Request for a review of the authorisations for GM crops with altered oil content

GeneWatch UK and TestBiotech

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GeneWatch UK and TestBiotech urge the European Commission to withdraw the market authorisations for the import and use in food and feed of the following nutritionally-altered genetically modified (GM) products (issued on 24th April 2015[1]):

- Monsanto's MON 87769 soybean: a stearidonic acid (SDA)-producing soybean;
- Monsanto's MON 87705 soybean: a glyphosate-tolerant low-linolenic, high-oleic soybean, known as Vistive Gold;
- Pioneer soybean 305423: a herbicide-tolerant (to (ALS)-inhibiting herbicides), high-oleic acid soybean, known as Plenish.

This is a formal request for internal review of these authorisations under Article 10 of Regulation (EC) No. 1367-2006. We are seeking a review of **Commission Implementing Decisions 2015/686, 2015/696 and 2015/698** of 30th April 2015, which grant market authorisations under Regulation 1829/2003 on genetically modified food.[2]

The three products are all soybeans which have been genetically engineered to express different fatty acids which alter the oil composition of the final crop. They are not regarded as "substantially equivalent" to existing conventional crops and therefore pose new challenges for regulators.

The EU regulations that are violated by all three market authorisations are: Regulation 178/2002 (General Principles and Requirements of Food Law), Regulation 1829/2003 (on genetically modified food and feed) and Commission Implementing Regulation 503/2013 (implementing 1829/2003).

The authorisations should not have been granted because:

1. EFSA has initiated but not completed a process of developing guidance for the assessment of GM crops with significantly altered nutritional content. As well as being incomplete, this process has not been independent or transparent. In the absence of this guidance, approvals should not have been granted for nutritionally-altered GM crops.
2. The lack of guidance has led to inconsistent and inadequate risk assessments for all three crops, which fail to meet the requirements of the legislation.
3. Labelling and post-marking monitoring proposals are also inadequate and inconsistent.
4. In addition, the impacts of pesticide residues have not been fully considered for the two herbicide-tolerant crops and the unintended effects of RNA interference have not been adequately assessed for MON 87705.

1. These authorisations are premature because specific requirements for the authorisation of nutritionally-altered GM crops have yet to be adopted as EFSA Guidance or an implementing decision

The European Food Safety Authority is mandated to issue guidance on the manner in which it will assess applications for authorisations for genetically modified organisms (GMOs). In particular:

- Under Article 23(b) of Regulation 178/2002, one of EFSA's tasks is that it must "*promote and coordinate the development of uniform risk assessment methodologies in the fields falling within its mission*";

• Under Articles 5(8) and 17(8) of Regulation 1829/2003 on genetically modified food and feed, EFSA "*shall publish detailed guidance to assist the applicant in the preparation and presentation of the application*".

EFSA recognises the importance of developing methodologies in Section 5.2 of its Policy on Independence and Scientific Decision-Making Processes[3] :
"*Over time, EFSA has invested significant resources to the development of a comprehensive body of good risk assessment practices and methodologies to guide the work of its Scientific Committee, Scientific Panels and its scientific staff to ensure their opinions respect the highest scientific standards[26]. This in itself represents an additional procedural guarantee of the excellence, objectivity and transparency of the scientific processes and standards followed by EFSA. Indeed, while maintaining a case-by-case assessment for each relevant substance or product,* ***the fact that general good risk assessment practices and methodologies have been developed helps avoiding a case-by-case approach that could otherwise be detrimental to the impartiality of the work of EFSA's scientific experts or the coherence of the scientific output***." [emphasis added].

Guidance is also important to ensure a "level playing field" so that all products in a similar category (such as nutrient-altered GM crops) are subject to the same standards of regulatory oversight and assessment. Without Guidance, it is difficult to ensure that regulation is applied in a non-discriminatory manner. The general objectives of food law in the EU include "fair practices in food trade" (Article 5, Regulation 178/2002) and Recital (47) of Regulation 178/2002 emphasises that the Community applies a high level of health protection in a non-discriminatory manner whether food or feed is traded on the internal market or internationally.

However, despite highlighting the importance of developing standard methodologies to ensure impartiality and coherence of its outputs, EFSA has not completed work that it initiated in 2012 to develop the necessary guidance for the assessment of nutritionally altered crops.

The risk assessment and approval of the three GM crops that are the subject of this objection should not have taken place before the adoption of such guidance.

In Mandate Number M-2012-0084, EFSA has itself recognised the need to develop and detail a strategy for the safety and nutritional assessment of nutritionally altered GM crops, and its (former) Director has commissioned the first step in this work. However, neither EFSA nor any other EU institution has taken subsequent steps to progress or finalise this work to create the necessary detailed strategy for the assessment of nutritionally-altered crops. The lack of any new EFSA Guidance on this topic, and a revised implementing regulation to implement it, fatally undermines the legality of the three decisions to authorise the import of the nutritionally-altered crops (as food and feed) which are the subject of this complaint.

Commission Implementing Regulation (EU) No. 503/2013 was adopted in 2013, in a process which followed consultation with the European Food Safety Authority (EFSA) and the adoption of EFSA's 2011 guidance for risk assessment of food and feed from genetically modified plants[4]. Regulation 503/2003 notes in Recital (13) that the type and necessity of studies required to ensure compliance with Regulation (EC) No. 1829/2003 may vary depending on the type of product: "*For example, genetic modifications which have negligible impact on the composition of a genetically modified food or feed or highly refined products that may be proven to be identical to products produced from the conventional counterpart* ***require different studies than a product resulting from complex genetic modification aiming to modify its nutritional characteristics***". [Emphasis added]. Recital (14) and Article 5(3) highlight that the requirements laid down in this regulation are <u>minimum requirements</u>

for all GM crops, which may need to be supplemented in specific cases. From Recital (13), it is clear that one such case is when the genetic modification aims to modify nutritional characteristics.

Under Mandate Number M-2012-0084, in June 2012, EFSA acknowledged that the process for evaluation of this new category of crops (including nutritionally enhanced foods with qualitative and quantitative changes in oils/lipids) required further study and development and commissioned an expert report at a cost of 75,000 euros.[5] EFSA's mandate letter cites EFSA's new (2011) Guidance for risk assessment of food and feed from genetically modified plants, which states (page 34): "*In cases where a comparative assessment is not applicable, a comprehensive food and feed safety and nutritional assessment of the GM plant and derived food and feed should be performed. This should include, among others, a detailed compositional analysis and specific toxicological/nutritional analyses, selected according to the agronomic and compositional properties of the food and feed under assessment.* ***Further development and detailing of this strategy is needed***." [emphasis added]. The mandate letter states: "*In practical terms, such strategy for a comprehensive food/feed safety assessment, although being addressed in the guidance documents of the EFSA Panel on Genetically Modified Organisms,* ***has so far not been fully described****. For the assessment of applications of GM plants developed to express new traits the EFSA GMO Panel is currently receiving ad-hoc support from Nutrition (NUTRI) Unit and members of the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA).* ***The definition of clear strategies for the assessment of these applications is becoming a relevant issue for the GMO Panel***." [emphasis added].

In September 2013, EFSA published the expert report resulting from Mandate Number M-2012-0084, which considers in more detail the studies that would be necessary for regulatory approval of "novel" GM traits, including altered nutrient content.[6] In this report (page 3):"*A number of recommendations for further work are given, including the need for a wider review of risk assessment strategies to inform the approach to risk assessment for 'novel' traits, further work to develop guidance on post market monitoring, guidance on cases where field trial design for 'novel' traits may need to be amended, further work on the concept of history of safe use and guidance on the management of the risk assessment process*." The report does not recommend a wholesale change to EFSA's risk assessment process but states: "*As such, it is recognised in the foreseeable scenario for risk assessments that approaches to risk assessment will be based on using a comparative approach as a starting point, with differences to the current EFSA guidance to make the process effective at assuring the safety of plants with 'novel' GM traits.*" There is no record of any of the recommended further work being undertaken, nor of any further steps being undertaken by EFSA to develop guidance for the risk assessment of nutrient-altered GM crops. No final guidance has been published or adopted.

It is unclear whether EFSA informed the European Parliament, the Commission and the Member States of the existence of Mandate Number M-2012-0084 or this expert report, as it is required to do under Article 32 of Regulation 178/2002. No correspondence on the subject is recorded in EFSA's Register of Questions. Thus, whilst it is clear that EFSA was aware that its existing Guidance was not fit-for-purpose, it is unclear whether other EU bodies were informed of this before being requested to approve the authorisations which are the subject of this complaint. However, if the risk manager (DG SANCO, rather than EFSA) made the decision not to allow or require EFSA to proceed with developing specific Guidance before authorising nutrient-altered GM crops, this also undermines the scientific quality of the risk assessments (as outlined below) and the legal basis of the approvals.

The principle of transparency in EU food law (Article 9, Regulation 178/2002) also requires that there is open and transparent public consultation during the preparation, evaluation and revision of food law. No such consultation has taken place in relation to the development and detailing of a strategy for the assessment of nutritionally-altered GM crops.

EFSA has repeatedly been criticised for developing inadequate rules on conflict-of-interest, or failing to enforce them, most recently in a case brought to the European Ombudsman by GeneWatch UK.[7] One of the research institutes commissioned to write the export report under Mandate Number M-2012-0084, Rothamsted Research, is involved in developing nutrient-altered GM crops, notably GM sativa with enhanced omega-3 oils. [8] The one altered-oil crop included as a future scenario in the report (Section 8) is a GM oil seed plant producing enhanced levels of long-chain polyunsaturated fatty acids (omega-3) oils such as DHA and EPA i.e. a product being developed through Rothamsted's own R&D. Several of the authors of this report therefore have a clear conflict-of-interest as they are employed by the institution hoping to commercialise this research, which could benefit financially from weak regulation of nutritionally-altered crops and minimal data requirements. Furthermore, the main overview articles cited in relation to developing a risk assessment process for nutritionally-altered GM crops are all written by industry authors (Constable et al., 2007; Chassy et al, 2007; Glenn, 2007&2008), although these industry-affiliations are not noted in the text. The authors highlight a number of areas of significant scientific disagreement in their report and acknowledge that: "*It also became apparent from preliminary searches of the literature that the types of records sourced would not contain extensive amounts of numerical data, rather dialogue, and to some extent opinion from the author or risk assessment body regarding strategies for risk assessment*" (Section 2.1.1). In Section 7 (Foreseeable scenarios for risk assessment) they state: "*Please note that this section is based on the judgements and discussion of members of the project team*…". The report states that it may not be considered as an output adopted by the Authority and it is clear that further steps should have been taken by EFSA to (i) complete the process it initiated to adopt new guidance; and (ii) ensure independence and transparency by, for example, commissioning further work from independent scientists, consulting with a wider range of stakeholders, conducting a public consultation, and keeping the relevant EU institutions fully informed.

In summary, the process of developing guidance for the risk assessment of GM crops with altered nutrient content has not been:

(i) Completed or adopted;
(ii) independent; or
(iii) transparent.

Therefore no legal basis exists for the assessment and approval of nutritionally-altered crops at the current time.

2. Failure to adopt Guidance prior to approvals for nutritionally-altered GM crops has led to violation of food safety requirements under Regulation (EC) No. 1829/2003 and Regulation (EC) 178/2002.

Failure to adopt specific EFSA Guidance and a revised implementing regulation for the case of nutritionally-altered crops means that the authorisation of these crops does not meet the requirement to protect human and animal health enshrined in Regulation 1829/2003 (on genetically modified food and feed) and in Regulation (EC) 178/2002 (covering the general principles of food law, establishing EFSA, and laying down procedures in matters of food safety), which requires "*assurance of a high level of protection of human health and consumers' interest in relation to food*…" (Article 1).

EFSA has published scientific opinions on MON 87769[9]; MON 87705[10,11]; and soybean 305423[12]. However, these opinions provide an inadequate basis on which to make a decision because the information meets only the minimum requirements necessary for non-nutritionally-altered crops, not the information necessary to protect human health in the case of crops that have altered

nutrient content. Important gaps exist because EFSA has yet to develop Guidance following from the 2013 expert report it commissioned under Mandate M-2012-0084. Further, because no such Guidance has been published there has been no opportunity for public consultation or for the adoption of any resulting changes to the relevant implementing regulation.

Thus EFSA has failed to publish risk assessments "*based on the available scientific evidence and undertaken in an independent, objective and transparent manner*" as required by Regulation 178/2002 (Article 6) or to provide the "best possible scientific opinions" as required by Regulation 173/2002 (Article 23).

Some specific problems with the risk assessments are highlighted below.

In a number of cases these reflect Member State comments on the risk assessments which have not been adequately addressed. [13,14,15]

2.1 Inadequate or missing literature reviews on health impacts

Article 6 of Regulation (EC) No. 1829/2003 requires applications to include a systematic review of studies published in the scientific literature and studies performed by the applicant on the potential effects on human and animal health of the GM food.

For MON 87769, the applicant cites published studies in humans and animals of the four fatty acids found in higher amounts in MON 87769 than in conventional soybean: SDA, GLA, 9c,12c,15t trans-ALA (18:3) and 6c,9c,12c,15t trans-SDA (Section 5.1.2.3 of EFSA's Scientific Opinion). The opinion cites intervention studies on humans with various amounts of SDA ethyl esters and/or SDA-containing plant derived oils, and with SDA-enriched soybean oil for between 14 and 84 days and at doses ranging from 0.05 to 4.2 g SDA/day, stating no adverse effects were reported. However, such studies are wholly inadequate to assess long-term effects such as cancer risk. Similarly, several studies cited in which human diets were supplemented with GLA at doses from 1 to 5 g/day for periods of one to six months shed little light on the overall, long-term safety of the product for approval.

Studies on the reduced linoleic acid (LA) levels in soybean MON 87769 are not included in this literature review and nor are studies on the intended impact of the product on omega-3 levels (which the applicant wishes to refer to on the label, see Section 3 below). SDA is a normal intermediate in the formation of the long chain omega-3 polyunsaturated fatty acids (PUFAs) eicosapentaenoic acid [(C20:5 (n-3)] (EPA) and docosahexaenoic acid [(C22:6 (n-3)] (DHA). However, in humans, the conversion of ALA to SDA is slow. Direct consumption of SDA avoids this step in the biosynthesis and EFSA's Scientific Opinion on this product states that the rationale for developing MON 87769 is that this may result in a more efficient synthesis of the higher chain-length PUFAs (EPA and DPA). There is some evidence of this from a study conducted by Monsanto and Southern Illinois University in rats[16] and a subsequent clinical trial of SDA soybean oil from biotechnology-derived soybean MON 87769 in humans.[17]

These omissions from the literature review for MON 87769 are important because the scientific literature includes evidence of potential harm to health from low linoleic acid (LA)[18] and from omega-3 fatty acids (increased prostate cancer risk).[19,20,21] Despite many claims to the contrary, there is no conclusive evidence of health benefit from increased omega-3.[22,23,24,25]

No literature review of health impacts is included for the altered fatty acid content of the soybeans in the other applications.

In relation to MON 87705 and soybean 305423, which increase oleic acid (a mono-saturated fat or MUFA), a literature review would have revealed:

- Studies suggesting a link between oleic acid/MUFAs and breast cancer[26,27] ; and
- Studies suggesting a link between MUFAs and poor memory function.[28]

Again, there is no consensus in the literature on the claimed on the benefits of MUFAs for cardiovascular disease risk.[29]

These findings are important because they suggest that the regulatory requirement to protect human health requires studies which are adequate to identify endpoints such as cancer risk or memory loss in humans. Identifying such endpoints normally requires long-term clinical studies in humans.

A literature review would also have identified many gaps in the literature, leading to a lack of understanding, for example, of the implications of altering fatty acid profiles in foods for babies, young children, pregnant women and people with specific health conditions (discussed further in Section 2.3 below).

Had Guidance been in place, it is likely that all applicants would have been aware of the requirement for a comprehensive literature review of the health impacts of the altered nutrients in their products and would have identified a number of likely or potential harms to human health. This would have allowed hypotheses regarding risks to human health to be developed and tested in the remainder of the assessment.

2.2 Inadequate food safety and nutritional assessment

EU food law states (Article 14, Regulation 178/2002) that food shall not be placed on the market if it is unsafe.

The three products that are the subject of this complaint feature significant changes in nutrient content:

- Soybean MON 87769 contains a single insertion consisting of two intact expression cassettes (Pj.D6D and Nc.Fad3) coding for the fatty acid Δ6 desaturase from *Primula juliae* (primrose) (Pj.D6D) and the fatty acid Δ15 desaturase from *Neurospora crassa* (red bread mold, a filamentous fungus) (Nc.Fad3). The newly expressed desaturases in soybean MON 87769 seeds result in an alteration of the fatty acid profile, leading to the appearance of four new fatty acids (stearidonic acid (SDA), also known as octadecatetraenoic acid; alpha-linolenic acid; and two trans-fatty acids, 9c,12c,15t trans-ALA (18:3) and 6c,9c,12c,15t trans-SDA (C18:4)) and a reduction in linoleic acid (LA). The compositional analysis also revealed increased protein and differences in the levels of amino acids. For the processed oil, statistically increased levels of palmitic acid, stearic acid, trans-ALA and vitamin E were observed, whereas the level of lignoceric acid was reduced. The level of LA was also extensively reduced (from 54.8–55.9 % in the conventional counterpart to 20.7–30.9 % of the fatty acids in soybean MON 87769). In addition to these changes, three of the new fatty acids identified in the whole seed were also seen in the refined oil from MON 87769 (SDA, GLA and trans-SDA). Small quantities of trans-ALA were present in all types of refined, bleached and deodorised soybean oil. LA in protein isolate from soybean MON 87769 was reduced, and trans-ALA and ALA increased. The fat phase of the protein isolate produced from soybean MON 87769 also contained SDA, GLA and trans-SDA. The crude lecithin derived from soybean MON 87769 contained SDA, GLA and trans-SDA, which are usually not detected in lecithin from conventional soybeans, and the level of linoleic acid (C18:2) was significantly reduced.

- Soybean MON 87705 contains the soybean FAD2-1A/FATB1-A gene fragments down-regulating endogenous FAD2 and FATB enzymes and the CP4 epsps gene cassette conferring tolerance to glyphosate-containing herbicides. MON 87705 differs from the conventional counterpart in the fatty acid profile (proportion of (C18:1) oleic acid increased and proportions of (C18:2) linoleic acid and (C16:0) palmitic acid decreased) in seeds and the presence of the CP4 EPSPS protein. The intended effects of the genetic modification and the effects on the fatty acid pattern seen in the analysis of unprocessed soybean seeds were also reflected in the composition of derived oil and additional differences were seen in heptadecenoic acid (C17:1 9c) and octadecadienoic acid (C18:2 6c, 9c).
- Soybean 305423 was developed through particle bombardment and contains gm-fad2-1 and gm-hra expression cassettes, conferring a high oleic acid profile and tolerance to acetolactate synthase (ALS)-inhibiting herbicides. Soybean 305423 expresses a fragment of the endogenous fad2-1 gene resulting, through RNA interference, in the silencing of the endogenous fad2-1 gene, which leads to a decreased level of the corresponding fatty acid desaturase. As a consequence, the conversion of oleic acid to linoleic acid is inhibited and the oleic acid level is elevated. Since linolenic acid is produced from linoleic acid, linolenic acid content is also decreased in soybean 305423. Some of the observed differences of the fatty acid profile are consistent with the intended effect of the genetic modification, i.e. an increase in oleic acid at the expense of PUFA, but changes in the levels of odd chain fatty acids are an unintended effect probably caused by the introduction of the ALS enzyme. Other parameters (calcium, zinc and glycitin and related total glycitein equivalents) also showed non-equivalence. Data was not provided for the compositional content of derived oil, despite this being the main product destined for human consumption.

In all three cases the nutritional content of the soybeans is clearly not (and is acknowledged not to be) "substantially equivalent" to conventional soybeans. In addition, the nutritional changes are complex and not limited to a single nutrient.

The terms of reference for this EFSA's Guidance on selection of comparators for the risk assessment of GM plants (page 6) include: "*the selection of comparators in cases where the current comparative approach may not be suitable for the risk assessment of the GM plants (e.g. where major compositional changes are targeted)*". It concludes (Summary)[30]:
"*In cases where appropriate comparators are not available (e.g. where significant compositional changes have been targeted) the EFSA GMO Panel considers to carry out a comprehensive safety/nutritional assessment on the GM plant per se*."
The Guidance (page 10) refers to "*Cases where appropriate comparators are not available and a comprehensive risk assessment is required*" and states:
"*The development of GM plants targeted towards major compositional changes is progressing rapidly. This includes, for example, the development of crops with modified metabolism and physiology to provide improved quality and enhanced nutritional profiles. In such cases plant composition may be modified to such an extent that for FF* [Food and Feed] *risk assessment an appropriate comparator cannot be identified for the species in question. In such cases the risk assessment requires an alternative approach*."
In Section 4 (Challenges and limitations to the selection of comparators), this document describes this situation in more detail:
"*The majority of GM plants applications concern modifications to agronomic traits such as herbicide tolerance and/or insect resistance. Currently, GM plants are being developed with quality traits modified by major modifications in metabolic pathways, possibly leading to extensive compositional alterations. Examples include nutritionally enhanced foods with qualitative and quantitative changes in proteins, amino acids, carbohydrates, oils/lipids, vitamins and minerals. Other GM plants will have*

new traits which facilitate adaptation to environmental stress conditions such as drought or high salinity. These crops may be cultivated in areas where they have never been grown before.
The selection of appropriate comparators for the risk assessment of these GM plants with complex modifications may be difficult. When no appropriate comparator is available, the risk assessment should be based primarily on the evaluation of the characteristics of the GM plant and derived products themselves".
EFSA states that data are then required on, *inter alia*, "*dietary intake and potential for nutritional impact*" (Section 4).

Regulation (EC) No 1829/2003 defines a conventional counterpart as "*a similar food or feed produced without the help of genetic modification and for which there is a well-established history of safe use*" (Article 2.12). The underlying assumption of the comparative approach is that traditionally cultivated crops have a history of safe use for consumers and/or domesticated animals. The range of natural variation is estimated from a set of non-GM reference varieties and this allows comparisons of the GM plant with a similar food or feed produced without the help of genetic modification and for which there is a well-established history of safe use.

However, all three plants that are the subject of this complaint have nutritionally-altered components that fall outside this natural variation (as detailed above) and therefore all three products lack a history of safe use. EFSA's Guidance for risk assessment of food and feed from genetically modified plants[31] states (Section 3.1.3):
"*Where no comparator can be identified, a comparative risk assessment cannot be made and a comprehensive safety and nutritional assessment of the GM plant and derived food and feed itself should be carried out. This would, for instance, be the case where the food and/or feed derived from a GM plant is not closely related to a food and/or a feed with a history of safe use, or where a specific trait or specific traits are introduced with the intention of changing significantly the composition of the plant*".
And:
"*In case an appropriate comparator is not available, a comparative assessment cannot be made and,* ***therefore a safety and nutritional assessment of the GM plant and derived products should be carried out as for other novel foods****. In such cases, the elements to be considered for the risk assessment are the same as those listed in Section 2.3*." [Emphasis added]
These are:
a) characteristics of the donor organisms and recipient plant;
b) genetic modification and its functional consequences;
c) agronomic and phenotypic characteristics of the GM plant;
d) compositional characteristics of GM plants and derived food and feed;
e) potential toxicity and allergenicity of gene products (proteins, metabolites) and the whole GM plant and its derived products;
f) dietary intake and potential for nutritional impact;
g) influence of processing and storage on the characteristics of the derived products.

The expert report commissioned by EFSA states (section 3.4):
"*Codex guidelines discuss the eventuality of a modification resulting in a food product, like vegetable oil, with a significantly different composition from its conventional counterpart. It is stated that in such cases it may be suitable to use conventional foods/ food components whose nutritional composition is closer to the food derived from the GM plant as appropriate comparators for assessing the nutritional impact of the food. A number of the 'novel' GM traits that will request authorisation in the future are nutritionally enhanced crops that contain a compound that is currently eaten within the diet but from another source (e.g. particular fatty acids from fish oils). One proposal for safety assessment of these compounds is to compare them with the current similar*

compounds consumed within the diet. For example this might be a commonly consumed food oil or protein from another food product (Constable et al., 2007). Varzakas et al. (2007) suggest GM material should be compared with the parent plant and material from the parent plant genetically modified to express an empty construct. This is useful in plant genetics research but comparison with parent plant may be more relevant to risk assessment."

However, because it did not complete the process of developing Guidance for the assessment of nutritionally-altered crops following receipt of the expert report, EFSA has taken no public view on this proposal, or how it should be applied in practice. All three soybeans that are the subject of this complaint contain altered fatty acid profiles (and in some cases other nutrients) but the changes are complex and not directly comparable to any other food with a history of safe use.

It should also be noted that Constable (2007)[32] is an industry-authored paper and alternative views have not been sought.

In relation to nutritionally altered crops, Codex guidance states[33]:
"*48. The assessment of possible compositional changes to key nutrients, which should be conducted for all recombinant-DNA plants, has already been addressed under 'Compositional analyses of key components'.* ***However, foods derived from recombinant-DNA plants that have undergone modification to intentionally alter nutritional quality or functionality should be subjected to additional nutritional assessment to assess the consequences of the changes and whether the nutrient intakes are likely to be altered by the introduction of such foods into the food supply****. A detailed presentation of issues to be considered can be found in Annex 2 to this document.*"

Examination of the Scientific Opinions reveals that studies of the effects of the intended and unintended nutritional changes in the three soybeans are totally inadequate:

- For MON 87769, the applicant used information from the United Kingdom (UK) National Diet and Nutrition Survey (adults 19–64 years old) and the US FDA information on serving sizes to calculated the intake of SDA-rich soybean oil and SDA. Making various assumptions, the applicant then calculated that the estimated mean per capita intake of SDA from the suggested use of SDA soybean oil would be equivalent to a dietary intake of around 0.4–0.8 g EPA/person/day and would result in a cumulative estimated intake below the level of 5 g/day of supplemental combinations of EPA and DHA and of 1.8 g of EPA alone per day, which were considered to be safe for adults by EFSA. The applicant also used the UK National Diet and Nutrition Survey to estimate the impact of replacing presently used vegetable oils in foods with SDA-rich soybean oil on the intake of other fatty acids, concluding that the dietary intake of n-3 PUFAs would increase by 2.70–2.85 g/day, whereas the intake of n-6 PUFAs would decrease by 0.85–0.62 g/day and the total saturated fatty acid intake would increase by 0.54–0.79 g/day. They conclude that the estimated reduction in LA intake is without concern with regard to the AI for LA established by EFSA. Upon request, the applicant performed an additional assessment of the changes in fatty acid intake of consumers owing to substitution of conventional soybeans in soybean foods including soybean oil, with soybeans MON 87769, using consumption data from the UK, France and Denmark. The greatest changes occurred in the UK and consisted of an increase in the ALA intake of 0.5 g/day, in the SDA intake of 3.4 g/day, in the GLA intake of 1.1 g/day and in the palmitic acid intake of 0.17 g/day, whilst the intake of LA decreased by 4.9 g/day and that of oleic acid by 0.5 g/day. This LA intake would correspond to about 3 E%, which is below the AI set by EFSA. A twenty-eight-day repeated dose toxicity study, a sub-chronic toxicity study, and a one generation reproductive toxicity study were also conducted with soybean oil in Sprague–Dawley rats.

- For MON 87705, the nutritional assessment is focused on the intended increase of oleic acid (C18:1) and the accompanying decreases of linoleic acid (C18:2) and palmitic acid (C16:0), of which the levels were outside the ranges of the natural variation. The mean per capita intake of soybean oil from the target foods is estimated for adult males and females only. EFSA's Opinion states that there would be a substantial increase in oleic acid intake, while the PUFA intake would be markedly reduced: however levels would remain within the range of dietary recommendations for both n-3 PUFA and n-6 PUFA. In response to a further request, the applicant provided exposure assessments based on total and partial substitutions of conventional soybean, rapeseed and sunflower oils with the soybean MON 87705 oil in foods (salad dressings, margarines and spreads, mayonnaise, crackers and salty snacks and soybean/rapeseed/sunflower oils in processed foods). The average and upper percentile intakes (expressed as g/day and as E % of the total diet) of five fatty acids (palmitic, stearic, oleic, linoleic and α-linolenic acid) arising from a total substitution of other oils by soybean MON 87705 oil were estimated, and the likely changes in total fatty acid consumption from the whole diet were calculated. EFSA has not set a dietary reference value (DRV) for SFAs or MUFAs. EFSA has proposed an adequate intake (AI) for ALA of 0.5 E %: the n-3 PUFA intake, around 1 E % at baseline in men and women, would fall by about 5 % in the substitution scenario. EFSA has proposed an AI for linoleic acid of 4 E %: intakes of n-6 PUFA for adults would fall by around 40% from above to below this level. Only adults are considered in the assessment. Diets containing defatted meal from soybean MON 87705 were tested in rats: no animal studies were undertaken for derived oil, which is the main product destined for human consumption.
- For soybean 305423, dietary intakes were estimated for five fatty acid groups (saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), n-6 PUFA, n-3 PUFA and trans fatty acids (TFA)). Average and upper percentile intake amounts of the relevant food groups containing soybean oil were calculated and compared with reference values and normal dietary intakes. EFSA has not set a dietary reference value for SFA or MUFA. EFSA has proposed an adequate intake (AI) for linoleic acid (LA, the main dietary n-6 PUFA in the human diet) of 4 E %: reduction below the AI was observed for toddlers, children and teenagers (3.2–3.8 E %). EFSA has proposed an AI for Alpha-linolenic acid (ALA, the main dietary n-3 PUFA) of 0.5 E %: this was exceeded in all subgroups studied and replacement of vegetable oils with soybean 305423 oil was calculated to result in an increase of the n-3 PUFA consumption for all age groups. On request of the EFSA GMO Panel, the applicant provided an exposure assessment for the odd chain fatty acids: however no reference values have been set for these unintended changes. The Scientific Opinion concludes that full replacement of vegetable oils with oil derived from soybean 305423 would not change substantially the average intake of SFA and n-3 PUFA, but would increase MUFA and odd chain fatty acids, and decrease n-6 PUFA intake. It states that these changes are small and without impact on health and nutrition. For animal studies, dehulled, fat-extracted toasted soybean meal was the principal product tested, with small amounts of hulls and/or oil added in rat and chicken studies i.e. these studies focused on the product likely to be consumed by animals, not on the oil for human consumption.

Codex Guidance states (para 51):
"*When the modification results in a food product, such as vegetable oil, with a composition that is significantly different from its conventional counterpart, it may be appropriate to use additional conventional foods or food components (i.e. foods or food components whose nutritional composition is closer to that of the food derived from recombinant-DNA plant) as appropriate comparators to assess the nutritional impact of the food*". All three assessments have taken one narrow aspect of this approach (comparison with dietary reference values for individual fatty acids, where available). However, they have omitted other important aspects identified by Codex.

For example, Codex Guidance states (para 52):
"*Because of geographical and cultural variation in food consumption patterns, nutritional changes to a specific food may have a greater impact in some geographical areas or in some cultural population than in others. Some food plants serve as the major source of a particular nutrient in some populations. The nutrient and the populations affected should be identified*".
The EFSA GMO Panel notes that vegetable oil consumption varies considerably between European Countries and may be much higher outside the UK, however UK data are relied on in all three assessments and estimates of impacts on other European populations are not considered, except for MON 87769 which uses some data from France and Denmark.

Codex Guidance states (para 50):
"*The use of plant breeding, including in vitro nucleic acid techniques, to change nutrient levels in crops can result in broad changes to the nutrient profile in two ways. The intended modification in plant constituents could change the overall nutrient profile of the plant product and this change could affect the nutritional status of individuals consuming the food. Unexpected alterations in nutrients could have the same effect. Although the recombinant-DNA plant components may be individually assessed as safe, the impact of the change on the overall nutrient profile should be determined*." However, all the assessments take a nutrient-by-nutrient approach and fail to assess the impact on health of the overall nutrient profile.

Codex guidance states (para 49): "*It is also important to ascertain to what extent the modified nutrient is bioavailable and remains stable with time, processing and storage*". However, bioavailability studies have not been included for any of the three soybeans.

Codex guidance also states (para 53):
"*Some foods may require additional testing. For example, animal feeding studies may be warranted for foods derived from recombinant-DNA plants if changes in the bioavailability of nutrients are expected or if the composition is not comparable to conventional foods. Also, foods designed for health benefits may require specific nutritional, toxicological or other appropriate studies. If the characterization of the food indicates that the available data are insufficient for a thorough safety assessment, properly designed animal studies could be requested on the whole foods*." However, only MON 87769 soybean oil has been tested in rats: the other animal studies in the applications focus on testing animal feed which has minimal oil content and is not comparable to the main product destined for the human diet. Further, the rat studies for MON 87769 soybean oil are inadequate to test long-term impacts in humans. Foods utilising the GMO (as opposed to the GMO itself) were not included in any animal feeding study so no data of relevance to human consumption of these foods was obtained and appropriate endpoints such as cancer risk in humans (which should have been identified by the literature review, see Section 2.1) were not considered.

Recently, the first study of the metabolic effects of genetically modified high oleic soybean oil in mice was presented at a conference. The authors designed a parallel diet in which the regular soybean oil was replaced, on a per gram basis, with GM high oleic acid soybean oil (Plenish soybean 305423).[34] To the authors' surprise this diet induced weight gain and fatty liver essentially identical to that of the unmodified soybean, although the mice remained insulin sensitive and had less adipose tissue. The results indicate that LA may contribute to insulin resistance and adiposity but that another as yet unidentified component of the soybean oil affects the liver and overall weight gain. The authors conclude that a thorough understanding of the metabolic effects of the GM soybean oil is essential before the adoption of yet another dietary trend that could have long lasting and impactful health consequences. However, EFSA has not required applicants to submit this study or any comparable studies for any of the soybeans.

It is widely recognised that human studies are needed to assess bioavailability of nutrients from nutrient-altered GM crops.[35,36,37,38,39,40] Monsanto has conducted a clinical trial of SDA soybean oil from biotechnology-derived soybean MON 87769 in humans (Lemke et al., 2010, cited in Section 2.1 above and in EFSA's Scientific Opinion) but (despite the title of the paper) this does not address the safety of the nutritional changes. For the other two products, data from human trials does not appear to be available.

For MON87769, the applicant focuses heavily on the intended physiological consequence of consuming the soybeans i.e. enhanced synthesis of the long chain omega-3 polyunsaturated fatty acids (PUFAs) EPA) and DHA. The EFSA Opinion relies heavily on the fact that EFSA has set an adequate intake (AI) level of 250 mg EPA + DHA/day for adults, based on considerations of cardiovascular health. This is inadequate for a number of reasons including: (i) the EFSA report which established the AI is out of date[41] and more recent studies must be included (e.g. studies suggesting increased prostate cancer risk as cited above in Section 2.1); (ii) it does not consider population subgroups who may be particularly affected by changes in the fatty acid profile of their food (discussed further below in Section 2.3); (iii) it requires an extrapolation, based on limited data, of the impacts of the product on EPA+DHA and ignores other nutritional changes (contrary to Codex Guidance cited above) (iii) it is not applicable to GMO foods which require a full safety assessment under Regulation (EC) No. 1829/2003.

In summary, the lack of Guidance for the assessment of nutritionally-altered GM crops has resulted in an inadequate assessment process which fails to protect human health. There are also major inconsistencies between the information supplied for different products.

2.3 Inadequate consideration of the potential impact of altered nutritional content on potentially vulnerable subpopulations

Article 14(4) of Regulation 178/2002 states:
4. In determining whether any food is injurious to health, regard shall be had:
(a) not only to the probable immediate and/or short-term and/or long-term effects of that food on the health of a person consuming it, but also on subsequent generations;
(b) to the probable cumulative toxic effects;
*(c**) to the particular health sensitivities of a specific category of consumers where the food is intended for that category of consumers***." [Emphasis added]

Implementing Regulation 503/2013 notes (Annex II, Part II, 1.6.3):
"*Genetically modified foods modified to provide additional health benefits to the consumer as compared to conventional foods, **may benefit specific populations or subpopulations while others may be at risk from the same food**. In cases where an altered bioavailability needs to be established and may raise concern for subpopulation(s), the level of the nutrient in the food shall be determined, taking into account all the different forms of the compound. The methods to test for bioavailability shall be selected on a case-by-case basis depending on the nutrient or other constituent, the food containing these constituents, as well as the health, nutritional status and dietary practices of the specific population(s) anticipated to consume the food*". [Emphasis added]

Codex Guidance also notes (Annex 2): "*Foods derived from recombinant-DNA plants modified for nutritional or health benefits may benefit certain populations/sub populations, while other populations/sub populations may be at risk from the same food*" and states (point 49):
"*Attention should be paid to the particular physiological characteristics and metabolic requirements of specific population groups such as infants, children, pregnant and lactating women, the elderly*

and those with chronic diseases or compromised immune systems. Based on the analysis of nutritional impacts and the dietary needs of specific population subgroups, additional nutritional assessments may be necessary".

The expert report commissioned by EFSA states (Section 3.8):
"*Exposure assessment should also consider population differences that may result in segregated risks. This applies also to vulnerable subsets/ at-risk groups of a population, including diabetics, nursing mothers, pregnant women, children, and the elderly, which should be separately evaluated for exposure, to determine whether the GM food crop may pose a separate risk to them*".

Thus, EFSA Guidance and Codex Guidelines require population subgroups to be considered in the nutritional and safety assessment. As well as categories by age, this should include other subgroups whose nutrient requirements may be different from the general population.

However, data provided for the Scientific Opinions is inconsistent between applications and too limited to assess risks to vulnerable subpopulations:

- In the dietary assessment for MON 87769, only average adult intakes are considered.
- In the main and supplementary assessment for soybean MON 87705 oil is assumed to replace conventional soybean, rapeseed and sunflower oils in foods consumed by the adult UK population only. No impacts on subpopulations are considered.
- For soybean 305423, consumption data are taken from the UK National Diet and Nutrition Survey (NDNS) of 2008–2010 and the sub-populations considered are toddlers (1–3 years), children (4–10 years), teenagers (11–18 years), adults (19–64 years) and the elderly (≥ 65 years).

No studies for any of the soybeans have been included for pregnant or lactating women.

Bioavailability studies in vulnerable subpopulations have not been included for any of the three soybeans.

Persons with chronic diseases have also been neglected. For example, there are a number of monogenic genetic disorders, e.g. in the category of Fatty Acid Metabolism Disorders (MCAD, LCAD and SCAD deficiencies) in which medium-chain triglycerides (MCTs) can't be broken down and linoleic acid deficiency may occur.[42] The implications of the low linoleic acid levels observed in soybean MON 87769 and soybean 305423 should have been considered for these vulnerable groups. Propionic acidemia and methylmalonic aciduria are genetic disorders of propionate catabolism which result in abnormality of odd-numbered Long-Chain Fatty Acids.[43] No studies are available to assess the health impacts on this group of the unexpected increases in odd-numbered Long-Chain Fatty Acids in soybean 305423.

The lack of such studies also impacts on the failure to meet labelling requirements (see below).

2.4 Failure to consider all processed forms of foods

Codex guidance states (para 47):
"*The potential effects of food processing, including home preparation, on foods derived from recombinant-DNA plants should also be considered. For example, alterations could occur in the heat stability of an endogenous toxicant or the bioavailability of an important nutrient after processing. Information should therefore be provided describing the processing conditions used in the production of a food ingredient from the plant. For example, in the case of vegetable oil, information should be provided on the extraction process and any subsequent refining steps*".

However, not all forms of the processed soybeans were fully tested before approval of the products which are the subject of this complaint:

- For MON 87769, soybeans were harvested from two of the five sites in the USA in 2006 in order to perform compositional analyses on processed fractions, including defatted and toasted meal; refined, bleached and deodorised oil; protein isolate; and crude lecithin. The soybean meal was analysed for proximates, fibre fractions, amino acids, fatty acids, phytic acid and trypsin inhibitors, the soybean oil for fatty acids and vitamin E, the protein isolate for amino acids, fatty acids and moisture and, finally, crude lecithin for fatty acids and phosphatides.
- For soybean MON 87705, the seeds were processed into refined bleached deodorised (RBD) oil, isolated soy protein, toasted defatted meal and crude lecithin for further composition tests. RBD oils were analysed for fatty acid composition and vitamin E, isolated soy protein was analysed for amino acids and crude lecithin was analysed for phosphatides. Seed samples to prepare soybean processed fractions were collected from field trials where MON 87705 and the conventional counterpart A3525 were grown in replicated plots at two sites in the USA during the 2007 growing season. The intended effects of the genetic modification and the effects on the fatty acid pattern seen in the analysis of unprocessed soybean seeds were also reflected in the composition of RBD oil. The main product for human use is soybean oil. However, EFSA's Scientific Opinion notes that in addition, soybean is used for the production of soybean milk, protein concentrates, flour, sprouts, baked or roasted soybeans, tofu, soybean sauce and other products for human consumption. No analyses were conducted for these products.
- For soybean 305423, the main product for human consumption is the oil, and other products for human consumption were not considered in EFSA's Scientific Opinion. For the exposure assessment, food items considered are the targeted foods (fried fish, meat, potatoes, vegetables and other fried foods, home-use; and from spray applications savoury snacks and crackers) and other foods (salad dressings, margarines and spread, mayonnaise). The fatty acid composition of the oil from soybean 305423 is taken from that of the unprocessed seeds from the field trial of 2011 and the oil is assumed to fully replace vegetable oils in the individual food items.

In all cases, the nutritional and safety assessment for humans in focused on use of soybean oil. However, there is inconsistency because the fatty acid composition of the oil itself (only the seed) is not used for soybean 305423 and the effects of processing are therefore not considered in this case. In addition, EFSA's Opinion for MON 87769 (Section 5.1.2.3 (c)) states that it is assumed that trans-SDA is mainly formed by trans-isomerisation of unsaturated fatty acids during the processing of the oil: but no specific studies have looked at the effects of consuming trans-SDA.

Other products for human consumption including soybean milk, protein concentrates, flour, sprouts, baked or roasted soybeans, tofu and soybean sauce are not assessed for their fatty acid content or health impacts for any of the three soybeans.

On request from the EFSA GMO Panel, the applicant supplied information on the oxidative stability of the SDA enriched oil obtained from soybean MON 87769. However, this information does not appear to have been required from other applicants.

In the absence of Guidance for the assessment of nutrient-altered crops, none of the applicants have tested all the forms of the soybean products which may be consumed by humans. This is inconsistent with the risk assessment of novel foods, as described in the 2012 expert report commissioned by EFSA, for which the starting point is considering the processing the crop would undergo and the products which would be manufactured or marketed to consumers.

2.5 Inadequate feed safety and nutritional assessment

EU food law states (Article 15, Regulation 178/2002) that feed shall be deemed to be unsafe for its intended use if it is considered to:

— have an adverse effect on human or animal health;

— make the food derived from food-producing animals unsafe for human consumption.

Based on the data provided, the EFSA GMO Panel concludes that feeding of full-fat soybean MON 87769 or inclusion of the oil derived from MON 87769 could alter the lipid content of animal tissues (Section 5.1.5.2 of the relevant Scientific Opinion). However, the Panel did not consider the nutritional impact from consuming products of animal origin derived from animals fed whole fat MON 87769 or its oil on consumers. In fact, none of the three scientific opinions provided by EFSA on nutritionally-altered soybeans assess the impact on the nutritional content of meat, milk or eggs. Therefore the opinions do not include the necessary assessment of whether food derived from food-producing animals fed on any of the three GM soybeans is safe for human consumption.

The addition of GM soybean oil or seeds to animal feed is an active topic of research, with the aim of altering milk fat composition[44] as has already been attempted using supplements.[45] Since potential food and feed uses have not been restricted, this use should fall within the scope of the assessments. Further, it is likely that a similar approach could be applied to meat and eggs where diet is known to affect fat composition.[46,47] Since such uses can be anticipated, nutrient (and anti-nutrient) composition should have been required for meat, milk and eggs from animals fed on all three nutrient-altered soybeans.

In its comments on MON 87769, Germany notes that the applicant should specify whether whole soybean MON 87769, processed material or the derived SDA-rich oil are intended to be used as animal feed and whether impacts on the food (e. g. meat or milk) derived from animals which were fed these materials are expected. However, EFSA responded that foods and feeds derived from animals fed soybean MON 87769, feed containing or consisting of soybean MON 87769 and feed produced from this soybean, are not within the application. It is hard to see how this response is consistent with the requirements of Article 15, Regulation 178/2002.

This important issue is unlikely to have been missed had EFSA developed Guidance for the assessment of nutrient-altered GM crops.

2.6 Inconsistency in field trials required to characterise the altered nutritional content of the soybeans

Codex Guidelines state (para 45):

"*The location of trial sites should be representative of the range of environmental conditions under which the plant varieties would be expected to be grown. The number of trial sites should be sufficient to allow accurate assessment of compositional characteristics over this range. Similarly, trials should be conducted over a sufficient number of generations to allow adequate exposure to the variety of conditions met in nature. To minimise environmental effects, and to reduce any effect from naturally occurring genotypic variation within a crop variety, each trial site should be replicated. An adequate number of plants should be sampled and the methods of analysis should be sufficiently sensitive and specific to detect variations in key components*."

And also (Annex 2, para 11):

"*With conventional fortification of food, typically a nutrient or a related substance is added at controlled concentrations and its chemical form is characterized. Levels of plant nutrients or related substances may vary in both conventionally bred and recombinant-DNA plants due to growing*

conditions. In addition, more than one chemical form of the nutrient might be expressed in the food as a result of the modification and these may not be characterized from a nutrition perspective. Where appropriate, information may be needed on the different chemical forms of the nutrient(s) or related substance(s) expressed in the portion of the plant intended for food use and their respective levels."

Environment and gene-environment interactions (GxE) are known to have important effects on nutrient (including fatty acid) composition of soybeans, [48] leading to significant alterations in fatty acid content in different environmental conditions (e.g. temperature and rainfall) and such effects can vary at different developmental stages[49]. It is therefore essential that data on nutrient composition of the edible pats of the plant is obtained from a wide variety of agronomic conditions, representative of expected growing conditions.

The data provided in the three relevant EFSA Opinions is inconsistent between applications and in some cases clearly inadequate to deal with the case of nutrient-altered crops. Specifically, according to the relevant EFSA opinions:

- Data on agronomic and phenotypic characteristics of soybean MON 87769, its conventional counterpart and a set of non-GM commercial varieties were collected in field trials performed in the USA over 2 years in 2006 and 2007. These field trials also supplied seed and forage material for compositional analysis of the various soybean materials. In both years, the field trial was carried out at five geographical sites representative of the soybean cultivation areas of the USA.
- The comparative analyses for MON87705 were carried out at 5 different geographical sites in 2007/08 (including data from the US and Chile) and at 5 sites in the USA in 2008 (one USA site was excluded from the analysis).
- For soybean 30542, analysis was undertaken of the GM-HRA protein and fatty acid profile of seeds collected across several locations in Chile, Argentina and the USA. Field trials for compositional data were performed at six locations in the USA and Canada in 2005 and at six locations during the season 2005–2006 in Chile and Argentina. An additional comparative field trial was performed at ten sites within soybean cultivation areas in the USA in 2011.

Of the three products, MON87769 is already authorised for commercial cultivation in Canada and the USA.[50] At minimum, data from Canadian trial sites is also required to establish the nutritional composition for this soybean due to likely very different cultivation conditions (e.g. climate, soil types).

The lack of Guidance for nutrient-altered crops means that EFSA has failed to specify requirements for composition data for nutrient-altered crops which take account of the importance of gene-environment interactions.

3. Failure to adopt Guidance has led to violation of labelling requirements in Regulation 178/2002 and Regulation 1829/2003

The lack of Guidance for the risk assessment of nutrient-altered foods has also resulted in a failure to appreciate the need to provide adequate information regarding the new nutritional content on labels.

EU food law aims at the prevention of practices which may mislead the consumer (Article 8, Regulation 178/2002) and Regulation 1830/2003 requires products consisting of or containing GMOs to be labelled and to be traceable via a unique identifier provided to the operator receiving or placing a product on the market (but not to the consumer). This Regulation does not specify detailed

labelling requirements for nutritionally-altered crops that may pose risk to specific subcategories of consumer. However, Article 14(3) of Regulation 178/2002 states:
"*3. In determining whether any food is unsafe, regard shall be had:*
(a) to the normal conditions of use of the food by the consumer and at each stage of production, processing and distribution, and
(b) ***to the information provided to the consumer, including information on the label, or other information generally available to the consumer concerning the avoidance of specific adverse health effects from a particular food or category of foods***."

Regulation (EC) 1829/2003 Recital (22) states:
"*In addition, the labelling should give* ***information about any characteristic or property which renders a food or feed different from its conventional counterpart with respect to composition, nutritional value or nutritional effects, intended use of the food or feed and health implications for certain sections of the population****, as well as any characteristic or property which gives rise to ethical or religious concerns*". [emphasis added].

Article 5 (1f) of Regulation 1829/2003 requires either an analysis, supported by appropriate information and data, showing that the characteristics of the food are not different from those of its conventional counterpart, having regard to the accepted limits of natural variations for such characteristics and to the criteria specified in Article 13(2)(a), or a proposal for labelling the food in accordance with Article 13(2)(a) and (3). Since the applicants accept the three soybeans are different from their conventional counterparts, labels have been proposed for all three products.

Article 13(2 and 3) of Regulation 1829/2003 state:
"*2. In addition to the labelling requirements referred to in paragraph 1, the labelling shall also mention any characteristic or property, as specified in the authorisation, in the following cases:*
(a) where a food is different from its conventional counterpart as regards the following characteristics or properties:
(i) composition;
(ii) nutritional value or nutritional effects;
(iii) intended use of the food;
(iv) implications for the health of certain sections of the population;
(b) where a food may give rise to ethical or religious concerns.
3. In addition to the labelling requirements referred to in paragraph 1 and as specified in the authorisation, the labelling of foods falling within the scope of this Section which do not have a conventional counterpart shall contain appropriate information about the nature and the characteristics of the foods concerned."
Article 14 highlights that detailed rules for implementing this Section, amongst other things regarding the measures necessary for operators to comply with the labelling requirements, may be adopted in accordance with the procedure referred to in Article 35(2). However, no such detailed rules have been adopted for nutrient-altered GM crops.

As a result of the lack of detailed rules, the proposed labelling does not conform to the legal requirements for any of the three soybeans which are the subject of this complaint, because (i) information is not provided about all the characteristics and properties that render the food or feed different from its natural counterpart; and (ii) no account as has been taken of the differing nutritional needs of different sections of the population, particularly children and those with metabolic disorders who may be adversely affected by altered nutrient content. More specifically:

- For MON87769, the applicant proposed that food and feed products within the scope of the application should be labelled as "genetically modified soybean containing SDA omega-3 oil" or "contains genetically modified soybean containing SDA omega-3 oil". This is factually

incorrect since there is no omega-3 oil produced by the soybean. Commission Implementing Decision (EU) 2015/686 of 24 April 2015 states that the words 'with stearidonic acid' shall appear after the name of the organism on the label or, where appropriate, in the documents accompanying the products. However, to meet legal requirements the label should describe the altered composition in full, including all the new fatty acids (stearidonic acid (SDA), also known as octadecatetraenoic acid; alpha-linolenic acid; and two trans-fatty acids, 9c,12c,15t trans-ALA (18:3) and 6c,9c,12c,15t trans-SDA (C18:4)) and the reduction in linoleic acid (LA).

- For MON 87705, the labelling proposal "increased oleic acid oil produced from genetically modified soybean" is inadequate because it fails to detail all the changes in the fatty acid profile, including the reduction in linoleic acid (LA). Commission Implementing Decision (EU) 2015/696 of 24 April 2015 states the words 'with increased monounsaturated fat and reduced polyunsaturated fat' shall appear after the name of the organism on the label or, where appropriate, in the documents accompanying the products. However, numerous GM soybeans with altered fatty acid profiles are in the GM industry pipeline with a wide variety of properties[51,52]. These products all have different fatty acid profiles and molecular characterisations and several could be described as having increased monounsaturated fat and reduced polyunsaturated fat, despite having substantially different fatty acid profiles (and in some cases other altered nutrients).
- For soybean 305423 the labelling proposal "genetically modified soybean with altered fatty acid profile" is inadequate for the same reason, as it also provides inadequate information on the nutritional changes including the reduction in linoleic acid (LA). Commission Implementing Decision (EU) 2015/698 of 24 April 2015 states that the words 'with increased monounsaturated fat and reduced polyunsaturated fat' shall appear after the name of the organism on the label or, where appropriate, in the documents accompanying the products. However, this implies equivalence with MON 97705, despite different fatty acid profiles.

For all three soybean products, it is particularly important that consumers are warned about low linoleic acid, given the potentially adverse effects of this nutritional change and the existence of vulnerable subgroups with Fatty Acid Metabolism Disorders (as described above). Consumer information is also important because a reduction below adequate intake (AI) for linoleic acid was observed for toddlers, children and teenagers in the assessment for soybean 305423 (children were wrongly omitted from the assessments for the other soybeans).

The failure to undertake comprehensive nutritional and safety assessments for vulnerable subgroups (as described above) also means there is inadequate information on which to base these labelling proposals as in most cases relevant subgroups (such as pregnant mothers) have not been considered.

To meet the legal requirements, it is essential that consumers and medical professionals are provided with more information on the label (i.e. a list of all fatty acids and other nutrients that are significantly increased or decreased) and the means to find more detailed information should this become necessary (i.e. the Unique Identifier). This is necessary because:

1. New information may become available in future about unexpected harms associated with the particular method of genetic modification or molecular characterisation (e.g. stability of a particular construct or off-target effects) which is only traceable via the Unique Identifier.
2. New information may become available regarding specific harms associated with specific types of fatty acid (e.g. confirming the reported association between omega-3 fatty acids and prostate cancer, or high oleic acid and breast cancer) which may lead to (some or all) consumers wishing to avoid some altered oil products but not others and/or retailers/manufacturers to withdraw some products. This can only be done if the fatty acid profile of each product is known and its source is traceable.

3. Subgroups of consumers (e.g. children or those suffering from a particular metabolic disorder) may find health problems are caused by some fatty acid profiles but not others (as described above). They may therefore wish (or need) to avoid specific fatty acids or groups of fatty acids.

Detailed consumer information regarding specific products is essential to allow specific subgroups of persons to avoid them. This can only be done if the fatty acid profile and its source is known to the consumer (and in some cases can be discussed with a medical professional) via information on its label.

For MON87769, the proposed label "contains genetically modified soybean containing SDA omega-3 oil" also conflicts with food claims legislation. Whilst the risks of GM crops are considered by EFSA under Regulation 1829/2003, claims about the health benefits of products may be added to labels on a voluntary basis under Regulation 1924/2006. Under Regulation (EC) No. 1924/2006 (Annex) the use of the claim "SOURCE OF OMEGA-3 FATTY ACIDS" is restricted. The Annex states:
"*A claim that a food is a source of omega-3 fatty acids, and any claim likely to have the same meaning for the consumer, may only be made where the product contains at least 0,3 g alpha-linolenic acid per 100 g and per 100 kcal, or at least 40 mg of the sum of eicosapentaenoic acid and docosahexaenoic acid per 100 g and per 100 kcal*". This is clearly not the case for MON 87769 – which contains enhanced SDA levels intended to alter omega-3 levels via the metabolism of the consumer - and therefore the implication for the consumer that the product contains omega3 fatty acids should be avoided. For all three soybeans, the altered nutrient levels were introduced with the objective for the applicants of making claims of health benefits, yet no such applications have been made under Regulation (EC) No. 1924/2006. Since the GMO assessment process considers only risks, it is not the right mechanism to approve or imply health claims for labels.

Although not currently provided for in the legislation, labelling of meat, milk and dairy products from animals fed on nutrient-altered soybeans as feed is also necessary, because the use the potential use of whole soybeans or soybean oil as dietary supplements can significantly alter the fatty acid profile of these products.

Lack of Guidance for the assessment of nutritionally-altered crops has led to a situation where the labelling requirements from such crops which are necessary to protect human health have not been developed. This has led to inconsistent and inadequate labelling proposals for the three soybean products which fail to meet the requirements of Regulation 1829/2003 and in one case conflict with food claims legislation.

4. Failure to adopt Guidance has led to inadequate and inconsistent post-market monitoring proposals

Commission Implementing Regulation (EU) No. 503/2013 notes in Recital (19) that it is appropriate to confirm the expected consumption, application of conditions of use or identified effects via post-market monitoring in cases where the GM food or feed has altered nutritional composition.

The proposed post-market monitoring (PMM) plans for all three products are inadequate to identify unintended health effects:

- For MON 87769, the Commission Implementing Decision states that: 1. The authorisation holder shall collect the following information: (i) quantities of MON-87769-7 soybean oil and MON-87769-7 soybeans for oil extraction, imported into the European Union for the placing on the market as or in products for food; (ii) in case of import of products referred to in point (i), results of searches in the FAOSTAT database on the quantities of vegetable oil

consumption by Member State, including shifts in quantities between the different types of oils consumed; (iii) in case of import of products referred to in point (i), data on the different categories of food and feed uses of MON-87769-7 oil in the EU; and 2. The authorisation holder shall, based on the information collected and reported, review the nutritional assessment conducted as part of the risk assessment.

- For MON 87705, the Commission Implementing Decision states that: 1. The authorisation holder shall collect the following information: (i) quantities of MON-877Ø5-6 soybean oil and MON-877Ø5-6 soybeans for oil extraction, imported into the European Union for the placing on the market as or in products for food; (ii) in case of import of products mentioned under (i), results of database searches in the FAOSTAT database on the quantities of vegetable oil consumption by Member State, including shifts in quantities between the different types of oils consumed. 2. The authorisation holder shall, based on the information collected and reported, review the nutritional assessment conducted as part of the risk assessment.
- For soybean 305423, the Commission Implementing Decision states that: 1. The authorisation holder shall collect the following information: (i) quantities of DP-3Ø5423-1 soybean oil and 305423 soybeans for oil extraction, imported into the European Union for the placing on the market as or in products for food; (ii) in case of import of products mentioned under (i), results of database searches in FAOSTAT database on the quantities of vegetable oil consumption by Member State, including shifts in quantities between the different types of oils consumed; and 2. The authorisation holder shall, based on the information collected and reported, review the nutritional assessment conducted as part of the risk assessment.

However, as noted in Section 2.2 above, data on expected consumption has been based largely on UK data for all three soybean applications. As stated in Regulation 503/2013 Recital (19), it is not appropriate to delay consideration of consumption data elsewhere in the EU to the post-market monitoring stage. Further, consumption data should also have been collected for all vulnerable groups prior to approval (as discussed in Section 2.3).

In addition, the failure to properly assess potential health impacts prior to authorisation (as discussed in Section 2) makes it impossible for PMM to fulfil the role of monitoring such effects. This is because prior hypotheses for adverse effects (such as potential effects on cancer risk) need to be formulated before the product is approved if a meaningful monitoring regime is to be implemented.

According to Codex:[53]
"*Post-market monitoring may be undertaken for the purpose of:*

A) verifying conclusions about the absence or the possible occurrence, impact and significance of potential consumer health effects; and

B) *monitoring changes in nutrient intake levels, associated with the introduction of foods likely to significantly alter nutritional status, to determine their human health impact*."

It is not possible for PMM to fulfil this role if intakes of relevant nutrient levels throughout the EU have not been established in the applications and if potential adverse health effects associated with changes in fatty acid levels raised in the scientific literature have not been considered (see Section 2.1 above).

Article 7 of Regulation 503/2003 specifies some requirements for post-market monitoring. Under Article 7.1, PMM is required when it is appropriate to confirm:
"(a) that specific recommendations of uses are followed by the consumer/animal owner;
(b) the predicted consumption of the genetically modified food or feed; or
(c) the relevance and intensity of effects and unintended effects detected during the pre-market risk assessment which can only be further characterised by post-market monitoring".

Article 7.2 specifies that the applicant shall ensure that the post-market monitoring is:
"*(a) developed to collect reliable information with respect to one or several of the aspects set out in paragraph 1. This information shall allow the detection of indications on whether any (adverse) effect on health may be related to genetically modified food or feed consumption;*
(b) based on strategies aiming at collecting relevant information from specific stakeholders including consumers and on a reliable and validated flow of information between the different stakeholders. More specific strategies shall be included when data on individual intakes of a specific food item or intakes of particular age groups have to be collected;
(c) accompanied by adequate justification and a thorough description of the selected methodologies for the proposed post-market monitoring including aspects related to the analysis of the collected information."

Again, it is not possible for PMM to fulfil these roles if intakes of relevant nutrient levels throughout the EU have not been established in the applications and if potential adverse health effects raised in the scientific literature have not been considered (see Section 2.1 above). In particular, there is no proposed collection of information to allow the detection of indications on whether any (adverse) effect on health may be related to genetically modified food or feed consumption, or to collect data from particular age groups.

Failure to develop Guidance for the assessment of nutrient-altered crops means the proposed monitoring plans for all three soybeans are inadequate.

5. Other issues

In addition to the issues outlined above, which relate specifically to nutrient-altered GM crops, a number of other issues should have not been fully considered in the risk assessments. In particular:

- MON 87705 and soybean 305423 are both genetically engineered to be tolerant to herbicides. As such, limitations in safety and nutritional testing described above should also have taken into account the presence of herbicide residues on these crops;
- In MON 87705, the genetic modification results in an inhibition of the expression of the FAD2-1A and FATB1-A genes by RNAi interference (RNAi). The use of RNA interference can give rise to unintended off-target effects[54,55] but this possibility has not been adequately investigated.

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