Outcome of the European Member States and Public consultations on the draft guidance for the risk assessment of the presence at low level of genetically modified plant material in imported food and feed under Regulation (EC)

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TECHNICAL REPORT

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European Food Safety Authority (EFSA)

Abstract

The European Food Safety Authority (EFSA) carried out a consultation to collect input from the scientific community and all interested parties for the risk assessment of the low level (LL) presence of genetically modified plant material in imported food and feed under Regulation (EC) No 1829/2003. A two-step approach was followed. The draft LL Scientific Opinion was prepared by the *ad hoc* Working Group of the EFSA Panel on Genetically Modified Organisms (GMO Panel) and endorsed by the Panel for a dedicated consultation with European Member States at its plenary meeting on 21 September 2016. EFSA received approximately 100 comments on the draft LL Scientific Opinion from 11 Member States. Based on the outcome of the dedicated consultation, a second draft LL Scientific Opinion was prepared and endorsed by the Panel for a dedicated consultation with European Member States at its plenary meeting on 5 April 2017. EFSA received approximately 60 comments on the draft LL Scientific Opinion from 7 interested parties. The current report summarises the outcome of the two-step consultation, and includes a brief description of the comments received and how the comments were addressed. Comments related to policy or risk management aspects were considered out of the remit of the GMO Panel and outside the scope of these consultations; therefore these are not addressed in this document. The GMO Panel prepared an updated version of the LL Scientific Opinion taking into account the comments under its remit received. EFSA and its GMO Panel wish to thank European Member States, all stakeholders and the general public for their contributions. The LL Scientific Opinion was adopted at the GMO Plenary meeting on 21 September 2017, and is published in the EFSA Journal.

Key words: guidance, low level, GMO, EU Member States, public consultation

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1. Introduction

1.1. Background as provided by the requestor

Genetically modified organisms (GMOs) and derived food and feed products are subject to a risk assessment and regulatory approval before they can enter the market in the European Union (EU). In this process, the role of the European Food Safety Authority (EFSA) is to independently assess and scientifically advise risk managers on any possible risk that the use of GMOs may pose to human's and animal's health and the environment. EFSA's scientific advice is elaborated by its GMO Panel with the scientific support of specific working groups and EFSA scientists.

Detailed guidance was adopted by EFSA in 2006 (EFSA, 2006) and updated for the last time in 2011 (EFSA GMO Panel, 2011a) to assist applicants in the preparation and the presentation of GMO applications submitted under Regulation (EC) No 1829/2003[1] (hereafter referred as to Reg. (EC) 1829/2003) on GM food and feed (hereafter referred as to "GMO standard applications"). The European Commission subsequently adopted in April 2013 Regulation (EU) No 503/2013[2] (hereafter referred as to Reg. (EU) 503/2013) on applications for authorisation of GM food and feed. Annex II of this Regulation lists the scientific requirements to be provided in accordance with Articles 5(3) and 17(3) of Reg. (EC) 1829/2003. Article 5(2) of Reg. (EU) 503/2013 states that by way of derogation a GMO application not satisfying all the requirements of Annex II may be submitted, provided that it is not scientifically necessary to supply such information.

Genetically modified (GM) plants and derived products, not intended to be exported to the EU, have been or are being developed for specific health or market needs in third countries. The accidental presence of some of these GM products at low levels cannot completely be excluded in exports to the EU. In 2009, *Codex Alimentarius* issued guidelines for the food safety assessment of low level presence (LLP) situations of recombinant DNA plant material in food.[3]

In 2014 the European Commission mandated EFSA, in accordance with Article 29 of Regulation (EC) No 178/2002, to advise whether or not all requirements of Annex II to Reg. (EU) 503/2013 are necessary to conclude on the safety of applications covering the unintended presence of GMOs in food and feed at the adventitious or technically unavoidable presence of 0.9% or below. If not, EFSA was required to indicate which requirements are unnecessary and to give the underlying rationale.

1.2. Terms of Reference

In 2015, following clarifications from the European Commission, EFSA accepted the mandate and committed to issue an EFSA Scientific Opinion providing guidance for the risk assessment of the presence at low level of genetically modified plant material in imported food and feed under Reg. (EC) 1829/2003. An *ad hoc* working group of the GMO Panel was set up to develop such Scientific Opinion (hereafter referred as LL Scientific Opinion). Additional tasks of this working group included two subsequent consultations on the draft LL Scientific Opinion, the first dedicated to EU MS and the second one for the public (including EU MS), each of these followed by review and revision of the draft LL LL Scientific Opinion accordingly.

[1] Regulation (EC) No 1829/2003 of the European Parliament and of the Council of 22 September 2003 on genetically modified food and feed. Official Journal of the European Communities, L268, 1–23.

[2] Commission Implementing Regulation (EU) No. 503/2013 of 3 April 2013 on applications for authorisation of genetically modified food and feed in accordance with Regulation (EC) No. 1829/2003 of the European Parliament and of the Council and amending Commission Regulations (EC) No. 641/2004 and (EC) No. 1981/2006. Off. J. Eur. Union L157, 1–48

[3] Annex 3 (Food safety assessment in situations of low-level presence of recombinant-DNA plant material in food - adopted 2008) of the Guideline for the conduct of food safety assessment of foods derived from recombinant-DNA Plants, CAC/GL 45-2003, adopted 2003 (*Codex alimentarius,* 2009).

1.3. Stakeholders involvement

In the context of the abovementioned mandate, the EFSA GMO Panel developed a draft LL Scientific Opinion providing guidance for the risk assessment of the presence at low level of genetically modified plant material in imported food and feed under Reg. (EC) 1829/2003. In line with EFSA's policy on openness and transparency, the EFSA engaged with Stakeholders (Member States, International partners, Academia, Non-governmental organisations and Industry) and the general public of the LL Scientific Opinion development.

EFSA followed a two-step approach.

The first consultation of the draft LL Scientific Opinion was dedicated to the EU Member States (MS) and allowed EFSA to engage them and gain their substantial contribution early in the LL Scientific Opinion development. Since no EFSA's website tools are available for such dedicated consultation, EFSA engaged the EFSA Focal Points (via the EFSA Advisory Forum) to distribute the draft LL Scientific Opinion to the official Competent Authorities under Reg 1829/2003 and to receive back comments on a dedicated form. The communication letter to EFSA Focal point, the draft guidance provided to EU Member States and all comments received are presented in Appendix A, B and C respectively.

Following this consultation process, the draft LL Scientific Opinion was revised by the *ad hoc* Working Group, and a second draft was prepared, endorsed by the GMO Panel and published on EFSA's website (https://www.efsa.europa.eu/en/consultations/call/170502).The public and stakeholders, including EU Member States contributed further to the LL Scientific Opinion development through an online consultation on a draft document during Spring 2017.

Accordingly, comments received are listed in Appendix D.

EFSA staff and the *ad hoc* Working Group of the GMO Panel revised the draft LL Scientific Opinion taking into account all the comments received. The updated LL Scientific Opinion was discussed and adopted at the GMO Panel plenary meeting on 21 September 2017, and it is published in the EFSA Journal (EFSA GMO Panel, 2017). With this document, EFSA is committed to publishing all the written comments received during the dedicated EU and during the public consultation, as well as a report on the outcome of these consultations.

2. Screening and evaluation of comments received

2.1. Comments received

EU Member States comments

EFSA received feedback on the first draft LL Scientific Opinion from 11 EU Member States. Approximately 100 written comments were received from the official Competent Authorities under Reg. (EC) 1829/2003. Other EU entities supporting MS activities under Reg. (EC) 1829/2003 provided about 30 additional written comments (see Table 1 for details).

Table 1: EU Member States that submitted comments through the dedicated EFSA electronic form.

Country	Competent Authority under Reg. (EC) 1829/2003	Other entities
Austria	Federal Ministry of Health and Women's Affairs	-
Czech Republic	Ministry of Agriculture	-

Denmark	Danish Veterinary and Food Administration (via Denmark Technical University, DTU)	-
France	Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES)	-
Germany	Federal Office of Consumer Protection and Food Safety (BVL)	Robert Koch Institute
		Federal Agency for Nature Conservation (BfN)
		Federal Research Centre of Cultivated Plants
Greece	Ministry of Rural Development and Food (YPAAT)	Hellenic Food Authority (EFET)
		General State Laboratory (GCSL)
Ireland	Ireland Food Safety Authority	-
Italy	Ministry of Health	Istituto Superiore di Sanita'
Poland	Competent Authority under Reg. (EC) 1829/2003	-
Netherlands	Ministry of Health, Welfare and Sport (Ministerie van Volksgezondheid, Welzijn en Sport, VWS) (via COGEM, RIKILT and BGGO)	-
Spain	Spanish Interminsterial Council for GMO	-

All written comments received are listed in Appendix C (after removal of duplicates and/or reiterated comments). All the comments were reviewed by EFSA Unit and by the *ad hoc* Working group. A summary of the comments falling under the remit of the GMO Panel as well as the considerations made by the GMO Panel and its *ad hoc* Working group is provided below in 2.2.

Comments related to policy or risk management aspects were considered out of the remit of the GMO Panel and outside the scope of this consultation; therefore these are not addressed in this document.

Public consultation comments

EFSA received approximately 60 written comments on the second draft LL Scientific Opinion from 7 interested parties, including risk assessment bodies from European Member States and from third countries, industrial and trade associations (see Table 2 for an overview).

Table 2: Organisations that submitted comments through the on-line consultation tool

Country	Organisation
Belgium	COCERAL (Comité du Commerce des céréales, aliments du bétail, oléagineux, huile d'olive, huiles et graisses et agrofournitures)
Belgium	EuropaBio
Canada	Government of Canada
France	ANSES
Germany	Bavarian State Ministry of the Environment and Consumer Protection
Germany	Federal Agency for Nature Conservation (BfN)
Germany	Federal Office of Consumer Protection and Food Safety (BVL)

All written comments received are listed in Appendix D (after removal of duplicates and/or reiterated comments). All the comments were reviewed by EFSA Unit and by the *ad hoc* Working group. A

summary of the comments falling under the remit of the GMO Panel as well as the considerations made by the GMO Panel and its *ad hoc* Working group is provided below in 2.2.

Comments related to policy or risk management aspects were considered out of the remit of the GMO Panel and outside the scope of this consultation; therefore these are not addressed in this document.

EFSA has also taken into account additional material received by e-mail from France, consisting in the "Scientific and technical support note by the French Agency for Food, Environmental and Occupational Health and Safety concerning the studies necessary for the assessment of GMOs developed for non-EU countries and that could be unintendedly present at low levels on the European market" (ANSES, 2015).

2.2. Comments related to general aspects of the document

2.2.1. Overall format of the guidance document

EU Member States comments and GMO Panel considerations

Some Member States (e.g. Austria, Czech Republic, Denmark, Germany) indicated that draft document should be revised in its format, since it was not easily consultable to identify requirements needed (and those not) in the case of presence of GMOs at low level in food/feed; that clarification on the underlying rationale should be provided; moreover, that references to chapters of Annex II of Reg. (EU) 503/2013 should be clarified.

The GMO Panel clarifies that the guidance has been issued to match the structure of Annex II of Reg. (EU) 503/2013, and to detail its scientific requirements that are considered necessary (and those not) in the case of LL situations. This is aligned with the mandate by European Commission. Based on the EU Member States received comments, further clarification was provided indicating that the applicant should not use this guidance as a stand-alone document but should read it in conjunction with Reg. (EU) 503/2013 (see EFSA GMO Panel, 2017, Section 3.1.1 for further details). Furthermore, references to specific sections and paragraph of Annex II of Reg. (EU) 503/2013 have been detailed.

Public comments

No specific comments were received on this aspect.

2.3. Comments related to the background and terms of reference, interpretation of the terms of reference and on the scope of the document

EU Member States comments

Comments were received from Austria, Czech Republic, Denmark, France, Germany (BVL, BfN), Greece (GCSL), Ireland, Italy, Netherlands and Poland.

Comments regarding the background and terms of reference included request for clarification on the rationale for selecting the 0.9% threshold, on possible inconsistency versus other EU regulations and on the process for accepting a LL application or to monitor LL situations (sampling, detection methods etc.). Furthermore it was commented that this guidance should mirror the LLP guidelines from Codex (2009), which are based on mutual recognition between countries and are intended for the assessment of low levels of GM plant materials that have already passed a food safety assessment according to the Codex in one or more countries.

The GMO Panel acknowledged these comments but considers that these are out of its remit, as they refer to to requirements and indications contained in the mandate received from the European

Commission and/or refer to risk management issues. Therefore the GMO Panel does not address these comments in this document.

Some Member States (Czech Republic, Greece [GSL]) found unclear the term "ingredient" or "per ingredient". The GMO Panel took into account these comments and clarified in the text the definition of ingredient (see EFSA GMO Panel, 2017 Section 1.2).

Some Member states (Austria, France and Greece [GSL]) indicated that further clarification was needed as regards the applicability of this guidance to GM fruits and vegetables consumed as such, asking to narrow the scope of the guidance to commodities such as grains.

The GMO Panel highlights that the EC mandate required EFSA to address situations up to a maximum of 0.9% of GMO in any food/feed, and covering commodities and fruits/vegetables. Based on the above predefined threshold and following interpretation of the terms of reference (see EFSA GMO Panel, 2017, Section 1.2) the GMO Panel considered that situations such as those linked to the presence/consumption of ingredients containing more than 0.9% of a GMO are precluded. This is for example the case of fruit/vegetables, constituting possibly more than 0.9% of an ingredient in a portion. The GMO Panel highlighted that that the decision to accept an application as LL is a risk management issues. The lack of applicability of this guidance to situations where a GMO is beyond 0.9% per ingredient defines a difference with Codex Alimentarius on LLP Codex Alimentarius, 2009, Annex 3), where no thresholds are indicated (see EFSA GMO Panel, 2017 – Annex 1 for further details).

France, Greece (GSL) and Ireland required clarification on the scope of the guidance as regards GMOs for cultivation purposes; GM microorganisms; GM animals; GMOs for non-food/feed uses, indicated to be out of the scope of Reg. (EC) 1829/2003. The GMO Panel clarified that this guidance is applicable to the risk assessment of GMO food and feed in the scope of Reg. (EU) 503/2013 (see EFSA GMO Panel, 2017 Section 3.1.2).

Public comments

Comments similar to those above were received from the Bavarian State Ministry of the Environment and Consumer Protection, Government of Canada, Coceral, Europabio, France (ANSES), Germany (BVL) and are addressed in the former section.

In addition the Bavarian State Ministry of the Environment and Consumer Protection reported that it is unclear the legal basis upon which the threshold of 0.9% was defined, in particular quoting the draft guidance sentence: "Following an exchange with the European Commission, it was further clarified that an application of GM food and feed at low levels submitted under Reg. (EC) 1829/2003 <…> covers a request for the authorisation of a GMO present at a level of maximum 0.9% per ingredient in any food and/or feed, due to adventitious or technically unavoidable circumstances".

The GMO Panel clarifies that based on the mandate received it was considered important to clarify versus what the low level (i.e. maximum 0.9%) of the GMO subject of a LL application was referring to. EC clarified to the working group that an application for low level presence covers a request for an authorisation of a GMO to be present at a level of maximum 0.9% *per ingredient* in all food (see Reg. (EC) 1829/2003 Section 2, Article 12, 2) and feed (in this case meaning feed and each individual feed, see Reg. (EC) 1829/2003 Section 2, Article 24, 2) from point of entry to the EU to the final consumer/animal due to an adventitious or technically unavoidable presence.

The Bavarian State Ministry of the Environment and Consumer Protection also commented that accidental or technically unavoidable reasons for an LLP situation cover both one-off and repeated contaminations, however, in supervision practice, only one-off cases in which GM material was identified at levels below 0.9% have been regarded as accidental or technically unavoidable, and repeated cases have not.

The GMO Panel considers that this is a risk management consideration and out of its remit. From the risk assessment view point "accidental/technically unavoidable" does not allow to infer single or repeated exposure to the GMO authorised for presence at low level, therefore both acute and repeated exposure scenario should be assessed.

2.4. Comments on scientific requirements for the risk assessment of LLP applications submitted under Reg. (EC) 1829/2003

2.4.1. General considerations

Public comments

Comments were received from the Bavarian State Ministry of the Environment and Consumer Protection that asked to clarify why some requirements from Annex II of Reg. (EU) 503/2013 are necessary for LL situations and others on a case-by-case basis only.

EFSA acknowledged the comment and clarified that the comprehensive characterisation of the transformation event and of its intended effects is considered necessary to frame the risk assessment of the GMO matter of a LL application; therefore requirements from Annex II of Reg. (EU) 503/2013 aiming at this are considered necessary. On the contrary, requirements for identifying unintended effects are not considered necessary on a routine basis in a LL situation, due to the limited impact of these effects on the safety and nutritional profile of the ingredient where the GMO is present at maximum 0.9%. These requirements include some data concerning the expression of the insert, *in silico* RNAi off target searches, routine comparative analysis studies of the genetically modified plant.

2.4.2. Stacked events

EU Member States comments

Comments were received from Germany (BVL), the Netherlands and France.

Germany (BVL) commented that it is very unlikely that combined transformation events stacked by conventional crossing impact the composition of the ingredient resulting in compound levels exceeding the natural variation in the final product under LL conditions.

The GMO Panel agrees that the the low exposure to the stack GMO in a LL situation is a relevant argument to consider, however clarifies that the stability of the transformation events combined in the stack serves to characterise the transformations event(s) and it is therefore considered necessary in a LL situation; while the expression of the transformation events is not considered necessary in a GM stack, since the likelihood for changes in the expression levels of the newly inserted sequences occurring as a consequence of interactions between the events and impacting the safety of the LL ingredient is negligible, given the low presence of the GM stack per LL ingredient (see Sections 3.2.3.2 and 2.4.3.1 of EFSA GMO Panel, 2017). Regarding potential synergistic or antagonistic effects resulting from the combinations of the transformation events the applicant should consider whether there is the expectation of such interactions that could lead to changes in the stack GMO of possible impact on the safety and nutritional impact of the ingredient. In such a case, the applicant should conduct targeted investigations accordingly (see Sections 3.2.2.2 and 3.2.3.3 of EFSA GMO Panel, 2017 for further details).

Netherlands requested clarification on the use of the term 'individual events' in the context of 'stacked transformation events'.

The GMO Panel took the comment into account and acknowledged that the term "individual event" is not used in the context of GM stacks in Reg. (EC) 1829/2013 or in Reg. (EU) 503/2013. The wording "individual event" has been substituted by "transformation event" or "single transformation event" in the Scientific Opinion (EFSA GMO Panel, 2017), with the only exception in section 1.1 *Background and Terms of reference as provided by the requestor*, since this is indicated in the EC mandate.

France commented that the comparison of the levels of newly expressed proteins in event 'stacks' with those measured in single events is necessary because it is one of the ways of identifying possible unexpected effects linked with the stacking.

It is recalled here that the GMO Panel in general considered necessary to characterise the transformation event(s) and its intended effects in order to frame the risk assessment of the specific GMO under a LL application; on the contrary requirements for identifying unintended effects are not considered necessary on a routine basis in due to the limited impact of these effects on the safety and nutritional profile of the ingredient. This is also applicable to stacks subject of LL applications. Specifically regarding the expression of the insert in a stack event on a case-by-case basis, when the nature or the characterisation of the transformation events combined in a stack suggests an interaction that may result in changes of the expression levels of the newly inserted sequences raising safety concerns in a LL situation, these data should be provided (see Section 3.2.3.2 of the EFSA GMO Panel, 2017 for further details).

Public comments

The Government of Canada commented that the EU requirements on the assessment of possible interactions in stacked events are overproportionate in LL applications considering the low exposuReg.

A response to a similar comment is provided above in the 'EU Member states comments' section.

Comments from EU Member States submitted during both consultations are addressed in the former section.

2.4.3. Hazard identification and characterisation

2.4.3.1. Molecular characterisation

EU Member States comments

Comments were received from Austria, Denmark, France and Germany (BVL and BfN).

Comments questioning the approach and data requirements for the assessment of potential risks associated with horizontal gene transfer (HGT) are addressed below in section 2.5 of this document (environmental risk assessment).

Austria, Germany (BfN) and Denmark commented concerning the requirements on the expression of the insert(s) (subsection 1.2.2.3 of Annex II of Reg. (EU) 503/2013) and in particular on the GMO Panel consideration that it would not be necessary for the applicant to routinely provide information on the expression levels of the newly inserted sequences for stacked transformation events. Austria noted the existence of literature indicating that i) despite the significantly lower presence (defined as 0.9 % per ingredient of a GMO) compared to a full-scope GMO application, the achieved concentration of an ingredient might still be sufficient to show an effect; ii) expression data may deviate considerably between stacks and their corresponding single events and therefore information on the expression of the inserts in a LL stack should be provided in all cases. France also questioned this derogation mentioning that the comparison of the levels of newly expressed proteins in LL stack GMOs

with those measured in single events should be considered necessary on a routine basis because this information serves to identify possible "unexpected effects" linked to the stacking of the single events. On the other hand, Denmark mentioned that since exposure in a LL situation per ingredient is expected to be ~ 100× lower relative to a full-scope GMO application, this should be reflected in considerably lower data requirements as regards information on the expression of the insert(s). In addition, Austria indicated insufficient clarity on whether all the single events used to produce a stack should be assessed prior to a stack LL application.

The GMO Panel clarified that information on new protein(s) expression data from those plant parts used for food and feed purposes, as well as the description of the methods used for expression analyses (point 1.2.2.3[a] and [e]) are considered necessary for characterising the GM plants in LL applications on single transformation events. Conversely, requirements such as those on "information on developmental expression of the insert during the life cycle of the plant" (point 1.2.2.3[b]) are not considered necessary for LL applications (see Section 3.2.3.2 of EFSA GMO Panel, 2017 for further details). In addition, given the defined level of presence of 0.9% of the GMO stack per LL ingredient, the GMO Panel considers that in the case of stacks, the likelihood for changes in the expression levels of the newly inserted sequences as a consequence of interactions between the events impacting the safety of the LL ingredient is negligible. Therefore information on the expression of the inserts in a LL stack is not considered necessary on a routine basis. In cases when the nature of the transformation events combined in a GM stack or the outcome of their characterisation suggests an interaction that may result in changes of the expression levels of the newly inserted sequences possibly raising a safety concern, these data should be provided. Finally, the GMO Panel also further clarified that for the risk assessment of LL applications of stacked events the applicant will provide a risk assessment of each single transformation event or, in accordance with Article 3(6) of Reg. 1829/2003, refer to already submitted application(s).

Comments were received from Germany (BVL) and France on the need of an *in silico* off-target analysis for RNAi mediated gene silencing for GMOs subject of LL situations on a routine basis. Germany (BVL) indicated that there is not sufficient clarity on whether or not an *in silico* off-target analysis for RNAi mediated gene silencing would be considered necessary for GMOs subject of LL situations. France mentioned that there is not yet a consensus on the possible associated risks of RNAi-based silencing approaches.

The GMO Panel considered these comments and clarified that based on current scientific knowledge, the likelihood of off-target effects resulting from silencing approaches by RNAi expression large enough to raise safety concerns in a LL situation is considered negligible. Therefore the potential 'off-target gene(s)' *in silico* search described in point 1.2.2.3(e) of Annex II.II of Reg. (EU) 503/2013 is not considered necessary.

Austria, Germany (BVL and BfN) and France questioned the GMO Panel consideration that it would not be necessary for the applicant to routinely provide information on the genetic stability of the insert and the phenotypic stability of the trait. They argued that these data form part of the molecular characterisation of the genetic modification as well as serve to indicate that detection methods specific to the GMO will continue to be valid in the long term. In addition, it was mentioned that the genetic stability of the insert may be essential for the identification of the LL GMO in case of an accidental release into the environment.

The GMO Panel took these comments into account and clarified that the scientific requirements in subsection 1.2.2.4 of Annex II.II of Reg. (EU) 503/2013 on the "genetic stability of the insert and phenotypic stability of the genetically modified plant" are considered necessary in LL applications on a routine basis.

Public comments

Comments on the molecular characterisation-related sections were received from the Government of Canada, the Bavarian State Ministry of the Environment and Consumer Protection and Europabio. Comments from EU Member States submitted during both consultations are addressed in the former section. Comments questioning the approach and data requirements for the assessment of potential risks associated with HGT are addressed below in section 2.5 of this document (ERA).

The Government of Canada questioned the need to routinely require data on interactions among single transformation events within a stack and their potential to cause synergistic or antagonistic effects.

The GMO Panel considers that data enabling the assessment of interactions serve to establish that the combination of events is stable and that no interactions between the stacked events, that may raise safety concerns compared to the single events, occur.

The Bavarian State Ministry of the Environment and Consumer Protection commented on the GMO Panel consideration that an *in silico* off-target analysis for RNAi mediated gene silencing is not considered necessary for GMOs subject of LL situations on a routine basis, noting that no sufficient justification for this derogation is provided and that the potential off-target effects cannot be foreseen. A response to similar comments is provided above in the 'EU Member states comments' section.

EuropaBio suggested that based on the low likelihood of expression of newly created ORFs and considering the defined level of presence of 0.9% of the GMO per LL ingredient, even if such an ORF was to be expressed, the likelihood of any adverse effect would be negligible; therefore data requirements described in point 1.2.2.3(d) should not be considered necessary.

The GMO Panel highlights that these data serve to characterise the potential unintended expression of newly created Open Reading Frames (ORFs) identified as raising a safety concern and are therefore considered necessary in a LL situation.

EuropaBio also mentioned that information on the "trait stability" is of very limited relevance to the safety assessment of GMOs intended only for import and processing into the EU and not for cultivation. Based on this, EuropaBio suggested that this requirement should be abolished due to negligible exposure for the environment.

The GMO Panel considers that data on the "genetic stability of the insert and phenotypic stability of the genetically modified plant" serve to characterise the genetic modification(s) of the plant and are threrefore considered necessary in LL applications.

2.4.3.2. Comparative analysis

EU Member States comments

Comments were received from Austria, Denmark, France and Germany (BVL).

Austria indicated that without the performance of field trials the risk assessment would have substantial data gaps in relation to potential unintended effects that become apparent only during growth and performance of the GM plant in the field. Therefore considered that a basic set of comparative analysis data should be always provided to inform whether the physiology of the plant has changed during the genetic modification process and changes in composition of safety relevance have occurred. In the case of hypothesis-driven comparative analysis, all requirements of paragraph 1.3 of Annex II of Reg. (EU) 503/2013 need to be followed. Clarification on the rationale why comparative analysis was considered not necessary on a routine basis and on the table supporting the exercise was requested by Denmark.

The GMO Panel took these comments into account and clarified the argumentation in the LL Scientific Opinion (EFSA GMO Panel, 2017). Considering the low level situation, not all differences identified in

comparative analysis may be relevant for safety of consumers and animals. On the basis of the current knowledge, variations in the level of compound(s) in the GMO subject of a LL application are unlikely to be large enough to impact the nutritional or safety characteristics of the LL ingredient, with the possible exception of GMOs with traits developed to improve nutrition (e.g. nutritionally enhanced crops); or in the cases of GMOs expected to show unintended compositional changes (e.g. EFSA GMO Panel, 2011b). More in general it is recalled here that the GMO Panel in general considered necessary to characterise the transformation event(s) and its intended effects in order to frame the risk assessment of the specific GMO under a LL application; on the contrary requirements for identifying unintended effects are not considered necessary on a routine basis in due to the limited impact of these effects on the safety and nutritional profile of the ingredient.

The acceptance of studies other than those performed in accordance paragraph 1.3 of Annex II of Reg. (EU) 503/2013 was also commented. Denmark considered that studies not aligned to Codex should be considered depending on the quality of the study. France agreed on the GMO Panel proposal of hypothesis-driven comparative analysis in LL situations, however, in alignment with Austria, indicated that when comparative analysis is required, it should be conducted in conformity with Reg. (EU) 503/2013.

The GMO Panel highlights that the objective of comparative analysis in a LL situation is to investigate compositional changes in composition triggered by a specific hypothesis and possibly impacting the safety and nutritional characteristics of the LL ingredient; and to support thereafter the assessment as regards safety and nutrition. Instead, a comparative analysis in LL situations is not intended to identify all possible unintended unexpected differences between the GMO and its conventional counterpart, as these are unlikely to be of safety/nutritional relevance, as explained befoReg. Compositional analysis should be conducted on endpoints triggered by a specific hypothesis with the objective to quantify the differences expected in the composition of the GMO compared to its conventional counterpart and to perform the subsequent risk assessment steps (i.e. exposure assessment and cumulative risk assessment). To meet this, the GMO Panel proposed adaptation to requirements set in Reg. (EU) 503/2013 while keeping the main aspects of experimental design and statistical analysis within the frame of Codex Alimentarius. Therefore conditions maximising expected change(s) in the composition of the GMO are considered necessary in LL situation, either field or greenhouse conditions, while information on the natural variability of this (these) endpoint(s) is considered not necessary on a routine basis.

France agreed on the EFSA proposal of targeted compositional analysis, however commented that, when needed, this should be conducted in accordance to Reg. (EU) 503/2013, in particular with regard to the number of test sites, the choice and number of the comparators, and the use of difference and equivalence test.

The GMO Panel considered that a target compositional analysis should addrees the specific hypothesis that raised the need. Therefore considered appropriate targeted study designs, aimimg at confirming the hypotheis and analytically determining the level of plant constituents different from the comparator. The information obtained will be use for next risk assessment steps.

Further clarification on the concept of target comparative analysis, experimental design and statistical analysis was requested (Germany BVL). The GMO Panel took the comment into account and revised the text of the LL Scientific Opinion to add clarity to the rationale of hypothesis-driven comparative analysis. Being compositional analysis targeted to address a specific hypothesis, case-by-case approaches should be followed, and thorough justification provided by the applicant.

Public comments

Comments were received from the Bavarian State Ministry of the Environment and Consumer Protection, the Government of Canada and Europabio.

The Bavarian State Ministry of the Environment and Consumer Protection commeted that the rationale for the derogation from the requirements laid down for risk assessment is based on the low concentration, however no scientific justification is provided.

The GMO Panel took note of the comment and clarified that since in LL situations the level of exposure of consumers and animals to the GMO is defined to be at a maximum 0.9% per ingredient, not all differences identified in the comparative analysis may be relevant. Rather, on the basis of current knowledge, the GMO Panel is of the opinion that variations in the level of compound(s) in GMOs are generally not large enough to impact the nutritional or safety characteristics of an ingredient in LL situations, with the possible exception of nutritionally enhanced crops or in general in the case of expected unintended compositional changes. In these situations a targeted compositional analysis is required.

The Government of Canada asked clarification of one of the conditions for which comparative compositional analysis in low level situations would be required, namely the one relating to compounds produced *de novo* in the GMO found at low level.

The GMO Panel thanks the Government of Canada for the comment and clarifies that *de novo* compounds refer to compounds "new", i.e. not constitutively expressed in a conventional crop. The text has been clarified accordingly.

Europabio required further clarification on the equivalence test, indicating that there was a contradicting indication on the exclusion of this test.

In the guidance it was clarified that in LL situations the objective is to quantify the level(s) of target compound(s) in the GMO with respect to its conventional counterpart, in accordance to the hypothesis that triggered the targeted composition analysis. In this context, the test of equivalence is considered not necessary in LL situations, since it has a different objective, which is to verify whether the GM plant is equivalent or not to reference varieties (apart from the introduced trait).

2.4.3.3. Toxicology

EU Member States

Comments were received from Austria, Germany (BVL) and Greece (GCSL).

Austria and Greece (GCSL) commented on the paragraph regarding *Information on altered levels of food and feed constituents (Reg. [EU] 503/2013; Annex II.II, 1.4.3)* indicating that since the submission of comparative data is not required, it is expected that changes in the levels of food and feed constituents that are of relevance for the toxicological risk assessment will be missed. Germany [BVL] also requested clarifying the text.

The GMO Panel highlights that, since the exposure is limited to 0.9% GMO per ingredient not all possible unintended differences in the composition (i.e. in the type and level of constituents) of the GMO compared to its conventional counterpart are likely to be of toxicological relevance in a LL situation. As indicated by Germany (BVL) a targeted compositional analysis will be conducted when a hypothesis is present; when changes in the levels of specific constituents of the GMO (i.e. compositional endpoints) are expected, these should be analytically confirmed and toxicologically assessed according to the scientific requirements laid down in paragraph 1.4.3 of Annex II.II of Reg. (EU) 503/2013.

Some comments were received on 90-day studies in rodents on the whole food/feed. Austria and Greece (GCSL) indicated the the necessity of such studies particularly considering to the lack of routine comparative data that would enable the development of a hypothesis-driven approach to investigate toxicological consequences of repeated exposure for a long-time period. Germany

requested clarification on which specific hypothesis can justify the requirement of animal feeding trials, considering the 0.9% presence of the GMO.

Subchronic studies in rodents (as well as other toxicity studies) are not considered necessary to corroborate information on the toxicological characteristics of the whole GM food and feed in rodents and/or to reduce the remaining uncertainties, considering the limited exposure to the GMO. On a case-by-case basis, depending on the GMO characteristics and on the results from preceding analysis, a 90-day study might be necessary if appropriate to test specific toxicological hypothesis.

Public comments

Comments were receved from Europabio. It was requested why a full assessment of the newly expressed protein (and non-protein) constituents is recommended in LL situations. Moreover, an approach based on a Tier approach (Tier I safety assessment (characterization, bioinformatics, stability, digestibility) followed by a Tier II (28-day study), if needed, is proposed. For non-protein constituents, Europabio recommends that the threshold of toxicological concern concept is used. Europabio considers that the outlined approach for not requiring a 90-day rat study for LLP assessment 90-day rat feeding study is well founded and more in general this study is not needed irrespective of exposure and should not be required for the LLP assessment.

The GMO Panel considers that a comprehensive characterisation of the transformation event and of its intended effects should be performed in LL situations. This includes the characterisation of newly expressed proteins and of their toxicological profile, as indicated by Reg. [EU] 503/2013; Annex II.II, 1.4. The GMO Panel agrees that the low exposure is the leading theme for the assessment of LL situations and indeed EFSA GMO Panel, 2017 has been based on this consideration. Regarding the use of the approach "threshold of toxicological concerns" this is not considered in Annex II of Reg. (EU) 503/2013. The GMO Panel acknowledged the comment on 90-day studies and considers that, depending on possible hypothesis identified, a 90-day study may be necessary.

2.4.3.4. Allergenicity

EU Member States comments

Comments were received from Austria, France, Germany (BVL, BfN, Robert Koch Institute, Federal Research Centre of Cultivated Plants) and from Greece (GCSL).

Austria commented that in the absence of a routine comparative analysis the identification of altered levels of endogenous constituents, possibly including altered levels of endogenous allergens, is missing; furthermore Austria indicated that for plant species for which to date no GMO has been assessed, it would probably be necessary to compile a list of allergens to be researched and quantified on a routine basis. France indicated that allergenicity assessment would not appear to be necessary for products consumed only in a mixture and/or after technological transformation, because any traces of allergens introduced by GM products will be extremely diluted; in the case of plant species that are known to be highly allergenic, an analysis of any change in the allergenicity of the food/feed could be required if other aspects of the application suggest that the GMO constitutes a risk. Germany (BVL) required clarifying whether measuring endogenous allergens on a routine basis is needed or not.

The GMO Panel took into account the comments and clarifies that the underlying principle of hypothesis-driven compositional analysis in LL situations (see Section 1.2 of EFSA GMO Panel, 2017) applies to all plant constituents, including endogenous allergens. Specifically, in the case there is the expectation of changes in the level of known endogenous allergens in the GMO possibly impacting the allergenicity of the LL ingredient, these should be analytically measured (see EFSA GMO Panel, 2017, Section 3.2.3.3) and the assessment of allergenicity of the food or feed from the GMO should be

conducted according to requirements of paragraph 1.5.2 of Annex II. II of Reg. (EU) 503/2013. This woud apply to GMOs not yet assessed and for which no list of endogenous allergens has been compiled yet.

France, Germany (BVL, BfN, Robert Koch Institute, Federal Research Centre of Cultivated Plants) and Greece (GCSL) required clarification on the significance of "large effects" applied to changes in the levels of endogenous allergens; in particular Germany (BVL) commented that, given the individuality of allergic subjects, the absence of a (uniform) threshold, the high natural variability of expression levels and the fact that the remaining 99.1% of the ingredient may already pose a risk to allergic persons, the interpretation of expression levels as well as of changes is difficult.

The GMO Panel agreed that the indication of "large" effect was not appropriate and revised the text accordingly: the changes in the endogenous allergens should be considered if impacting the allergenicity of the LL ingredient; it will be upon to the applicant to discuss the impact of these changes on the allergeniciy of the LL ingredient.

France commented that the assessment of adjuvanticity is a weak requirement by the current regulation.

The GMO Panel took note of the comment, however highlights that this is not specific to LL situation and therefore not in the remit of this mandate.

Public comments

Clarifications were requested on the scientific rationale why endogenous allergens should not be routinely measured (Bavarian State Ministry of the Environment and Consumer Protection).

Comments from EU Member States submitted during both consultations are addressed in the former section.

As explained above, the GMO Panel highlights that the underlying principle of hypothesis-driven compositional analysis in LL situations (see Section 1.2 of EFSA GMO Panel, 2017) applies to all plant constituents, including endogenous allergens. The text was further clarified to reflect this (see Section 3.1.2 of EFSA GMO Panel, 2017).

2.4.4. Risk characterisation

Public comments

Germany (BVL) suggested keeping primary version of this topic: "Considering that the LLP applications are intended to support the authorisation of a GMO at a maximum level of 0.9 % in an ingredient of food and feed, no post market monitoring is foreseen".

The GMO Panel took the comment into account however highlights that since the exposure to a GMO subject of a LL application could be repeated, on a case by case situation, depending on the characteristics of the GMO and on the basis of the LL assessment a PMM might be needed.

2.4.5. Cumulative risk assessment

EU Member States comments

Clarification was requested (Austria, France and Germany [BVL]) on the cumulative assessment and the significance of "similar traits" and "same plant species" and their relevance in the exercise, in particular whether different GMOs of the same plant species or GMOs belonging to different plant species should be taken into account in the cumulative assessment.

The comments were taken on board by the GMO Panel and the text revised to improve clarity. In the case of multiple GMOs showing similar trait(s), e.g. nutritionaly enhanced crops, the relative

contribution to the ingredient of each of these GMOs should be taken into account to allow an estimation of their total contribution, via the addition of the respective trait-related constituent(s).

France also asked how the process will be managed in the time frame.

Considering the decision on whether a given GMO can constitute a LL application is a risk management issue (see Section 1.2 of EFSA GMO Panel, 2017), it is not in the remit of this guidance to define a process relevant for the cumulative risk assessemnt.

From the risk assessment point of view, for the time being it is not possible to predict the number and type of GMOs matter of LL applications and therefore the GMO Panel cannot provide precise indications how to perform the cumulative risk assessment.

Public comments

Europabio asked similar comments as EU MS; these are addressed above. Comments from EU Member States submitted during both consultations are addressed in the former section.

2.5. Comments on Environmental risk assessment

EU Member States comments

Comments on the ERA-related sections were received from Austria, Germany (the Federal Office of Consumer Protection and Food Safety [BVL] and the Federal Agency for Nature Conservation [BfN]) and the Netherlands.

Several of the comments questioned the approach and data requirements for ERA of GM plant applications for import and processing for food/feed uses (e.g., exposure pathways [e.g., release of non-viable GM plant material into the environment; environmental exposure via intact (viable) seeds in faecal material]; likelihood of illegitimate recombination of DNA for HGT; minimum DNA sequence length sufficient for homologous recombination for HGT; formation of mosaic genes; persistence, invasiveness and vertical gene flow scenarios proposed in the ERA scheme/diagram). Since these comments are not specific to LL conditions, they are not considered further in this report.

Germany (BVL) and the Netherlands indicated a discrepancy in the level of detail with which applicable data requirements are described in the LL draft LL Scientific Opinion that underwent consultation. Data requirements for ERA were considered less specific than for the other areas of risk covered by the LL draft document. The GMO Panel attributes this discrepancy to the less prescriptive nature of Directive 2001/18/EC in terms of data requirements, compared to the Reg. (EU) 503/2013. Since more detailed data requirements are given in its guidance document on the ERA of GM plants (EFSA GMO Panel, 2010), and to ensure consistency in data requirements between GM plant applications for import and processing for food/feed uses and LL applications, the GMO Panel recommends applicants to follow the principles and approach outlined in EFSA GMO Panel (2010) and other applicable EFSA guidelines when determining the applicable data requirements for the ERA of GM plants under LL conditions. Moreover, in its revised LL guidance, the GMO Panel put additional emphasis on the importance of problem formulation to assess the GM plant using existing knowledge, and identify potential hazards and exposure routes on a case-by-case basis. Taking this information into account, applicants should identify which areas of risk need to be addressed and hence the data requirements to inform the ERA. Risk should then be characterised by testing specific hypotheses about the likelihood and severity of adverse environmental effects that may occur. These hypotheses may be tested with existing information.

The Netherlands questioned the need to assess the probability and consequences of HGT under LL conditions, and suggested a more targeted approach for this assessment by focusing on the potential of intended traits to enhance the potential for HGT. Instead, Austria and Germany (BfN) confirmed the necessity to assess HGT and its potential consequences under LLP conditions. In this context, the

GMO Panel took into account the requirements of Directive 2001/18/EC and the Implementing Reg. (EU) 503/2013, which require the assessment of the environmental impact of a gene transfer from GMOs to other organisms, and the potential risk associated with HGT from the product to humans, animals and microorganisms, respectively. Moreover, although it is well recognised that the likelihood of transfer of recombinant DNA from GM plants to microorganisms is extremely low, and may be further reduced under LL conditions, the GMO Panel considers that currently no exposure threshold can be established from which HGT can be excluded.

Germany (BfN) considered there was a need to conduct a full ERA for GM plants with high persistence and invasiveness potential (scenarios 3 and 4, as described in the draft LL Scientific Opinion that underwent consultation) under LL conditions. In these cases, Germany (BfN) is of the opinion that a full dataset "for compositional analysis, comparative approach, protein expression and agricultural and environmental parameters" needs to be provided. For protein expression Germany (BfN) considers that information on the expression of the insert(s) should be supplied in additional tissues than those typically used for the food/feed safety assessment. In its revised LL Scientific Opinion, the GMO Panel no longer explicitly refers to previously introduced scenarios to group plants in terms of their persistence and invasiveness, and hybridisation potential. Instead, the revised LL Scientific Opinion refers to problem formulation to identify potential hazards and exposure routes requiring further consideration in the risk assessment. To determine the specific data requirements for ERA of GM plants under LL conditions, the revised LL Scientific Opinion recommends applicants to follow the principles and approach outlined in EFSA GMO Panel (2010) and other applicable EFSA guidelines (EFSA GMO Panel, 2017b). Therefore, information on the expression of the insert(s) in tissues other than those used for food/feed purposes is not considered necessary on a routine basis. Likewise, the revised LL Scientific Opinion specifies that the agronomic/phenotypic and compositional characterisation of the GM plant may be needed to support the risk assessment on a case-by-case basis depending on the persistence, invasiveness and hybridisation potential of the GM plant, as well as the nature of the intended traits.

In the LL Scientific Opinion that underwent consultation, the GMO Panel suggested applicants to conclude on what management measures to take, including post-market environmental monitoring (PMEM). EU Member States expressed contradicting views on the need for post-market environmental monitoring under LL conditions. Some considered it mandatory, while others not. Since PMEM is related to risk management, the European Commission was consulted on this matter. Based on this consultation, the GMO Panel decided to no longer explicitly refer to risk management measures in the revised LL Scientific Opinion. Instead, reference is made to EFSA GMO Panel (2010) to determine the necessary data requirements for ERA of GM plants under LL situations, and under which conditions risk management measures may be required.

Public comments

Comments on the ERA-related sections were received from Europabio, the Government of Canada and Germany (BfN). Comments from EU Member States submitted during both consultations are addressed in the former section.

Europabio and the Government of Canada questioned the requirement to assess the likelihood of and risks associated with HGT under LL conditions, requesting scientific justification for not derogating from this requirement. Since currently no exposure threshold can be established at which HGT can be excluded, the GMO Panel recommends applicants to consider the exposure of microbial communities to recombinant DNA in the gastrointestinal tract of animals fed GM plant material or recombinant DNA in faecal material (manure and faeces) of these animals, and the potential for transgene transfer, and the environmental and human/animal health impacts thereof. This rationale has not been provided in the EFSA GMO Panel, 2017, because the mandate received from the European Commission asked the

GMO Panel to indicate which requirements of the Reg. (EU) 503/2013 are unnecessary, and give the underlying rationale only for such derogations.

3. Conclusions

All comments received on this guidance during the consultations (both the EU Member States and the following public consultation) were scrutinised and considered by the EFSA GMO Unit and by the EFSA GMO Panel through its *ad hoc* Working Group. Comments related to policy or risk management aspects were considered out of the remit of the GMO Panel and outside the scope of these consultations; therefore these are not addressed in this document. Comments under the GMO Panel remit were taken into account for the revision of the draft LL Scientific Opinion enhancing its scientific quality, usability and clarity (EFSA GMO Panel, 2017). The GMO Panel acknowledges the usefulness of the dedicated EU MS consultation step in the guidance development, and would like to thank all stakeholders and the general public for their interest and input to the EFSA work.

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Glossary

LL situation: a situation where a GMO (i.e. a GM plant and/or its derived products or food or feed use) not previously authorised in the EU is present at a level of maximum 0.9% per ingredient in any food and/or feed, due to adventitious or technically unavoidable circumstances. A LL situation can occur from point of entry into the EU, through the food/feed production processing chain, up to the food (or feed) portion consumed.

LL application: an application for a GMO (and derived food/feed) at low levels (i.e. under a LL situation), submitted under Reg. (EC) 1829/2003.

LL ingredient: the mixture of the GMO and the same plant species and/or derived product, at the predefined proportion of a maximum of 0.9% and 99.1% respectively.

Standard GMO application: an application submitted under Reg. (EC) 1829/2003 for food/feed, import and processing and assessed according to Reg. (EU) 503/2013 and relevant EFSA guidance documents (EFSA GMO Panel, 2010, 2011a).

Abbreviations

DNA	Deoxyribonucleic acid
EC	European Commission
ERA	Environmental Risk Assessment
EFSA	European Food Safety Authority
EU	European Union
GM	Genetically Modified
GMO	Genetically Modified Organism
LL	Low Level
LLP	Low Level Presence
OECD	Organisation for Economic Co-operation and Development
ORF	Open Reading Frame
RNAi	Ribonucleic acid interference
WG	Working Group

Appendix A – Documentation of the dedicated European Member States consultation

E-mail sent to Focal points by AF Secretariat - Advisory Forum and Scientific Cooperation Unit Communications and External Relations Department EFSA on 28/10/2016

Dear Focal Points,

As anticipated and detailed in my email below please find attached to this e-mail the material for the EU MS consultation on the draft guidance for the risk assessment of the low level presence of genetically modified plant material in imported food and feed under Regulation (EC) No 1829/2003 (LLP Guidance).

In detail you find:

1. the draft guidance document endorsed by the GMO Panel in .pdf format. This document is protected by a password, that will be sent to you in a separate e-mail. This document is intended for reading only, and not as a file for being commented directly by editorial tools.

2. a document in .docx format. This is the working document intended to be used to collect EU MS comments. The structure of this document fully mirrors the structure and the content of draft guidance above mentioned and it is meant to be used in conjunction with it. It is set to collect MS comments on the draft guidance in two ways: at line-by-line level; and at paragraphs level. Line-by-line commenting is intended to offer the possibility of punctual editorial changes on the draft guidance text; paragraph commenting is proposed to allow general comments on the paragraph(s) part of it. This document is also protected by a password, that will be sent to you in a separate e-mail.

As indicated, the consultation is intended to be completed in 6 weeks from the receipt of the material to delivery back to EFSA and therefore the deadline for comments is close of business Friday 9 December.

These documents are CONFIDENTIAL. Please share these with official Competent Authorities under Regulation (EC) No 1829/2003 only.

Should you have any request for clarification, please to not hesitate to contact Anna Lanzoni at Anna.LANZONI@efsa.europa.eu (in copy of this mail).

Anna is the coordinator of the activities of the ad hoc Working Group of GMO Panel dedicated to the development of a guidance on the Low Level Presence (LLP) of GMO.

SCIENTIFIC OPINION

ADOPTED: x Month 201X PUBLISHED: dd mmmm yyyy AMENDED: dd mmmm yyyy

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Appendix B – Draft Guidance provided to European Member States for dedicated consultation

Draft guidance for the risk assessment of the low level presence of genetically modified plant material in imported food and feed under Regulation (EC) No 1829/2003

EFSA Panel on Genetically Modified Organisms (GMO)

Abstract

This document provides draft guidance for the *a priori* risk assessment of the unintended, adventitious or technically unavoidable low level presence in food and feed of genetically modified (GM) plant material and derived products developed for third countries and not intended to be exported to Europe. The low level presence is defined to be maximum 0.9% of a GMO per ingredient. This document is a draft that will undergo two consultations aimed to collect contributions to enhance its quality and clarity. The first consultation will be dedicated to EU Member States; following this consultation process, the document will be revised and will undergo a public consultation where stakeholders, including EU Member States can contribute further to the guidance development.

Keywords: guidance document, GMO, low level presence, risk assessment, 1829/2003, food, feed

Requestor: European Commission

Question number: EFSA-Q-2015-00433

Correspondence: GMO@efsa.europa.eu

Panel members: Andrew Nicholas Birch, Josep Casacuberta, Adinda De Schrijver, Mikolaj Antoni Gralak, Philippe Guerche, Huw Jones, Barbara Manachini, Antoine Messean, Hanspeter Naegeli, Elsa Ebbesen Nielsen, Fabien Nogue, Christophe Robaglia, Nils Rostoks, Jeremy Sweet, Christoph Tebbe, Francesco Visioli and Jean-Michel Wal.

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The EFSA Journal is a publication of the European Food Safety Authority, an agency of the European Union.

43 # Summary

44 A summary will be provided after the public consultation.

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a) Introduction

a. Background and Terms of Reference as provided by the requestor

Genetically modified organisms (GMOs) and derived food and feed products are subject to a risk assessment and regulatory approval before they can enter the market in the European Union (EU). In this process, the role of the European Food Safety Authority (EFSA) is to independently assess and scientifically advise risk managers on any possible risk that the use of GMOs may pose to human's and animal's health and the environment. EFSA's scientific advice is elaborated by its GMO Panel with the scientific support of specific working groups and EFSA scientists.

Detailed guidance to assist applicants in the preparation and the presentation of GMO applications submitted under Regulation (EC) No 1829/2003 on GM food and feed was adopted by EFSA in 2006 (EFSA, 2006) and last updated in 2011 (EFSA GMO Panel, 2011). In April 2013, the European Commission subsequently adopted Regulation (EU) No 503/2013 on applications for authorisation of GM food and feed. Annex II of this Regulation lists the scientific requirements to be provided in accordance with Articles 5(3) and 17(3) of Regulation (EC) No 1829/2003. Article 5(2) of Regulation (EU) No 503/2013 further states that by way of derogation, a GMO application not satisfying all the requirements of Annex II may be submitted, provided that it is not scientifically necessary to supply such information.

Genetically modified (GM) plants and derived products, which are not necessarily intended to be exported to the EU, have been or are being developed for specific health or market needs in third countries. The presence of some of these GM products at low levels cannot completely be excluded in exports to the EU. Therefore, applicants might be willing to submit applications to request the authorisation of the unintended presence of low levels of GMOs to the EU market.

In 2009, *Codex Alimentarius* issued guidelines for the food safety assessment in situations of low level presence (LLP) of recombinant DNA plant material in food (Codex Alimentarius, 2009, Annex 3).

In 2015, the European Commission mandated EFSA, in accordance with Article 29 of Regulation (EC) No 178/2002, to advise whether or not all requirements of Annex II to Regulation (EC) No 503/2013 are necessary to conclude on the safety of applications covering the unintended presence of GMOs in food and feed at the adventitious or technically unavoidable presence of 0.9% or below. If not, EFSA is required to indicate which requirements are unnecessary and to give the underlying rationale. Following a request for clarification by EFSA[4], the European Commission further clarified[5] that:

- the GMO Panel LLP guidelines should be applicable to low level presence of GM products, independently of the existence or not of a third country risk assessment;
- LLP applications should only concern GM products developed for specific health or market needs in third countries not intended for the EU market; therefore should not be submitted for GM products for which a full scope application was previously submitted;
- both exposure scenarios i.e. through commodities or foods consumed whole and undiluted should be considered under the EFSA LLP guidance;
- a cumulative risk assessment should be performed in case of similar traits present in different LLP applications;
- for stacks, the same principles as those referred to in Regulation (EC) No 503/2013 will apply;
- for stacks, the implementation of the 0.9% threshold should follow the same rules as for labelling purposes i.e. the threshold applies to individual events.

[4] Ref. BU/PB/EW/AL/shv(2014) - out - 11201195
[5] Ref. Ares(2015)1362776 – 27/03/2015

b. Interpretation of the Terms of Reference

Following an exchange with the European Commission, it was further clarified that a LLP application covers a request for the authorisation of a GMO (i.e., a GM plant and derived food and feed products, in alignment with the scope of Regulation (EC) No 1829/2013[6]) present at a level of maximum 0.9% per ingredient in any food and/or feed containing the same ingredient, due to its adventitious or technically unavoidable presence.

In the context of this guidance, "ingredient" is the mixture of the GMO and the same type of plant and/or derived product at the predefined proportions of maximum 0.9% and 99.1% respectively.

It is presupposed that in a LLP application the GMO is present at a level of maximum 0.9% per ingredient from point of entry into the EU, through the food/feed production and processing chain, up to the food (or feed) portion (or ration) consumed.

Therefore the following situations are not in the remit this guidance:

- large sized fruit/vegetables consumed as such (e.g. papaya, potato); these would constitute either a full portion (or ration) or part of a portion (or ration) resulting in an exposure higher than 0.9% of consumers (or animals) to that GMO;
- the 0.9% of the GMO is exceeded in the ingredient at any given step of the production chain, resulting in localised higher concentrations to which consumers (or animals) may be exposed.

The decision on whether a given GMO can constitute a LLP application is a risk management issue, and is therefore not in the remit of this guidance.

In its mandate, the European Commission referred to Codex Alimentarius for the assessment of LLP GMO situations (Codex Alimentarius, 2009, Annex 3) as a relevant document to consider during the development of this guidance. The GMO Panel took into consideration principles and requirements outlined in Codex Alimentarius (Codex Alimentarius, 2009, Annex 3), and identified some differences between the Codex approach on LLP and the terms of reference of this mandate. These differences are listed in Box 1.

Box 1: Differences in principles and requirements of Codex Alimentarius (Codex Alimentarius, 2009, Annex 3) and the terms of reference of the LLP mandate of the European Commission

Scope

- Codex Alimentarius (Codex Alimentarius,2009, Annex 3) provides an approach for the risk assessment of food. Instead the GMO Panel guidance on LLP is intended to cover the risk assessment of food and feed, in accordance with Regulation (EC) No 1829/2003.
- Codex Alimentarius (Codex Alimentarius, 2009, Annex 3) considers only the dietary exposuReg. In contrast, the GMO Panel guidance on LLP is requested to cover all possible routes of exposure to consumers/animals in addition to the diet, in accordance with Regulation (EC) No 1829/2003.
- Codex Alimentarius (Codex Alimentarius, 2009, Annex 3) is applicable to LLP situations either before or after these have occurred (*a priori* and *a posteriori* assessment). Instead, the GMO Panel guidance on LLP is intended to support only the risk assessment of LLP situations before these occur (*a priori* assessment).
- In contrast to Codex Alimentarius (Codex Alimentarius,2009, Annex 3), the GMO Panel guidance on LLP includes environmental risk assessment (ERA) considerations, as the Implementing Regulation (EU) No 503/2013 requires the ERA of GMOs or food and feed containing, or consisting of, GMOs to be performed according to the principles outlined in Annex II to Directive 2001/18/EC of the

[6] Regulation (EC) No 1829/2003. Chapter II Genetically modified food, Article 3. Scope. a) GMOs for food use; (b) food containing or consisting of GMOs; (c) food produced from or containing ingredients produced from GMOs; Chapter III Genetically modified feed: Article 15. Scope. (a) GMOs for feed use; (b) feed containing or consisting of GMOs; (c) feed produced from GMOs.

European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of GMOs and repealing Council Directive 90/220/EEC, and the applicable GMO Panel guidance (EFSA GMO Panel, 2010).

Pre-requisites to identify an LLP situation

- Codex Alimentarius (Codex Alimenatrius, 2009, Annex 3) recognises that an increased number of GMOs is undergoing authorisation and commercialisation at different rates in different countries (asymmetric authorisations). As a consequence, LLP situations may occur in importing countries where the GMO has not yet been assessed according to Codex Alimentarius (2009). The Codex Alimentarius on LLP (Codex Alimentarius, 2009, Annex 3) stipulates that a GMO can only be considered for LLP risk assessment if it has undergone a risk assessment according its guidelines in a third country. In contrast, this mandate requires the GMO Panel to set guidance for LLP applications for any GMO, independently of the existence of a third country risk assessment.

Threshold definition

- Codex Alimentarius (Codex Alimentarius, 2009, Annex 3) proposes a risk assessment strategy for LLP situations based on the expectation of a low exposure to the GMO, but does not define which amount of GMOs constitutes a LLP situation. In the GMO Panel LLP guidance instead the threshold for LLP situations has been defined by European Commission as a level of maximum 0.9% of the GMO per ingredient in any food or feed containing the same ingredient.

Possible dietary exposure scenarios in case of LLP situations and risk assessment strategies

- Codex Alimentarius (Codex Alimentarius, 2009, Annex 3) distinguishes two categories of food possibly subject of LLP situations; and associates these to two distinct dietary exposure scenarios:
    - food commodities small in particle size (e.g. grains, beans); these would constitute the most frequent LLP situation. In this case, any inadvertently commingled GM material is expected to be present at low level in any individual serving of food, based on various assumptions (e.g. commodities are derived from multiple plants, are sourced from multiple farms, and/or are commingled during the food chain processing);
    - food commodities large in particle size (e.g. tomato, papaya), and commonly consumed whole; these are expected to constitute a less frequent LLP situation. In this case each particle of such food might constitute an entire consumed portion of the GMO.

  The risk assessment strategy and methodology advocated by Codex Alimentarius (Codex Alimentarius, 2009, Annex 3) differs for the two dietary exposure scenarios, with compositional data (limited to key toxicants and allergens) required only for the second scenario. Instead this GMO Panel guidance on LLP is requested to cover an exposure scenario for which a GMO is present at a level of maximum 0.9% per ingredient in the final food or feed. Food commodities of large particle size commonly consumed whole are therefore excluded from the scope of the GMO Panel guidance on LLP.

b) Data and Methodologies

a. Data

In delivering this guidance, the GMO Panel took into account the data requirements outlined in Regulation (EC) No 1829/2003, Regulation (EU) No 503/2013, Codex Alimentarius (2009) and EFSA GMO Panel, 2010.

b. Methodologies

EFSA established an *ad hoc* Working Group (LLP WG) to address the mandate and develop the risk assessment of the low level presence of genetically modified plant material in imported food and feed

under Regulation (EC) No 1829/2003. In accordance with the Terms of Reference of the mandate, the LLP WG scrutinised which data requirements of Annex II of Regulation (EU) No 503/2013 are necessary to conclude on the safety of GMOs present in food and feed and derived products at the adventitious or technically unavoidable level of maximum 0.9% per ingredient; possible derogations from existing requirements were identified, and justified reasons provided.

In order to adequately take EU Member States and stakeholder comments into account, two consultations are organised in a stepwise manner. The first consultation will be dedicated to EU Member States. Following this consultation process, the document will be revised and will undergo a second public consultation where all stakeholders, including EU Member States, can contribute further to the development of the guidance document. As an outcome, a technical report will be published in the EFSA website together with the adopted guidance document.

c) Assessment

a. Introduction

i. Key definitions

Key definitions applicable to this guidance document are given below:

- **Low level presence (LLP)**: a situation where a GMO (i.e. a GM plant and/or its derived products for food or feed use, referred to hereafter as GMO) not previously authorised in the EU, is present at a level of maximum 0.9% per ingredient in any food and/or feed containing the same ingredient, due to adventitious or technically unavoidable reasons. A LLP situation can occur from point of entry into the EU, through the food/feed production processing chain, up to the food/feed portion consumed.
- **Ingredient:** the mixture of the GMO subject of a LLP application and the same type of plant and/or derived product at the predefined proportions of maximum 0.9% and 99.1% respectively.
- **LLP application**: an application prepared by an applicant in accordance to GMO Panel guidance on LLP.
- **Standard application**: an application submitted under Regulation (EC) No 1829/2003, for food/feed, import and processing and assessed according to Regulation (EU) No 503/2013 and relevant EFSA guidance documents (EFSA GMO Panel, 2010, 2011).

ii. Scope of the guidance

This document provides guidance for the risk assessment of LLP situations within the framework of Regulation (EC) No 1829/2003 and according to Regulation (EU) No 503/2013. In particular, this document is intended to assist applicants in the preparation of LLP applications by indicating which technical requirements of Annex II of Regulation (EU) No 503/2013 are necessary and which are not, in this case providing justification, in order to conclude on the safety of a GMO in the scope of a LLP application.

Definitions and requirements of Regulation (EC) No 503/2013 other than those indicated in its Annex II apply to this guidance.

This guidance does not cover GMOs for cultivation purposes; GM microorganisms; GM animals; GMOs for non-food/feed uses, as these are not in the scope of Regulation (EC) No 1829/2003.

This guidance does not consider issues related to risk management (traceability, labelling, and coexistence). Socio-economic and ethical issues are also outside the scope of this guidance.

iii. Risk assessment considerations for LLP situations compared to standard GMO applications

The risk assessment strategy followed for standard GMO applications is driven by the comparative assessment principle, which aims to demonstrate that the GMO is as safe and as nutritious as traditionally cultivated crops (and derived products) with a history of safe use for consumers and/or animals (Codex Alimentarius, 2009; EFSA GMO Panel, 2011). Within this comparative frame, a standard GMO application is assessed assuming the possibility of a 100% replacement of the corresponding conventional crop and derived products (worst-case scenario). To achieve this objective, the GMO Panel identified scientific requirements and deployed a wide range of tools and methods (EFSA GMO Panel, 2011), which have been incorporated in Annex II of Regulation (EU) No 503/2013 by the European Commission and EU Member States. These requirements are followed in standard GMO applications submitted under Regulation (EC) No 1829/2003.

In a LLP situation as defined in this guidance, exposure to the GMO will be at maximum 0.9% per ingredient. This pre-defined threshold implies a lower exposure to a GMO than that foreseen in standard GMO applications. The GMO Panel considers that the adventitious or technically unavoidable reasons leading to an LLP situation do not exclude the possibility of repeated exposure of consumers/animals. Therefore, both single and repeated exposure scenarios are considered.

Based on the above considerations and in alignment with the Codex Alimentarius on LLP (Codex Alimentarius, 2009, Annex 3), the GMO Panel considers that derogation from and adaptation of certain requirements for the risk assessment of standard GMO applications are possible in LLP situations. These are discussed in Section 3.2 of this guidance.

b. Scientific requirements for the risk assessment of LLP applications submitted under Regulation (EC) No 1829/2013

Introduction (Annex II. I)

This paragraph applies.

d) Definitions (Annex II. I, 1)

The GMO Panel considered the requirements of the risk assessment of GM plants and derived food and feed (EFSA GMO Panel, 2011) and endorsed by Regulation (EU) No 503/2013; and recommends adaptations and derogations to Annex II for LLP applications as described below.

e) Specific considerations (Annex II. I, 2)

f) Insertion of marker genes and other nucleic acid(s) sequences not essential to achieve the desired tract (Annex II. I, 2.1)

This paragraph applies.

g) Risk assessment of genetically modified food and feed containing stacked transformation events (Annex II. I, 2.2)

In accordance with the term of reference of this mandate, the same principles as those referred to in Regulation (EC) No 503/2013 apply for genetically modified food and feed containing stacked transformation events (stacks), for which the risk assessment includes an assessment of the following aspects:

a. stability of the transformation events;

b. expression of the transformation events;

c. potential synergistic or antagonistic effects resulting from the combinations of the transformation events in accordance with sections 1.4 (Toxicology), 1.5 (Allergenicity) and 1.6 (Nutritional assessment).

In Regulation (EC) No 503/2013, data requirements to address the above principles are provided in specific molecular characterisation and food and feed sections. Applicability, adaptation or possible derogation to these requirements are provided in the specific sections of this guidance.

Requirements laid down in Regulation (EC) No 503/2013 as regards the assessment of sub combinations in stacked events apply in LLP applications.

Scientific requirements (Annex II. II)

h) Hazard identification and characterisation (Annex II. II, 1)

i) Information relating to the recipient or (where appropriate) to parental plants (Annex II. II, 1.1)

All requirements described in paragraph 1.1 of the Annex II of Regulation (EU) No 503/2013 apply.

j) Molecular characterisation (Annex II. II, 1.2)

The molecular characterisation of the GM plant serves two purposes: first it allows the characterisation of the event, and second, it is the first step to detect potential unintended effects linked to the genetic modification.

In the case of LLP situations, the exposure to the GMO is defined to be at a maximum 0.9% for any specific ingredient, allowing derogation from some of the molecular characterisation data requirements specified in Annex II of Regulation (EU) No 503/2013. In the following sections, data requirements that do not apply or apply on a case-by-case basis for the risk assessment of a GMO in a LLP situation and the scientific rationale for derogation are described.

k) Information relating to the genetic modification (Annex II. II, 1.2.1)

Data requirements of this section serve to characterise the genetic modification(s) of the plant. Therefore, all requirements described in paragraph 1.2.1 of Annex II of the Regulation (EU) No 503/2013 apply.

l) Information relating to the genetically modified plant (Annex II. II, 1.2.2)

Paragraph 1.2.2.1. General description of the trait(s) and characteristics which have been introduced or modified

Data requirements within this paragraph of Annex II of the Regulation (EU) No 503/2013 serve to characterise the genetic modification(s) and therefore apply.

Paragraph 1.2.2.2. Information on the sequences actually inserted/deleted

All requirements within this paragraph of Annex II of the Regulation (EU) No 503/2013 serve to characterise the genetic modification(s) and therefore apply.

Paragraph 1.2.2.3. Information on the expression of the insert(s)

Annex II of the Regulation (EU) No 503/2013 describes the requirements as regards the information on the expression of the insert(s) to demonstrate whether the inserted/modified sequence results in the intended changes in the GM plant, and to characterise the potential unintended expression of new Open Reading Frames (ORFs) identified, as indicated in paragraph 1.2.2.2 of Annex II of the Regulation (EU) No 503/2013, as raising a safety concern. Whereas the description of the methods used for expression analyses as well as protein expression data related to the conditions in which the crop is grown [points 1.2.2.3(a) and (e) respectively of Annex II of the Regulation (EU) No 503/2013] should apply in order to characterise the GM plant, only the expression levels from those part(s) of the plant used for food and feed purposes, are considered necessary to complete the risk assessment. Therefore points 1.2.2.3(b) (information on developmental expression of the insert during the life cycle of the plant); and 1.2.2.3(c) (parts of the plant where the inserted/modified sequences are

expressed) of Annex II of the Regulation (EU) No 503/2013 do not apply for the risk assessment of GM plants in an LLP situation.

Point 1.2.2.3 (d) of Annex II of the Regulation (EU) No 503/2013, requiring the analysis of potential unintended expression of new ORFs identified under point 1.2.2.2(f), which raise a safety concern in an LLP situation, applies.

In the case of LLP applications of stacked transformation events, the GMO Panel considers that the likelihood for changes in the expression levels of the newly inserted sequences as a consequence of interactions between the transformation events and in comparison to the assessed single transformation events, that would be large enough to raise safety concerns is negligible in a LLP situation. Hence it is not considered necessary to provide data on the expression levels of the newly inserted sequences for stacked transformation events. Therefore, point 1.2.2.3(f) of the Annex II of Regulation (EU) No 503/2013 is not routinely required.

On a case-by-case basis, and when the nature or the characterisation of the transformation events combined in a stack LLP GMO suggests an interaction that may result in changes of the expression levels of the newly inserted sequences large enough to raise safety concerns in a LLP situation, this data should be provided.

Paragraph 1.2.2.4. Genetic stability of the insert and phenotypic stability of the genetically modified plant

Given that a LLP situation only applies for the presence of GMO product(s) in food and feed due to the adventitious or technically unavoidable presence below or equal to 0.9 %, potential risks associated with instability of the event are considered negligible and it is therefore not considered necessary to provide information on the genetic stability of the insert and the phenotypic stability of the trait. Therefore, the data requirements described under paragraph 1.2.2.4. of Annex II of Regulation (EU) No 503/2013 do not apply.

Paragraph 1.2.2.5. Potential risk associated with horizontal gene transfer

All requirements within this paragraph of Annex II of the Regulation (EU) No 503/2013 apply.

m) Conclusions of the molecular characterisation (Annex II. II, 1.2.3)

Based on considerations from the above paragraphs, the conclusion should contain information on of the molecular characterization of the event as well as indications whether the genetic modification(s) raises safety concerns considering the scope of a LLP application. Derogation from Annex II of Regulation (EC) No 503/2013 applies for data requirements described under points (b) and (c) of paragraph 1.2.2.3 (*Information on the expression of the insert[s]*) as well as for data requirements of paragraph 1.2.2.4 (*Genetic stability of the insert and phenotypic stability of the genetically modified plant*). On a case-by-case basis, requirements under point (f) of paragraph 1.2.2.3 regarding the data for the expression levels of the newly inserted sequences for stacked transformation events may be considered necessary.

n) Comparative analysis (Annex II. II, 1.3)

The methodological approach to conduct the comparative assessment on GMOs is detailed in paragraph 1.3 of Annex II of Regulation (EU) No 503/2013, including criteria for the selection of appropriate comparator, experimental design of field trials and statistical analysis of results, selection of endpoints to measure, and effects of processing.

Since in LLP situations the level of exposure of consumers/animals to the GMO is defined to be at a maximum 0.9% per ingredient, in order for the GMO fraction of the ingredient to have an impact on the nutritional or safety characteristics of the ingredient as a whole, it is necessary that the level of its compound(s) largely differs from that of the plant and/or derived product constituting the remaining part of the ingredient. Table 1 illustrates examples of the impact on the level of a compound in an ingredient by the GMO, which shows differences in the level of this compound compared to the plant (and/or derived products) constituting the remaining part of the ingredient. It is noted that a decrease

in the level of a compound in the GMO translates in a decrease in the ingredient never larger than 0.991 folds respect to the ingredient without the GMO.

a) Impact of the presence of a GMO on the level of a compound in the ingredient.

Ratio between the level of compound in the GMO and in the other plant (and/or derived product)[(a)]	**Impact on the level of compound in the ingredient[(b)]**
0 X	0.991 X
0.001 X	0.991009 X
0.01 X	0.99109X
0.1 X	0.9919X
1 X	**1 X**
10 X	1.081 X
20 X	1.171 X
50 X	1.441 X
90 X	1.801 X
100 X	1.891 X
200 X	2.791 X

(a) Ratio calculated as X fold change between the GMO and the plant (and/or derived product) constituting the remaining part of the ingredient.
(b) Impact calculated as X fold change respect to the ingredient without the GMO.

Large variations in the level of compound(s) in GMOs are known to occur in the case of nutritionally enhanced crops, including GMOs with output traits developed to improve nutrition (e.g. Perez-Massot et al., 2013).

The GMO Panel is of the opinion that differences in the level of a compound in the GMO large enough to impact the composition of the ingredient are unlikely to occur and considers that comparative compositional analysis is not necessary, recommending derogation from paragraph 1.3 of Annex II of Regulation (EU) No 503/2013 requirements, unless:

- the intended trait targets the composition of the GMO;
- a specific hypothesis can be formulated, as in the case of unintended compositional changes anticipated by the precedent molecular characterisation;
- compounds are *de novo* expressed in the GMO.

In these cases, the GMO Panel considers that the comparative compositional analysis is necessary to confirm and quantify differences, to perform an exposure assessment and to provide information relevant for cumulative risk assessment. In these cases, adaptations to requirements laid down in paragraph 1.3 of Annex II of Regulation (EU) No 503/2013 (paragraphs 1.3.1, 1.3.2, 1.3.3 and 1.3.4) are possible and described below.

o) Choice of conventional counterpart and additional comparators (Annex II. II, 1.3.1)

In the case compositional comparative assessment of GMO is necessary in a LLP application, requirements laid down in this paragraph apply, including requirements regarding stacked transformation events.

p) Experimental design and statistical analysis of data from field trials for comparative analysis (Annex II. II, 1.3.2)

Paragraph 1.3.2.1. Description of the protocols for the experimental design

Principles of experimental design

In the case compositional comparative analysis is necessary in a LLP application, studies for the compositional characterisation should be conducted under conditions where the expected change(s) in the composition of the GMO are observed (based on available knowledge), in order to collect analytical data for further risk assessment considerations. Criteria for the selection of specific study conditions (e.g. field trials or greenhouse studies) should be described and scientifically justified.

When required, the comparative compositional analysis should include a difference test, in accordance with requirements laid down in Regulation (EU) No 503/2013. Instead, derogation is possible for the test of equivalence, aimed to verify if the GM plant is equivalent to the non-GM reference varieties. In fact, the estimation of equivalence limits to establish natural ranges of variability for compositional endpoints is not needed in case of LLP applications, where the aim is to confirm and quantify differences versus the conventional counterpart and support following risk assessment (i.e. exposure assessment and cumulative risk assessment).

Specific protocols for experimental design

In derogation to requirements laid down in Regulation (EU) No 503/2013, in case the comparative assessment is performed in a field trial, the number of sites to support the comparative assessment in LLP applications could be less than the eight prescribed. One site could be sufficient, provided this is adequate to confirm and quantify differences in the composition of the GMO and to perform subsequent risk assessment steps (i.e. exposure assessment and cumulative risk assessment). Similarly, in case the comparative assessment is performed under greenhouse conditions, justifications for the specific conditions selected should be provided to demonstrate adequacy to confirm and quantify differences in the composition of the GMO and to perform subsequent risk assessment steps (i.e. exposure assessment and cumulative risk assessment).

All the other requirements, including the inclusion of a sufficient number of replicates to obtain reliable analytical compositional data, apply to both field trials and greenhouse studies.

Paragraph 1.3.2.2. Statistical analysis

The requirements laid down in this paragraph apply for LLP applications, with derogations as regards the equivalence test (as explained above).

q) Selection of material and compounds for analysis (Annex II. II, 1.3.3)

The requirements laid down in this paragraph apply. In particular, as in standard applications, the comparative analysis should be conducted on raw agricultural commodities, with additional analysis of processed products conducted where appropriate on a case-by-case basis.

r) Comparative analysis of composition (Annex II. II, 1.3.4)

In derogation to the requirements laid down in this paragraph of Regulation (EU) No 503/2013, in LLP applications the analysis of the composition may not include a range of compounds (i.e at least proximates, key macro and micro-nutrients, ant nutritional compounds, natural toxins and already identified allergens, as referred to in plant-specific OECD Consensus Documents). The selection of compounds should be targeted to address the specific hypothesis triggering the need for compositional data; justification on the choice of the compounds should be provided.

s) Comparative analysis of agronomic and phenotypic characteristics (Annex II. II, 1.3.5)

The inclusion of agronomic and phenotypic characteristics endpoints in the comparative assessment studies laid down in Regulation (EU) No 503/2013 is intended to identify unintended effects related to the genetic modification and to address plant biology and agronomic traits. Considering that the main objective of comparative analysis in the context of LLP situations is to confirm and quantify compositional differences versus the conventional counterpart, a comparative analysis of agronomic and phenotypic characteristics to address the above requirements is not considered mandatory in the context of LLP situations, representing a possible derogation to Annex II requirements of Regulation (EU) No 503/2013.

t) Effects of processing (Annex II. II, 1.3.6)

The requirement laid down in this paragraph of Regulation (EU) No 503/2013 regarding the assessment of the possible impact of the processing and/or preserving technologies on the characteristics of the derived products of the GMO applies in LLP applications.

In the case comparative compositional assessment is required (see above Comparative analysis, Annex II. II, 1.3), in alignment with the requirements of Regulation (EC) No 503/2013 processed products may be assessed together with the assessment of the genetically modified plant or separately, and it is applicant's responsibility to provide the scientific rationale for the risk assessment of these products. On a case by case basis, the submission of additional experimental data should be considered by the applicant.

On a case-by-case basis, in alignment with the requirement laid down in this paragraph of Regulation (EU) No 503/2013 and depending on the nature of the newly expressed protein(s), the extent to which the processing steps lead to concentration or elimination, denaturation and/or degradation of these proteins in the final product should be determined.

u) Comparative assessment studies performed under non-EU regulatory frames: applicability in LLP applications.

In derogation to Regulation (EU) No 503/2013, the GMO Panel considers that comparative assessment studies that have been conducted in accordance to Codex Alimentarius, 2009 could support the comparative compositional assessment in LLP situations, provided that the relevant compositional endpoints, i.e. of interest on the basis of the hypothesis triggering the analysis, or addressing the output trait, have been reliably measured; and that all Codex Alimentarius, 2009 principles and requirements have been duly fulfilled.

In contrast, compositional analysis studies not aligned to requirements of Codex Alimentarius, 2009 are not considered appropriate by the GMO Panel.

v) Combined transformation events stacked by conventional crossing

On a case-by-case basis, when the expectation of interactions between the combined transformation events stacked by conventional crossing leading to differences in the composition of GMO possibly impacting the composition of the ingredient exists, experimental data is needed.

w) Conclusions (Annex II. II, 1.3.7)

Based on considerations from the above paragraphs, the conclusions of the compositional comparative assessment in LLP applications should be adapted with respect to Annex II of Regulation (EU) No 503/2013 as follows.

The applicant should state the rationale for conducting the compositional assessment, or the justification why it was not conducted.

In the case a comparative compositional analysis has been conducted, the applicant should indicate if the outcome of the targeted compositional analysis confirms the expectations and if it allows to properly quantify differences versus the conventional counterpart, to perform an exposure assessment and to provide information relevant for cumulative risk assessment; or if further investigation is needed.

Relevant differences in the agronomic and phenotypic characteristics of the GM plant versus the conventional counterpart should be provided on a case-by-case basis, depending upon ERA-driven hypothesis.

In the case of stacks, when an expectation of interactions between the combined transformation events stacked by conventional crossing leading to differences in the composition of GMO possibly impacting the composition of the ingredient exists, experimental data is needed.

x) Toxicology (Annex II. II, 1.4)

Annex II of the Regulation (EU) No 503/2013 (paragraph 1.4) states that the toxicological impact of any change on the whole GM food/feed resulting from the genetic modification such as the introduction of new genes, gene silencing or over-expression of an endogenous gene shall be assessed.

More specifically, Annex II of the Regulation (EU) No 503/2013 requires assessing:

- the toxicity of individual compounds, represented by newly expressed proteins (paragraphs 1.4.1 and 1.4.5) and/or new constituents (paragraphs 1.4.2 and 1.4.5); and by possible altered levels of food and feed constituents (paragraphs 1.4.3 and 1.4.5);
- the toxicity of the whole genetically modified food and feed (paragraphs 1.4.4 and 1.4.5).

y) Testing of newly expressed proteins (Annex II. II, 1.4.1)

Requirements laid down in paragraph 1.4.1 of Annex II of Regulation (EU) No 503/2013 apply.

z) Testing of new constituents other than proteins (Annex II. II, 1.4.2)

Requirements laid down in paragraph 1.4.2 of Annex II of Regulation (EU) No 503/2013 apply.

aa) Information on altered levels of food and feed constituents (Annex II. II, 1.4.3)

The GMO Panel considers that the requirements laid down in paragraph 1.4.3 for the toxicological assessment of altered levels of natural constituent(s) [i.e. compound(s) constitutively expressed in the GMO] in the GMO apply only if the expected changes in the level of natural constituent(s) have been confirmed (section Comparative assessment). In this case, the conclusion of the assessment should indicate whether the information on the natural constituent(s) provides indications of potential adverse effects, in particular whether and at which doses adverse effects were identified in specific studies (paragraph 1.4.5 *Conclusions*).

bb) Testing of whole genetically modified food and feed (Annex II. II, 1.4.4)

The GMO Panel considers that the requirements of testing of whole GM food and feed laid down in paragraph 1.4.4 of Annex II of Regulation (EU) No 503/2013 need adaptation, as detailed in the below paragraphs.

Paragraph 1.4.4.1. 90-day feeding study in rodents with whole genetically modified food and feed

The GMO Panel considers that, if no specific hypothesis has been identified by preceding analysis or information, a 90-day study in rodents with the whole GM food and feed does not provide information on the toxicological properties of the whole food feed relevant in a LLP situation, and the requirement of such a study studies does not apply under LLP situations.

If a specific hypothesis requiring a 90-day study on the whole GM food/feed in rodents has been identified by preceding analysis or information, requirements laid down in Annex II of Regulation (EU) No 503/2013 apply.

Paragraph 1.4.4.2. Animal studies with respect to reproductive and developmental toxicity testing.

Requirements laid down in paragraph 1.4.4.2 of Regulation (EU) No 503/2013 apply.

Paragraph 1.4.4.3. Animal studies to examine the safety and the characteristics of genetically modified food and feed.

Requirements laid down in paragraph 1.4.4.3 of Regulation (EU) No 503/2013 apply.

Paragraph 1.4.4.4. Interpretation of relevance of animal studies.

Requirements laid down in paragraph 1.4.4.4 of Regulation (EU) No 503/2013 apply.

cc) Conclusions of the toxicological assessment (Annex II. II, 1.4.5)

This paragraph applies. The GMO Panel notes that the conclusions of the toxicological assessment do not routinely include considerations from the 90-day studies in rodents on the whole food/feed.

dd) Allergenicity (Annex II. II, 1.5)

Considerations and requirements relative to the allergenicity assessment of the GMO of Annex II to Regulation (EU) No 503/2013 refer to:

- assessment of allergenicity of newly expressed proteins and adjuvanticity (paragraphs 1.5.1, 1.5.3 and 1.5.4);
- assessment of allergenicity of the GM food or feed (paragraphs 1.5.2 and 1.5.4).

ee) Assessment of allergenicity of newly expressed proteins (Annex II. II, 1.5.1)

Requirements laid down in paragraph 1.5.1 of Annex II of Regulation (EU) No 503/2013 apply.

ff) Assessment of allergenicity of the genetically modified food or feed (Annex II. II, 1.5.2)

The GMO Panel considers that due to the 0.9% contribution of the GMO to the ingredient, derogation from requirements laid down in paragraph 1.5.2 of Annex II of Regulation (EU) No 503/2013 is possible, unless large changes in the level of endogenous allergens in the GMO have been confirmed (section Comparative assessment). In this case, requirements from this paragraph apply.

gg) Assessment of adjuvanticity (Annex II. II, 1.5.3)

Requirements laid down in paragraph 1.5.3 of Annex II of Regulation (EU) No 503/2013 apply.

hh) Conclusions of the allergenicity assessment (Annex II. II, 1.5.4)

The requirements for the conclusions of the allergenicity assessment laid down in Annex II of Regulation (EU) No 503/2013 applies as regards the novel proteins (point a). Derogation is foreseen for the assessment of the allergenicity of GM food or feed, which should be conducted if the large changes in endogenous allergens occur. In this case, and if large changes in endogenous allergens are identified compared to the conventional counterpart, the conclusion of the assessment should indicate whether the GM food or feed is likely to be more allergenic than its appropriate comparator under the specific circumstances of a LLP application.

ii) Nutritional assessment (Annex II. II, 1.6)

jj) Objectives of the nutritional assessment (Annex II. II, 1.6.1)

In standard applications, the nutritional assessment is intended to address two objectives:

1) demonstration that the introduction of the GM food and feed into the market is not nutritionally disadvantageous to humans or animals, respectively;

2) demonstration that unintended effects of the genetic modification that were identified or that may be assumed to have occurred based on the preceding molecular, compositional or phenotypic analysis have not adversely affected the nutritional value of the GM food and feed.

The GMO panel considers that these objectives are not fitting into the scope of a LLP application, which is limited to the unavoidable, adventitious presence of 0.9% of a GMO per ingredient and not covering the introduction in the EU market of that GMO. Only if the GMO subject of a LLP application affects the level of a (some) compound(s) in the ingredient, and if this has been confirmed by the comparative compositional analysis (see Comparative assessment), a nutritional assessment is needed. This should focus on the evaluation of the nutritional impact of the GMO at 0.9% incorporation in an ingredient after acute and repeated exposuReg.

For stacked transformation events combined by conventional crossing, on a case by case basis, the applicant should provide an assessment of the potential changes in nutritional value that may arise from synergistic or antagonistic effects of the gene products including compositional changes, if these impact the ingredient containing the stacked GMO.

kk) Points to consider for the nutritional assessment of genetically modified food and feed. (Annex II. II, 1.6.2)

In the case a nutritional assessment is deemed necessary, requirements laid down in paragraph 1.6.2 of Regulation (EC) No 503/2013 apply.

ll) Nutritional studies of genetically modified food (Annex II. II, 1.6.3)

In the case a nutritional assessment is deemed necessary, requirements laid down in paragraph 1.6.3 of Regulation (EC) No 503/2013 apply.

mm) Nutritional studies of genetically modified feed (Annex II. II, 1.6.4)

In the case a nutritional assessment is deemed necessary, requirements laid down in paragraph 1.6.4 of Regulation (EC) No 503/2013 apply.

nn) Conclusion of the nutritional assessment (Annex II. II, 1.6.5)

The conclusion of the nutritional assessment of a GMO under the circumstances of a LLP application should indicate if the GMO at 0.9% incorporation in an ingredient has a nutritional impact on the ingredient after acute and repeated exposuReg.

oo) Standardised guidelines for toxicity tests (Annex II. II, 1.7)

Paragraph 1.7 of Annex II of Regulation No 503/2013 applies.

pp) Exposure assessment — Anticipated intake/extent of use (Annex II. II, 2)

The exposure to a GMO under the circumstances of LLP applications is defined to be maximum 0.9% per ingredient, under acute or repeated intake scenarios. The GMO Panel considers that the exposure assessment requirements laid down in Annex II. II, 2 of Regulation (EU) No 503/2013 should be based on this predetermined exposure level and adapted accordingly.

In particular exposure considerations should be focused on newly produced components (e.g. newly expressed proteins) and on natural constituent(s) showing levels altered enough to impact the nutritional or safety characteristics of the ingredient (see Comparative assessment).

qq) Risk Characterisation (Annex II. II, 3)

The GMO Panel considers that adaptations and derogations to requirements of Annex II of Regulation (EU) No 503/2013 on risk characterisation are needed for LLP applications, considering the 0.9% contribution of the GMO to the ingredient. Requirements regarding demonstration of completeness, quality and use of information and estimation of uncertainties apply.

rr) Issues to be considered for risk characterisation (Annex II. II, 3.2)

ss) Molecular characterisation (Annex II. II, 3.2.1)

Paragraph 3.2.1 applies.

tt) Comparative analysis (Annex II. II, 3.2.2)

The goal of the comparative analysis in the context of an LLP application is to confirm and quantify changes expected in the composition of the GMO, which can impact the safety/nutritional profile of the ingredient when the GMO is mixed at the maximum level of 0.9%. The applicant shall demonstrate that the compositional analysis with respect to the relevant compositional characteristics of the GMO has been carried out in accordance with the indications presented in this guidance (section Comparative assessment).

uu) Food and feed safety in relation to intake (Annex II. II, 3.2.3)

This aspect of the risk characterisation should consider the data generated to estimate possible short- and long-term risks to human or animal health associated with the consumption of food/feed containing the ingredient with the GMO matter of an LLP application. Requirements described in paragraph 3.2.3 apply, providing these are adapted to the specific context of LLP.

Considering that LLP applications are intended to support the authorisation of GM food/feed at maximum 0.9% level, no post market monitoring is foreseen.

vv) The result of risk characterisation (Annex II. II, 3.3)

In accordance with these requirements of Annex II of Regulation (EU) No 503/2013, the applicant should ensure that the final risk characterisation clearly demonstrates that the GMO does not impact the safety and nutritional characteristics of the ingredient (where it is unavoidably, adventitiously present at maximum 0.9%) to such an extent that the normal consumption of the ingredient would be nutritionally disadvantageous for the consumer or for animals.

The applicant should clearly indicate what assumptions have been made during the risk assessment in order to predict the probability of occurrence and severity of adverse effect(s) in a given population, and the nature and magnitude of uncertainties associated with establishing these risks.

Information justifying the inclusion or not of a proposal for labelling in the application is not required, considering the boundaries of the scope of LLP applications.

ww) Cumulative risk assessment

Derogations and adaptations to Annex II of Regulation (EU) No 503/2013 described in this guidance are based on a pre-defined maximum 0.9% per ingredient exposure level to the GMO. In this context, the expected effects of the genetic modification(s) are characterised as regards its/their safety. These include the assessment of novel compound(s) (e.g. new protein) and of endogenous compound(s) showing large variations with respect to the ingredient counterpart.

In the case of multiple LLP applications for GMOs showing similar traits, the possible cumulative contribution from the various GMOs to the ingredient should be taken into consideration in the risk assessment.

For example, if a similar output trait is expressed in different GMOs objects of multiple LLP applications, the relative contribution to the ingredient of each of these GMOs should be taken into account to allow an estimation of the total contribution of all these GMOs, via the addition of the respective trait-related compound(s). Information from the outcome of comparative assessment (section Comparative assessment) of each of these GMOs is relevant to establish the strategy to perform the cumulative assessment, on a case-by-case basis.

a. Environmental risk assessment[7]

The GMO Panel considers that LLP applications require an ERA that uses the same approach as described in the GMO Panel Guidance Document on the ERA of GM plants for imported viable GM plant material for food/feed uses only (EFSA GMO Panel, 2010), but that data requirements will depend on the identified and characterised hazards and level of exposuReg.

The ERA of standard applications is case-specific, and it begins with an explicit problem formulation where the GM plant is described, and potential hazards and exposure pathways are identified and characterised. Taking this information into account, problem formulation identifies which areas of risk

7 As mentioned in the Implementing Regulation (EU) No 503/2013, the ERA of GMOs or food and feed containing or consisting of GMOs should be performed according to the principles outlined in Annex II to Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of GMOs and repealing Council Directive 90/220/EEC, and the applicable EFSA GMO Panel guidance. Since the 2010 Guidance Document on the ERA of GM plants provides guidance for the ERA of GM plants submitted under Directive 2001/18/EC and Regulation (EC) No 1829/2003 on GM food and feed, the GMO Panel took this guidance as a basis to determine the approach and data requirements for ERA of GM plants in LLP situations.

need to be addressed and hence the data requirements to inform the risk analysis. Risk is then characterised testing specific hypotheses about the likelihood and severity of adverse environmental effects that may occur. Applicants should follow the same approach as for the ERA of standard applications under LLP situations.

As for standard applications, the ERA of LLP applications needs to consider the same exposure pathways described in EFSA GMO Panel, 2010 for imported GM plant material for food/feed uses only: (1) exposure of microbial communities to recombinant DNA in the gastrointestinal tract of animals fed GM plant material and environments exposed to faecal material (manure and faeces) of these animals (exposure pathway 1 in Figure 1); and (2) accidental release into the environment of imported viable material from the GM plant during transportation and processing (exposure pathway 2 in Figure 1). These two exposure pathways need to be accounted for in the problem formulation as described in EFSA GMO Panel, 2010.

The ERA also requires assessment of the consequences of plant-to-microorganism gene transfer, as well as assessment of the potential for the establishment, spread and dispersal of viable GM plant material and flow of transgenes into cross-compatible wild relatives, in order to determine if the low exposure conditions are likely to continue or whether exposure is expected to increase, potentially leading to environmental harm.

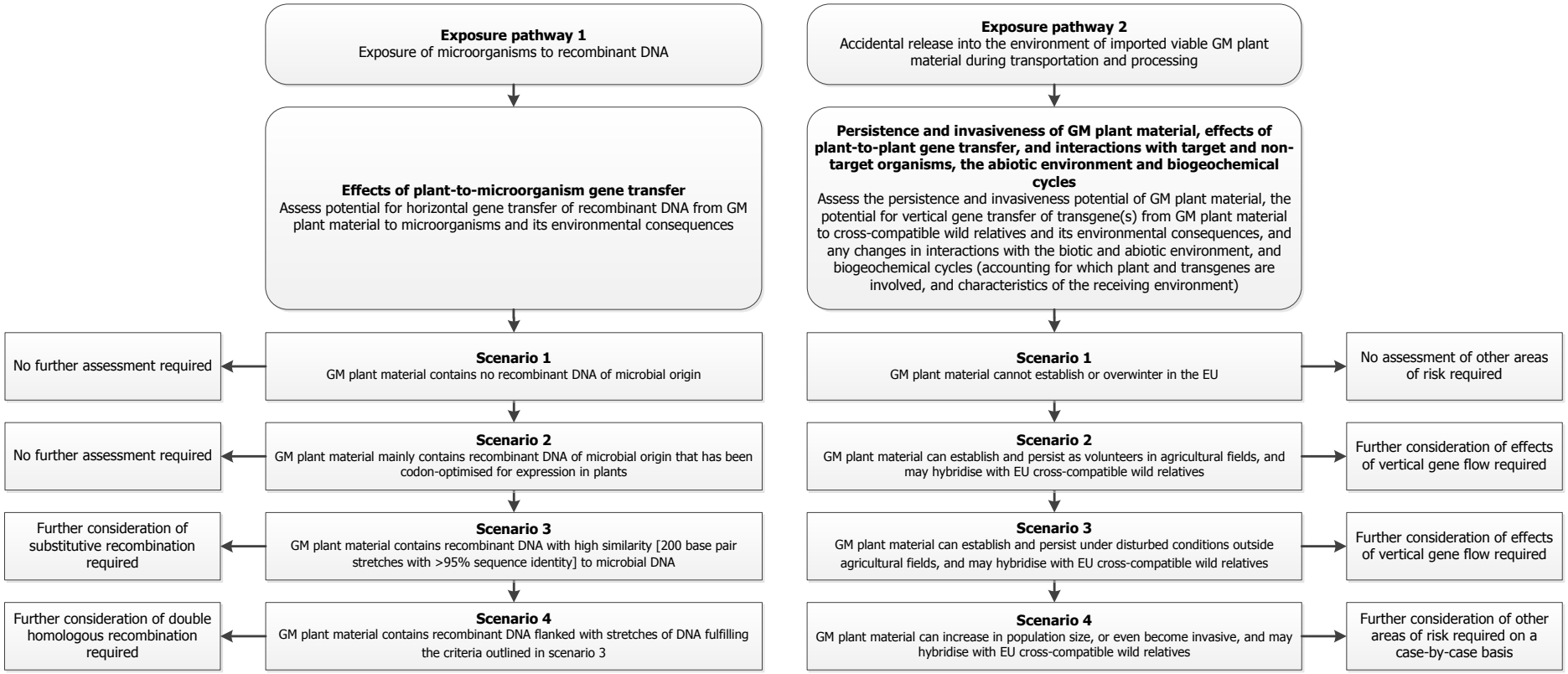

Diagram outlining under which circumstances specific areas of risk require further consideration during the ERA of imported GM plant material under LLP situations.

Figure 1: Overview of areas risk requiring consideration during the environmental risk assessment (ERA) of genetically modified (GM) plant material under conditions of low level presence (LLP) in imported food/feed into the European Union

i. Exposure pathway 1: Exposure of microorganisms to recombinant DNA

Although it is generally considered to be a very rare event (EFSA GMO Panel, 2009; EFSA, 2015), microorganisms present in the gastrointestinal tract of animals fed GM plant material and environments exposed to faecal material (manure and faeces) of these animals may be exposed and incorporate (parts of) recombinant DNA via horizontal gene transfer (HGT). Microorganisms inhabiting the gastrointestinal tract are continuously shed and thus, provided they would have incorporated recombinant plant DNA, these are also released into the environment. In addition, soil, water and other environments may be exposed to animal feed, processed products and plant waste materials where microorganisms, mostly bacteria, will degrade the plant material and become exposed to recombinant DNA.

Successful HGT requires the transfer of a recombinant DNA sequence from the GM plant material to microorganisms, its stabilisation into the recipient organism by autonomous replication or integration in the genome, its expression, and potential selective advantages conferred to the recipient by acquisition of the foreign DNA molecules. If microbial recipients gain a selective advantage by the expression of recombinant DNA from GM plants, then HGT may potentially raise a concern for the environment.

xx) Risk assessment approach

The assessment of the environmental impact of HGT has two facets: one linked to characterising the probability of HGT events under natural conditions; and the other to identifying environmental hazards that the expression of a transgene transferred by HGT would have in a microbial recipient. To assess the probability of HGT, exposure and mechanisms which would facilitate HGT need to be considered. The LLP situation limits the exposure of microorganisms to recombinant DNA compared to a situation covered by a standard application and reduces the probability of HGT to occur, but there are superimposing factors, such as the amount of GMO fed to animals over time, which need to be taken into account. Independent of establishing the probability, the identification of hazards should be based on a worst-case scenario, meaning that any recombinant gene of the GM plant could be expressed in a microbial recipient. This worst-case scenario addresses the possibility of illegitimate recombination between GM plant DNA and genomes of microorganisms, even if highly unlikely, and only theoretically possible; it has never been shown to allow HGT of recombinant DNA from GM plants to microorganisms under natural conditions.

Homologous recombination (HR) is the most important mechanism facilitating HGT. In order to identify potential sites for HGT, stretches of sequence identity (as detailed in EFSA, 2015) between the recombinant DNA and DNA from microorganisms need to be identified (scenarios 3 and 4 in Figure 1). In case of single sequence identities, HR may result in substitutive recombination, i.e. one gene or parts of one gene of a recipient are replaced, or, in case of two or more sequence identities, double HR (DHR) may cause the transfer and genomic incorporation of additional genes located between two stretches with sequence identity. The assessment of potential HR and DHR is therefore required under LLP situations. The relevant information, which can be extracted from the molecular characterisation, must be provided.

To finalise the risk assessment, in cases that HR or DHR scenarios have been identified at the molecular level, applicants need to consider their environmental consequences as outlined in GMO Panel (2010).

i. Exposure pathway 2: Accidental release into the environment of imported viable GM plant material during transportation and processing

In case of imports of viable plant material such as grains and seeds containing a low level of GM plant material, accidental release of viable GM plant material may occur during handling, transportation, storage and processing (OECD, 2013; Roberts et al., 2013). Spillage of grains or seeds may occur near shipping centres such as ports or railroad stations or near milling and processing plants or alongside transport routes (Bagavathiannen and Van Acker, 2008; Devos et al., 2012). Depending on which plant and which transgenes are involved, and on the characteristics of the receiving environment, spilled viable GM plant material may grow and establish transient or self-perpetuating populations in the EU. The exposure of the environment to these feral GM plants is the starting point of the ERA (EFSA GMO Panel, 2010; Roberts et al., 2013), as these plants may mediate transgene movement among cross-compatible plants in the landscape, and impact other organisms (including target and non-target organisms), the abiotic environment, biogeochemical cycles or ecosystem services. The potential for establishment, persistence and invasiveness of the GM plant, and its hybridisation potential with cross-compatible wild relatives (also termed plant-to-plant gene transfer hereafter) (both step 1, below) will determine whether it is necessary to assess interactions of the GM plant material with target and non-target organisms, the abiotic environment, and biogeochemical cycles (step 2, below).

yy) Risk assessment approach

The assessment of the persistence and invasiveness, and hybridisation potential of GM plants in LLP situations is concerned mainly with the environmental consequences of accidental release of viable GM plant material which can survive and/or propagate.

A first step in the ERA is to consider the potential of environmental exposure to the GM plant material in LLP situations, covering both single and repeated imports. This includes determining whether the GM plant material will establish, persist and/or invade in receiving environments. If the GM plant can establish, it is important to determine whether it can hybridise with cross-compatible wild relatives, and whether the intended trait(s) can increase environmental exposure compared to the parent species.

If establishment and hybridisation are predicted, then the second step of the ERA would be to examine whether the intended trait(s) may result in environmental consequences in terms of adverse biotic and abiotic impacts in different potential receiving environments. These impacts, such as displacing or depleting indigenous populations of plants, or effects on ecosystem functions or services, should be determined according to the data requirements outlined in EFSA GMO Panel (2010).

zz) Information for determining the likelihood of persistence and invasiveness of GM plants and their hybridisation potential

Based on a staged approach proposed by EFSA GMO Panel (2010), the following four scenarios were identified to group plants in terms of their persistence and invasiveness, and hybridisation potential:

- Scenario 1 considers GM plant material that cannot establish or overwinter in the EU;
- Scenario 2 considers GM plant material that can establish and persist as volunteers in agricultural fields (e.g., maize, rice, soybean, oilseed rape), and may hybridise with cross-compatible wild relatives present in the EU;

- Scenario 3 considers GM plant material that can establish and persist under disturbed conditions outside agricultural fields forming feral populations, which may hybridise with cross-compatible wild relatives present in the EU (e.g., cotton, oilseed rape);
- Scenario 4 considers GM plant material that can establish and persist in semi-natural environments, and could also increase in number or even become invasive depending on the novel trait(s), and can hybridise with cross-compatible wild relatives present in the EU (e.g., oilseed rape under certain conditions[8], clover, alfalfa, grasses).

Various types of information can be considered for determining the likelihood of establishment, persistence and invasiveness of GM plants and their hybridisation potential (EFSA GMO Panel, 2010; Raybould et al., 2012; Roberts et al., 2013). As outlined in the Section 3.1.2 of EFSA GMO Panel (2010), applicants should describe the persistence and invasiveness, and hybridisation potential of the parent organism[9], as well as the critical biological and abiotic factors limiting this potential.

Applicants are also requested to indicate whether the intended trait(s) has(ve) the potential to alter the persistence and invasiveness of the parent species and its hybridisation potential. Characteristics that provide resistance or tolerance to biological and abiotic stressors likely limiting fitness (e.g., drought, temperature, salt, disease, pest, competition with other species) may allow the GM plant to spread more easily including in environments where the plant is normally not grown (Warwick et al., 2009). This requires consideration of the various life cycle stages of the parent species, as this will make explicit which life cycle stage(s) limits or facilitates the persistence of a species, and whether the transgene will allow the GM plant to overcome limiting factors.

aaa) Environmental consequences of persistence and invasiveness of the GM plant and plant-to-plant gene transfer

If the GM plant material cannot establish and persist in the receiving environment under LLP conditions (scenario 1, above), then there is less likelihood of plant-to-plant gene transfer, and environmental interactions of the GM plant material will be restricted and much reduced. In these cases, interactions with target and non-target organisms, the abiotic environment, and biogeochemical cycles at these low levels of exposure are unlikely to lead to environmental harm, and so assessment of these interactions is not required.

If the GM plant material is likely to establish and persist in the receiving environment as occasional plants which do not multiply, and exposure is likely to remain low and confined to agricultural or ruderal habitats when released at low levels into the environment (scenarios 2-3, above), then the potential for plant-to-plant gene transfer is likely to remain low, but its consequences still need to be considered. However, it is unlikely that interactions of the GM plant with target and non-target organisms, the abiotic environment, and biogeochemical cycles require assessment.

If the GM plant material is likely to establish, persist or be invasive, and hybridise with cross-compatible wild relatives found in the EU (scenario 4, above), then specific information outlined in EFSA GMO Panel (2010) is required to determine the impacts under LLP situations, including additional characterisation of

[8] Oilseed rape genetically modified to provide tolerance to biological and abiotic stressors likely limiting fitness such as disease, pest, drought, salt and temperature

[9] Such information is widely available for most major crops and summary biology documents produced by governments or international organisations (such as, Canadian Food Inspection Agency (CFIA): http://www.inspection.gc.ca/plants/plants-with-novel-traits/applicants/directive-94-08/biology-documents/eng/1330723572623/1330723704097; Organisation for Economic Co-operation and Development (OECD): http://www.oecd.org/env/ehs/biotrack/consensusdocumentsfortheworkonharmonisationofregulatoryoversightinbiotechnologybiologyofcrops.htm; and Office of the Gene Technology Regulator (OGTR): http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/biology-documents-1)

the potential for plant-to-plant gene transfer and its environmental consequences, and interactions of the GM plant material with target and non-target organisms, the abiotic environment, and biogeochemical cycles.

i. Risk management

Where critical uncertainties or risks are identified in the ERA, applicants should conclude on what management measures to take including post-market environmental monitoring. These risk management strategies should aim to reduce the identified risks to a level of no concern and should consider defined areas of uncertainty.

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Glossary

Low level presence (LLP): a situation where a GMO (i.e. a GM plant and/or its derived products for food or feed use, referred to hereafter as GMO) not previously authorised in the EU, is present at a level of maximum 0.9% per ingredient in any food and/or feed containing the same ingredient, due to adventitious or technically unavoidable reasons. A LLP situation can occur from point of entry into the EU, through the food/feed production processing chain, up to the food/feed portion consumed.

Ingredient: the mixture of the GMO subject of a LLP application and the same type of plant and/or derived product at the predefined proportions of maximum 0.9% and 99.1% respectively.

LLP application: an application prepared by an applicant in accordance to GMO Panel guidance on LLP.

Standard application: an application submitted under Regulation (EC) No 1829/2003, for food/feed, import and processing and assessed according to Regulation (EU) No 503/2013 and relevant EFSA guidance documents (EFSA GMO Panel, 2010, 2011).

Abbreviations

DHR	Double Homologous Recombination
DNA	Deoxyribonucleic acid
EC	European Commission
ERA	Environmental Risk Assessment
EFSA	European Food Safety Authority
EU	European Union
GM	Genetically Modified
GMO	Genetically Modified Organism
HGT	Horizontal Gene Transfer
HR	Homologous Recombination
LLP	Low Level Presence
OECD	Organisation for Economic Co-operation and Development
ORF	Open Reading Frame
WG	Working Group

Appendix C – Table of comments from the dedicated European Member States consultation submitted by means of electronic forms sent by EFSA to Focal points

Table of comments received from Competent Authorities under Reg. (EC) 1829/2003 during the dedicated European Member States consultation on the draft guidance on genetically modified plants at low levels (after removal of duplicates and/or of reiterated comments).

Country	Organisation	Section	Complete comment
Austria	Federal Ministry of Health and Women's Affairs	1.2. Interpretation of the Terms of Reference	Are fruits of smaller size (e.g. peanuts) excluded from the remit of the guidance? As also plant derived products are included (see abstract line 9) there is the possibility that derived products are contaminated technically unavoidable with GM variants of "small" sized fruits up to 0.9%.
Austria	Federal Ministry of Health and Women's Affairs	2.2 Methodologies	*…a technical report will be published in the EFSA website…* Proposal: a technical report will be published on the EFSA website…
Austria	Federal Ministry of Health and Women's Affairs	3.2.Scientific requirements for the risk assessment of LLP applications	Please replace "Regulation (EC) No 1829/2013" by "Regulation (EC) No 1829/2003. As an explicit reference to Regulation (EC) No 1829/2003 was selected in the headline it is expected that the following references to Annex II.I, Annex II.1, 1 etc. are referring to chapters present in Regulation 1829/2003. However, these Annexes are in fact part of Commission Implementing Regulation (EU) No 503/2013. In our opinion, this kind of presentation is confusing. It should be made clear that the Annexes are from Commission Implementing Regulation 503/2013. We would like to suggest to use the following heading: "Scientific requirements for the risk assessment of LLP applications submitted under Regulation (EC) No 1829/2003 under special consideration of Commission Implementing Regulation (EU) No 503/13.
Austria	Federal Ministry of Health and Women's Affairs	Paragraph 1.2.2.3. Information on the expression of the insert(s)	It should be made clear that "…Data on expression levels from those parts of the plant used for food and feed purposes shall be provided in all cases". 273 – 285: Sentences are too long and too complex (>50 words per

			sentence). Please simplify. We do not concur with the notion of the EFSA GMO panel stating that *…it is not considered necessary to provide data on the expression levels of the newly inserted sequences for stacked transformation events* for the following reasons: 1) Expression data may deviate considerably between single event and stacked combinations (Agapito-Tenfen et al. 2014) 2) The presented EFSA draft guideline provides no requirements that single events have to be characterized before the applicant is applying for approval of LLP contaminations caused by stacked events. Therefore, we are of the opinion that expression data from the transgenic plant used as an ingredient – whether it is a single or a stacked event – should be provided in any case."
Austria	Federal Ministry of Health and Women's Affairs	Paragraph 1.2.2.4. Genetic stability of the insert and phenotypic stability of the genetically modified plant	Given that risk assessments from third countries are not a requested prerequisite (…*This mandate requires the GMO Panel to set guidance for LLP applications for any GMO, independently of the existence of a third country risk assessment*. See Box 1; lines 147-148) and, thus, a non-risk assessed transgenic plant (in a worst case scenario) may be subject to an LLP application data on genetic and phenotypic stability should be provided. Line of reasoning: 1) Data on genetic and phenotypic stability are a cornerstone of the molecular characterization of a transgenic plant providing invaluable information on the proper (i.e. the intended) functioning of the transgenic insert over several generations. This is in the utmost interest of the producer of the genetically modified plant. 2) As the producer is interested in a stably transformed transgenic plant line the respective data should be available anyway in the files of the applicants. 3) Concerning the negligibility of safety concerns due to low amounts of

			GMO products (equal or below 0.9%) in a given commodity we would like to indicate that a contaminating transgenic plant line might be producing highly active and stable enzymes and/or pharmaceutical compounds (Tschofen et al. 2016). The achieved concentrations under LLP conditions might still be sufficient to show an effect if present only at 1/100 of their maximum possible concentration especially considering long-term or life-long exposuReg. For instance Lv et al. reported that only 40 g of the transgenic seeds containing Bispora sp. MEY-1 ß mannanase per kilogram of a conventional maize/soybean diet (equalling 4% transgenic content of the tested commodity) is sufficient to achieve the greatest feed efficiency (Lv et al. 2013)."
Austria	Federal Ministry of Health and Women's Affairs	Conclusions of the molecular characterisation (Annex II. II, 1.2.3)	We do not concur with the derogations as proposed by the EFSA GMO Panel concerning the proposed information requirements on the expression of the inserts of stacked events and concerning the requirement for data on genetic stability of the insert and phenotypic stability of the genetically modified plant for the following reasons: 1) Expression data may deviate significantly between single event and stacked combinations (Agapito-Tenfen et al. 2014) 2) The presented EFSA draft guideline provides no requirements that single events have to be characterized before the applicant is applying for approval of LLP contaminations caused by stacked events. Therefore the situation may arise that there are not even expression data for the single events presented/available. 3) Data on genetic and phenotypic stability are a cornerstone of the molecular characterization of a transgenic plant providing invaluable information on the proper (i.e. the intended) functioning of the transgenic insert over several generations and of potential unintended effects (EFSA 2011a). A stable insert mediating the intended phenotype is in the utmost interest of the producer of the genetically modified plant. 4) As the producer is interested in a stably transformed transgenic plant line the respective data should be available anyway in the files of the applicants.

			5) The concentrations of highly active and stable enzymes and/or pharmaceutical compounds (Tschofen et al. 2016) achieved under LLP conditions due to a contaminating transgenic plant line might still be sufficient to show adverse effects if present only at 0.9% in the tested commodity."
Austria	Federal Ministry of Health and Women's Affairs	Comparative analysis (Annex II. II, 1.3)	The EFSA Draft Guidance points out: *The GMO Panel is of the opinion that differences in the level of a compound in the GMO large enough to impact the composition of the ingredient are unlikely to occur and considers that comparative compositional analysis is not necessary*. We argue that only on a case-by-case basis it can be decided whether existing differences in compounds may give reasonable grounds to believe that a risk exists for humans or animals, and whether these differences need to be further addressed or deserve special attention. Field tests are an essential instrument for understanding the behavior of GM plants in the natural environment and for observing and measuring important characteristics (appearance, agronomic traits, composition, etc.). Field tests are considered a key element to understand whether the GM plant develops and reacts as it is expected when it is grown in the field. Such behavioural characteristics of plants cannot be predicted by molecular characterisation alone (Kleter and Noordam 2015). We would further like to point to current EFSA Guidance which lays down that any identification of compositional and agronomic differences should be further assessed with respect to potential impact on human and animal health (EFSA 2011b). Furthermore, to our knowledge, there is no evidence of a third country risk assessment of GM plants which does not include field tests in some form. It is thus difficult to understand why this EFSA Draft Document states that field test are not needed for drawing conclusions on the risk assessment of the low level presence of genetically modified plant material in imported food and feed.

			The crucial point is that differences in compounds provide an indication that the physiology of the plant has changed during the genetic modification process. Such changes may lead to higher concentrations of minor nutrients or of secondary plant metabolites some of which are known to be poisonous to humans (Ames et al. 1990). We think it is rather irresponsible for GM plants and derived food and feed products included in the daily diet (even at a level of only 0.9%) to exclude potential harmful effects a priori and to conduct no field trials in order to complete the risk assessment and minimise potential consumer risks. It is also rather irresponsible for GM plants the risk characterisation to be based entirely on the molecular assessment which is known to produce data that are subject to scientific uncertainties (Wilson et al. 2006). Unwanted effects at the molecular level such as rearrangements of plant genomic DNA, unintended insertions of additional sequences, pleiotropic effects, somaclonal variation are well known for GM plants (Filipecki and Malepszy 2006). Such effects may only become visible during field trial studies. We think that a basic set of comparative data should be submitted by the applicant. We therefore propose amending the EFSA Draft Guidance, Chapter Comparative analysis (Annex II. II, 1.3) (Line 341 ff.) as follows: The submission of comparative data is needed allowing an estimate that the GM plant shows no substantial differences in compositional or agronomic characteristics (as compared to its conventional counterpart) that could be of relevance for the risk assessment even when considering a 0.9% threshold in food and feed. The requirements as laid down in Chapter 1.3 of Annex II of Regulation (EU) No 503/2013 apply, but derogations are possible of paragraphs 1.3.2 (Experimental design and statistical analysis of data from field trials for comparative analysis) and 1.3.4 (Comparative analysis of composition). All requirements as laid down in paragraph 1.3 of Annex II of Regulation (EU) No 503/2013 need to be followed when:

			- the intended trait targets the composition of the GMO, or - a specific hypothesis can be formulated, as in the case of unintended compositional changes anticipated by the precedent molecular characterisation, or - compounds are de novo expressed in the GMO. Please explain and define the term "de novo expressed". In a broad sense of view all transgenic events could be considered theoretically as de novo expressed in a novel genetic background. However, this kind of interpretation would invalidate the derogation as proposed by the EFSA GMO Panel in lines 341 – 344.
Austria	Federal Ministry of Health and Women's Affairs	Comparative analysis of composition (Annex II. II, 1.3.4)	Please check the correctness of the elements presented in brackets. In the presented configuration of the sentence exactly these important parameters are NOT requested to be presented by a LLP applicant. A suggested correct version would be:"in LLP 394 applications the analysis of the composition may not include a range of compounds. However, at least information on proximates, key macro and micro-nutrients, ant nutritional compounds, natural toxins and already identified allergens, as referred to in plant-specific OECD Consensus Documents should be provided.
Austria	Federal Ministry of Health and Women's Affairs	Information on altered levels of food and feed constituents (Annex II. II, 1.4.3)	The EFSA Draft Guidance states: *The GMO Panel considers that the requirements laid down in paragraph 1.4.3 for the toxicological assessment of altered levels of natural constituent(s) [i.e. compound(s) constitutively expressed in the GMO] in the GMO apply only if the expected changes in the level of natural constituent(s) have been confirmed (section Comparative assessment).* Since the submission of comparative data is not required (according to the EFSA Draft Document at hand), it is expected that changes in the levels of food and feed constituents that are of relevance for the toxicological risk assessment will be missed. As outlined before (see Austrian Comment on Chapter "Comparative Analysis"), we point out that without the performance of field trials the

			risk assessment would have substantial data gaps in relation to potential unintended effects that become apparent only during growth and performance of the GM plant in the field. It thus cannot be excluded a priori (and solely on basis of molecular characterisation data) that an altered level of a minor compound (secondary plant metabolite or micronutrient) exists that would be of no harm because the inclusion level is only 0.9%. It is therefore important that field trials in some way are carried out by the applicant in order to fill these data gaps"
Austria	Federal Ministry of Health and Women's Affairs	Paragraph 1.4.4.1. 90-day feeding study in rodents with whole genetically modified food and feed	The EFSA Draft Guidance states: *The GMO Panel considers that, if no specific hypothesis has been identified by preceding analysis or information, a 90-day study in rodents with the whole GM food and feed does not provide information on the toxicological properties of the whole food feed relevant in a LLP situation, and the requirement of such a study studies does not apply under LLP situations*. The EFSA Draft Guidance shows here weaknesses in its argumentation: Since the submission of comparative data is not required (according to the EFSA Draft Document at hand), it can be expected that significant differences (between the GMO and its conventional counterpart) that would enable (and make necessary) the development of a hypothesis-driven approach to investigate toxicological consequences of repeated exposure for a long-time period would remain undetected. Therefore, the EFSA Draft Guidance at hand should be amended as to avoid important data gaps in relation to the toxicological assessment of GM plants that are present at a level of maximum 0.9% per ingredient in food and feed products."
Austria	Federal Ministry of Health and Women's Affairs	Assessment of allergenicity of the genetically modified food or feed (Annex II. II, 1.5.2)	The EFSA Draft Guidance states: *The GMO Panel considers that due to the 0.9% contribution of the GMO to the ingredient, derogation from requirements laid down in paragraph 1.5.2 of Annex II of Regulation (EU) No 503/2013 is possible, unless large changes in the level of endogenous allergens in the GMO have been confirmed (section Comparative assessment)*. Again, the EFSA Draft Guidance shows weaknesses in its argumentation.

			Without appropriate field trials and comparative studies, potential unintended changes in physiology and composition of the GM plant would remain hidden and altered levels of food and feed constituents that are of relevance for the risk assessment potentially be missed. It is not out of the question that such changes are substantial and may concern allergen patterns of GM food. It is rather likely that such unanticipated effects are not identifiable by molecular characterisation studies alone. Therefore, the EFSA Draft Guidance at hand should be amended as to avoid data gaps in relation to the allergenicity assessment of GM plants that are present at a level of maximum 0.9% per ingredient in food and feed products"
Austria	Federal Ministry of Health and Women's Affairs	Risk Characterisation (Annex II. II, 3)	We would like to point to the fact that a LLP application may comprise of transgenic plants which may produce highly active pharmaceutical compounds (Tschofen et al. 2016). An amount of 0.9% of the transgenic part may therefore still contain a significant number of biologically active molecules which may induce adverse effects in the consumer upon ingestion.
Austria	Federal Ministry of Health and Women's Affairs	Cumulative risk assessment	Please define "similar traits". Is this referring for instance to all recombinant Bt-proteins or only to GMOs e.g. carrying Cry1Ab. Has the applicant take into account products from different producers?
Austria	Federal Ministry of Health and Women's Affairs	3.3. Environmental risk Assessment 3.3.1. Exposure pathway 1: Exposure of microrganisms to recombinant DNA	We would like to re-iterate that the frequency of horizontal gene transfers in bacterial populations is not very informative for predicting long-term effects (Pettersen et al. 2005). Rare events like the formation of mosaic genes with a calculated probability of 10E-24 have evolved into clinical threats severely hampering antimicrobial therapy of infectious diseases (please compare mosaic penicillin binding proteins) (Heinemann and Traavik 2004). It is astonishing that this argument ("rare event") is still perpetuated at the most prominent positions in current risk assessment guidelines although frequency estimates are not of decisive importance in this context. *Risk assessment approach:* We would like to point to the fact that a

			worst case LLP situation (assuming a GM concentration of 0.9% in the diet) would reduce the exposure level of bacterial populations to transgenic DNA roughly by a factor of 100. This means if the mammalian gastrointestinal tract would be exposed to e.g. 10E10 copies of the transgenic insert via a diet consisting of 100% GMO still 10E8 transgenic copies would be available for bacterial transformation in the LLP diet. The probability for HGT would be indeed reduced (supposedly by the factor of 100) but this reduction is completely irrelevant considering the remaining copy number of transgenic elements available for interaction with the bacterial community in the gastrointestinal tract. ""…it has never been shown to allow HGT of recombinant DNA from GM plants to microorganisms under natural conditions." Assuming a rather low horizontal gene transfer frequency (from plant to bacteria) of 10E-15 would result in roughly 1 recombinant bacterial cell per square meter of a typical agricultural field (Heinemann and Traavik 2004). However, by using the currently available detection technology (e.g. real time PCR) this single recombinant would be only detectable if 3 tons of soil would have been sampled (please see table 1 in reference Heinemann and Traavik 2004). Horizontal gene transfer under field conditions is hard to detect: But not because this process is not taking place but because the available tools for analysing this process are inadequate (Nielsen et al. 2014). Additionally, we would also like to refer to several reports indicating plant-to-bacteria gene transfer in natural environments (Netherwood et al. 2004; Pontiroli et al. 2009; Pontiroli et al. 2010; Nikolaidis et al. 2014). We would also prefer the EFSA GMO Panel to remember their seminal conclusions on the "Use of Antibiotic Resistance Genes as Marker Genes in Genetically Modified Plants" where they pointed to the fact that "…The transfer of antibiotic resistance marker genes from GM plants to bacteria has not been shown to occur either in natural conditions or in the laboratory in the absence of sequence identity in the recipient bacterial cell" (EFSA 2009). This is the correct description of the situation and is distinctly different compared to the corresponding text element as

			presented in this draft guidance."
Czech Republic	Ministry of Agriculture	General	General comment on the current text: too complicated to be used as a guideline, not very clear in some para.
Czech Republic	Ministry of Agriculture	Title and Keywords	Better include "unapproved" as title like this is a bit misleading.
Czech Republic	Ministry of Agriculture	1.2. Interpretation of the Terms of Reference	It is a bit misleading to use the term ingredient or per ingredient, if in case of mixed matrices one component or contamination is not listed how to cope with the situation. Contaminants by other species usually are not listed among ingredients. Definition of LLP: 0,9% - is generally accepted as labelling limit according EU legislation. In other legislation (e.g. feed. LLP is set at 0.1% (619/2011)) Please cope on that in threshold definition – no reference on EU regulation given theReg.
Denmark	Danish Veterinary and Food Administration	1.1. Background and Terms of Reference as provided by the requestor	What about products that are also intended for the EU market but due to the very long approval process in the EU the risk of unintended presence of a GMO is high. A short process for approval of unintended presence might be of relevance and useful. The idea with the LLP guidelines from Codex (2009) is based on some mutual respect between countries in the sense that when the OECD guidelines "for the conduct of food safety assessment of foods derived from recombinant-DNA plants" have been used for an approval for marketing of a GM-plant in a country outside the EU, it would be considered "almost" safe for EU citizens as well. This would be true when considering that presence of 0.9% or even much higher would hardly be a problem if 100% is approved in another country. Examples of situations where this is not the case seems to be rather speculative and therefore the information requirements seem to be exaggerated. *the GMO Panel LLP guidelines should be applicable to low level presence of GM products, independently of the existence or not of a third country risk assessment.* This sentence is highly problematic. It seem that EU do not from a scientific point of view respect, to a certain degree, approval in another

			country as is the basic idea in the codex guidance concerning the LLP and accepted by EU. From a scientific point of view a GMO approved for marketing in one country where the Codex guidelines have been followed for risk assessment can hardly be considered as being of a health risk considering the exposure in general will be 100 times lower. Examples or cases illustrating the problem that exist are missing to document this is a health problem and not a management problem. The mandate does not state that a situation where an assessment in a third country exists cannot be treated differently
Denmark	Danish Veterinary and Food Administration	General comment	In general this draft guidance makes it difficult for the applicant to know which level of information is sufficient for the GMO panel, e.g. comparative analysis. It should be indicated that due to the foreseen difference in exposure (100x) both GMP with positive opinion from EFSA and non-segregant can be accepted as both counterpart and references for the compositional analysis. Otherwise indicate the scientific reasons why not.
Denmark	Danish Veterinary and Food Administration	1.2. Interpretation of the Terms of Reference (in the final guidance Appendix 1)	Box 1 . "…*the GMO Panel guidance on LLP is intended to support only the risk assessment of LLP situations before these occur (a priori assessment*)." This is not very logic since we know that unintended presence will occur irrespective of any EU approval's.
Denmark	Danish Veterinary and Food Administration	2.2. Methodologies	*In accordance with the Terms of Reference of the mandate, the LLP WG scrutinised which data requirements of Annex II of Regulation (EU) No 503/2013 are necessary to conclude on the safety of GMOs* From a scientific point of view EFSA has never succeeded to argument for all the present requirement of data for an application for marketing. It is therefore also highly uncertain what criteria are used by EFSA for this evaluation of which data is necessary for LLP assessment. The EU regulation 503/2013 is a mixture of requirement based on science and management.
Denmark	Danish Veterinary and Food Administration	3.1.3. Risk assessment considerations for LLP situations compared to	In general this draft guidance makes it difficult for the applicant to know which level of information is sufficient for the GMO panel, e.g. comparative analysis. It should be indicated that due to the foreseen difference in exposure (100x) both GMP with positive opinion from EFSA

		standard GMO applications	and non-segregant can be accepted as both counterpart and references for the compositional analysis. Otherwise indicate the scientific reasons why not.
Denmark	Danish Veterinary and Food Administration	Insertion of marker genes and other nucleic acid(s) sequences not essential to achieve the desired tract (Annex II. I, 2.1)	It make no sense for LLP to refer to the sentence in the Annex "In order to facilitate the risk assessment, the applicant shall endeavour to minimise the presence of inserted nucleic acid(s) sequences not essential to achieve the desired trait
Denmark	Danish Veterinary and Food Administration	Paragraph 1.2.2.3. Information on the expression of the insert(s)	Since the exposure is expected to be more than 100 times lower for a LLP acceptance relative to a normal application for marketing as food and feed, this should be reflected in considerable lower requirement for this point. The guidance does not reflect the fact of a considerable lower exposuReg. Exposure is part of the scientific assessment and should therefore be reflected in this chapter. In general the guidance do not properly take into consideration the 100 times or more lower exposure also considering the lack of examples where GMP is found unexpected different from traditional bred plants and their variation
Denmark	Danish Veterinary and Food Administration	Comparative analysis (Annex II. II, 1.3)	Concerning table 1: Instead of a table that is not wrong but neither useful in relation to assessment of risk the first five row could be replaced by a sentence saying that one kernel out of 100 will make no relevant changes if the level of different compounds are lower even if the GM-kernel is "empty". In order to make any essential differences one of the key substances should probably be considerable higher than 100 times the content in that of the traditional plant which is again considerable higher that the "large variations" mentioned in line 338. From the experience we have today this is almost unthinkable and in order to make sense from a scientific point of view and not leave it as just a speculation this should be illustrated by an example. Without some examples to illustrate what can go wrong we would categorize this as pure speculation and not related to scientifically sound approach or method. *On a case-by-case basis, requirements under point (f) of paragraph 1.2.2.3 regarding the data for the expression levels of the newly inserted*

			sequences for stacked transformation events may be considered necessary. (Line 349) Replace "is necessary" to "may be necessary"
Denmark	Danish Veterinary and Food Administration	Comparative assessment studies performed under non-EU regulatory frames-applicability in LLP applications.	*In derogation to Regulation (EU) No 503/2013, the GMO Panel considers that comparative assessment studies that have been conducted in accordance to with Codex Alimentarius, 2009 could support the comparative compositional assessment in LLP situations* (Line 426) replace with "could be used for…" *In contrast, compositional analysis studies not aligned to requirements of Codex Alimentarius, 2009 are not considered appropriate by the GMO Panel.* (Comment to line 431-432): It depends hopefully on the quality of the compositional analysis studies. We do not agree that the Codex Alimentarius require the analysis but maybe recommend an approach. This leave room for using years of experience to lower the demand for data
Denmark	Danish Veterinary and Food Administration	Combined transformation events stacked by conventional crossing	When reading the sentence "on a case by case basis……..data is needed" the sentence seems to be in conflict with itself
France	ANSES	Title, Abstract, Summary	Préciser que ce document ne s'applique qu'aux graines et leurs produits consommés en mélange et non pas aux plantes consommées entières comme les légumes ou les fruits. En effet, ce n'est qu'à la ligne 135 que les fruits et légumes sont explicitement exclus du champ des lignes directrices. Proposition de titre: « Draft guidance for the risk assessment of the low level presence of genetically modified plant material in imported food and feed commodities, such as grains, beans or oil seeds, under Regulation (EC) No 1829/2003". Proposition de rédaction (*abstract*): "This document provides draft guidance for the a priori risk assessment of the unintended, adventitious

			or technically unavoidable low level presence in food and feed commodities, such as grains, beans or oil seeds, of genetically modified (GM) plant material […]". (*Summary*) Il faudra veiller à préciser que ce document ne s'applique qu'aux graines et leurs produits consommés en mélange et non pas aux plantes consommées entières comme les légumes ou les fruits. English translation: State that this document applies only to grains and the products thereof when consumed in a mixture and not to plants consumed whole such as fruit or vegetables. Fruits and vegetables are not explicitly excluded from the scope of the guidance until line 135. Suggested title: 'Draft guidance for the risk assessment of the low level presence of genetically modified plant material in imported food and feed commodities, such as grains, beans or oil seeds, under Regulation (EC) No 1829/2003'"'State that this document applies only to grains and the products thereof when consumed in a mixture and not to plants consumed whole such as fruit or vegetables. Suggested wording *(Abstract)*: 'This document provides draft guidance for the a priori risk assessment of the unintended, adventitious or technically unavoidable low level presence in food and feed commodities, such as grains, beans or oil seeds, of genetically modified (GM) plant material […]'" (*Summary*) Care must be taken to state that this document applies only to grains and the products thereof when consumed in a mixture and not to plants consumed whole such as fruits or vegetables
France	ANSES	1.1. Background and Terms of Reference as provided by the requestor	*In 2009, Codex Alimentarius issued guidelines for the food safety assessment in situations of low level* Vérifier la date de cette référence, car il s'agit du document suivant : Commission du Codex Alimentarius (2008). Directive régissant la conduite de l'évaluation de la sécurité sanitaire des aliments dérivés de

			plantes à ADN recombiné. In Aliments dérivés des biotechnologies modernes, Deuxième édition. Organisation des Nations Unies pour l'alimentation et l'agriculture (FAO)/Organisation Mondiale de la Santé (OMS), Eds, Rome, pp. 7-37. *In 2015, the European Commission mandated EFSA, in accordance with Article 29 of Regulation (EC)* Le mandat date de septembre 2014 *For stacks, the implementation of the 0.9% threshold should follow the same rules as for labelling purposes i.e. the threshold applies to individual events*. Commentaire : Il est intéressant de voir que la Commission européenne a confirmé à l'AESA que, dans le cas des hybrides, le seuil d'exemption d'étiquetage de 0,9% s'applique pour chaque évènement parental de l'hybride. Cette précision bien utile figure dans le projet de lignes directrices alors que les Etats membres n'ont jamais réussi à avoir cette interprétation par écrit English translation *In 2009, Codex Alimentarius issued guidelines for the food safety assessment in situations of low level.* Check the date of the reference because the document in question is the Codex Alimentarius Commission (2008). Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Plants In Foodstuffs derived from modern biotechnological methods, Second Edition. United Nations Food and Agriculture Organization (FAO) / World Health Organization (WHO), Eds, Rome, pp. 7-37". *In 2015, the European Commission mandated EFSA, in accordance with Article 29 of Regulation (EC).* The mandate was given in September 2014. *For stacks, the implementation of the 0.9% threshold should follow the same rules as for labelling purposes i.e. the threshold applies to*

			individual events. Comment: It is worth noting that the European Commission has confirmed to the EFSA that for hybrids the 0.9% labelling exemption level applies to each parental event in the hybrid. This very useful clarification is stated in the draft guidance although the Member States have never succeeded in securing this interpretation in writing."
France	ANSES	1.2. Interpretation of the Terms of Reference	La note de bas de page n°3 qui vise à préciser le type d'utilisation pouvant être couvert par le présent projet de lignes directrices est ambiguë dans la mesure où elle cite les semences (cf. « Article 3. Scope. a) GMOs for food use » and « Article 15. Scope. a) GMOs for feed use ») alors que la ligne 194 du document précise que ce document ne couvre pas les OGM pour la cultuReg. *the 0.9% of the GMO is exceeded in the ingredient at any given step of the production chain* Clarifier le sens de cette phrase. En effet, l'évaluation de risque ne porte que sur des présences inférieures à 0,9 % et cette phrase suggère que l'OGM pourrait finalement se trouver à des niveaux plus élevés dans les ingrédients. L'objectif de ce point est-il de préciser que ce document ne couvre pas les présences supérieures à 0,9% en amont de la filière alimentaire quand bien même, du fait des étapes de transformation, l'ingrédient en aval tel qu'il est consommé serait effectivement inférieur à 0,9% ? *The decision on whether a given GMO can constitute a LLP application is a risk management issue* Sur le principe, cette séparation entre évaluateur du risque et gestionnaire du risque est correcte. Toutefois, il conviendrait de préciser ce point pour les futurs pétitionnaires afin qu'ils ne déposent pas des dossiers pour finalement voir leur demande rejetée par les Etats membres au motif qu'elle ne peut être assimilée à un cas de LLP… En particulier, à la ligne 135, les « larges » fruits et légumes sont exclus du champ du document sans que cette notion ne soit précisée : qu'en est-il

			du raisin, des cerises par exemple ? *Pre-requisites to identify an LLP situation : […] In contrast, this mandate requires the GMO Panel to set guidance for LLP applications for any GMO, independently of the existence of a third country risk assessment.* Ce point pose problème car, pour mémoire, en 2005, lorsque les Etats-Unis avaient proposé que le Codex travaille sur la question des LLP, l'UE n'avait pas donné son accord car le périmètre envisagé par les Etats-Unis incluait la présence d'OGM non autorisé et ceux en phase d'essais. Un consensus avait finalement était trouvé en 2006 après avoir précisé que les travaux du Codex ne s'appliquaient qu'à des OGM autorisés à la commercialisation (cf. on parle d'ailleurs « d'autorisations asynchrones »). Le projet de lignes directrices est donc moins exigeant que les normes Codex, ce qui est assez inhabituel : ce point doit donc faire l'objet de discussion entre la Commission, les Etats membres et l'AESA. <u>English translation</u> Footnote 3, which aims to clarify the type of use covered by this draft guidance is ambiguous to the extent that it refers to seeds (see 'Article 3. Scope. a) GMOs for food use' and 'Article 15. Scope. a) GMOs for feed use') whereas line 194 of the document states that it does not cover GMOs for cultivation purposes. *the 0.9% of the GMO is exceeded in the ingredient at any given step of the production chain* Clarify the meaning of this phrase. The risk assessment relates only to a concentration below 0.9% and this phrase suggests that GMO levels could ultimately be higher in the ingredients. Is the purpose of this point to state that this document does not cover concentrations greater than 0.9% upstream in the supply chain even when, as a result of processing, the downstream concentration in the product as consumed would actually be lower than 0.9%? *The decision on whether a given GMO can constitute a LLP application is a risk management issue*

			In principle, the separation between the risk assessor and the risk manager is correct. Nonetheless it would be useful to clarify this point for future applicants so that they do not lodge applications that will ultimately be rejected by the Member States on the ground that they cannot be regarded as constituting an LLP. In particular, in line 135 'large' fruits and vegetables are precluded from the scope of the document without any clarification as to what that means: what about grapes or cherries, for example? *Pre-requisites to identify an LLP situation : […] In contrast, this mandate requires the GMO Panel to set guidance for LLP applications for any GMO, independently of the existence of a third country risk assessment.* For the record, this point is problematic because the EU did not agree to the proposal made in 2005 by the United States that the Codex should work on LLP; this was because the scope envisaged by the US included the presence of non-authorised GMOs and GMOs in trials. A consensus was finally reached in 2006 after clarifying that the Codex work applied only to GMOs authorised for commercial purposes (cf. we also refer to 'asynchronous authorisations'). The draft guidance is therefore, unusually, less demanding than the Codex standard; this point should therefore be discussed by the Commission, the Member States and the EFSA"
France	ANSES	2.1. Data	*Regulation (EC) No 1829/2003, Regulation (EU) No 503/2013, Codex Alimentarius (2009) and EFSA GMO Panel, 2010* Codex alimentarius (**2008**). Ajouter la référence EFSA GMO Panel (2011) <u>English translation</u> Add the reference EFSA GMO Panel (2011)"
France	ANSES	3.1.2. Scope of the guidance	*Definitions and requirements of Regulation (EC) No 503/2013 other than those indicated in its Annex II apply to this guidance*. Clarifier le sens de cette phrase. En effet, si seules les définitions de

			l'article 2 du RUE n°503/2013 s'appliquent (et non celles de l'annexe II), le mot « definitions » peut être supprimé puisque le RUE n°503/2013 ne définit aucun terme nouveau mais renvoie aux définitions des RCE n°1829/2003 et 178/2002. English translation Clarify the meaning of this phrase. If only the definitions in Article 2 EU Reg No 503/2013 apply (and not those set out in Annex II) then the word 'definitions' can be removed because EU Reg No 503/2013 does not define any new terms; instead, it refers the reader to the definitions given in EC Regulations Nos 1829/2003 and 178/2002 *This guidance does not cover GMOs for cultivation purposes; GM microorganisms; GM animals; GMOs for non-food/feed uses, as these are not in the scope of Regulation (EC) No 1829/2003*. Phrase à clarifier car (1) les termes " as these are not in the scope of Regulation (EC) No 1829/2003" s'appliquent-ils uniquement aux OGM autres que des denrées/aliments (cf. « for non-food/feed uses »)? et (2) dans l'affirmative, ce point est inexact puisque l'article 2.c) des décisions d'autorisation au titre du RCE n°1829/2003 vise justement ce cas de figure… English translation Clarify this sentence because (1) does the wording 'as these are not in the scope of Regulation (EC) No 1829/2003' apply only to GMOs other than in food/feed (cf. 'for non-food/feed uses')? and (2) if so, this is incorrect because Article 2(c) on authorisation decisions pursuant to EC Reg No 1829/2003 refers to that precise scenario *This guidance does not consider issues related to risk management (traceability, labelling, and coexistence). Socio-economic and ethical issues are also outside the scope of this guidance.* Phrase à compléter car le paragraphe 3.3.3 (lignes 767 à 771) aborde la question des plans de surveillance des effets sur l'environnement.

			Proposition de rédaction : " This guidance does not consider issues related to risk management (traceability, labelling, and coexistence) but assists applicants if management measures are necessary based on the ERA." English translation This sentence needs to be expanded because paragraph 3.3.3 (lines 767-771) addresses plans to monitor environmental effects. Suggested wording: 'This guidance does not consider issues related to risk management (traceability, labelling, and coexistence) but assists applicants if management measures are necessary based on the ERA.'
France	ANSES	3.2.Scientific requirements for the risk assessment of LLP applications	Corriger No 1829/2013 par No 1829/2003. Voir proposition pour les lignes 224 à 226. English translation Correct 'No 1829/2013' to read 'No 1829/2003'. See suggested wording for lines 224-226.
France	ANSES	Introduction (Annex II. I)	*Line 122: This paragraph applies* Supprimer la ligne 222 (car, dans l'annexe II du RUE n°503/2013, il s'agit juste d'un titre et il n'y a aucune exigence). English translation Delete line 222 (because Annex II of EU Reg No 503/2013 is merely a title and there are no requirements).
France	ANSES	Definitions (Annex II. I, 1)	*Line 223: Definitions (Annex II. I, 1)* *Lines 224-226: The GMO Panel considered the requirements of the risk assessment of GM plants and derived food and feed (EFSA GMO Panel, 2011) and endorsed by Regulation (EU) No 503/2013; and recommends adaptations and derogations to Annex II for LLP applications as described below.* Supprimer la ligne 223 puisqu'il est indiqué aux lignes 192 et 193 que les

			définitions de l'annexe II ne s'appliquent à ce document. Placer les lignes 224 à 226 tout de suite après la ligne 220 (cf. titre du point 3.2) afin qu'elles constituent un paragraphe introductif aux exigences qui suivent, paragraphe qu'il convient de compléter afin de préciser que les paragraphes de l'annexe II du Règlement d'exécution (UE) n° 503/2013 qui ne sont pas cités peuvent ne pas faire l'objet d'un examen. Proposition de rédaction: " The GMO Panel […] and recommends adaptations and derogations to Annex II for LLP applications as described below. Those paragraphs of the Annex II of Regulation (EU) No 503/2013 that are not listed can be omitted from consideration." English translation Delete line 223 because lines 192 and 193 state that the definitions in Annex II do not apply to this document. Place lines 224-226 immediately after line 220 (see title of point 3.2) so that they form an introductory paragraph to the requirements that follow; the paragraph should be expanded to state that the paragraphs in Annex II of Implementing Regulation (EU) No 503/2013 that are not referred to can be omitted from consideration. Suggested wording: `*The GMO Panel […] and recommends adaptations and derogations to Annex II for LLP applications as described below. Those paragraphs of Annex II of Regulation (EU) No 503/2013 that are not listed can be omitted from consideration.*"'
France	ANSES	Molecular characterisation (Annex II. II, 1.2)	L'Anses indique que pour les produits consommés uniquement en mélange et/ou après transformation technologique, une caractérisation moléculaire complète est requise, le demandeur doit notamment fournir des informations permettant de démontrer la stabilité génétique de l'insert et la stabilité phénotypique de la plante génétiquement modifiée (cf. point 1.2.2.4 de l'annexe II) English translation

			ANSES notes that for products consumed only in a mixture and/or after technological transformation, full molecular characterisation is required, the applicant must inter alia supply information to demonstrate the genetic stability of the insert and the phenotypic stability of the genetically modified plant (see point 1.2.2.4 of Annex II).
France	ANSES	Information relating to the genetic modification (Annex II. II, 1.2.1)	Il conviendrait de préciser si c'est uniquement le point 1.2.1 qui s'applique ou également les sous-sections du point 1.2.1. En effet, le fait que pour le point suivant (cf. 1.2.2), les sous-sections soient explicitement visées peut laisser penser que pour le point 1.2.1 la situation est différente… English translation It would be useful to clarify whether only point 1.2.1 applies or if the subsections of point 1.2.1 also apply. The fact that the following point (see 1.2.2) refers explicitly to the subsections may give the impression that the situation for point 1.2.1 is different.
France	ANSES	Paragraph 1.2.2.4. Genetic stability of the insert and phenotypic stability of the genetically modified plant	La stabilité génétique devrait être démontrée y compris pour des OGM LLP car (1) cela fait partie de la démonstration de l'innocuité de l'OGM LLP et (2) cela permet de s'assurer que les méthodes de détection fonctionneront sur le long terme pour détecter l'OGM LLP puisque l'insert sera bien stable. English translation Genetic stability should be demonstrated, including for LLP GMOs because (1) it is part of demonstrating the safety of LLP GMOs and (2) it ensures that detection methods will function in the long term and will detect LLP GMOs because the insert will be very stable.
France	ANSES	Conclusions of the molecular characterisation (Annex II. II, 1.2.3)	Une caractérisation moléculaire complète reste nécessaire pour les OGM LLP, le demandeur doit notamment fournir des informations permettant de démontrer la stabilité génétique de l'insert et la stabilité phénotypique de la plante génétiquement modifiée (cf. point 1.2.2.4 de l'annexe II) English translation

			Full molecular characterisation is still necessary for LLP GMOs; the applicant must inter alia supply information to demonstrate the genetic stability of the insert and the phenotypic stability of the genetically modified plant (see point 1.2.2.4 of Annex II).
France	ANSES	Comparative analysis (Annex II. II, 1.3)	Intérêt du tableau 1 à préciser… L'Anses rejoint l'AESA sur le fait qu'une analyse comparative n'est pas nécessaiReg. En revanche, cette position vaut y compris pour les trois exemptions listées par l'AESA. English translation Explanation required for Table 1. ANSES shares the view of the EFSA that a comparative analysis is not necessary. Conversely, ANSES also maintains this position with regard to the three exemptions listed by the EFSA.
France	ANSES	Experimental design and statistical analysis of data from field trials for comparative analysis (Annex II. II, 1.3.2) Paragraph 1.3.2.1. Description of the protocols for the experimental design b) Specific protocols for experimental design	Lorsqu'une analyse comparative est demandée, celle-ci devrait être menée conformément au Règlement d'exécution (UE) n° 503/2013. En particulier, un test de différence réalisé à partir de données collectées sur un seul site sur une seule année présente-il un intérêt? En effet, l'AESA n'a, par le passé, jamais accepté un tel dispositif expérimental puisque: - Dans les lignes directrices de 2006, il était préconisé de faire les essais au champ sur plusieurs sites et plusieurs saisons (sans plus de précision); - Le RUE n°503/2013 reprend ce qui figurait déjà dans les lignes directrices de 2011, à savoir que chaque essai au champ doit être répliqué sur au moins huit sites et que ces essais peuvent être menés sur une seule année. De même, pour démontrer l'équivalence avec le produit conventionnel, il faut réaliser un test d'équivalence et donc intégrer des variétés

			commerciales dans le dispositif experimental. English translation Where a comparative analysis is required, it should be conducted in conformity with Implementing Regulation (EU) No 503/2013. In particular, is a test of difference that is conducted using data collected at a single site in a single year relevant? The EFSA has never accepted experimental designs of this kind in the past because: - The 2006 Guidance advocated field trials at several sites and in several seasons (without going into any more detail); - EU Reg No 503/2013 reiterates the 2011 Guidance, namely that each field trial must be replicated at a minimum of eight sites and may be conducted in a single year. Moreover, in order to demonstrate equivalence with the conventional counterpart, an equivalence test must be performed and therefore commercial varieties must be incorporated into the experimental design."
France	ANSES	Toxicology (Annex II. II, 1.4)	L'Anses rejoint l'AESA sur le fait qu'une étude de toxicité de 28 jours est requise si la (les) protéine(s) nouvellement exprimée(s) n'a (n'ont) jamais fait l'objet d'une évaluation toxicologique. Si les résultats de cette étude ou d'autres éléments du dossier suggèrent que l'OGM présente un risque, d'autres études pourraient être demandées. English translation ANSES shares the view of the EFSA that a 28-day toxicity study is required if the newly expressed protein(s) has (have) never been the subject of a toxicological evaluation. If the outcome of the study or other aspects of the application suggest that the GMO constitutes a risk, other studies could be required.
France	ANSES	Allergenicity (Annex II. II, 1.5)	L'Anses estime que, pour les produits consommés uniquement en mélange et/ou après transformation technologique, l'évaluation de

			l'allergénicité ne paraît pas nécessaire, car pour les produits consommés en mélange et/ou après transformation technologique, les traces d'allergènes amenées par la PGM vont être extrêmement diluées. Pour les espèces végétales connues pour être fortement allergéniques, une analyse de la modification éventuelle de l'allergénicité de la denrée/aliment pourrait être demandée si d'autres éléments du dossier suggèrent que l'OGM présente un risque. English translation ANSES is of the view that allergenicity assessment would not appear to be necessary for products consumed only in a mixture and/or after technological transformation, because any traces of allergens introduced by GM products will be extremely dilute. In the case of plant species that are known to be highly allergenic, an analysis of any change in the allergenicity of the food/feed could be required if other aspects of the application suggest that the GMO constitutes a risk.
France	ANSES	Assessment of allergenicity of the genetically modified food or feed (Annex II. II, 1.5.2)	L'AESA estime que l'évaluation de l'allergénicité de la denrée/l'aliment GM reste nécessaire lorsque l'analyse comparative a démontré des changements important (cf. « large changes ») dans le niveau des allergènes endogènes mais (1) l'analyse comparative n'est plus obligatoire pour les OGM LLP sauf dans quelques rares cas cités aux points 345 à 348 et (2) qu'entend-on par « large changes » ? English translation EFSA is of the view that assessment of the allergenicity of the GM food/feed remains necessary where the comparative analysis showed large changes in the level of endogenous allergens but (1) comparative analysis is no longer mandatory for LLP GMOs except in a few cases referred to in points 345-348 and (2) what is meant by 'large changes'?
France	ANSES	Nutritional assessment (Annex II. II, 1.6)	L'Anses estime que pour les produits consommés uniquement en mélange et/ou après transformation technologique, une évaluation nutritionnelle n'est pas nécessaiReg.

			English translation ANSES is of the view that nutritional assessment is not appear necessary for products consumed only in a mixture and/or after technological transformation.
Germany	BVL	Abstract/general	It is appreciated that the EFSA GMO Panel makes an effort to draft supplementary guidance for the risk assessment of the low level presence of genetically modified plant material in imported food and feed, which takes into consideration the specifics of LLP-situation. However, the actual format of the draft is debatable: Due to many references to Annex II of Regulation (EU) 503/2013 and defined derogations from the Annex, it is difficult to follow and to clearly decide which requirements are foreseen for the risk assessment of GMO under LLP situation. In many sections of the draft the performance of further assessment is dependent on the outcomes of the comparative assessment, which is mandatory only for some defined scenarios. It is not clear how to perform the further risk assessment in case the comparative assessment is not necessary. Creation of a clearer decision path/decision tree is necessary to represent explicit and definite requirements for risk assessment taking into account all characteristics of an LLP situation. Due to the definition of LLP situation in the current draft, the central point of the risk assessment should concern the question, whether an ingredient with a maximum GMO content of 0,9% can be considered as safe as the same product without any GMO content. If the creation of a consistent stand-alone document is not possible for legal rationale, then more detailed comments should be provided in the sections, which refer to the paragraphs where the part of requirements is defined by this draft as derogation from Annex II of Regulation (EU) 503/2013. This applies in particular to sections such as allergenicity, toxicological assessment and ERA
Germany	BVL	1.2. Interpretation of the Terms of Reference	"Same type of plant" is very general; should be more specific, i.e. replace by "same plant species" Non-GMO portions are present at a proportion of minimum 99.1%; therefore please change to … maximum 0.9% and minimum 99.1%,

			respectively.
Germany	BVL	3.1.2. Scope of the guidance	In line 192 and 193, reference is made to the definitions and requirements of Regulation (EU) No 503/2003. It is unclear, if the constraint "other than those given in Annex II" applies only to the requirements or also to the definitions. In Regulation (EU) No 503/2003 itself, regarding the definitions reference is made to Regulation (EC) No 1829/2003 and the only specific definitions are given in Annex II. These seem to apply for the LLP applications as well. Regarding the requirements, in the LLP guidance all sections of Regulation (EU) No 503/2003 Annex II are listed and classified as "apply" or "don't apply". The sentence in line 192/193 should be rephrased to make it more precise.
Germany	BVL	3.1.3. Risk assessment considerations for LLP situations compared to standard GMO applications	100% replacement of a conventional crop and derived products by a GMO should not be called a "worst-case-scenario". Considering that extensive safety evaluation and risk assessment is done for standard GMO applications, it can be assumed that only those products get marketing permits that are safe for human and animal health and the environment. Therefore, the bracket with the term "worst case scenario" should be deleted.
Germany	BVL	3.2.Scientific requirements for the risk assessment of LLP applications	Reference should be made to Regulation (EU) No 503/2013 in the headline as otherwise it could be misleading that the following sections refer to Regulation (EC) No 1829/201
Germany	BVL	Information relating to the genetically modified plant (Annex II. II, 1.2.2) Paragraph 1.2.2.1. General description of the trait(s) and characteristics which have been introduced or modified	This paragraph mainly deals with phenotypic traits and metabolic changes associated with the introduced traits. Therefore be more specific and replace "genetic modification" by "plant phenotype and metabolic changes associated with the genetic modification".
Germany	BVL	Paragraph 1.2.2.3. Information on the expression of the	"In paragraph 1.2.2.3(e) there is a section on RNAi mediated gene silencing, demanding in-silico analysis to evaluate possible effects on the expression of other genes. However, the LLP draft document does not

		insert(s)	consider this aspect. If the necessity for in-silico analysis can be neglected under LLP conditions, for clarity reasons this should be mentioned in the document The sentence "Hence it is not considered necessary to provide data on the expression levels of the newly inserted sequences for stacked transformation events" is probably not in accordance with the demand in lines 280-281 that expression levels from plant parts used for food and feed purposes are necessary. However, it should be clearly stated what is meant here: 1. Is the focus here on the comparison between stacked event and single transformation events? Then change this sentence to: "Hence it is not considered necessary to provide data comparing the expression levels of the newly inserted sequences in stacked transformation events to those in the single transformation events" or 2. Do you mean that in the case of LLP applications of stacked transformation events, only data on the expression levels in the single events are necessary?"
Germany	BVL	Conclusions of the molecular characterisation (Annex II. II, 1.2.3)	According to the statement on point 1.2.2.3(f) data on the expression levels of the newly inserted sequences in stacked events – or rather on the comparison of expression levels in stacked vs. single transformation events (see above comment) - are not considered necessary for LLP applications. Now in the conclusions it is stated that on a case-by-case basis these data requirements may be considered necessary. Are there examples for these cases? Please specify.
Germany	BVL	Experimental design and statistical analysis of data from field trials for comparative analysis (Annex II. II, 1.3.2) Paragraph 1.3.2.1. Description of the protocols for the	If equivalence test is not necessary, it would be helpful to provide a support for interpretation of significant differences taking into consideration all specifics of LLP situation.

		experimental design	
Germany	BVL	b) Specific protocols for experimental design	L 376 ... 383: the description provides little guidance how to decide. Perhaps more tangible examples could help ... EFSA should provide support how to decide what is "adequate to confirm and quantify differences…" A "sufficient number of replicates" should be more specified.
Germany	BVL	Paragraph 1.3.2.2. Statistical analysis	Taking into consideration that the equivalence test is not required and other requirements for field trials as defined in the Annex II of Regulation (EU) 503/2013 are foreseen, the paragraph should be adapted and provide clear requirements how to perform the statistical analysis of composition in LLP applications.
Germany	BVL	Comparative analysis of composition (Annex II. II, 1.3.4)	The first sentence is unclear and misleading. Does this sentence mean, that the compounds listed in the brackets must or may not be measured? If the compounds may not be measured "at least" should be deleted. Certainly it should be considered, that some following paragraphs (i.e. allergenicity, toxicology) refer to outcomes of those measurements. In this case, following sections need more detailed comments how to deal with situations in which the applicant has justifiably not performed a comparative assessment. If the compounds must be measured irrespective whether comparative assessment is necessary or not, the paragraph should be rephrased, e.g. "The selection of compounds should be targeted to address the specific hypothesis triggering the need for compositional data… However the applicant is required to provide at least ……".
Germany	BVL	Combined transformation events stacked by conventional crossing	It is very unlikely, that combined transformation events stacked by conventional crossing impact the composition of the ingredient resulting in compound levels exceeding the natural variation in the final product under LLP conditions.
Germany	BVL	Conclusions (Annex II. II, 1.3.7)	The text in line 448-450 seems to be in contradiction to lines 401-408 as the driver "ERA-driven hypothesis" is not included in the descriptive section, but only mentioned in the conclusion. If it is wanted, it should

			be added to the section 401-408, reference to section 3.3 should be added and the abbreviation should be introduced. According to lines 406-407, a comparative analysis of agronomic and phenotypic characteristics in order to identify unintended effects is not considered mandatory in the context of LLP situations. According to the conclusions, however, relevant differences in the agronomic and phenotypic characteristics of the GM plant versus the conventional counterpart should be provided on a case-by-case basis, depending on ERA-driven hypothesis. The ERA for LLP situations, however, focuses only on the exposure of microorganisms to recombinant DNA and on accidental release of viable GM plant material – both not suitable for elaborating a risk hypothesis connected to unintended compositional changes related to the genetic modification Discrepancy to lines 400-408 (the collection of agronomic and phenotypic data is not considered mandatory?) Discrepancy to lines 400-408 (the collection of agronomic and phenotypic data is not considered mandatory?) Discrepancy to lines 400-408 (the collection of agronomic and phenotypic data is not considered mandatory?) Repetition of lines 434-453 without substantial additional information.
Germany	BVL	Information on altered levels of food and feed constituents (Annex II. II, 1.4.3)	According to the section on "Comparative Analysis", comparative compositional analysis is only necessary in specific cases. Therefore determining the levels of natural constituents should not be generally taken for granted with respect to toxicological assessment. Therefore the second part of the first sentence may be changed to: ... apply only if comparative compositional analysis was considered necessary and if the expected changes in the level of natural constituent(s) have been confirmed (section Comparative assessment). In line 471/472, "expected" should be deleted and "confirmed" should be replaced by "observed" – in case, the decision was made to perform a comparative assessment (due to the rationale as given in section 1.3), observed significant changes, which are biological relevant under LLP conditions, no matter whether expected or unexpected, should trigger the

			toxicological assessment as outlined in 1.4.3
Germany	BVL	Testing of whole genetically modified food and feed (Annex II. II, 1.4.4)	Taking into account that the exposure to LLP-GMO will be maximum 0,9% per ingredient of a product, the question arises, which specific hypothesis can justify the requirement of animal feeding trials
Germany	BVL	Assessment of allergenicity of the genetically modified food or feed (Annex II. II, 1.5.2)	The reference to the paragraph compositional analysis generates a kind of discrepancy since the analysis of composition is not mandatory for LLP applications. Or should the endogen allergens be measured in 0,9 % GMO fraction irrespective whether comparative assessment has been performed or not? EFSA should define clear requirements at this point. Changes in the level of one or more endogenous allergens in a given GMO present at a level of maximum 0.9% per ingredient in any food/feed do not necessarily increase (or decrease) the overall allergenicity of such food/feed. Given the individuality of allergic subjects, the absence of a (uniform) threshold, the high natural variability of expression levels and the fact that the remaining 99.1% of the ingredient may already pose a risk to allergic persons, interpretation of expression levels as well as of changes is difficult. Therefore, clear indications would be important as to how changes in expression levels are to be interpreted. In this regard, the phrase "LARGE changes" should be specified with regard to the biological relevance of a given increase in endogenous allergen levels "…possible, unless large changes in the level of endogenous allergens in the GMO have been confirmed observed…Do you really mean "changes" or "increase" of in the level of endogenous allergens? Please specify.
Germany	BVL	Conclusions of the allergenicity assessment (Annex II. II, 1.5.4)	The sentence in line 515-517 and the first half of the following sentence in line 517-518 seem to be redundant and should be rephrased. Following the recommendation in lines 506-510, this section would need to be rephrased
Germany	BVL	Food and feed safety in relation to intake (Annex II. II, 3.2.3)	Line 582: "Subject" instead of "matter" is in line with the wording of the document containing the ingredient with the GMO ~~matter~~ subject of an LLP application. Requirements described in

			The sentence is proposed to be reworded to make it more precise, e.g.: "Considering that the LLP applications are intended to support the authorisation of a GMO at a maximum level of 0.9 % in an ingredient of food and feed, no post market monitoring is foreseen."
Germany	BVL	Cumulative risk assessment	"There are actually two different scenarios of multiple LLP applications and possible cumulative contributions: 1. LLP of different GMOs of the same plant species, together amounting to < 0.9% of the ingredient; 2. LLP of GMOs belonging to different plant species, each amounting to < 0.9% of the respective ingredient Does the second scenario fall or not within the scope of the guidance? The second "compound" in line 609 should be changed to "constituent" as this is in line with the usage in the documents. " include the assessment of novel compound(s) (e.g. new protein) and of endogenous compound(s) constituent(s)
Germany	BVL	3.3. Environmental risk assessment	The restriction is not needed for understanding and is not part of the title of GMO Panel, 2010, but might lead to misunderstandings It is questionable whether the identification of four scenarios based on a stepwise approach (EFSA, 2010) is necessary under LLP conditions, especially since the inclusion of endpoints relating to agronomic and phenotypic characteristics is not considered mandatory. Under LLP conditions, which significantly reduce the exposition of GMO by loss and spillage, mainly the case in which the genetic modification directly targets the ability of a plant to persist and outcross in the non-natural environment is conceivable to be a candidate for ERA. In Exposure pathway 2 there is one scenario missing: GM plant material can establish and persist as volunteers in agricultural fields, but does not hybridise with EU cross-compatible wild relatives/there are no cross-compatible wild relatives in the EU (example: maize, potato); Consider to explicitly display a decision tree ... yes vs. no. It may be more "ergonomic" for readers

Germany	BVL	3.3.1. Exposure pathway 1: Exposure of microrganisms to recombinant DNA	even if… only theoretical possible" –the question arise, if the risk assessment of HGT under LLP conditions is necessary?
Germany	BVL	3.3.2. Exposure pathway 2: Accidental rlese into the environment of imported viable GM plant material during transportation and processing	"Plant-to-plant gene transfer" is usually defined broader and should not be equated with "hybridisation with cross-compatible wild relatives"; therefore it may be replaced here by the term "interspecific plant-to-plant gene transfer" It is questionable whether the identification of four scenarios based on a stepwise approach (2010) is necessary under LLP conditions, especially since the inclusion of endpoints relating to agronomic and phenotypic characteristics is not considered mandatory. Under LLP conditions, which significantly reduce the exposition of GMO by loss and spillage, mainly the case in which the genetic modification directly targets the ability of a plant to persist and outcross in the non-natural environment is conceivable to be a candidate for ERA.
Germany	BVL	Information for determining the likelihood of persistence and invasiveness of GM plants and their	It is recommended to delete the crop listing in lines 725, 729 and 733 as it is incomplete and the categorization of a certain crop will highly depend on the LLP product, the GM trait and the regions within the EU. A similar list is not given in other cited documents as GMO Panel, 2010. The categorization should to be substantiated by the applicant as part of the application. The categorization is to be evaluated by risk assessors. See comment on Fig. 1. For example there are no wild relatives for maize in Europe and therefore no hybridisation with cross-compatible wild relatives is expected in the EU
Germany	BVL	Glossary	"Same type of plant" is very general; should be more specific, i.e. replace by "same plant species" Non-GMO portions are present at a proportion of minimum 99.1%; therefore please change to … maximum 0.9% and minimum 99.1%, respectively.
Germany	BfN	1.1. Background and Terms of Reference as provided by the	The reason for a threshold of 0.9% remains unclear. In comparison to the rules given in Regulation 619/2011 which allows a LLP of up to 0.1%

		requestor	in GM feed for certain conditions the higher threshold given in the mandate by the commission is not supported.
Germany	BfN	Paragraph 1.2.2.3. Information on the expression of the insert(s)	For Food and Feed safety it might be sufficient to characterize the expression of transgenes in the parts of the plant used for food and feed purposes. But if plants establish and/or persist outside of agricultural fields (Exposure pathway 2, Scenario 3 and 4), for the ERA the potential of exposition of the environment needs to be assessed. Therefore information on the whole plant as requested in the original paragraph (b, c) could be pivotal to ensure that a satisfactory environmental risk assessment is possible (e.g. pollen expression in bt-maize). The same is true for the possible safety concerns of stacked events.
Germany	BfN	Paragraph 1.2.2.4. Genetic stability of the insert and phenotypic stability of the genetically modified plant	The genetic stability of the insert may be essential for the identification of the GMP in case of an accidental release into the environment. A partial loss of the transgene renders the identification of possible residual transgenic sequences difficult and enhances the probability of false negatives
Germany	BfN	Comparative analysis (Annex II. II, 1.3)	In the draft guidance document EFSA states that a compositional analysis to examine the nutritional equivalence of the GMO will not be necessary if only present at low levels (up to 0.9%). In our opinion in case of plants that can establish and persist, the evaluation of toxicological and allergenic potential of the GMO requires a compositional analysis even if no precise hypothesis can be formulated. The approach proposed by EFSA will miss effects which are not directly caused by the transgene or it components and are unintended or unexpected.
Germany	BfN	Experimental design and statistical analysis of data from field trials for comparative analysis (Annex II. II, 1.3.2) Paragraph 1.3.2.1. Description	*a) Principles of experimental design* In case of plants that establish and persist, an estimation of equivalence limits might be necessary after identifying significant deviations in a difference test. *b) Specific protocols for experimental design*

		of the protocols for the experimental design	In case of plants that establish and persist, a full comparative assessment with a minimum of eight sites as recommended in Regulation (EU) No 503/2013 is required.
Germany	BfN	Comparative analysis of agronomic and phenotypic characteristics (Annex II. II, 1.3.5)	A comparative analysis of agronomic and phenotypic characteristics should be considered, depending on the characteristics of the plant concerning its ability to establish and persist.
Germany	BfN	Conclusions of the toxicological assessment (Annex II. II, 1.4.5)	*The GMO Panel notes that the conclusions of the toxicological assessment do not routinely include considerations from the 90-day studies in rodents on the whole food/feed.* 90-day studies in rodents are obligatory according to Regulation (EU) No 503/2013. It would be desirable to state that this paragraph clearly refers to a LLP situation. Otherwise the last sentence should be deleted.
Germany	BfN	Assessment of allergenicity of the genetically modified food or feed (Annex II. II, 1.5.2)	The draft guideline proposes derogation from Annex II in cases where "no large changes in the level of endogenous allergens in the GMO have been confirmed". The derogated Comparative assessment does not require testing if no hypothesis is formulated. In our opinion this means that non-intended and unexpected changes which are not caused by a novel component could not be identified as those components will not be tested in comparative assessment in the first place. Furthermore as allergenic effects can be caused by low levels of harmful ingredients derogation should be avoided.
Germany	BfN	3.3. Environmental risk assessment	For the environmental risk assessment of LLP of viable seeds it is essential to take the following points into account. 1. Even if the applied event only occurs with a presence of less than 0.9% in commodities, it can, depending on the frequency of import and the amount of the imported seeds, at the end become a huge total amount of GM seeds that will be imported. 2. Furthermore, for plants that can establish and persist outside of agricultural habitats and may cross with wild relatives Low Level

			Presence does not exclude dissemination. If establishment occurs, the exposition of the environment can become high in the long run independent of the low level portion at the beginning. Therefore a full environmental risk assessment needs to be performed if viable seeds of plants of scenario 3 and 4 are imported. In this case, the full data set for compositional analysis, comparative approach, protein expression and agricultural and environmental parameters needs to be provided. *ERA diagram:* Minimal sequence length sufficient for homologous recombination varies between microorganisms and can be lower than the 200bp recommended by the EFSA explanatory note on DNA sequence searches (2015) (e.g. 23bp for E. coli (Shen and Huang 1986) or 96bp for Xylella fastidiosa (Kung et al. 2013)). To exclude a potential risk of HGT by HR and respecting the precautionary principle laid down in Directive 2001/18/EC we recommend to either substantially lower or remove the suggestion for a minimal sequence length that triggers further consideration from the EFSA guidance document. Kung SH, Retchless AC, Kwan JY, Almeida RP. Effects of DNA size on transformation and recombination efficiencies in Xylella fastidiosa. Appl Environ Microbiol. 2013 Mar;79(5):1712-7. doi: 10.1128/AEM.03525-12 Shen P, Huang HV. Homologous recombination in Escherichia coli: dependence on substrate length and homology. Genetics. 1986 Mar;112(3):441-57.
Germany	BfN	Environmental consequences of persistence and invasiveness of the GM plant and plant-to-plant gene transfer	It would be desirable in this paragraph to clearly state that in a scenario 3 and 4 situation a full ERA according to EFSA GMO Panel (2010) is necessary. *If the GM plant material is likely to establish and persist in the receiving environment as occasional* That only applies, if it includes the assumption that it does not hybridize with wild relatives *However, it is unlikely that interactions of the GM plant with target and*

			non-target organisms, the abiotic environment, and biogeochemical cycles require assessment In our opinion, for plants that can establish and persist outside of agricultural habitats and may cross with wild relatives a full environmental risk assessment needs to be performed as due to the establishment exposition of the environment may be high in the long run
Germany	BfN	3.3.3. Risk management	Post-market environmental monitoring (PMEM) is a compulsory part of the authorisation and a measure within the frame of the precautionary principle, that aims to detect potential adverse effects of the GMO on human health and the environment, which might be direct, indirect, immediate or delayed" (RL 2001/18/EC, Article 13 No 2,Article 19 No 3 Annex VII; Council Dec. 2002/811/EC Annex A). Current wording suggests, that PMEM would be part of the risk management and would not be imperative. Therefore the indicated subordinary clause should be deleted
Germany	Federal Research Centre of Cultivated Plants	Assessment of allergenicity of the genetically modified food or feed (Annex II. II, 1.5.2)	Allergenicity of GM food is a sensitive issue regarding consumer protection. Therefore requirements laid down in para 1.5.2 of Annex II should apply
Germany	Robert Koch Institute	Experimental design and statistical analysis of data from field trials for comparative analysis (Annex II. II, 1.3.2) Paragraph 1.3.2.1. Description of the protocols for the experimental design b) Specific protocols for experimental design	One site could be largely impacted by climate factors. Therefore, at least 3 sites should be recommended to compensate climate effects
Germany	Robert Koch Institute	Assessment of allergenicity of the genetically modified food or feed (Annex II. II, 1.5.2)	As allergenicity is no question of amount, the requirements as outlined in section 1.5.2 of Annex II of the Regulation (EU) No 503/2013 should apply. Line 509 "large changes" should be defined otherwise "large" should be

			deleted.
Greece	Ministry of Rural Development and Food (YPAAT)	1.1. Background and Terms of Reference as provided by the requestor	There is no reference to Reg (EU) No 619/2011 which lays down the methods of sampling and analysis for the official control of feed as regards presence of genetically modified material for which an authorisation procedure is pending or the authorisation of which has expired. In our opinion, the above Regulation should be taken into account as it regulates LLP issues in feed.
Greece	Ministry of Rural Development and Food (YPAAT)	1.2. Interpretation of the Terms of Reference	Regulation (EU) No 619/2011 sets a technical limit of 0.1% for the presence of genetically modified material in feed. On the contrary, the present Draft guidance sets a maximum limit of 0.9%. We ask for clarifications about the different approach on the determination of the upper limit of presence of genetically modified material
Greece	Ministry of Rural Development and Food (YPAAT)	3.1.2. Scope of the guidance	In spite of the fact that GMOs for non-food/feed uses are not in the scope of Regulation (EC) 1829/2003, Commission Decisions approve the uses other than food and feed.
Greece	EFET-DERE	Title	Change to "Draft guidance for the a priori risk assessment of the low level presence authorization of genetically modified plant material in imported food and feed under Regulation (EC) No 1829/2003"
	EFET-DERE	Keywords	Insert 503/2013
	EFET-DERE	1.2. Interpretation of the Terms of Reference	A more specific determination of "large sized fruit/vegetable consumed as such" is needed
Greece	EFET-DERE	3.1.1. Key definitions	Key definitions are very satisfactory
Greece	EFET-DERE	3.1.2. Scope of the guidance	Scope of the guidance is very clear and satisfactory
Greece	EFET-DERE	ERA Diagram	Very Informative and satisfactory
Greece	EFET-PDMK	Insertion of marker genes and other nucleic acid(s) sequences not essential to achieve the desired tract (Annex II. I, 2.1)	trait (instead of tract)
Greece		Risk assessment of genetically	terms (instead of term)

		modified food and feed containing stacked transformation events (Annex II. I, 2.2)	
Greece	EFET-PDMK	b) Specific protocols for experimental designin derogation to requirements	b) Specific protocols for experimental design in derogation to the requirements
Greece	GCSL	1.1. Background and Terms of Reference as provided by the requestor	The low level presence should be defined at a maximum level of 0,1%, as defined in LLP Regulation (619/2011) for feed for asynchronous GMOs. It is not reasonable to set the threshold for asymmetric or not yet approved (even in third countries) GMOs at higher level than the threshold for asynchronous GMOs (0,1%) and at the same level of the threshold applied for labelling of approved GMOs(0.9%). The maximum level of 0,9% should be corrected to 0,1% to the whole text. *...concern GM products developed for specific health or market needs in third countries* Proposal:...concern GM products developed and authorised or submitted for authorisation for specific health or market needs in third countries It is obvious that an LLP application should include GMOs to be legally used (for experimental or commercial purposes) in a third country, otherwise there is no reason to find these GMOs as an adventitious and unavoidable presence in food/feed imported in the EU.
Greece	GCSL	3.1.1. Key definitions	A definition for "asymmetric" or "not yet approved in third countries" GMO should be added for the purposes of this guidance. Proposal: Asymmetric or not yet approved in third countries GMO - a GMO authorised or submitted for authorisation in third countries (outside EU) and for which no application has been submitted for authorisation in EU. Ingredient: as defined in the Regulation (EU) 1169/2011. For the purposes of LLP presence the ingredient is a mixture derived from a GM and non-GM plant (both GM and non-GM material is derived from the same plant species). Furthermore the legal definition of ingredient should

			not be ignored, because it is linked with the term ingredient in the Regulation (EC) 1829/2003
Greece	GCSL	3.1.2. Scope of the guidance	The scope of the Regulation (EC) 1829/2003 (articles 3 and 15) is general and it is not limited to GM plants. Furthermore, the same Regulation, under the principle "one door-one key", covers GMOs for cultivation purposes and non-food/feed uses". Please see relevant authorisation decisions according to the Reg (EC) 1829/2003 for non food and feed uses. On the other hand, Regulation (EU) 503/2013 covers only GM plants for food/feed uses (article 1).
Greece	GCSL	Information on altered levels of food and feed constituents (Annex II. II, 1.4.3)	If the comparative analysis has not been fully carried out, we may have not enough data to decide if there are significant changes in the level of natural constituents.
Greece	GCSL	Paragraph 1.4.4.1. 90-day feeding study in rodents with whole genetically modified food and feed	An incomplete comparative assessment should be followed at least by a 90-day feeding study in rodents with the whole GM food/feed.
Greece	GCSL	Assessment of allergenicity of the genetically modified food or feed (Annex II. II, 1.5.2)	There are no defined thresholds for allergenicity. The term "large" is not and cannot be adequately defined. *...unless large changes...* Proposal: ...unless any changes...
Ireland	Food Safety Authority of Ireland	3.1.1. Key definitions	Should read: LLP application: an application prepared by an applicant in accordance to with GMO Panel 180 guidance on LLP LLP application: an application prepared by an applicant in accordance to GMO Panel guidance on LLP
Ireland	Food Safety Authority of Ireland	3.1.2. Scope of the guidance	Im not sure I understand why GMMs and GM animals, both for food use are automatically excluded as they are not excluded from 1829/2003? It may just be the wording that makes it look like they are excluded?
Ireland	Food Safety Authority of Ireland	Insertion of marker genes and other nucleic acid(s) sequences not essential to achieve the desired tract (Annex II. I, 2.1)	"tract (Annex II. I, 2.1) Should read "achieve the desired trait""'

Ireland	Food Safety Authority of Ireland	Comparative assessment studies performed under non-EU regulatory frames: applicability in LLP applications.	"studies that have been conducted in accordance to Codex Alimentarius studies that have been conducted in accordance to with Codex Alimentarius"
Ireland	Food Safety Authority of Ireland	Conclusions (Annex II. II, 1.3.7)	"to differences in the composition of GMO possibly to differences in the composition of a GMO possibly"
Italy	Istituto Superiore di Sanita (ISS)	General	The risk assessment strategy followed in the guidance is able to wholly achieve the a priori risk assessment of the low level presenceof genetically modified plants. The identified requirements of Annex II to Regulation (EC) No 503/2013 are those necessary to conclude on the safety of this kind of applications. It is not fully clear the normative framework of an LLP application. Finally a validated event specific method of detection, identification and quantification and control samples and reference material should be provided.
Italy	Ministero della Salute Direzione generale per l'igiene e la sicurezza degli alimenti e la nutrizione Ufficio 6 - Igiene delle tecnologie alimentari	General	In reference to the request for comments on "GMO Guidance document on LLP", also taking into consideration the assessment of the National Reference Laboratory for GM food and feed, c/o IZS of Latium and Tuscany, for its area of competence, please find the following observations. From a technical and scientific point of view, there is no evidence to refute the approach of EFSA panel to conduct the assessment of GM events at low level concentration. However, we express concerns about the legislation on which this issue could refer. At present, with the exception of feed regulated by the Regulation UE 619/2011, the presence of unauthorized GMOs, although at low levels, foresees the activation of RASFF and the Regulation EC 1829/2003 doesn't provide for the possibility of submitting an application for authorising a GMO at low level presence. These concerns are even more substantial in the light of outcomes of the

			SCPAFF of 8th July 2016, in which the Commission presented to Member States technical study to assess the need for harmonization of sampling and analysis methods for GM material in food at low concentrations. Based on the study results and the ensuing discussion, Member States agreed that the harmonization of sampling and analysis methods for food would not be justified, taking into account technical aspects and the economic impact. So, the Commission encouraged the proper implementation of the existing legislation and, where possible, a higher convergence between Member States' practices. Therefore, for the abovementioned reasons, the final purpose of the guideline proposal doesn't appear so clear.
Netherlands	Ministry of Health, Welfare and Sport (Ministerie van Volksgezondheid, Welzijn en Sport, VWS). The question was answered by COGEM, RIKILT and BGGO on request of the Ministry of Health, Welfare and Sport	General	General comments: In general it can be concluded that the selection of items from the Implementation Regulation 503/2013 that are considered to apply in a LLP situation, seems fully in line with the IR as such. Most items of the IR are deemed applicable, but in most cases less data need to be supplied routinely. It can, however, be questioned, how often these LLP stipulations will be applicable, and helpful: if a GMO has not received market approval anywhere, the data required in the current document are not likely to be available. In those cases it will require much time and effort to generate even the reduced datasets. In practice this will likely mean that there will still be a zero tolerance for this group of GMOs. In those cases where the GMO has already received market approval elsewhere, the LLP stipulations can be of help, as in those cases dossiers will be available, but these stipulations, although less rigid than the Implementation Regulations as such, may still hamper trade as safety dossiers that may underpin the safety of the GMO, but may not include all data as stipulated in the LLP guidance, can still not be considered sufficient to allow LLP of the GMO in import flows. A more flexible case-by-case approach to assess the safety of LLP GMOs would have been more applicable and helpful in practice, also taking into account the fact that so far no GMOs have been identified that justify a very stringent approach at the level of 0.9% (per ingredient). Overall conclusion:

			The guidance document provides a detailed overview of the information required to assess the potential risks for food and feed safety in case of adventitious LLP of GM plant material in imported food or feed. The guidance, however, does not provide sufficient guidance on the information required to assess potential environmental risks. Descriptions of potential exposure pathways and scenarios to categorise plants in different groups are provided, but these do not result in clear descriptions of the information needed for the different situations. In addition, the guidance could be improved by ensuring that the different sections in the guidance document are interconnected, for instance by mentioning the types of information which may be needed to assess environmental risks in the corresponding paragraphs in the sections of the guidance describing the scientific requirements (3.2). "
Netherlands	Ministry of Health, Welfare and Sport (Ministerie van Volksgezondheid, Welzijn en Sport, VWS). The question was answered by COGEM, RIKILT and BGGO on request of the Ministry of Health, Welfare and Sport	1.2. Interpretation of the Terms of Reference	"Further information needed on the LLP threshold for stacked events According to the clarifications of the European Commission, in case of stacked transformation events the 0.9% threshold for 'low level presence' applies to individual events (line 122). The use of the term 'individual events' in the context of 'stacked transformation events' leads to confusion. Therefore, further information should be provided on the threshold for 'low level presence' for stacked events. "
Netherlands	Ministry of Health, Welfare and Sport (Ministerie van Volksgezondheid, Welzijn en Sport, VWS). The question was answered by COGEM, RIKILT and BGGO on request of the Ministry of Health, Welfare and Sport	3. Assessment	Applications for LLP authorisations limited to non-viable plant material may be submitted A substantial part of the food and feed imported in the EU consists of non-viable plant material (such as maize gluten or soybean meal). The guidance document and the potential future authorisation procedure should take into account that applications for authorisations limited to LLP of non-viable plant material may be submitted. In such cases, only the food/feed safety has to be assessed. As the environmental risks do not have to be assessed, a considerable lower number of safety studies will be required. Guidance on environmental risk assessment requirements limited and insufficiently incorporated in other sections of the guidance

			The guidance describes the information required to assess food/feed safety as well as the environmental risks of adventitious LLP of GM plant material in imported food/feed. The structure of the guidance reflects the separate status of the environmental risk assessment. It has to be noted that data deemed unnecessary to assess food or feed safety (e.g. expression levels from plant parts which are not consumed, and the comparative analysis of agronomic and phenotypic characteristics) may be required to assess environmental risks. This is not mentioned in the section on scientific requirements (Annex II.II). The interconnectivity of the different sections in the guidance document could amongst others be improved by incorporating the (potential) ERA requirements in the other sections. In addition, the section on the environmental risk assessment does not provide sufficient guidance on the information required to assess potential environmental risks. Different exposure pathways are described and scenarios are provided to categorise plants according to their potential for persistence, invasiveness and hybridisation potential. The guidance on the information required to assess the environmental risks for each of these different pathways and scenarios is, however, limited. Examples of the information required for different types of GM plants would provide insight in the kind of information that is needed to assess potential environmental risk"
Netherlands	Ministry of Health, Welfare and Sport (Ministerie van Volksgezondheid, Welzijn en Sport, VWS). The question was answered by COGEM, RIKILT and BGGO on request of the Ministry of Health, Welfare and Sport	Comparative analysis of agronomic and phenotypic characteristics (Annex II. II, 1.3.5)	"Information on agronomic and phenotypic characteristics is required in some cases According to the guidance, a comparative analysis of agronomic and phenotypic characteristics is not mandatory for LLP situations (lines 405-407). However, information on agronomic and phenotypic characteristics are also used to identify differences in plant fitness (as mentioned in line 403), which is particularly relevant in the case of the fourth scenario described in chapter 3.3 on the environmental risk assessment. Therefore, the statement that information on agronomic and phenotypic characteristics is not necessary in case of LLP has to be adapted to reflect that information may be needed on a case-by-case basis to inform

			the environmental risk assessment, i.e. in accordance with the statement in lines 448 to 450 "Relevant differences in the agronomic and phenotypic characteristics of the GM plant versus the conventional counterpart should be provided on a case-by-case basis, depending upon ERA-driven hypothesis.”"
Netherlands	Ministry of Health, Welfare and Sport (Ministerie van Volksgezondheid, Welzijn en Sport, VWS). The question was answered by COGEM, RIKILT and BGGO on request of the Ministry of Health, Welfare and Sport	Combined transformation events stacked by conventional crossing	"Incorporate paragraph on events stacked by conventional crossing in the comparative analysis paragraph The guidance contains a separate paragraph on 'combined transformation events stacked by conventional crossing' (lines 433 to 436). As this paragraph only describes that experimental data may be needed if interactions between the combined transformation events could lead to differences in composition, this paragraph could better be incorporated as a fourth case in the enumeration given in lines 345 to 348 of the paragraph on comparative analysis. "
Netherlands	Ministry of Health, Welfare and Sport (Ministerie van Volksgezondheid, Welzijn en Sport, VWS). The question was answered by COGEM, RIKILT and BGGO on request of the Ministry of Health, Welfare and Sport	Molecular characterisation (Annex II. II, 3.2.1)	"Incorporation of environmental risk assessment requirements in required molecular characterisation The molecular characterisation of a GM plant provides information that is relevant to the food/feed safety assessment and the environmental risk assessment. The guidance follows the lay-out of Regulation 503/2013 leading to a focus on aspects relevant to the food/feed safety assessment. For instance, in paragraph 1.2.2.3 (information on the expression of the insert(s)) the following is stated "…, only the expression levels from those part(s) of the plant used for food and feed purposes, are considered necessary to complete the risk assessment" (lines 280-281). However, to assess environmental risks information on expression levels in other plant parts may be relevant, e.g. in case of the fourth scenario described in lines 730 to 733 of the section on the environmental risk assessment"
Netherlands	Ministry of Health, Welfare and Sport (Ministerie van Volksgezondheid, Welzijn en Sport, VWS). The question was	3.3. Environmental risk assessment	"Requirements to assess environmental risks insufficiently elaborated The section on the environmental risk assessment is far less elaborate than the section on food/feed safety requirements and does not provide much guidance on the information required to assess environmental risks

	answered by COGEM, RIKILT and BGGO on request of the Ministry of Health, Welfare and Sport		of LLP. In the case of scenarios 2, 3 and 4 (exposure pathway 2) it is mentioned that the environmental consequences need to be considered, but no further details are provided on cases in which certain aspects of the 'EFSA environmental risk assessment guidance' are and are not considered relevant. To enhance the applicability of the guidance, more elaborate information on the data required to assess the environmental risks has to be provided. Improve clarity of environmental risk assessment requirements by including release of non-viable GM plant material in exposure pathways In the section on the environmental risk assessment it is only briefly mentioned that an assessment of these risks is only required for viable GM plant material (lines 614-615). The inclusion of an additional exposure pathway (both in the text and in figure 1), i.e. the release of imported non-viable GM plant material (such as soybean meal, maize gluten, etc.), would improve the clarity of the guidance. Viable seeds in faecal material more appropriately discussed in exposure pathway 2 The guidance distinguishes two exposure pathways: 1) exposure of microbial communities to recombinant DNA in the GI tract of animals fed GM plant material and environments exposed to faecal material of these animals, and 2) accidental release into the environment of imported viable material from the GM plant during transportation and processing (lines 626-629). According to these descriptions, environmental exposure via intact (viable) seeds in faecal material is part of the first exposure pathway. Potential scenarios associated with the introduction of intact seeds into the environment via faecal material are, however, not mentioned in figure 1 or 3.3.1. More importantly, the assessment of risks posed by such seeds has more in common with the risk assessment of GM plants introduced via accidental spillage. Therefore, the requirements to assess potential risks of intact seeds could be more appropriately discussed as part of exposure pathway 2."
Netherlands	Ministry of Health, Welfare and	3.3.1. Exposure pathway 1:	"Assessment of horizontal gene transfer has to be based on the presence

	Sport (Ministerie van Volksgezondheid, Welzijn en Sport, VWS). The question was answered by COGEM, RIKILT and BGGO on request of the Ministry of Health, Welfare and Sport	Exposure of microrganisms to recombinant DNA	of introduced traits potentially enhancing its occurrence The rationale to request information to assess the probability and consequence of horizontal gene transfer, which is a very rare event, is insufficiently substantiated. According to the guidance, illegitimate recombination should be addressed even though there is no evidence that it occurs under natural conditions and illegitimate recombination is considered highly unlikely and only theoretically possible (lines 669-672). Since illegitimate recombination is improbable, this requirement appears to be superfluous. In addition, EFSA is of the opinion that in view of the amount of GMOs fed to animals over time, the possibility of homologous recombination should be assessed even though horizontal gene transfer is a very rare event. Instead of requesting sequence identity comparisons between the recombinant DNA and DNA from microorganisms, an approach to assess horizontal gene transfer potential that is based on the potential presence of introduced traits which could enhance the occurrence of horizontal gene transfer is better suited.[1] [this comment is also relevant to paragraph 1.2.2.5 'potential risk associated with horizontal gene transfer' (this comment is also relevant to paragraph 1.2.2.5 'potential risk associated with horizontal gene transfer') COGEM (2011). Comments on the 'Guidance on the environmental risk assessment of GM plants' and on the 'LL Scientific Opinion on the assessment of potential impacts of GM plants on NTOs'. COGEM advice CGM/110214-02"
Netherlands	Ministry of Health, Welfare and Sport (Ministerie van Volksgezondheid, Welzijn en Sport, VWS). The question was answered by COGEM, RIKILT and BGGO on request of the Ministry of Health, Welfare and Sport	3.3.2. Exposure pathway 2: Accidental release into the environment of imported viable GM plant material during transportation and processing	"Not all plant species fit to the given scenarios In the EFSA guidance four different scenarios are described to group plants. There are, however, plant species with properties that do not seem to fit to the given scenarios. For instance, plant species which can establish and persist in a natural environment; or plant species which can establish and persist in semi-natural environments, but which cannot hybridise with wild relatives. In addition, the distinction between the four scenarios is not unambiguous, as is illustrated by oilseed rape which is

			mentioned as an example in both scenario 2 and 3. The description of the different scenarios has to be reconsidered. Scenario 1 of exposure pathway 2 describes a hypothetical situation Scenario 1 refers to GM plants that cannot establish or overwinter in the European Union. It is doubtful whether there are plant species which are within the scope of the guidance and cannot establish or overwinter anywhere in the European Union. A plant species which comes to mind is papaya, but large sized fruits and vegetables such as papaya fall outside the scope of the guidance. Mentioning that this scenario reflects a hypothetical situation, would add to the clarity of the guidance document. In addition, the description of scenario 1 at line 723 has to be adapted. In line 750 it is mentioned that in scenario 1 there is less likelihood of plant-to-plant gene transfer, but at line 723 it is not mentioned that hybridisation with cross-compatible wild relatives may occur. This can be added to the description at line 723. Furthermore, because hybridisation with cross-compatible wild relatives is not excluded in this scenario, information to assess environmental risks may be required in some cases. The conclusion of EFSA that in this scenario (thus for all cases) environmental harm is unlikely and therefore assessment of interactions with target and non-target organisms, the abiotic environment, and biogeochemical cycles is not required (lines 752 to 754), has to be adapted accordingly. Description of scenarios of exposure pathway 2 do not reflect routes of exposure by accidental spillage of imported food or feed The guidance describes the information required in case of LLP of GM plant material in imported food/feed. In the description of the scenarios of exposure pathway 2 (figure 1, lines 724 to 729 and 756) situations are mentioned which are improbable in case of GM plants introduced via

			accidental spillage of imported food or feed. Scenario 2 in particular does not seem to be relevant as introduction in agricultural fields is not very likely in case of adventitious presence of imported commodities or food/feed. The same is true for scenario 3 which refers to persistence under disturbed conditions outside agricultural fields. Also, as the risk assessment approach for scenarios 2 and 3 is equal (lines 755 to 760), it is unclear why these two different scenarios are distinguished"
Netherlands	Ministry of Health, Welfare and Sport (Ministerie van Volksgezondheid, Welzijn en Sport, VWS). The question was answered by COGEM, RIKILT and BGGO on request of the Ministry of Health, Welfare and Sport	Environmental consequences of persistence and invasiveness of the GM plant and plant-to-plant gene	"Considerable amount of seeds may be introduced even in case of LLP presence Lines 755 to 758 refer to a situation where the GM plants are likely to establish and persist in the environment as occasional plants which do not multiply and may hybridise with wild relatives (scenarios 2 and 3). It is concluded that it is unlikely that interactions of the GM plant with target and non-target organisms, the abiotic environment, and biogeochemical cycles would require assessment (lines 759 to 760) when the GM plant material is released at low levels in the environment and exposure is likely to remain low and confined to agricultural or ruderal habitats (lines 756 to 757). Even in case of LLP a considerable amount of plant material can be released into the environment. A single kilo of oilseed rape seeds contains approximately 310,000 seeds.[1] In case of LLP (a maximum of 0.9% of a GMO) this would correspond to ~2800 GM oilseed seeds per kilo. If 0.1% of the seeds is accidentally spilled, this would correspond to approximately 3 GM oilseed seeds per kilo. As tonnes of oilseed rape seeds are imported each year, the number of GM seeds that could potentially be introduced in the environment by accidental spillage during transportation and processing is, even in case of LLP, considerable. This is demonstrated by the numerous reports of oilseed rape (Brassica napus) populations and GM oilseed rape plants alongside road verges and railway tracks.[2] Therefore, it cannot be concluded in advance that it is unlikely that interactions of the GM plant with target and non-target organisms, the abiotic environment, and biogeochemical cycles would require assessment (as is stated in lines 759 to 760 for scenarios 2 and

			3). Depending on the plant species and the introduced traits, information to assess potential environmental risks may be required. The conclusion has to be adapted accordingly. In case of scenario 4 of exposure pathway 2 derogation of the information requirements in Regulation 503/2013 is probably not possible Scenario 4 refers to a situation where the GM plants increases in population size (or becomes invasive) and may hybridise with EU cross-compatible wild relatives. In this scenario GM pollen could be produced and may subsequently fertilise conventional varieties. This would result in the presence of GM material in harvest material. Because of this, it is questionable whether in case of scenario 4 derogation of the information requirements listed in Regulation (EU) 503/2013 is possible. In case of scenario 4 of exposure pathway 2 derogation of the information requirements in Regulation 503/2013 is probably not possible Scenario 4 refers to a situation where the GM plants increases in population size (or becomes invasive) and may hybridise with EU cross-compatible wild relatives. In this scenario GM pollen could be produced and may subsequently fertilise conventional varieties. This would result in the presence of GM material in harvest material. Because of this, it is questionable whether in case of scenario 4 derogation of the information requirements listed in Regulation (EU) 503/2013 is possible. 2.Tamis WLM & De Jong TJ (2010). 'Transport chains and seed spillage of potential GM crops with wild relatives in the Netherlands' COGEM research report CGM/2010-02; 3. COGEM (2013). GM oilseed rape (Brassica napus): Aspects in relation to the environmental risk assessment and post-market environmental monitoring of import applications. COGEM advice CGM/130402-01"
Poland		General	Insufficient data (citations) regarding the testing of the modified DNA on LLP level
Poland		1.1. Background and Terms of Reference as provided by the	Additional justification for the preparation of guidelines is needed, ie. examples that the presence of modified DNA at the low level (<0.9%) may pose a risk of toxicity, allergenicity and therefore the preparation of

		requestor	guideline is appropriate in this regard.
Poland		References	References should be supplemented with information on testing data of GMO products at LLP level in various materials and feeds, methods of calculation of the results on the mass fraction and how to interpret results

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Appendix D – Table of the public consultation submitted by means of electronic forms

Country	Organisation	Section	Complete comment
Belgium	COCERAL	General comment	COCERAL, the European association of trade in cereals, rice, feedstuffs oilseeds, olive oil, oils and fats and agrosupply, would like to comment on the draft guidance for the risk assessment of the Low Level Presence (LLP) of genetically modified (GM) plant material in imported food and feed. COCERAL acknowledges that the European Commission's mandate to the European Food Safety Authority (EFSA) was to focus on the risk assessment of LLP of GMOs before the situation of LLP occurs (i.e. "a priori" risk assessment – as per letter ref. Ares(2015)1362776 of 27 March 2015). However, COCERAL would like to underline that the distinction between "a priori" and "ex post" risks to be too artificial, and does not necessarily provides for any scientific utility in the risk assessment per se. COCERAL would also like to draw EFSA's attention to the following. The draft guidance in its current form is not providing enough indication on the approach adopted for exposure modelling. While it is clear that EFSA's intention is to assess exposure resulting from low level of presence in the commodity to which the GM event belongs (sort specific LLP) it is not clear whether EFSA would also consider the potential for intermittent presence at low level of the GM event at stake as a botanical impurity in other food commodities imported from the region(s) growing the GM event under consideration. COCERAL would therefore welcome a clarification on the approach adopted for exposure scenarios.
Belgium	EuropaBio	1.1 Background and Terms of Reference as provided by the requestor	Lines 114-115: We recommend that the exact wording of the mentioned article is used as follows: an application may be submitted that does not satisfy all the requirements of Annex II provided that is not scientifically necessary. Lines 136-137: It is not clear whether the term 'similar traits' refers to similar traits in the same crop or in different crops. Moreover, it would be challenging to gain this information since traits are developed by different companies and at different times. The

			first LLP application cannot contain any cumulative RA. It also remains unclear how many similar traits would qualify for a cumulative risk assessment. Consequently, we suggest that the requirement of the cumulative risk assessment is deleted.
Belgium	EuropaBio	1.2 Interpretation of the Terms of Reference	Lines 145-152: A reference to the products 'not intended for the EU market' is missing. Lines 161-162: The draft guidance does not specify how the decision on whether a given GMO constitutes a LLP application. We recommend that precise criteria concerning which products could qualify and when are laid down in the guidance. Line 167: The differences between the Codex and the terms of reference of this mandate would not allow for adopting an approach towards global harmonization of LLP policy. This runs counter Article 13 of Regulation (EC) No. 178/2002.
Belgium	EuropaBio	2.1 Data	Line 171: We suggest that the terms "requirements" or "scientific requirements" are used consistently through the document.
Belgium	EuropaBio	2.2 Methodologies	Line 187: We recommend that the technical report (on received comments) is published on the EFSA website to cover both consultations (i.e. the one with Member States and the public consultation).
Belgium	EuropaBio	3.1.1. Scope of the guidance	Line 193: Instead of using the term 'technical requirement', we suggest that the terms "requirements" or "scientific requirements" are consistently used throughout the document.
Belgium	EuropaBio	3.1.2. General risk assessment considerations for LLP situations	Line 205: We recommend that the term 'traditionally cultivated crops' is substituted with "conventionally cultivated crops".
Belgium	EuropaBio	3.2.2.1. Insertion of marker genes and other nucleic acid(s) sequences not essential to achieve the desired tract (Regulation [EU] No 503/2013; Annex II. I, 2.1)	Line 235: There is a typographical error in the section header: "tract" should be replaced by "trait".

Belgium	EuropaBio	3.2.2.2. Risk assessment of genetically modified food and feed containing stacked transformation events (Regulation [EU] No 503/2013; Annex II. I, 2.2)	Line 243: Trait stability is of very little relevance to the safety assessment for LLP of a GMO that will not be cultivated or marketed in the EU. Therefore, we recommend that this requirement is deleted due to negligible exposure argument towards the environment.
Belgium	EuropaBio	3.2.3.2. Molecular characterisation (Regulation [EU] No 503/2013; Annex II. II, 1.2)	Lines 295-296: The likelihood of expression of newly formed ORFs is very low. Consequently, even if an ORF is expressed at the level of 0.9%, the likelihood of any adverse effect is negligible. Hence, the identification of new ORFs, their expression analysis and risk assessment is not scientifically necessary and will not add to the safety assessment of the GM plant in LLP.
Belgium	EuropaBio	3.2.3.3. Comparative analysis (Regulation [EU] No 503/2013, Annex II. II, 1.3)	Line 415: There is a discrepancy between this line and line 387. In this paragraph, the draft guidance states that there is a "possible" exception of the equivalence test, whereas the equivalence test is explicitly excluded in line 387. Lines 439 - 446: This statement appears to contradict earlier statements (lines 393-411) that articulate acceptable conditions for generating test material for LLP assessment that potentially deviate from the Codex Guidelines. We suggest that lines 445-446 are deleted.
Belgium	EuropaBio	3.2.3.4. Toxicology (Regulation [EU] No 503/2013; Annex II. II, 1.4)	Line 468: Following the principles of comparative analysis described in section 3.2.3.3, we consider that the testing of newly expressed proteins should not be provided on a routine basis. Due to the maximum 0.9% contribution of the LLP GMO to the ingredient, the actual exposure to the newly expressed proteins is negligible. Line 469: The draft guidance states that 'Requirements laid down in this paragraph are considered necessary in LLP applications'. We are of the opinion that the risk assessment shall start with the exposure part, the same being applied to new constituents. However, we would welcome further clarification.

			Lines 468-471: It is not clear why a full assessment of the expressed protein and non-protein constituents is recommended by the LLP draft guidance. More specifically, the rationale for a 28-day repeat dose study is unclear in the case that other endpoints in the protein assessment demonstrate that the protein is labile and when the anticipated exposure is exceedingly low due to situation of low level presence. The need for a 28-day repeat dose study should be triggered by other protein endpoints, e.g., only if Tier I safety assessment (characterization, bioinformatics, stability, digestibility) raises safety concerns. Furthermore, we note that the argument of very low levels of anticipated exposure presented in LLP the draft guidance should also apply for a protein that is novel and/or has an insufficient HOSU (i.e., no need for 28-day repeat dose study). For non-protein constituents, we recommend that the threshold of toxicological concern concept is used. Lines 486-489: The outlined approach for not requiring a 90-day rat study for LLP assessment is well-founded, based on the limited exposure to the LLP GMO. We recommend that it is applied to the protein and non-protein constituent evaluations in lines 468-471 as well as to the environmental risk assessment in Section 3.3. While we agree that limited exposure should be a primary consideration to be used throughout the LLP risk assessment (including in the protein and non-protein constituent evaluations in lines 468-471), we are of the strong opinion that a 90-day rat feeding study is not needed irrespective of exposure and should not be required for the LLP assessment.
Belgium	EuropaBio	3.2.5.3. Cumulative risk assessment	Lines 610-624: According to Regulation (EC) No 1829/2003, the authorization and the risk assessment is performed for each individual GMO and respective food/feed independently. It is thereby irrelevant for the individual GMO risk assessment if multiple products exist (similar or not) and receive an independent approval following the risk assessment, as outlined in the draft LLP guidance. Therefore, we suggest that the section on cumulative risk assessment is deleted. Line 616: Since the definition of "similar" trait is vague, it remains uncertain which

			events should be considered in the cumulative assessment. The standard GMO authorization procedure does not refer to "similar" traits. Thus, we suggest that the cumulative risk assessment in the LLP guidance is deleted for the sake of consistency. Line 617: It would be difficult to conduct a cumulative risk assessment, especially if traits are developed by different companies and at different times. Lines 621-624: The applicant would not be entitled to access the results of the comparative analysis of each of "the LLP GMOs applications" of different applicants. Therefore, the proposed approach of performing the cumulative assessments seems to be neither feasible, nor justifiable, as applications are usually stand-alone documents.
Belgium	EuropaBio	3.3. Environmental risk assessment	Lines 641-644: It is unclear what the risk hypothesis is to support testing of GM plants in LLP situations for their potential impact to the microbial communities in the gastrointestinal (GI) tract of animals or the potential presence of rDNA in fecal material based on the low levels of anticipated exposuReg. We recommend that the approach outlined for the 90-day rat study is applicable here and suggest that exposure can be considered as a mitigating factor in determination of data requirements for LLP applications. Lines 649-651: We suggest that the following sentence is deleted: "However, such analysis may be need…." As the same approach outlined for the 90-day study applies in this case, the characteristics of the crop are of little relevance.
Belgium	EuropaBio	General comments	The EFSA draft guidance on LLP risk assessment introduces and acknowledges the concept of a limited amount of data needed for LLP risk assessment and the acceptance of a non-zero threshold, that is distinct from the "technical zero" threshold (0.1%) for feed. Europabio supports this approach. However, we consider the scope of the guidance as unnecessarily narrow as it currently covers "GM products developed for specific health or market needs in third countries and not intended for the EU market". Furthermore, the draft text indicates that the decision on whether a given GMO can constitute an LLP application is a risk management issue. We suggest that precise

			criteria concerning which products could qualify for a LLP risk assessment and when are defined, with a view to broadening the scope of the draft guidance and avoiding the risk manager taking decisions on the applicability of the risk assessment guidance to individual applications without clear criteria. We note that the scope of this guidance concerns GM products developed for specific health or market needs (i.e., products with modified composition). However, the derogation on compositional analysis would not apply in the case of products with output traits developed to improve nutrition (see line 348-353 of the draft guidance). As mentioned above, the draft guidance states that it applies to products not intended for the EU market. On the other hand, it sets the maximum threshold of 0.9% of the LLP GMO per ingredient as a pre-requisite to identify a LLP situation. However, the 0.9% threshold exposure is irrespective of the origin of the GM event. Although the EU agreed on and supported the adoption of the LLP Annex on "Food safety assessment in situation of Low-Level Presence of recombinant DNA-plant material in food" at Codex Alimentarius in 2008, the European Commission's mandate to EFSA framing the scope of the LLP draft guidance does not consider the value and additional safety assurance provided by the existence of a completed third country safety assessment for GM products. This is a fundamental aspect of the LLP Codex Annex and it should be reflected in the draft guidance. Furthermore, we believe that the draft guidance deviates from international LLP considerations (Global Low Level Presence Initiative – GLI). It appears from the current text that the EU does not support the aim of global harmonization for LLP policies. This seems to be in contradiction with Article 13 of Regulation (EC) No 178/2002, which lays down the general principles and requirements of food law, which puts the European Union and the Member States under the obligation to contribute to the food and feed international standards.

			In addition, the amount of information requested by EFSA for the risk assessment of LLP applications appears disproportionate to the likely risk. In fact, it is not significantly different from what is required in a standard application. Moreover, many requirements may be considered necessary on a case-by-case basis with a lot of room for interpretation. This brings about uncertainty. Clear derogations are provided only for a limited number of requirements. Therefore, the practical value of LLP applications is questionable, mainly for technology developers, including public research institutes and small enterprises.
Belgium	EuropaBio	General Comment	Given that the term "LLP" (as articulated in the internationally agreed Codex LLP Annex) is applicable to products that have completed a safety assessment compatible with the Codex Plant Guidelines, we are of the strong opinion that a 0.9% threshold is unnecessarily conservative. At international for a, such as the Global LLP Initiative, thresholds of up to 5% are being discussed. The 0.9% threshold set forth in the European Commission mandate thus seems to be an arbitrary value (tied to existing GMO labeling provisions), and not based on sound science or risk assessment principles.
Canada	Government of Canada	1.2 Interpretation of the Terms of Reference	Canada will appreciate receiving additional technical information on how the EU will determine whether or not a food or feed ingredient contains more or less than 0.9% of a given genetically modified organism. This would include sampling regimes, detection and quantification procedures including in processed products, and whether the level will be expressed on a weight or other basis, and how validated tests and reference samples would be obtained.
Canada	Government of Canada	3.1.1. Scope of the guidance	(1/2) Canada appreciates the European Union's (EU) efforts in providing guidance and proposing a regulatory process for genetically modified (GM) food or feed developed in other countries and not intended to be exported to the EU. However, this effort falls short of providing a trade-facilitative and pragmatic solution to the issue of low level presence (LLP). The scope of the document does not cover all

			potential instances of LLP, i.e., of GM food and feed materials for which a full safety assessment has been conducted according to Codex Guidelines. More specifically, the scope should include GM crop materials for which a complete submission for authorization has been submitted through the EU's regulatory approval process, which are the most likely source of LLP in EU imports. In the face of the EU's zero tolerance towards LLP, these create the largest potential for trade disruptions, despite the fact that these have been fully assessed for safety. A fully functional LLP solution must be able to address asynchronous approvals, and thus provide a temporary solution to address the potential presence of materials that have already been assessed for safety elsewhere, but that have not been approved yet. Canada notes that the use of the term "low level presence" in this document is not consistent with its use by the Codex Alimentarius Commission, which refers to recombinant DNA plant material that has passed a food safety assessment according to Codex guidelines. The definition presented in the document is based on commercialization intent, rather than on the fact that the safety of the product has already been assessed, the latter being a central concept supporting the internationally recognized definition. A previous Codex-consistent approval significantly reduces uncertainty about the risk of genetically modified food, whereas its commercialization intent does not. In addition, there is a significant potential that this may result in the discriminatory treatment of imports from countries seeking approvals in the EU, including from Canada, which would not be treated on the same footing as products developed mainly for use by non-exporters. This limitation in scope could create an incentive not to seek full approvals in the EU market. Canada also questions the practicality of such a definition in terms of enforcement; i.e. • how will the EU determine the intent of a developer in third countries? • how will the EU address instances of adventitious presence covered by the definition, given that a submission package for full authorization with the necessary data to complete a risk assessment is unlikely to be available? • once an "LLP" application is completed and authorized, what would happen if a full

			submission is provided? Would that annul the tolerance level and result in a zero tolerance approach being applied, even if it was determined that there was no risk? Due to the definitional issues described above, we would strongly encourage the EU to avoid using the term LLP to describe the situation to which this guidance applies. We would suggest using "unapproved GM food products not destined to the EU market" when referring to the issue this guidance is meant to address, including in the title. Under 3.1.1, it is stated that "This document is intended to assist applicants in the preparation of LLP applications", and the term "LLP application" is frequently used in the document. Canada would appreciate further clarification as to what would trigger a risk assessment process as described in this document: would an "application" need to be filed by a developer in a third market to trigger the risk assessment process? If so, this guidance is unlikely to provide a trade-facilitative solution even to those crops that would be covered by its scope, as it would be incumbent on developers who have no interest in the EU market to ensure trade-facilitative responses from the EU, rather than on the EU to remain proactive in providing for trade-facilitative solutions in managing unapproved GM crops in its imports. Canada notes that traces of a crop species that a country does not export to the EU can inadvertently be present in exports of other crops or products, and believe that trade-facilitative approaches for such situations are equally needed. From this perspective, Canada also seeks a justification for not including in the scope of this guidance low levels of material from a plant species that would not otherwise present in exports.
Canada	Government of Canada	3.2.2.2. Risk assessment of genetically modified food and feed containing stacked transformation events (Regulation [EU] No 503/2013; Annex II. I,	Canada has previously noted that some information requirements in Regulation (EU) No 503/2013 may be scientifically unjustified for a full-scale approval. Please provide a scientific justification for requiring the following information for material present at 0.9% or below, particularly in the case when such material has been previously approved according to Codex guidelines • potential synergistic or antagonistic effects among transformation events within a

		2.2)	stack (3.2.2.2 - lines 245-248 on page 8) • the risk of horizontal gene transfer (3.2.3.2 - lines 310-311 on page 10) • exposure of recombinant DNA to microbial communities in the gut and faeces of animals (3.3 lines 642-644) on page 17.
Canada	Government of Canada	3.2.3.2. Molecular characterisation (Regulation [EU] No 503/2013; Annex II. II, 1.2)	Canada has previously noted that some information requirements in Regulation (EU) No 503/2013 may be scientifically unjustified for a full-scale approval. Please provide a scientific justification for requiring the following information for material present at 0.9% or below, particularly in the case when such material has been previously approved according to Codex guidelines • potential synergistic or antagonistic effects among transformation events within a stack (3.2.2.2 - lines 245-248 on page 8) • the risk of horizontal gene transfer (3.2.3.2 - lines 310-311 on page 10) • exposure of recombinant DNA to microbial communities in the gut and faeces of animals (3.3 lines 642-644) on page 17.
Canada	Government of Canada	3.2.3.3. Comparative analysis (Regulation [EU] No 503/2013, Annex II. II, 1.3)	Canada would appreciate clarification of one of the conditions for which comparative compositional analysis in low level situations would be required, that relating to compounds produced de novo in the GMO found at low level (line 360 on page 11 of the draft guidance). Would this capture all genetically modified plants that produce a new compound including those naturally produced by the plant and those not naturally produced by the plant? If so, this would capture the great majority of all GM plants cultivated to date.
Canada	Government of Canada	3.3. Environmental risk assessment	Canada has previously noted that some information requirements in Regulation (EU) No 503/2013 may be scientifically unjustified for a full-scale approval. Please provide a scientific justification for requiring the following information for material present at 0.9% or below, particularly in the case when such material has been previously approved according to Codex guidelines • potential synergistic or antagonistic effects among transformation events within a stack (3.2.2.2 - lines 245-248 on page 8) • the risk of horizontal gene transfer (3.2.3.2 - lines 310-311 on page 10) • exposure of recombinant DNA to microbial communities in the gut and faeces of

			animals (3.3 lines 642-644) on page 17.
Germany	Bavarian State Ministry of the Environment and Consumer Protection	1.1 Background and Terms of Reference as provided by the requestor	Aus dem Dokument geht nicht hervor, ob die in Drittstaaten entwickelten GVO, auf die sich die Leitlinien beziehen, in diesem oder einem anderen Land zugelassen sind bzw. zugelassen sein müssen. Vielmehr heißt es unter Punkt 1.1 (Zeile 128-129), dass eine Risikobewertung eines Drittstaates für einen jeweiligen GVO nicht vorliegen muss. Dies impliziert, dass für GVO in der EU ein LLP Antrag gestellt werden kann, auch wenn ein GVO unter Umständen weltweit keine Zulassung besitzt. Wir halten dies für bedenklich. English translation It is unclear from the document whether the GMOs developed in third countries and referred to in the guidelines are authorised in this country or in another, or are to be authorised. Rather, in section 1.1 (lines 128–129), it states that it is not necessary for a risk assessment to have been performed by a third country for any given GMO. That implies that an LLP request can be submitted in the EU for GMOs, even in circumstances where a GMO has not been authorised anywhere in the world. We see that as alarming
Germany	Bavarian State Ministry of the Environment and Consumer Protection	1.2 Interpretation of the Terms of Reference	Unter Punkt 1.2 (Zeilen 145 ff) wird bemerkt, dass nach einem nicht näher erläuterten Meinungsaustausch ("exchange") zwischen der Kommission und EFSA ein Antrag auf Zulassung eines GVO nach Verordnung (EG) Nr. 1829/2003 im niederen Konzentrationsbereich möglich sei. Es ist u.E. nicht ersichtlich, auf welcher rechtlichen Grundlage dies erfolgen soll. In der Verordnung ist eine (Teil) Zulassung von GVO bis 0,9 % für zufällige oder technisch unvermeidbare Verunreinigungen von Lebens- und Futtermitteln weder explizit vorgesehen, noch erwähnt. English translation In section 1.2 (line 145 et seq.) it is noted that, following an 'exchange' between the Commission and EFSA – about which no further details are provided –, an application

			for authorisation of a GMO in low concentrations is possible under Regulation (EC) No 1829/2003. In our view, the legal basis for that is unclear. The regulation neither explicitly provides for nor mentions a (partial) authorisation for GMOs up to 0.9% resulting from accidental or technically unavoidable contamination of food or feed.
Germany	Bavarian State Ministry of the Environment and Consumer Protection	3.1.1. Scope of the guidance	Unter Punkt 3.1.1. Zeilen 201 – 202 wird darauf hingewiesen, dass die Leitlinien Aspekte zu Risikomanagement (z.B. Rückverfolgbarkeit) usw. nicht beinhalten. Die Überwachung derartiger Verunreinigungen mit gv Material ist jedoch ohne ausreichende Dokumentation und Eigenkontrollmaßnahmen nicht möglich. Aus unserer Sicht sind generell bestimmte Aspekte des Risikomanagements zu berücksichtigen. Fragen der Koexistenz sowie sozioökonomische Belange sollten bei der Risikobewertung mit bewertet werden, wenn die Lebens- oder Futtermittel lebensfähige GVO enthalten können, die beim Transport oder anderweitig in die Umwelt gelangen könnten. <u>English translation</u> In section 3.1.1, lines 201–202, it is noted that the guidelines do not contain any information regarding risk management (e.g. traceability), etc. However, it is impossible to supervise such contaminations with GM material without sufficient documentation and self-monitoring procedures. In our view, particular aspects of risk management must be observed as standard. Where the food or feed may contain viable GMOs which could be released into the environment during transport or by other means, coexistence and socio-economic concerns should be evaluated as part of the risk assessment.
Germany	Bavarian State Ministry of the Environment	3.1.2. General risk assessment considerations for LLP situations	Unter Punkt 3.1.2 (Zeile 214) ist von einem vordefinierten Schwellenwert ("pre-defined threshold") von 0,9 % pro Zutat die Rede. Der Schwellenwert von 0,9 % bezieht sich in der Verordnung (EG) Nr. 1829/2003 auf zugelassene GVO. Nach VO (EU) Nr. 619/2011 gilt für bestimmte, nicht zugelassene, aber sicherheitsbewertete GVO in Futtermitteln ein Schwellenwert von 0,1 %. In Lebensmitteln gilt für nicht zugelassene GVO bisher

	and Consumer Protection		die Nulltoleranz. Die Einführung eines weiteren Schwellenwerts für Futtermittel und die de facto Abschaffung der Nulltoleranz bei Lebensmitteln lässt sich u.E. sachlich nicht begründen. 5. Unter Punkt 3.1.2 (Zeilen 215-218) ist angemerkt, dass zufällige oder technisch unvermeidbare Gründe für eine LLP Situation sowohl einzelne als auch wiederholte Expositionen einschließen. Als zufällig oder technisch unvermeidbar werden in der Überwachungspraxis bisher jedoch nur solche Fälle angesehen, bei denen vereinzelt, jedoch nicht wiederholt gv Material kleiner 0,9% festgestellt wird. Systematische (wiederholte) Gehalte von gv Material müssen demnach gekennzeichnet werden. English translation Section 3.1.2 (line 214) refers to a 'pre-defined threshold' of 0.9% per ingredient. In Regulation (EC) No 1829/2003, the threshold of 0.9% applies to authorised GMOs. Under Regulation (EU) No 619/2011, a threshold in feed of 0.1% applies for specific unauthorised but safety-assessed GMOs. There has always been zero tolerance for unauthorised GMOs in food. In our view, there are no objective grounds for the introduction of an additional threshold for feed or the de facto lifting of the zero-tolerance policy for food. In section 3.1.2 (lines 215–218), it is noted that accidental or technically unavoidable reasons for an LLP situation cover both one-off and repeated contaminations. However, in supervision practice, only one-off cases in which GM material was identified at levels below 0.9% have been regarded as accidental or technically unavoidable. Repeated cases have not. Systematic (repeated) levels of GM material must be signalled accordingly.
Germany	Bavarian State Ministry of the Environment	3.2 Scientific requirements	Zu Kap. 3.2.: Die Leitlinien sehen für LLP Anträge verschiedene Abweichungen von den Anforderungen zur Risikobewertung nach Anhang II der Durchführungsverordnung (EU) Nr. 503/2013 vor. Diese Abweichungen, die im Wesentlichen darin bestehen, dass bestimmte Aspekte der Risikobewertung wegfallen, oder nur im Einzelfall („on a case-by-case basis") zu prüfen sind, müssten nach Art. 5 Abs. 2 VO (EU) Nr. 503/2013 bei

	and Consumer Protection		regulären Zulassungsanträgen technisch fundiert begründet werden. Bei vorliegenden Leitlinien sind anstelle von wissenschaftlich fundierten Begründungen pauschale Aussagen wie „not considered necessary" oder „negligible in LLP situation". Es werden auch keinerlei Hinweise aufgeführt, wann ein sogenannter "Einzelfall" vorliegt. English translation Chapter 3.2: As regards LLP applications, the guidelines provide for various derogations from the requirements for risk assessment set out in Annex II of Implementing Regulation (EU) No 503/2013. For regular authorisation applications, Article 5(2) of Regulation (EU) No 503/2013 indicates that those derogations, whose primary effect is that particular elements of the risk assessment are omitted or are only to be evaluated 'on a case-by-case basis', must be technically well founded. In the present guidelines, scientifically well-founded reasons are replaced by sweeping statements such as 'not considered necessary' or 'negligible in LLP situation'. There are also no indications provided as to what is to be classified as a so-called 'one-off case
Germany	Bavarian State Ministry of the Environment and Consumer Protection	3.2.3.2. Molecular characterisation (Regulation [EU] No 503/2013; Annex II. II, 1.2)	Unter Punkt .3.2.3.2. Molecular characterisation (Zeilen 291-294) wird beispielsweise gesagt, dass sogenannte off-target Effekte (unvorhergesehene, unerwünschte Effekte), die durch die Methode des RNAi Silencing (Abschalten von Genen mittels RNA-Molekülen) in einer LLP Situation, also bei Konzentrationen von bis maximal 0,9 % genetisch veränderten Materials, zu vernachlässigen ("considered negligible") seien (Anhang II. II, 1.2.2 Unterpunkte 1.2.2.3 (e) VO (EU) Nr. 503/2013). Dies wird jedoch in keiner Weise wissenschaftlich oder anderweitig begründet. Das Wesen von off-target Effekten ist es aber gerade, dass nicht bekannt ist oder sicher vorherzusagen ist, welcher Art diese Effekte sind und welche (z.B. gesundheitlichen) Auswirkungen diese haben können. Daher ist die Behauptung, solche (unbekannten) Effekte seien hier zu vernachlässigen wissenschaftlich nicht haltbar. Ziel einer Risikobewertung ist es, alle denkbaren und überprüfbaren potentiellen Risiken zu analysieren und zu bewerten und nicht pauschal eine Risikobewertung aufgrund einer angenommenen geringen

			Konzentration von unerwünschten Stoffen auszuschließen. Auch wenn eben gerade nicht alle off-target Effekte vorhersehbar sind, so ist es immerhin möglich mittels gezielter DNA-Sequenzanalyse potentielle Beeinflussung anderer Gene zumindest hypothetisch zu untersuchen. Dies sollte in jedem Fall erfolgen. Zudem kann auch bei einem LLP von GVO nicht ausgeschlossen werden, dass solches Material auch in höheren als der maximal vorgesehenen Konzentration von 0,9 % in den Handel gelangt. English translation In section 3.2.3.2, 'Molecular characterisation' (lines 291–294), it is stated for example that so-called off-target effects (unforeseen, undesirable effects) caused by the RNAi silencing method (deactivation of genes using RNA molecules) in an LLP situation, that is to say at concentrations up to max. 0.9% genetically modified material, are to be 'considered negligible' (Annex II, II, 1.2.2.3(e) of Regulation (EU) No 503/2013). However, no justification for that is provided, scientific or otherwise. Off-target effects by their very nature are effects whose type and potential consequences (e.g., for health) are unknown, or certainly cannot be foreseen. The assertion that such (unknown) effects are to be considered negligible here is therefore scientifically untenable. The objective of a risk assessment is to analyse and assess all conceivable and investigable risks and it should not be ruled out on the mere ground that the concentrations of undesirable substances are assumed to be low. Even though, as stated, not all off-target effects are foreseeable, it is nevertheless possible to investigate their potential influence on other genes, at least hypothetically, using targeted DNA sequence analysis. This should be carried out in every case. Moreover, even at a GMO LLP, it cannot be ruled out that such material could also find its way into goods in concentrations higher than the maximum of 0.9%.
Germany	Bavarian State	3.2.3.3. Comparative analysis (Regulation [EU]	Unter Punkt 3.2.3.3. Comparative analysis (Zeilen 329-333) zielt die Begründung für die Abweichung von vorgesehenen Anforderungen zur Risikobewertung ähnlich wie unter

	Ministry of the Environment and Consumer Protection	No 503/2013, Annex II. II, 1.3)	Punkt 3.2.3.2 auf die Konzentration ab. Eine wissenschaftliche Begründung fehlt. Eine vergleichende Analyse der agronomischen und phänotypischen Eigenschaften wird in einer LLP Situation für nicht notwendig angesehen (Anhang II. II, 1.3.5 VO (EU) Nr. 503/2013). English translation In section 3.2.3.3, 'Comparative analysis' (lines 329–333), the rationale for the derogation from the requirements laid down for risk assessment is, as in section 3.2.3.2, based on the concentration. No scientific justification is provided. A comparative analysis of agronomic and phenotypic characteristics is regarded as unnecessary in an LLP situation (Annex II, II, 1.3.5 of Regulation (EU) No 503/2013).
Germany	Bavarian State Ministry of the Environment and Consumer Protection	3.2.3.5. Allergenicity (Regulation EU No 503/2013; Annex II. II, 1.5)	Unter Punkt 3.2.3.5 (Zeilen 519 – 521) und Punkt 3.2.3.6 (Zeilen 538 – 540) sind eine Bewertung der Allergenität der gv Lebens- und Futtermittel sowie eine ernährungsphysiologische Bewertung aufgrund des angenommen Wertes von 0,9 % an gv Material routinemäßig nicht vorgesehen (Anhang II. II, 1.5.2 und 1.6 VO (EU) Nr. 503/2013). Auch hier fehlt wie bei den Punkten 3.2.3.2 und 3.2.3.3 eine wissenschaftliche Begründung. English translation In section 3.2.3.5 (lines 519–521) and section 3.2.3.6 (lines 538–540), an assessment of the allergenicity of the GM food and feed and a nutritional assessment are not provided for as standard owing to the assumed level of GM material of 0.9% (Annex II, II, 1.5.2 and 1.6 of Regulation (EU) No 503/2013). As in sections 3.2.3.2 and 3.2.3.3, no scientific justification is provided here either
Germany	Bavarian State Ministry of	Assessment	1 Zu Punkt 3. Assesment (Zeile 189): Ungeklärt bleibt aus Sicht der amtlichen Überwachung/Analytik auch, wie rechtlich zu verfahren wäre, wenn in Proben bei Analysen von LLP Material Gehalte von größer 0,9 % festgestellt würden.

	the Environment and Consumer Protection		English translation Section 3, Assessment (line 189): From the point of view of surveillance/analysis, it also remains unclear what legal proceedings can be brought where levels exceeding 0.9% are identified in samples during analysis
Germany	BfN	1.1 Background and Terms of Reference as provided by the requestor	Line 130 to 139 Neither the scope that exclusively only addresses GM products not intended for the EU market, nor the threshold of 0.9% is comprehensible. In comparison to the rules given in Regulation 619/2011 which allows a LLP of up to 0.1% in GM feed for certain conditions the higher threshold given in the mandate by the commission implies that rules counting for GMOs intended for the market do not apply for GMOs that are not intended for the market.
Germany	BfN	3.3. Environmental risk assessment	For the environmental risk assessment of LLP of viable seeds it is essential to take the following points into account. • Even if the applied event only occurs with a presence of less than 0.9% in commodities, it can, depending on the frequency of import and the amount of the imported seeds, at the end become a huge total amount of GM seeds that will be imported. • Furthermore, for plants that can establish and persist outside of agricultural habitats and may cross with wild relatives Low Level Presence does not exclude dissemination. If establishment occurs, the exposition of the environment can become high in the long run independent of the low level portion at the beginning. Therefore a full environmental risk assessment needs to be performed if viable seeds of plants of scenario 3 and 4 are imported. In this case, the full data set for compositional analysis, comparative approach, protein expression and agricultural and environmental parameters needs to be provided.
Germany	BVL	1.2 Interpretation of the Terms of Reference	Line 152: Non-GMO portions are present at a proportion of minimum 99.1%; therefore please change to … maximum 0.9% and minimum 99.1%, respectively.
Germany	BVL	3.1.1. Scope of the guidance	It would be advisable to clarify, whether the situation in which a non-authorized GMO is present at the maximum level of 0.9% in a given food/feed containing not the same

			ingredient (e.g. mustard seeds containing 0.9 % of non-authorized GM oilseed rape), does or does not fall within the scope of the LLP-guidance.
Germany	BVL	3.2.2.1. Insertion of marker genes and other nucleic acid(s) sequences not essential to achieve the desired tract (Regulation [EU] No 503/2013; Annex II. I, 2.1)	Line 235: Trait instead of tract?
Germany	BVL	3.2.5.3. Cumulative risk assessment	Lines 616-621: There are actually two different scenarios of multiple LLP applications and possible cumulative contributions: 1. LLP of different GMOs of the same plant species, together amounting to < 0.9% of the ingredient 2. LLP of GMOs belonging to different plant species, each amounting to < 0.9% of the respective ingredient It would be advisable to clarify, whether the second scenario fall or not within the scope of the guidance The second "compound" in line 609 should be changed to "constituent" as this is in line with the usage in the documents.
Germany	BVL	Experimental design and statistical analysis of data from field trials for comparative analysis (Regulation [EU] No 503/2013; Annex II. II, 1.3.2, subsections 1.3.2.1a,b, 1.3.2.2)	Lines 390-392: If equivalence test is not necessary, it would be helpful to provide a support for interpretation of significant differences taking into consideration all specifics of LLP situation, e.g. the applicant should discuss the biological relevance of possible detected significant differences in LLP context.
Germany	BVL	Food and feed safety in relation to intake (Regulation [EU]	Line 597: The question is whether the post market monitoring under LLP conditions (labeling obligation from threshold level of 0,9%) is possible. Therefore, we suggest keeping primary version of this topic: "Considering that the LLP applications are

		No 503/2013; Annex II. II, 3.2.3)	intended to support the authorisation of a GMO at a maximum level of 0.9 % in an ingredient of food and feed, no post market monitoring is foreseen.”
France	Anses	1.1 Background and Terms of Reference as provided by the requestor	Modifier l'ordre des paragraphes de manière à faire le lien entre les lignes 116-119 et les lignes 122-143. Proposition de nouvelle rédaction : "Genetically modified (GM) plants and derived products, not intended to be exported to the EU, have been or are being developed for specific health or market needs in third countries. The accidental presence of some of these GM products at low levels cannot completely be excluded in exports to the EU. In this context and in accordance with Article 29 of Regulation (EC) No 178/2002, the European Commission mandated EFSA in 2014 to advise whether or not all requirements of Annex II to of Regulation (EU) No 503/2013 are necessary to conclude on the safety of applications covering the unintended presence of GMOs in food and feed at the adventitious or technically unavoidable presence of 0.9% or below. If not, EFSA is required to indicate which requirements are unnecessary and to give the underlying rationale. Following a request for clarification by EFSA, the European Commission further clarified that:[…] In 2015, EFSA accepted the mandate from the European Commission and committed to issue an EFSA LL Scientific Opinion providing guidance on possible derogations of to existing requirements for applications of GM food and feed at low levels submitted under Regulation (EC) No 1829/2003. The differences in principles and requirements between this guidance document and the guidelines issued in 2009 by Codex Alimentarius for the food safety assessment of low level presence (LLP) situations of recombinant DNA plant material in food (Codex Alimentarius, 2009, Annex 3) are detailed in Appendix A of this LL Scientific Opinion." L'unité du "0.9%" devrait être précisée (ADN, masse, etc.). Par ailleurs, les dérogations décrites dans ce document ne sont acceptables que si la teneur en OGM au total est inférieure à 0,9 % dans la denrée alimentaire ou l'aliment pour animaux. Elles ne le

			sont plus si cette teneur est en fait de n x 0,9 % du fait de la présence de n événements de transformation à une teneur de 0,9 % chacun. Editorial: justifier le texte dans les notes de bas de page. <u>English translation</u> Change the order of the paragraphs to create a link between lines 116–119 and lines 122–143. Suggested new wording: 'Genetically modified (GM) plants and derived products, not intended to be exported to the EU, have been or are being developed for specific health or market needs in third countries. The accidental presence of some of these GM products at low levels cannot completely be excluded in exports to the EU. In this context and in accordance with Article 29 of Regulation (EC) No 178/2002, the European Commission mandated EFSA in 2014 to advise whether or not all requirements of Annex II to of Regulation (EU) No 503/2013 are necessary to conclude on the safety of applications covering the unintended presence of GMOs in food and feed at the adventitious or technically unavoidable presence of 0.9% or below. If not, EFSA is required to indicate which requirements are unnecessary and to give the underlying rationale. Following a request for clarification by EFSA, the European Commission further clarified that:[…] In 2015, EFSA accepted the mandate from the European Commission and committed to issue an EFSA LL Scientific Opinion providing guidance on possible derogations of to existing requirements for applications of GM food and feed at low levels submitted under Regulation (EC) No 1829/2003. The differences in principles and requirements between this guidance document and the guidelines issued in 2009 by Codex Alimentarius for the food safety assessment of low level presence (LLP) situations of recombinant DNA plant material in food (Codex Alimentarius, 2009, Annex 3) are detailed in Appendix A of this LL Scientific Opinion.'

			The unit to which '0.9 %' refers should be specified (DNA, mass, etc.). In addition, the derogations described in this document are acceptable only where the total level of GMOs is below 0.9 % in the food or feed. They are no longer acceptable where that level is actually n x 0.9 % owing to the occurrence of n transformation events each at a level of 0.9 %. Editorial: justify the text in the footnotes."
France	Anses	1.1 Background and Terms of Reference as provided by the requestor	Ligne 110 : Editorial: remplacer "as to" par "to as". Line 110: Editorial: replace 'as to' with 'to as'.
France	Anses	1.2 Interpretation of the Terms of Reference	L'unité du "0.9%" devrait être précisée (ADN, masse, etc.). Par ailleurs, les dérogations décrites dans ce document ne sont acceptables que si la teneur en OGM au total est inférieure à 0,9 % dans la denrée alimentaire ou l'aliment pour animaux. Elles ne le sont plus si cette teneur est en fait de n x 0,9 % du fait de la présence de n événements de transformation à une teneur de 0,9 % chacun. Ne pas aller à la ligne entre les lignes 155 et 156 : elles sont liées puisqu'il y a le terme "therefore" dans la phrase de la ligne 156. Dans la mesure où l'Article 5(2) du Règlement d'exécution (UE) n° 503/2013 rend dores et déjà possibles des dérogations pour tous les types de produits et où les fruits et légumes font partie du mandat donné à l'EFSA par la Commission Européenne, il est nécessaire de développer un guide pour ces produits. Dans le cas contraire, la liste des produits concernés par le présent guide (ou les critères qui permettent de les identifier) doit être définie. "The decision on whether a given GMO can constitute a LLP application is a risk management issue, and is therefore not in the remit of this guidance." : qui sera en charge de prendre la décision ? A l'heure actuelle, les demandes d'autorisation de mise sur le marché au titre du Règlement (CE) n° 1829/2003 sont déposées auprès de

			l'EFSA, qui en gère la recevabilité avant de les examiner. Un autre circuit va-t-il être mis en place pour les dossiers LLP ? English translation "The unit to which '0.9 %' refers should be specified (DNA, mass, etc.). EFSA: 0.9% refers to the ingredient. In addition, the derogations described in this document are acceptable only where the total level of GMOs is below 0.9 % in the food or feed. They are no longer acceptable where that level is actually n x 0.9 % owing to the occurrence of n transformation events each at a level of 0.9 Do not insert a line break between lines 155 and 156: they are linked by the word 'therefore' in the sentence in line 156. Insofar as Article 5(2) of Implementing Regulation (EU) No 503/2013 already renders the derogations for all types of goods possible and insofar as fruits and vegetables are covered by EFSA's mandate from the European Commission, a guidance document must be compiled for those goods. If this is not the case, the list of goods covered by the present guidance document (or the criteria enabling them to be identified) must be specified. 'The decision on whether a given GMO can constitute a LLP application is a risk management issue, and is therefore not in the remit of this guidance': who will be responsible for making the decision? At the present time, applications for marketing authorisation under Regulation (EC) No 1829/2003 are submitted to EFSA, which assesses their admissibility before examining them. Will an additional channel be put in place for LLP files? "
France	Anses	2.1 Data	Lignes 172-173 : Editorial : ajouter "Annex 3" après "Codex Alimentarius, 2009" dans la parenthèse (Codex Alimentarius, 2009, Annex 3). English translation Lines 172-173: Editorial: insert 'Annex 3' after 'Codex Alimentarius, 2009' in the

			parenthesis (Codex Alimentarius, 2009, Annex 3).
France	Anses	2.1 Data	Ligne 180 : Editorial : remplacer "from" par "to" dans la phase "derogations from to existing requirements" English translation Line 180: Editorial: replace 'from' with 'to' in the phrase 'derogations from to existing requirements'
France	Anses	3.1.1. Scope of the guidance	Lignes 199-200 : pour plus de clarté, remplacer les points-virgules par des virgules. Proposition de rédaction : "This guidance does not cover GMOs for cultivation purposes, GM microorganisms, GM animals, GMOs for non-food/feed uses and novel foods, as these are not in the scope of Regulation (EU) No 1829/2003." English translation Lines 199–200: for greater clarity, replace the semi-colons with commas. Suggested wording: 'This guidance does not cover GMOs for cultivation purposes, GM microorganisms, GM animals, GMOs for non-food/feed uses and novel foods, as these are not in the scope of Regulation (EU) No 1829/2003.'
France	Anses	3.1.2. General risk assessment considerations for LLP situations	L'utilisation du terme "comparative assessment" ligne 204 est ambiguë, car elle peut laisser penser que l'évaluation des dossiers ne repose que sur le volet "Evaluation comparative", alors qu'elle prend également en compte les volets "Caractérisation moléculaire", "Toxicologie", "Allergénicité" et "Evaluation nutritionnelle". Proposition de rédaction : "The risk assessment strategy for GMO standard applications is based on the appraisal of the elements provided by the applicant to demonstrate that the GMO is as safe and as nutritious as traditionally cultivated crops (and derived products) with a history of safe use for consumers and/or animals (Codex Alimentarius, 2009; EFSA GMO Panel, 2011a)." L'unité du "0.9%" devrait être précisée (ADN, masse, etc.). Par ailleurs, les dérogations décrites dans ce document ne sont acceptables que si la teneur en OGM au total est

			inférieure à 0,9 % dans la denrée alimentaire ou l'aliment pour animaux. Elles ne le sont plus si cette teneur est en fait de n x 0,9 % du fait de la présence de n événements de transformation à une teneur de 0,9 % chacun. Lignes 219-224, simplifier la rédaction, par exemple : "Based on the above considerations and in line with the Codex Alimentarius guidelines on LLP situations (Codex Alimentarius, 2009, Annex 3), the GMO Panel considers that certain requirements for the risk assessment of GMO standard applications are necessary in LLP situations and that others are not or should be adapted. Detailed description of the possible derogations to the requirements of Annex II of Regulation (EU) No 503/2013 in the case of LLP applications are given in Section 3.2 of this guidance." <u>English translation</u> "The use of the term 'comparative assessment' in line 204 is ambiguous because it could lead to the conclusion that the evaluation of the files is based solely on the 'comparative analysis' component when it also takes into account the elements 'molecular characterisation', 'toxicology', 'allergenicity' and 'nutritional analysis'. Suggested wording: 'The risk assessment strategy for GMO standard applications is based on the appraisal of the elements provided by the applicant to demonstrate that the GMO is as safe and as nutritious as traditionally cultivated crops (and derived products) with a history of safe use for consumers and/or animals (Codex Alimentarius, 2009; EFSA GMO Panel, 2011a).' The unit to which '0.9 %' refers should be specified (DNA, mass, etc.). In addition, the derogations described in this document are acceptable only where the total level of GMOs is below 0.9 % in the food or feed. They are no longer acceptable where that level is actually n x 0.9 % owing to the occurrence of n transformation events each at a level of 0.9 %.

			Lines 219–224: simplify the wording, for example: 'Based on the above considerations and in line with the Codex Alimentarius guidelines on LLP situations (Codex Alimentarius, 2009, Annex 3), the GMO Panel considers that certain requirements for the risk assessment of GMO standard applications are necessary in LLP situations and that others are not or should be adapted. Detailed description of the possible derogations to the requirements of Annex II of Regulation (EU) No 503/2013 in the case of LLP applications are given in Section 3.2 of this guidance.'"
France	Anses	3.2.2.1. Insertion of marker genes and other nucleic acid(s) sequences not essential to achieve the desired tract (Regulation [EU] No 503/2013; Annex II. I, 2.1)	Editorial : "All requirements described in Paragraph 2.1 of Annex II.I of Regulation (EU) No 503/2013 are considered necessary for LLP applications." English translation Editorial: 'All requirements described in Paragraph 2.1 of Annex II.I of Regulation (EU) No 503/2013 are considered necessary for LLP applications.'
France	Anses	3.2.3.2. Molecular characterisation (Regulation [EU] No 503/2013; Annex II. II, 1.2)	Dans sa note d'Appui Scientifique et Technique du 26 août 2015, l'Anses considère qu'une caractérisation moléculaire complète est nécessaire (Anses, 2015). Parmi les dérogations proposées par l'EFSA, celles qui concernent les paragraphes 1.2.2.3(b) et 1.2.2.3(c) sont acceptables. En revanche, l'évaluation du risque d'effets indésirables ("off-target effects") des RNAi, telle que décrite dans le paragraphe 1.2.2.3(e), est nécessaiReg. En effet, dans l'état actuel des connaissances scientifiques, il n'existe pas de consensus au sujet du risque associé à l'utilisation de cette technique et la recherche in silico décrite dans ce paragraphe est faisable sans engager beaucoup de moyens humains et financiers. De même, la comparaison des niveaux d'expression des protéines nouvellement exprimées dans les événements empilés ("stacks") avec ceux mesurés dans les événements simples (paragraphe 1.2.2.3(f)) est nécessaire, car elle est l'un des moyens d'identifier d'éventuels effets inattendus liés à l'empilement. English translation

			"In its scientific and technical support note of 26 August 2015, Anses considers that a complete molecular characterisation is necessary (Anses, 2015). Of the derogations proposed by EFSA, those concerning paragraphs 1.2.2.3(b) and 1.2.2.3(c) are acceptable. However, a risk assessment for 'off-target effects' of RNAi, as described in paragraph 1.2.2.3(e), is necessary. At the current stage of scientific knowledge, there is no consensus on the subject of the risk associated with the use of that technique and the in silico research described in that paragraph is feasible without excessive staffing or financial costs. Likewise, the comparison of the levels of newly expressed proteins in event 'stacks' with those measured in single events (paragraph 1.2.2.3(f)) is necessary because it is one of the ways of identifying possible unexpected effects linked with the stacking."
France	Anses	3.2.3.2. Molecular characterisation (Regulation [EU] No 503/2013; Annex II. II, 1.2)	Lignes 267-268 : Editorial. Proposition de rédaction : "by-case basis. In the following sections, the rationale for considering that specific requirements are necessary or not specific requirements is described." <u>English translation</u> Lines 267–268: Editorial. Suggested wording: 'by-case basis. In the following sections, the rationale for considering that specific requirements are necessary or not specific requirements is described.'
France	Anses	3.2.3.3. Comparative analysis (Regulation [EU] No 503/2013, Annex II. II, 1.3)	Lignes 319-324, les phrases "It aims at identifying similarities and differences in composition (intended and unintended alterations) between the GM plant and its conventional counterpart, and between the food and feed derived from the GM plant and those derived from the conventional counterpart. It also aims at identifying similarities and differences in agronomic performance and phenotypic characteristics (intended and unintended alterations) between the GM plant and its conventional counterpart." sont ambiguës du fait de l'utilisation du singulier pour "counterpart". Cela donne l'impression que l'OGM n'est comparé qu'avec un équivalent non génétiquement

			modifié, alors qu'il est comparé au témoin (isogénique) par des tests de différence et à des variétés commerciales de référence par des tests d'équivalence, comme indiqué dans le guide du Panel GMO de l'EFSA de 2011 (EFSA GMO Panel. 2011. "Guidance for risk assessment of food and feed from genetically modified plants." EFSA Journal 9 (5): 2150, 37 pp.), qui a été repris dans l'Annexe II du Règlement d'exécution (UE) n° 503/2013. Pour les produits consommés uniquement en mélange et/ou après transformation technologique, l'Anses rejoint l'EFSA sur le fait qu'une analyse comparative n'est pas nécessaire (Anses, 2015). Si toutefois une analyse comparative est demandée, alors celle-ci doit être menée conformément au Règlement d'exécution (UE) n° 503/2013, notamment en ce qui concerne le nombre de sites d'essais, le choix et le nombre des comparateurs et la mise en œuvre de tests statistiques de différence (comparaison de la plante génétiquement modifiée (PGM) avec son équivalent non génétiquement modifié) et d'équivalence (comparaison de la PGM avec des variétés commerciales de référence). En effet, l'étape précédant l'évaluation comparative est la caractérisation moléculaire de la PGM, qui n'est pas suffisante pour détecter et formuler des hypothèses concernant tous les effets potentiels inattendus liés à la modification génétique, en particulier pour les PGM empilées (a fortiori si la comparaison des niveaux d'expression des protéines nouvellement exprimées dans les événements empilés ("stacks") avec ceux mesurés dans les événements simples n'est pas demandée). Dans ces conditions, la démonstration du fait que la PGM peut être considérée comme équivalente à une plante non génétiquement modifiée reste d'actualité. <u>English translation</u> "Lines 319–324: the following sentences are ambiguous owing to the use of the singular 'counterpart': 'It aims at identifying similarities and differences in composition (intended and unintended alterations) between the GM plant and its conventional counterpart, and between the food and feed derived from the GM plant and those

			derived from the conventional counterpart. It also aims at identifying similarities and differences in agronomic performance and phenotypic characteristics (intended and unintended alterations) between the GM plant and its conventional counterpart.' It gives the impression that the GMO can be compared to only one non-GM equivalent, whereas it is compared to the control (isogenic) through differential tests and to reference commercial varieties through equivalence tests, as indicated in the guidance document of the EFSA GMO Panel of 2011 (EFSA GMO Panel. 2011. 'Guidance for risk assessment of food and feed from genetically modified plants.' EFSA Journal 9 (5): 2150, 37 pp.), which was incorporated into Annex II to Implementing Regulation (EU) No 503/2013. For goods consumed only in a mixture and/or after technological transformation, Anses concurs with EFSA that a comparative analysis in unnecessary (Anses, 2015). Where an analysis is nevertheless called for, it should be carried out in accordance with Implementing Regulation (EU) No 503/2013, in particular with regard to the number of test sites, the choice and number of the comparators, and the use of differential expression analysis (the genetically modified plant (GMP) is compared to its non-genetically modified equivalent) and equivalence (the GMP is compared to commercial reference varieties). The stage preceding the comparative analysis is the molecular characterisation of the GMP, which is insufficient for detecting and formulating hypotheses concerning all of the potential unexpected effects linked to genetic modification, in particular for stacked GMPs (all the more so where the comparison of the levels of newly expressed proteins in event 'stacks' with those measured in single events is not called for). In those circumstances, demonstrating that the GMP could be considered to be equivalent to a non-GM plant is still an issue."
France	Anses	3.2.3.4. Toxicology (Regulation [EU] No 503/2013; Annex II. II, 1.4)	L'Anses rejoint l'EFSA sur le fait qu'une étude de toxicité de 28 jours est requise si la (les) protéine(s) nouvellement exprimée(s) n'a (n'ont) jamais fait l'objet d'une évaluation toxicologique et sur le fait que d'autres études pourraient être demandées, au cas par cas, si les résultats de cette étude ou d'autres éléments du dossier

			suggèrent que l'OGM présente un risque. English translation Anses concurs with EFSA that a 28-day toxicity study is required where the newly expressed protein(s) has (have) never been the subject of a toxicology test and that other studies could be called for, on a case-by-case basis, where the results of that study or other elements in the file suggest that the GMO constitutes a risk.
France	Anses	3.2.3.5. Allergenicity (Regulation EU No 503/2013; Annex II. II, 1.5)	Pour les produits consommés uniquement en mélange et/ou après transformation technologique, l'évaluation de l'allergénicité ne paraît pas nécessaire, car pour ces produits, les traces d'allergènes amenées par la PGM vont être extrêmement diluées (Anses, 2015). Pour les espèces végétales connues pour être fortement allergéniques, une analyse de la modification éventuelle de l'allergénicité de la denrée/aliment pourrait être demandée si d'autres éléments du dossier suggèrent que l'OGM présente un risque. Enfin, pour les espèces végétales pour lesquelles aucun OGM n'a été évalué jusqu'à aujourd'hui, il sera sans doute nécessaire de définir une liste d'allergènes à rechercher et quantifier. English translation An allergenicity assessment would not appear to be necessary for products consumed only in a mixture and/or after technological transformation, because any traces of allergens introduced by GM products will be extremely dilute (Anses, 2015). In the case of plant species that are known to be highly allergenic, an analysis of any change in the allergenicity of the food/feed could be required if other aspects of the application suggest that the GMO constitutes a risk. Finally, for plant species for which to date no GMO has been assessed, it would probably be necessary to compile a list of allergens to be researched and quantified.
France	Anses	3.2.3.6. Nutritional assessment (Regulation	L'Anses rejoint l'EFSA sur le fait que pour les produits consommés uniquement en mélange et/ou après transformation technologique, une évaluation nutritionnelle n'est

		[EU] No 503/2013; Annex II. II, 1.6)	sans doute pas nécessaire (Anses, 2015). L'Anses est d'accord avec les propositions présentées dans ce paragraphe, qui est clair et explicite sur les attentes. English translation Anses concurs with EFSA that a nutritional assessment is certainly unnecessary for products consumed only in a mixture and/or after technological transformation (Anses, 2015). Anses concurs with the proposals set out in that paragraph, which is clear and explicit as regards expectations.
France	Anses	3.2.5.3. Cumulative risk assessment	Comment cela va-t-il être géré dans le temps ? (e.g. des autorisations sont données pour 3 dossiers LLP et 3 ans plus tard, 5 nouveaux dossiers sont déposés : que fait-on si le risque cumulé devient inacceptable ?) Par ailleurs, est-ce que le(s) caractère(s) introduit(s) est (sont) vraiment le bon critère ? En effet, le danger n'est pas forcément lié au(x) caractère(s) introduit(s) dans la PGM. English translation How will this be managed in the time frame? (e.g. three LLP files are granted authorisation and three years later, five new files are submitted: what happens if the cumulative risk becomes unacceptable?) Also, is (are) the introduced characteristic(s) really the correct criterion? After all, the risk is not necessarily linked to the characteristic(s) introduced into the GMP.
France	Anses	Abstract	L'unité du "0.9%" devrait être précisée (ADN, masse, etc.). Par ailleurs, comment faut-il interpréter la phrase "maximum 0.9% of a GMO per ingredient" si plusieurs événements de transformation de la même espèce végétale et/ou un (des) événement(s) empilé(s) est (sont) présent(s) ? Les dérogations décrites dans ce document ne sont acceptables que si la teneur en OGM au total est inférieure à 0,9 % dans la denrée alimentaire ou l'aliment pour animaux. Elles ne le sont plus si cette teneur est en fait de n x 0,9 % du fait de la présence de n événements de transformation à une teneur de 0,9 % chacun.

			<u>English translation</u> The unit to which '0.9 %' refers should be specified (DNA, mass, etc.). Furthermore, how is the phrase 'maximum 0.9 % of a GMO per ingredient' to be interpreted where several transformation events of the same plant species are present and/or one or several stacked events is (are) present? The derogations described in this document are acceptable only where the total level of GMOs is below 0.9 % in the food or feed. They are no longer acceptable where that level is actually n x 0.9 % owing to the occurrence of n transformation events each at a level of 0.9 %.
France	Anses	Assessment of adjuvanticity (Regulation [EU] No 503/2013; Annex II. II, 1.5.3)	Le problème de la recherche d'une activité adjuvante reste entier dans la mesure où les directives actuelles (recherche d'identités avec les toxines d'une banque) demeurent insuffisantes. La question du caractère adjuvant des proteins Cry fait débat et reste toujours posée. <u>English translation</u> The problem with researching an adjuvant activity persists since the current directives (research identifying toxins from one databank) remain insufficient. The question of the adjuvant characteristic of Cry proteins is controversial and continues to be raised.
France	Anses	Testing of whole genetically modified food and feed (Regulation [EU] No 503/2013; Annex II. II, 1.4.4 subsections 1.4.4.1-1.4.4.3)	Le paragraphe 1.4.4.4. n'est cité nulle part : qu'en est-il ? S'applique-t-il in extenso ou des adaptations sont-elles proposées ? <u>English translation</u> What about paragraph 1.4.4.4? It is not cited anywheReg. Does it apply in its entirety or have amendments been proposed?