investigations are required. In addition, hazard identification at an early stage tends to narrow down all further step of risk assessment.

To avoid these problems, the first step in ERA should be based on a broad generation of empirical data that is not already confined to certain hypotheses. In general, risk assessment in plants has to be organised in such a way that it challenges the hypotheses and findings from earlier steps at each level of the process.

2. Define the correct starting point for step-by-step risk assessment

EU Directive 2001/ 18 requires step-by-step risk assessment. However, the first step of collecting relevant data still needs to be defined. As mentioned above, the first step in ERA should be based on the broad generation of empirical data not already confined to certain hypotheses.

This kind of empirical data would give researchers a higher degree of understanding of the biological characteristics of the genetically engineered organism – and are essential to formulating and developing any refined hypothesis on risks and potential hazards.

As shown in several publications, the insertion of the additional genetic material can change plant gene activity. In addition, there are several publications showing that genetically engineered plants do not react to environmental stress in the same way as plants derived from conventional breeding. The consequences of change as a stress reaction can be various: The plants might show higher susceptibility to pests, or yield may be lower, or resistance to conditions, such as climate change, may be lower. But it can also lead to higher fitness (such as a higher pollen count or seeds), or an increased content of unhealthy compounds. These unintended changes might only emerge under specific environmental conditions or after several generations. Compared to the past when Directive 2001/18 was being discussed and adopted, there is in the present much greater urgency to these

issues due to ongoing climate change.

Therefore, even before any further steps in risk assessment are undertaken e.g. field trials, it is essential that sufficient data on the genetic stabilities and functionalities of the genetically engineered organism are collected. To generate such data, the genetically engineered organisms have to be subjected to a sufficiently broad range of defined environmental stressors under controlled conditions.

It would not require a huge effort to collect more relevant data, for example, by using climate chambers. Further, the so-called omics (metabolomics, transcriptomics, proteomics) can be quite useful in this context, since they allow lots of data on changes in gene regulation and metabolism in the plants to be generated. These data might not allow any direct conclusions to be drawn on the risks, but they can provide important information to facilitate more targeted down-stream investigations.

3. Define sufficient mandatory testing and quality control in data

Not only the first step in risk assessment, but the whole process, is dependent on sufficient data of a reliable quality. However, so far, several levels of risk assessment as carried out by EFSA lack a comprehensive mandatory testing regime. Consequently, risk assessment can be easily narrowed down and become flawed through using a range of data that is too small. To organise a sufficiently broad process, a set of mandatory tests need to be defined in a way that excludes avoidance due to superficial or wrong hypothesising. While it is true that risk assessment needs to be flexible enough to add additional points when being carried out, a basic set of mandatory tests also need to be defined.

A lack of mandatory testing and empirical data has, in addition, serious implications for monitoring and surveillance at a later stage. To fulfil requirements, monitoring must be able to identify relevant risks correctly. In many cases, the specifications for monitoring will only mirror those risks that have already been identified and not aim to examine unexpected effects in detail. Thus, those risks that are not identified during risk assessment also have a greater chance of escaping monitoring and general surveillance.

For example, Bt toxins are currently only assessed in keeping with GMO regulation, but not pesticide regulation. Consequently, their mode of action and toxicity in target and non-target organisms is not known in all relevant details. This makes improvement in the interplay of GMO and pesticide regulation essential in order to ensure that all the data are made available and current gaps in environmental risk assessment are closed.

Further, the quality of the data needs to be scrutinised. In particular, fully validated methods for the measuring of new gene products, such as new proteins, have to be made available to enable independent control. For example, it is currently almost impossible to measure the precise concentration of Bt-toxins in the fields because no fully validated methods are available for this purpose.

Further, it is necessary to establish independent controls at each step of data generation. Currently,

data generation from field trials is the sole responsibility of the companies, without any independent control. Consequently, companies may feel free to present data selected in accordance with their own interests.

To avoid the presentation of selective data, the companies must be required to make all risk relevant data available, including the data that does show results that might have been expected.

Finally, immediately after filing the application, the company must be required to grant access to all relevant material needed for further independent research. At present, access can be blocked by patents, or by not making relevant comparators available.

4. Investigate combinatorial effects in detail

Directive 2001/18 explicitly requests that the assessment of interactions between genetically engineered plants and cumulative effects are taken into account during risk assessment. Recital (1) reads:

> *A case-by-case environmental risk assessment should always be carried out prior to a release. It should also take due account of potential cumulative long-term effects associated with the interaction with other GMOs and the environment. Cumulative effects and potential interactions have to be taken into account as well in the parallel cultivation and imports of different genetically engineered plants and in the case of stacked events in single transgenic plants.*

Current EFSA practice ignores this request completely. Therefore, the Annex should be re-phrased and be more explicit about data and assessment.

For example, it is known that cumulative effects can result from a combination of traits, such as insect resistance and herbicide tolerance. Further, cumulative effects have been described between different Bt toxins as well as between combined applications of complementary herbicides. In addition, it is also known that factors such as plant compounds and external stressors can enhance the toxicity of Bt toxins.

The Annex to the Directive should contain much more detail in regard to cumulative effects. Potential interactions need to be taken into account, including cultivation of several events in parallel, imports of different genetically engineered plants and the cumulative effects and interactions relevant to stacked events.

5. Define cut-off criteria

There is some serious concern that we are already seeing the uncontrolled spread of transgenic plants into native populations in several regions. No one can predict how these plants will evolve in further evolutionary processes, which will, amongst other things, be influenced by ongoing climate change.

From a regulatory point of view, the spatio-temporal control of genetically engineered organisms is a fundamental precondition for any reliable risk assessment. In general, it is very difficult to predict the long-term ecological impact of transgenes that escape spatio-temporal control. Long-term, evolutionary processes make it possible for events with a low probability of ever happening to turn

into events that may feasibly happen.

From the perspective of the intention of the precautionary principle, any release of genetically engineered organisms that might persist in the environment must be prohibited. As yet, however, there are no clear “cut-off” criteria to reject applications where there is no effective spatio-temporal control in place for the genetically engineered organisms.

There are further cut-off criteria that should be defined. These include gaps in knowledge, genetic stability as a response to environmental stressors and non-sustainable practices in agriculture that prevent any conclusions on safety.

6. The EC Proposal

The Annexes to EU Directive 2001/18 now will be revised for the first time, since the Directive was adopted. According to Article 27 of the Directive,

> “Sections C and D of Annex II, Annexes III to VI, and section C of Annex VII shall be adapted to technical progress”.

“Technical progress” is not defined in the Directive. However, from the content of the Annexes and the scope of the Directive, it is clear that the level of protection for health and the environment must not be reduced by any update of the Annexes.

Further, the purpose of the Annexes must be upheld in any proposed updates. For example, the purpose of Annex II is outlined in Article 2 of the Directive stating:

> “environmental risk assessment’ means the evaluation of
> risks to human health and the environment, whether direct or indirect, immediate or delayed, which the deliberate release or the placing on the market of GMOs may pose and carried out in accordance with Annex II.”

This is also generally relevant for the current EU Commission initiative (EC), which was started on the basis of the Council Conclusions from 2008. In its Conclusions, the Council stresses the need to update and strengthen the environmental risk assessment of genetically engineered plants, particularly in regard to the assessment of any long-term environmental effects.

However, as analysis of the EC proposal shows (see Annex), the aim of strengthening environmental risk assessment would not be achieved and could, in fact, even weaken risk assessment. Some of the proposals would reduce the scope of Directive 2001/18 to such an extent that the protection of health and the environment would be substantially weakened. For example, the assessment complementary herbicides application to the plants is a crucial element in environmental risk assessment under the requirements of Directive 2001/18 and cannot be excluded by any update of the Annexes. Such a proposal is not within the competence of the EC, which does not have a mandate to narrow down the scope of the Directive.

Furthermore, the EC proposal is mostly based on EFSA guidance from 2010. However, the task of the EC, as expressed in the Council conclusions and Article 27, is much more general and not restricted to any guidance prepared by EFSA. Whatever the case, the EFSA guidance cannot be regarded as being comprehensive. The guidance was already adopted in 2010 and further adoptions will be necessary.

If the EU Commission wants fulfil its obligations, the following levels of “technical progress” have

to be considered:

1. New methods that were developed to improve risk assessment;
2. New areas of risk assessment that were not central issues when the Directive was adopted;
3. New evidence showing that specific issues have to be considered in more depth than previously thought;
4. New scientific findings indicating specific uncertainties or limits of knowledge that require a greater level of precaution.

Below is a tabled overview of the proposed changes with some initial comments. A non-exhaustive list of requirements that should be taken into account can be derived from our comments:

- usage of -omics studies
- detailed assessment of all new gene products, not only proteins
- investigation of changes in signalling pathways
- investigation of interactions between plants and their microbiome
- investigation of reactions of genetically engineered plants to stressors and climate change
- assessment of changes to susceptibility to plant diseases
- detailed assessment of combinatorial, cumulative and long-term effects
- cut-off criteria to prevent cultivation-independent establishment of genetically engineered plants.

However, none of these topics were taken into account in the EU Commission proposal. Further, in regard to the interplay of pesticide regulation and GMO regulation, the proposal made by the EU Commission is not in line with the Council conclusions and it also in contradicts the EFSA opinion:

The Council is demanding improved interplay between pesticide regulation and GMO regulation. Nothing in the Council conclusion can be interpreted in a way that implies lowering the standards for GMO environmental risk assessment or that the application of the complementary herbicide should be left aside. In fact, the Council is calling for the exact opposite: Active substances produced by the genetically engineered plants (GMP) that have pesticidal qualities (such as Bt toxins) should be assessed according to both regulations – the pesticide and the GMO regulation:

> *" (…) the mandate includes examination of the criteria and requirements for assessing all GMPs, including GMPs that produce active substances covered by directive 91/414/EEC and herbicide-tolerant GMPs with a view to reviewing them if necessary; UNDERLINES in particular the need to study the potential consequences for the environment of changes in the use of herbicides caused by herbicide-tolerant GMPs and to ensure coherence between risk assessments of GMPs which produce active substances covered by directive 91/414/EEC and those of the corresponding plant protection products; RECALLS that the use of plant protection products implies authorisations at national level and EMPHASISES THE NEED for competent authorities involved with the implementation of Directive 2001/18/EC and of Council Directive 91/414/EEC concerning the placing of plant protection products on the market, within the Commission and at national level, to co-ordinate their action as far as possible."*

The need to assess the usage of the complementary herbicides under both regulations is also emphasised by the EFSA GMO panel:[1]

> " *Interplay between ERA of GMOs and associated pesticides*

1EFSA 2015: Scientific Panel On GMO, Minutes of the 94th Plenary meeting of the Scientific Panel on GMO Held on 3-4 December 2014, Parma

The GMO Panel was informed of the European Commission initiative to transpose the EFSA GMO Panel ERA Guidance document 5 into regulation. In this context, the EC will consider and address the interplay between the ERA of GMOs and of the pesticides associated to these GMOs.
Preliminary discussion with the Member States took place in November 2014. The GMO Panel agreed that the consequences to possible changes in crop management practices, including the herbicide treatments, should remain as an integral part of the ERA of GMOs. Members of the GMO Panel confirmed their scientific responsibility to consider environmental effects of herbicide-tolerant systems such as reductions in arable plants, insects and bird-food, and expressed doubts that any proper environmental risk assessment could be concluded if such considerations were excluded. The Chair of the GMO Panel provided evidence for his view that there was no current alternative regulatory process within the EU that provided an appropriate assessment of such indirect herbicidal effects."

Therefore, interplay between these regulations has to be defined to make sure that current gaps in environmental risk assessment are closed. However, the proposal of the EU Commission would have the opposite effect and widen the gaps and weakness in current ERA.

For references see:

Then C. & Bauer-Panskus A. (2016a) Risks and side effects for humans and animals: What really goes wrong in the regulation of genetically engineered plants – Risk assessment of genetically engineered plants used for food and feed - and flaws in the work of the European Food Safety Authority EFSA, Testbiotech Report, www.testbiotech.org/node/1668.

Then C. & Bauer-Panskus A. (2016b), Cultivation of genetically engineered maize: Risks not under control, Testbiotech Background 24 - 11 – 2016, www.testbiotech.org/node/1759.

7. Annexes

Annex 1: Overview on intended changes and comments made by Testbiotech on Annex II of the Directive 2001/18.

ANNEX II

PRINCIPLES FOR THE ENVIRONMENTAL RISK ASSESSMENT

C Methodology

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
…….		
A. Objective		
B. General Principles		
C. Methodology		
C.1. Characteristics of GMOs and releases	C.1. General and specific considerations for the e.r.a.	
	1. Intended and Unintended Effects	
	The e.r.a shall identify and characterise the intended and unintended effects of the genetic modification with respect to possible adverse impacts on human and animal health and the environment.	The objective of the Directive is to detect direct, indirect, immediate and delayed effects. Further cumulative long-term effects have to be analysed. This also has to be reflected in the methodology. Intended and unintended effects are only some of the elements necessary to achieve these objectives.
	"Intended effects" are those that are designed to occur and which fulfil the original objectives of the genetic modification.	See above
	"Unintended effects" are consistent (non-transient) differences between the GMO	See above. In addition, the word non-transient has to be deleted, since some of the relevant

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
	and its chosen comparator, which go beyond the intended effect(s) of introducing the genetic modification.	effects might only get apparent under specific environmental conditions.
	2. Delayed effects For notifications under Part C of this Directive the e.r.a shall be relevant to the receiving environment(s) and intended use(s) of the GMO(s) and shall include an assessment of the potential delayed environmental effects in the form of a desk based study using one or more of the following; – evidence from previous experiences; – available data sets/literature; – mathematical models predictions.	The objective of the Directive is to detect direct, indirect, immediate and delayed effects. Further cumulative long-term effects have to be analysed. This also has to be reflected in the methodology. Assessment of delayed effects should notld be reduced to desk-based studies, but also imply empirical investigations if possible.
	3. Data	
	To carry out an e.r.a. the notifier shall generate the necessary data.	
	Where applicable, data already available from scientific literature may be used.	It has to be made clear that available scientific literature can only be used additionally, and cannot replace empirical data required from the specific event.
	Information from any previous releases of the same or similar GMOs and organisms with similar traits and their biotic and abiotic interaction with similar receiving environments shall be considered in the e.r.a, subject to Article 6(3) or Article 13(4). Data provided in the e.r.a shall comply with the following requirements:	All risk related data have to be made available, no matter whether the applicant considers them to be relevant or not.

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
	(a) The use of data generated outside Europe shall be justified with regard to relevance to European receiving environment(s).	It has to be made clear that data from outside Europe can only be used additionally and not as a substitute for data from the receiving environment(s) in Europe.
	(b) Toxicological studies carried out to assess risk(s) to human or animal health shall be conducted in facilities which comply with the:	It has to be made clear that data not meeting these standards still have to be presented and considered.
	(i) requirements of Directive 2004/10/EC; or	See above
	(ii) 'OECD Principles on Good Laboratory Practice' (GLP), if carried out outside the Union.	See above
	The applicant shall provide evidence to demonstrate such compliance.	Add: Applications already accepted or filed before this Directive comes into force and which do not comply with the relevant standards must be amended.
	(c) Studies other than toxicological studies shall:	
	(i) comply with the principles of Good Laboratory Practice (GLP) laid down in Directive 2004/10/EC; or	It has to be made clear that data not meeting these standards still have to be presented and considered. New methods used to support risk assessment such as metabolomic data that, as yet, do not fulfil all necessary standards should not be excluded, but required as additional, supportive data.
	(ii) be conducted by organisations accredited under the relevant ISO standard.	See above
		Add: The applicant must be required to provide evidence to demonstrate

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
		compliance. Applications already accepted or filed before this Directive comes into force and which do not meet the relevant standards, must be amended.
	(d) Information on the study protocols and the results obtained from the studies referred to points (b) and (c) shall be comprehensive and include the raw data in an electronic format, suitable for carrying out statistical or other analysis.	
	(e) Selection of sites for field studies shall be representative of the receiving environments where the GMO(s) may be released and shall be justified explicitly.	
	(f) The non-genetically modified comparator shall be appropriate for the relevant receiving environment(s) have a genetic background comparable to the GMO and its choice shall be justified in the e.r.a.	Replace: The real comparator should have an isogenic background. The other reference groups used for comparison should have a comparable genetic background.
		Data on genetic stability have to be based on controlled studies with a broad range of defined biotic and abiotic stressors. The selection of these stressors should not only reflect the receiving environments in their current state, but also more extreme conditions due to further climate change or other developments that might impact genetic stability within the duration of the authorisation.
		The data should not only be related to compositional analysis, but also take

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
		metabolomic, transcriptomic and proteomic studies into account.
		Data on gene expression and concentration of intended newly produced proteins, such as Bt toxins, should be based on methods that are fully described and validated by independent laboratories.
		The data have to integrate all new gene products, no matter whether intended or unintended, or which are proteins or not.
		Data on changes in the associated microbiome have to be taken into account including a) soil organisms b) mycorrhizae c) associated micro-organisms in other parts of the plants (microbiome) d) intestinal microbiomes of humans and animals after consumption.
		Data on residues from spraying with the complementary herbicide have to be generated by taking into account changes in agricultural practices, changes in plant composition and cumulative effects.
		Methods to detect and assess direct, indirect, immediate and cumulative long-term effects have to be defined. The methods should also take metabolomic, transcriptomic and proteomic studies into account.
		Data have to be made available that allow a general conclusion on the control of the GMO in its

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
		spatio-temporal dimension.
		Independent controls have to be established for all relevant steps of data generation.
	4. Stacked transformation events	
	For the e.r.a. of GMOs containing stacked transformation events obtained by conventional crossing of organisms containing one or several transformation event(s) the notifier shall provide an e.r.a. for each single transformation event or refer to already submitted notifications in accordance with Article 6(3) or Article 13(4).	Replace: Data from stacked events have to at least meet the same requirements as those of the parental single events. As additional comparators for the assessment of the stacked events, the parental single plants should be grown in the same field trials.
	The notifier shall consider the potential for progeny of the GMO containing various subcombinations of the transformation events to occur and assess the need to consider sub combinations of the higher stack in the risk assessment.	Replace: Assessment of the sub-combinations has to be requested in each case.
	The e.r.a. of GMOs containing stacked transformation events shall include an assessment of the following aspects:	All the data used for the assessment of the following topics have to be based on empirical studies.
	(a) stability of the transformation events; (b) expression of the transformation events;	To generate these data, it is necessary to grow the parental single plants in field trials together with the stacked event. Further, these data have to be based on controlled studies with a broad range of relevant biotic and abiotic stressors. The selection of these stressors should not only reflect the receiving environments, but also more extreme conditions

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
		due to further climate change or other developments that can impact genetic stability within the duration of the authorisation. The data should not only be related to compositional analysis but also take metabolomics, transcriptomic and proteomic studies into account. Data on concentration in regard to intended newly produced proteins such as Bt toxins have to be based on methods that are fully described and validated by independent laboratories.
	(c) potential additive, synergistic or antagonistic effects resulting from the combination of the transformation events.	The assessment has to be based on empirical studies with relevant non-target organisms, such as pollinators and protected species, taking into account the residues from spraying with the complementary herbicide. The same standards apply for health risks assessment.
	C.2. Characteristics of the GMO	
Depending on the case the e.r.a. has to take into account the relevant technical and scientific details regarding characteristics of:	The notifier shall take into account the relevant technical and scientific details regarding characteristics of:	
. the recipient or parental organism(s);	No changes	
. the genetic modification(s), be it inclusion or deletion of genetic material, and relevant information on the vector and the donor;	No changes	
. the GMO;	No changes	

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
. the intended release or use including its scale;	No changes	
. the potential receiving environment; and	the potential receiving environment(s) into which the GMO will be released and into which the transgene may spread; and	
		Data should include the associated microbiome of the recipient organism and changes that go along with its genetic modification.
. the interaction between these.	No changes	
		Data from spraying with the complementary herbicide have to be taken into account, including the resulting residues, the impact on plant composition and interaction with other potential stressors.
Information from releases of similar organisms and organisms with similar traits and their interaction with similar environments can assist the e.r.a.	Deletion	
	Information on the recipient, donor, vector, genetic modification and the GMO shall be independent of the environment and the conditions of the release.	
C.2. Steps in the e.r.a.	C 3 Steps in the e.r.a	
In drawing conclusions for the e.r.a. referred to in Articles 4, 6, 7 and 13 the following points should be addressed:	The e.r.a. referred to in Articles 4, 6, 7 and 13 shall be conducted following the six steps below:	
1. Identification of characteristics which may cause adverse effects:	**1. Problem formulation including hazard identification:**	
	The problem formulation shall:	
	– define assessment endpoints	Replace: The endpoints should

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
	that are representative of the protection goals;	represent the protection goals, but problem formulation should not be restricted to them. In general, risk assessment should not be overly simplistic and able to deal with non-knowledge and unexpected effects as well as new areas of knowledge at each step.
	– identify the hazards;	Replace: Identify any potential hazards, by applying worst case scenarios.
	– describe the pathway to harm;	
	– formulate testable hypotheses that are clearly phrased and easily transferable to data to be generated or evaluated;	Not all relevant hypotheses can be easily transferred into data to be generated or evaluated. Nevertheless, such hypothesis can be relevant for overall conclusions. In general, risk assessment should not be overly simplistic and able to deal with non-knowledge and unexpected effects as well as new areas of knowledge at each step.
	– define measurement endpoints as measurement units for both hazard and exposure;	This might not be applicable for each case. In general, risk assessment should not be overly simplistic and able to deal with non-knowledge and unexpected effects as well as new areas of knowledge at each step.
	– define the magnitude of tolerable effect;	This should be the responsibility of the risk manager, who has to take various factors into account.
	– consider possible uncertainties, including knowledge gaps and methodological limitations.	
		Define cut-off criteria such as

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
		- lack of control of the genetically engineered organisms and their newly introduced genetic information in their spatio-temporal dimension. - knowledge gaps and uncertainties that do not allow final conclusions to be drawn.
Any characteristics of the GMOs linked to the genetic modification that may result in adverse effects on human health or the environment shall be identified. A comparison of the characteristics of the GMO(s) with those of the non-modified organism under corresponding conditions of the release or use, will assist in identifying the particular potential adverse effects arising from the genetic modification. It is important not to discount any potential adverse effect on the basis that it is unlikely to occur.	Any characteristics of the GMOs linked to the genetic modification that may result in adverse effects on human health or the environment shall be identified. Potential adverse effects shall not be discounted on the basis that they are unlikely to occur.	This should include the assessment of the usage of complementary herbicides, their residues and interactions.
Potential adverse effects of GMOs will vary from case to case, and may include:	Potential adverse effects of GMOs will vary from case to case, and may include:	
. disease to humans including allergenic or toxic effects (see for example items II.A.11. and II.C.2(i) in Annex III A, and B 7 in Annex III B);	disease to humans, including allergenic or toxic effects;	
. disease to animals and plants including toxic, and where appropriate, allergenic effects (see for example items II.A.11. and II.C.2(i) in Annex III A, and B 7 and D 8 in Annex III B);	disease to animals and plants, including toxic, and, where appropriate, allergenic effects;	Add: [animals] including wildlife species
. effects on the dynamics of	effects on the dynamics of	

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
populations of species in the receiving environment and the genetic diversity of each of these populations (see for example items IV B 8, 9 and 12 in Annex III A);	populations of species in the receiving environment and the genetic diversity of each of these populations;	
. altered susceptibility to pathogens facilitating the dissemination of infectious diseases and/or creating new reservoirs or vectors;	altered susceptibility to pathogens facilitating the dissemination of infectious diseases or creating new reservoirs or vectors;	
. compromising prophylactic or therapeutic medical, veterinary, or plant protection treatments, for example by transfer of genes conferring resistance to antibiotics used in human or veterinary medicine (see for example items II.A.11(e) and II.C.2(i)(iv) in Annex III A); .	compromising prophylactic or therapeutic medical, veterinary, or plant protection treatments, for example by transfer of genes;	
effects on biogeochemistry (biogeochemical cycles), particularly carbon and nitrogen recycling through changes in soil decomposition of organic material (see for example items II.A.11(f) and IV.B.15 in Annex III A, and D 11 in Annex III B).	effects on biogeochemistry (biogeochemical cycles), including carbon and nitrogen recycling through changes in soil decomposition of organic material.	
Adverse effects may occur directly or indirectly through mechanisms which may include:	Adverse effects may occur directly or indirectly through exposure pathways which may include:	
. the spread of the GMO(s) in the environment,	No changes	
. the transfer of the inserted genetic material to other organisms, or the same organism whether genetically modified or not,	No changes	
. phenotypic and genetic instability,	No changes	
		Changes in the microbiome of the plant.
		Emergence of gene products

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		that are biologically active, such as miRNA.
. interactions with other organisms,	No changes	
		Cumulative effects such as combinatorial effects of several GMOs being grown or consumed in parallel.
. changes in management, including, where applicable, in agricultural practices.	No changes	
2. Evaluation of the potential consequences of each adverse effect, if it occurs	**2 Hazard characterisation**	
The magnitude of the consequences of each potential adverse effect should be evaluated. This evaluation should assume that such an adverse effect will occur. The magnitude of the consequences is likely to be influenced by the environment into which the GMO(s) is (are) intended to be released and the manner of the release.	The magnitude of the consequences of each potential adverse effect shall be evaluated. This evaluation shall assume that such an adverse effect will occur. The e.r.a shall consider that the magnitude of the consequences is likely to be influenced by the receiving environment(s) into which the GMO(s) is (are) intended to be released and the scale and conditions of the release.	Add: worst case scenarios, delayed, long-term and cumulative effects have to be taken into account.
	The evaluation shall be expressed where possible in quantitative terms. If expressed in qualitative terms, a categorical description ("high”, "moderate", "low" or "negligible") shall be used and an explanation of the scale of effect represented by each description provided.	This might not be applicable for each case. In general, risk assessment should not be overly simplistic and able to deal with non-knowledge and unexpected effects as well as new areas of knowledge at each step.
3. Evaluation of the likelihood of the occurrence of each identified potential adverse effect	**3. Exposure characterisation**	

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A major factor in evaluating the likelihood or probability of adverse effects occurring is the characteristics of the environment into which the GMO(s) is intended to be released, and the manner of the release.	The likelihood or probability of each identified potential adverse effect occurring shall be evaluated to provide a qualitative or quantitative assessment of the exposure. A qualitative assessment shall be further defined using an appropriate scale, which may notably consist in a numerical scale from 0 to1. The characteristics of the receiving environment(s), and the scope of the application shall be taken into consideration.	This might not be applicable for each case. In general, risk assessment should not be overly simplistic and able to deal with non-knowledge and unexpected effects as well as new areas of knowledge at each step.
4. Estimation of the risk posed by each identified characteristic of the GMO(s)	**4. Risk characterisation**	
An estimation of the risk to human health or the environment posed by each identified characteristic of the GMO which has the potential to cause adverse effects should be made as far as possible, given the state of the art, by combining the likelihood of the adverse effect occurring and the magnitude of the consequences, if it occurs.	The risk shall be characterised by combining the magnitude of the consequences of a hazard and the likelihood of the adverse effects occurring to provide a quantitative or semi quantitative estimation of the risk. Where relevant the uncertainty for each identified risk shall be described and expressed in quantitative terms.	This might not be applicable for each case. In general, risk assessment should not be overly simplistic and able to deal with non-knowledge and unexpected effects as well as new areas of knowledge at each step.
5. Application of management strategies for risks from the deliberate release or marketing of GMO(s)	**5. Risk management strategies**	
The risk assessment may identify risks that require management and how best to manage them, and a risk management strategy should be defined.	An evaluation of the overall risk of the GMO(s) shall be made taking into account the results of the risk characterisation (step 4), the proposed risk management strategies (step 5) and the associated levels of uncertainty. The overall risk evaluation and conclusions shall determine the requirements for the Post	Add: worst case scenarios, delayed, long-term and cumulative effects have to be taken into account.

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	Market Environmental Monitoring (PMEM) plan of the GMO(s) and the monitoring of the efficacy of the proposed risk management measures.	
6. Determination of the overall risk of the GMO(s)	**6. Overall risk evaluation and conclusions**	
An evaluation of the overall risk of the GMO(s) should be made taking into account any risk management strategies which are proposed.	An evaluation of the overall risk of the GMO(s) shall be made taking into account the results of the risk characterisation (step 4), the proposed risk management strategies (step 5) and the associated levels of uncertainty. The overall risk evaluation and conclusions shall determine the requirements for the Post Market Environmental Monitoring (PMEM) plan of the GMO(s) and the monitoring of the efficacy of the proposed risk management measures.	Add: worst case scenarios, delayed, long-term and cumulative effects have to be taken into account. The assessment has to conclude on cut-off criteria such as ● lack of control of the genetically engineered organisms and their newly introduced genetic information in the spatio-temporal dimension ● knowledge gaps and uncertainties that do not allow final conclusions to be drawn.

D. Conclusions

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
D. Conclusions on the potential environmental impact from the release or the placing on the market of GMOs	**D. Conclusions on the specific areas of risk of the e.r.a.**	
On the basis of an e.r.a. carried out in accordance with the principles and methodology outlined in sections B and C, information on the points listed in sections D1 or D2 should be included, as appropriate, in notifications with a view to assisting in drawing	Conclusions on the potential environmental impact in relevant receiving environments from the release or the placing on the market of GMOs shall be drawn on each of the points listed in sections D1 or D2, on the basis of an e.r.a. carried out in accordance	

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
conclusions on the potential environmental impact from the release or the placing on the market of GMOs:	with the principles outlined in section B and following the methodology described in section C, and on the basis of the information required pursuant to Annex III."	
D.1. In the case of GMOs other than higher plants	No changes	
1. Likelihood of the GMO to become persistent and invasive in natural habitats under the conditions of the proposed release(s).	No changes	Worst case scenarios have to be taken into account on all following topics. The assessment has to conclude on cut-off criteria such as lack of control of the GMO and its newly introduced genetic information in its spatio-temporal dimension.
2. Any selective advantage or disadvantage conferred to the GMO and the likelihood of this becoming realised under the conditions of the proposed release(s).	No changes	
3. Potential for gene transfer to other species under conditions of the proposed release of the GMO and any selective advantage or disadvantage conferred to those species.	No changes	
4. Potential immediate and/or delayed environmental impact of the direct and indirect interactions between the GMO and target organisms (if applicable).	No changes	
5. Potential immediate and/or delayed environmental impact of the direct and indirect interactions between the GMO with non-target organisms, including impact on population levels of competitors, prey,	No changes	Assessment of environmental impacts has to take into account further relevant issues, such as interactions with associated microbiomes, impact on signalling pathways and wild life species.

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
hosts, symbionts, predators, parasites and pathogens,		
6. Possible immediate and/or delayed effects on human health resulting from potential direct and indirect interactions of the GMO and persons working with, coming into contact with or in the vicinity of the GMO release(s).	No changes	
7. Possible immediate and/or delayed effects on animal health and consequences for the feed/food chain resulting from consumption of the GMO and any product derived from it, if it is intended to be used as animal feed.	No changes	
8. Possible immediate and/or delayed effects on biogeochemical processes resulting from potential direct and indirect interactions of the GMO and target and non-target organisms in the vicinity of the GMO release(s).	No changes	
9. Possible immediate and/or delayed, direct and indirect environmental impacts of the specific techniques used for the management of the GMO where these are different from those used for non-GMOs.	No changes	
D.2. In the case of genetically modified higher plants (GMHP)	D.2. In the case of genetically modified higher plants (GMHP)	
	The term ‘higher plants’ means plants which belong to the taxonomic group Spermatophytae (Gymnospermae and Angiospermae).	
1. Likelihood of the GMHP becoming more persistent than the recipient or parental plants	1. Persistence and invasiveness of the GMHP, including plant to plant gene flow	Add: worst case scenarios, delayed, long-term and cumulative effects have to be

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
in agricultural habitats or more invasive in natural habitats.		taken into account. The assessment has to conclude on cut-off criteria, such as lack of control of the GMHP and its newly introduced genetic information in its spatio-temporal dimension.
2. Any selective advantage or disadvantage conferred to the GMHP.	deletion	The original paragraph should not be deleted. In addition, it should read: taking into account the application of complementary herbicides.
3. Potential for gene transfer to the same or other sexually compatible plant species under conditions of planting the GMHP and any selective advantage or disadvantage conferred to those plant species.	2. Plant to micro-organisms gene transfer	Add: and other interactions with the microbiome of the GMHP and intestinal microorganism after consumption.
4. Potential immediate and/or delayed environmental impact resulting from direct and indirect interactions between the GMHP and target organisms, such as predators, parasitoids, and pathogens (if applicable).	3. Interactions of the GMHP with target organisms	Replace: Potential immediate and/or delayed environmental impact resulting from direct and indirect interactions between the GMHP and target organisms
5. Possible immediate and/or delayed environmental impact resulting from direct and indirect interactions of the GMHP with non-target organisms, (also taking into account organisms which interact with target organisms), including impact on population levels of competitors, herbivores, symbionts (where applicable), parasites and pathogens.	4. Interactions of the GMHP with non-target organisms	The original paragraph should not be replaced. Further, it should be added: .. including wildlife species as well as impacts on the microbiome of the GMHP and intestinal microorganism after consumption.
6. Possible immediate and/or delayed effects on human health	7 . Effects on human and animal health.	The original paragraph should not be replaced.

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
resulting from potential direct and indirect interactions of the GMHP and persons working with, coming into contact with or in the vicinity of the GMHP release(s).		
7. Possible immediate and/or delayed effects on animal health and consequences for the feed/food chain resulting from consumption of the GMO and any products derived from it, if it is intended to be used as animal feed.	deletion	The original paragraph should not be deleted.
8. Possible immediate and/or delayed effects on biogeochemical processes resulting from potential direct and indirect interactions of the GMO and target and non-target organisms in the vicinity of the GMO release(s).	6. Effects on biogeochemical processes	The original paragraph should not be replaced.
9. Possible immediate and/or delayed, direct and indirect environmental impacts of the specific cultivation, management and harvesting techniques used for the GMHP where these are different from those used for non-GMHPs.	5. Impacts of the specific cultivation, management and harvesting techniques.	The original paragraph should not be replaced.
		Add: impacts on plant health and its susceptibility to abiotic or biotic stressors.

Annex 2: Overview on intended changes and comments made by Testbiotech on Annex III B of the Directive 2001/18 (similar comments are relevant for changes in Annex III C)*

* similar comments are relevant to changes in Annex III C

ANNEX III B

INFORMATION REQUIRED IN NOTIFICATIONS CONCERNING RELEASES OF GENETICALLY MODIFIED HIGHER PLANTS (GMHPs) (GYMNOSPERMAE AND ANGIOSPERMAE)

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
	II INFORMATION REQUIRED IN NOTIFICATIONS SUBMITTED PURSUANT TO ARTICLES 13	
A. GENERAL INFORMATION	No Changes	
1. Name and address of the notifier (company or institute),	No Changes	
2. Name, qualifications and experience of the responsible scientist(s),	No Changes	
3. Title of the project,	Designation and specification of the GMHP.	
	4. Scope of the notification. (a) Cultivation or growing (b) Other uses.	
B. INFORMATION RELATING TO (A) THE RECIPIENT OR (B) (WHERE APPROPRIATE) PARENTAL PLANTS	B. SCIENTIFIC INFORMATION	
	All the subsets of information listed below shall be provided in the notification, except where the notifier can justify that a	

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
	specific subset is not relevant or necessary in the context of the notification concerned.	
	1. Information relating to the recipient plant or, where appropriate, to the parental plants	
1. Complete name:	(a) Complete name:	
(a) family name	No Changes	
(b) genus	No Changes	
(c) species	No Changes	
(d) subspecies	No Changes	
(e) cultivar/breeding line	No Changes	
(f) common name.	No Changes	
	(b) Geographical distribution and cultivation of the plant within the Union.	
		Data on associated micro-organisms that are considered to be the microbiome of the GMHP. In this respect, the GMHP has to be regarded as a holobiont that is connected as part of the hologenome of the GMPH itself and its associated microbiome.
2. (a) Information concerning reproduction:	(c) Information concerning reproduction:	
(i) mode(s) of reproduction	No Changes	
(ii) specific factors affecting reproduction, if any	No Changes	
(iii) generation time.	No Changes	
(b) Sexual compatibility with other cultivated or wild plant species, including the distribution in Europe of the	(d) No Changes	

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
compatible species.		
3. Survivability:	(e)	
(a) ability to form structures for survival or dormancy	No Changes	
(b) specific factors affecting survivability, if any.	No Changes	
4. Dissemination:	(f)	
(a) ways and extent (for example an estimation of how viable pollen and/or seeds declines with distance) of dissemination	(i) ways and extent of dissemination (for example an estimation of how viable pollen and/or seeds declines with distance)	
5. Geographical distribution of the plant.	Deletion (see above)	
6. In the case of plant species not normally grown in the Member State(s), description of the natural habitat of the plant, including information on natural predators, parasites, competitors and symbionts.	Where a plant species is not grown in the Union, a description of the natural habitat of the plant, including information on natural predators, parasites, competitors and symbionts.	
7. Other potential interactions, relevant to the GMO, of the plant with organisms in the ecosystem where it is usually grown, or elsewhere, including information on toxic effects on humans, animals and other organisms.	Other potential interactions of the plant, that are relevant to the GMHP, with organisms in the ecosystem where it is usually grown, or elsewhere, including information on toxic effects on humans, animals and other organisms.	
		8. A list of plant diseases that are common for the GMO in the receiving environment.
	2. Molecular characterisation	
C. INFORMATION RELATING TO THE GENETIC MODIFICATION	No Changes	
1. Description of the methods used for the genetic modification.	No Changes	
2. Nature and source of the vector used.	No Changes	
3. Size, source (name) of donor	(iii) Source of the nucleic	If the DNA used for

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
organism(s) and intended function of each constituent fragment of the region intended for insertion.	acid(s) used for transformation, size, and intended function of each constituent fragment of the region intended for insertion.	transformation was changed in its structure compared to its natural templates, all changes have to be fully described as well as intended changes in their biological function.
D. INFORMATION RELATING TO THE GENETICALLY MODIFIED PLANT	(b) No Changes	
1. Description of the trait(s) and characteristics which have been introduced or modified.	No Changes	
2. Information on the sequences actually inserted/deleted:	No Changes	
(a) size and structure of the insert and methods used for its characterisation, including information on any parts of the vector introduced in the GMHP or any carrier or foreign DNA remaining in the GMHP;	size and copy number of all detectable insert(s), both partial and complete and methods used for its/their characterisation;	
	the organisation and sequence of the inserted genetic material at each insertion site in a standardised electronic format;	
(b) in case of deletion, size and function of the deleted region(s);	in case of deletion, size and function of the deleted region(s) whenever possible;	
(c) copy number of the insert;	Deletion	
(d) location(s) of the insert(s) in the plant cells (integrated in the chromosome, chloroplasts, mitochondria, or maintained in a non-integrated form), and methods for its determination.	subcellular location(s) of the insert(s) in the plant cells (integrated in the nucleus, chloroplasts, mitochondria, or maintained in a non-integrated form), and methods for its/their determination.	
	-In the case of modifications other than insertion or deletion, function of the modified genetic material before and after the modification, as well as direct	

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
	changes in expression of genes as a result of the modification;	
	– sequence information in a standardised electronic format for both 5’ and 3’ flanking regions at each insertion site;	
	– nucleotide sequence that contains a string of codons that is uninterrupted by the presence of a stop codon in the same reading frame (Open Reading Frames, hereafter referred to as ‘ORFs’) created as a result of the genetic modification either at the junction sites with genomic DNA or due to internal rearrangements of the insert(s).	
3. Information on the expression of the insert:	(iii) No Changes	
(a) information on the developmental expression of the insert during the lifecycle of the plant and methods used for its characterisation;	the method(s) used for expression analysis together with their performance characteristics;	The method used has to be validated by independent laboratories.
(b) parts of the plant where the insert is expressed (for example roots, stem, pollen, etc.).	parts of the plant where the insert is expressed.	
	information on the developmental expression of the insert during the lifecycle of the plant;	Data on all parts of the plant, including the roots have to be made available. All pathways of environmental exposure via roots, pollen or other parts of the plant have to be examined.
	potential unintended expression of new ORFs identified under the sixth indent of point (ii), which raise a safety concern;	All newly expressed gene products have to be fully characterised, including miRNA (not only those that raise clear safety concerns).

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
	– protein expression data, including the raw data, obtained from field trials and related to the conditions in which the crop is grown;	Expression should include all newly expressed gene products, including miRNA. Data on gene expression and concentration of intended newly produced proteins, such as Bt toxins, should be based on methods that are fully described and validated by independent laboratories.
	– expression data with regard to the stacking of transformation events by conventional crossing and, where concerns arise, additional information.	See above
5. Genetic stability of the insert and phenotypic stability of the GMHP.	(iv) Genetic stability of the insert and phenotypic stability of the GMHP.	
		Expression data from studies with a broad range of defined biotic and abiotic stressors have to be included. The selection of these stressors should not only reflect the current status of the receiving environments, but also possible changes due to further climate changes or other developments that can impact genetic stability within the duration of the authorisation. Data from transcriptomics, proteomics and metabolomics have to be used to support risk assessment.
	(c) Conclusions of molecular characterisation	
	3. Comparative analysis (a) Choice of conventional counterpart and additional comparators.	
	(b) Choice of representative site locations.	

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
	(c) Experimental design and statistical analysis of data from field trials for comparative analysis	
	(i) Description of field trial design	
	(ii) Description of relevant aspect of the receiving environments	
	(iii) Statistical analysis	
	(d) Selection of plant material and compounds for analysis, if applicable.	
	(e) Comparative analysis of agronomic and phenotypic characteristics, if applicable.	
	(f) Comparative analysis of composition, if applicable.	
		Data from transcriptomics, proteomics and metabolomics have to be used to support risk assessment.
		Data on secondary plant compounds and signalling pathways have to be included.
	(g) Conclusions of comparative analysis.	
4. Information on how the genetically modified plant differs from the recipient plant in:	**4. Information on specific areas of risk**	
	For each of the seven areas of risk referred to in Section D.2 of Annex II the notifier shall first describe the pathway to harm explaining in a chain of cause and effect how the deployment of the GMHP could lead to harm, taking into account both hazard and exposure.	Add: worst case scenarios, delayed, long-term and cumulative effects have to be taken into account as well as knowledge gaps and uncertainties. Impact of the usage of the complementary herbicide on plant composition, impact on target and non-target organisms,

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
		persistence and invasiveness, biochemical processes and health
(a) mode(s) and/or rate of reproduction; (b) dissemination; (c) survivability.	(a) **Persistence and invasiveness** including plant to plant gene flow	
6. Any change to the ability of the GMHP to transfer genetic material to other organisms.	(i) Assessment of the potential for the GMHP to become persistent or invasive or to transmit transgene(s) to relatives and the environmental consequences thereof.	
	(ii) Conclusions on impacts of persistence and invasiveness including plant-to-plant gene flow.	
	(b) **Plant to micro-organism gene transfer**	Replace: Plant and micro-organism interaction
	(i)Assessment of the potential impact of transfer or long-term establishment of newly inserted DNA from the GMHP to microorganisms;	The assessment should include data on the impact of the genetic modification and on the microbiome of the GMHP. The assessment should include data on signalling pathways, including miRNA.
	(ii) Assessment of the potential impact of the transfer of newly inserted DNA for human and animal health and the environment;	The assessment should include data on the impact on the intestinal microbiome after consumption of the GMHP. The assessment should include data on signalling pathways, including miRNA.
	(iii) Conclusions on impacts of plant to microorganism gene transfer.	Replace: Conclusion on impact of plant and microorganism interactions
9. Mechanism of interaction between the genetically modified plant and target organisms (if applicable).	(c) **Interactions of the GMHP with target organisms**	
	(i) Assessment of the potential immediate and delayed environmental impact(s) resulting from undesired	

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
	changes in the direct and indirect interactions between the GMHP and target organisms;	
	(ii) Assessment of the potential immediate and delayed environmental impact(s) resulting from the development of resistance of the target organism to the expressed protein based on the history of development of resistance to conventional pesticides or transgenic plants expressing similar traits;	
	(iii) Conclusions on interactions of the GMHP with target organisms.	
10. Potential changes in the interactions of the GMHP with non-target organisms resulting from the genetic modification.	(d) Interactions of the GMHP with non-target organisms.	
	(i) Assessment of the possible immediate and delayed environmental impact(s) resulting from direct and indirect interactions of the GMHP with non-target organisms, (also taking into account organisms which interact with target organisms), including impact on population levels of a representative subset of species of herbivores, predators, parasitoids, parasites and pathogens, entomopathogenic organisms, pollinators, decomposers and plant symbionts (where applicable), and taking into account the potential impact(s) on relevant ecosystem services;	Wild life species, such as birds and mammals should be mentioned explicitly. The assessment should include data on signalling pathways, including volatile bio-chemicals and miRNA.
	(ii) Conclusions on interactions of the GMHP with non-target	

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
	organisms.	
	(e) Impacts of the specific cultivation, management and harvesting techniques	
	(i) For GMHPs for cultivation, assessment of the possible immediate and delayed, direct and indirect environmental impacts of the specific cultivation, management and harvesting techniques used for the GMHP;	The assessment should include data on changes in the susceptibility of the GMHP to biotic or abiotic stressors / plant diseases.
	(ii) Conclusions on impacts of the specific management and harvesting techniques.	
	(f) Effects on biogeochemical processes	
	f) Effects on biogeochemical processes (i) Assessment of the possible immediate and delayed effects on biogeochemical processes in the production site, which comprises the soil, plants, animals and microorganisms within the area in which the GMHP is to be grown;	The assessment should include data on signalling pathways including miRNA and other interactions between plant x microorganism.
	(ii) Assessment of the possible immediate and delayed effects on biogeochemical processes in the wider environment, which comprises land, water and air outside the production site, with which the GMHP and its management might interact;	
	(iii) Conclusions on effects on biogeochemical processes.	
7. Information on any toxic, allergenic or other harmful effects on human health arising from the genetic modification.	(g) Effects on human and animal health	
8. Information on the safety of the GMHP to animal health, particularly regarding any toxic,	(i) Assessment of possible immediate and delayed effects on human health resulting from	

Original 2001/18	Proposed Changes by Commission	Comments (Testbiotech)
allergenic or other harmful effects arising from the genetic modification, where the GMHP is intended to be used in animal feedstuffs.	potential direct and indirect interactions of the GMHP and persons working with, coming into contact with the GMHP release(s) (products such as pollen or dust from processed plants);	
	(ii) For GMHPs not destined for human consumption but where the recipient or parental organism(s) may be considered for human consumption the likelihood of accidental intake;	
	(iii) Possible immediate and delayed effects on animal health and consequences for the feed/food chain resulting from the unintended or accidental exposure to the GMHP and products derived from it;	Delete: resulting from the unintended or accidental exposure to the GMHP. Even if these data were made available under Regulation 1829/ 2003, they would have to be integrated into the assessment for cultivation.
	(iv) Conclusions on the effects on human and animal health.	
11. Potential interactions with the abiotic environment.	Deletion	This criteria should not be deleted but extended by listing relevant abiotic and biotic stressors that have to be taken into account.
	(h) Overall risk evaluation and conclusions.	Worst case scenarios, delayed, long-term and cumulative effects have to be taken into account as well as knowledge gaps and uncertainties.
12. Description of detection and identification techniques for the genetically modified plant.	5. Description of detection and identification techniques for the GMHP.	For stacked events, specific methods have to be made available to identify them in comparison to occasional mixtures of GMOs
13. Information about previous releases of the genetically modified plant, if applicable.	6. Information about previous releases of the GMHP, if applicable.	All risk-related data have to be made available, no matter whether the applicant considers them to be relevant or not.