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Re : A1073 – Genetically engineered Soybean DAS44406-6 tolerant to three Dow herbicides.

Dear FSANZ Submission Committee,

GE Free NZ in Food and Environment Incorporated is a voluntary non-governmental organisation. We are set up to inform and educate the GE issue to our members and the public. We have made many submissions on relevant applications to FSANZ.

GE Free NZ in Food and Environment are notably concerned at the lack of scientific analysis that has been conducted in support of this application, A1073. There is no detailed critique or cross referencing to other studies due to the lack of vital information on how the new transgenic food will affect human consumers.

We are entering this dialogue as part of the consumer consultation process as outlined in The FSANZ Application Handbook and because there is a major variation in process for a genetically engineered (GE) food application, namely A1073. We note that:

> *FSANZ needs to ensure that it has collected sufficient evidence, including from outside experts if necessary, in order to be able to undertake a rigorous analysis of each case. In some situations the best available scientific evidence is irrefutable. In others there might be conflicting scientific views, a lack of evidence or some uncertainty in the science. Where the evidence is in dispute, FSANZ will ensure that it sets out the reasoning and logic used to reach its decision/s.*[1]

The FSANZ Science Strategy 2012 -2015 talks about data gathering, peer reviewed science and looks at enhancing"our"science by a risk analysis that is evidence and outcome based.

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1 Community involvement and consultation during the assessment process http://www.foodstandards.govt.nz/foodstandards/changingthecode/informationforapplicants/communityinvolvement3610.cfm

FSANZ ensures that food regulatory measures are based on the best available scientific evidence, using a risk analysis framework. The successful application of science is critical to the effectiveness and appropriateness of food regulatory measures, and underpins the risk management decision making process. [2]

It is concerning that in every FSANZ assessment of an application for a GE food the public is led to believe that the experts at FSANZ are assessing the safety of eating these products based on hard scientific evidence from outside experts as well as industry.

Of note, the same statement made in this assessment appeared in the last two FSANZ statements when assessing risk of GE foods -

> *The Safety Assessment did not identify any public health and safety concerns associated with the genetic modification used to produce …*

This leads the public to assume that safety studies have been conducted on either human or animals. Yet when asked for this scientific information for the results of the whole GE plant being fed to animals or humans, **it is identified that the research has not been done**. The assessment process is not evidence-based as the evidence simply does not exist. There is no scientific data to support the above statement though FSANZ says in the FSANZ Application Handbook and the FSANZ Science Strategy 2012 -2015, that such data are a requirement.

FSANZ has the discretion to "stop the clock" to ask for more information[3]. The current application for A1073 is devoid of any scientific analysis in relation to ingestion safety and must be immediately put on hold until sufficient safety feeding data is obtained.

FSANZ is charged with protecting human health in Australasia in relation to section 18 (b) to protect human or animal life or health from risks arising from additives, contaminants, toxins or disease-causing organisms in foods, beverages or feedstuffs.

We believe that under section 50 (i) (ii)(iii) of the FSANZ Act, when the application for A1073 was considered, the following requisite information (p.38) was not available:

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[2] Our Science
www.foodstandards.govt.nz/scienceandeducation/scienceinfsanz/

[3] FSANZ will have the discretion to 'stop the clock' for up to 18 months for Applications if the Ministerial Council has notified FSANZ that it is developing policy guidelines on a specific, clearly defined issue or subject matter.
http://www.foodstandards.govt.nz/scienceandeducation/publications/annualreport/fsanzannualreport20062007/ourregulatorymeasures/newproceduresforamen3670.cfm

- the initial requirements to the protection of public health and safety;
- the provision of adequate information relating to food to enable consumers to make informed choices;
- the prevention of misleading or deceptive conduct; [4]

A1073 is a major variation of legal requirements[5] with no preceding safety studies conducted on the soybean product in question. We believe that FSANZ needs to maintain its duty to protect public health. For this to occur, adequate information needs to be made available to submitters to make informed submissions in this democratic process of stakeholder engagement. We are specifically seeking scientific data on the biological effects of eating the proposed food product.

As FSANZ is one of the first Food Authorities in the world to receive and assess this application, there needs to be a careful review of the scientific evidence in support of the application.

We note that the Technical Expert Committee appointed by the Supreme Court in India has submitted a report[6] setting down protocols for safety assessment of GMO's. This report follows the Cartagena and OECD guidelines and should set a base for all Food Authorities to be guided by. The Committee made 11 specific recommendations of which two are related to food assessment stating:

2. long term and inter-generational studies in rodents to be added to the tests and performed for all products whether already approved or yet to be approved: And

3. acute and sub-chronic feeding studies for all applications including those in progress should be completed before BRLI, as also molecular analysis and allergenicity tests. If these studies indicate potential risks of any kind, the GM event should be rejected outright to save time, resources and contamination",

It is of great concern that in the rush to approve this transgenic Soybean for commercialisation, environmental and ingestion studies have not been completed, the latter relevant for FSANZ's statutory responsibilities for food safety under Codex.

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4 Food Standards Australia New Zealand Act 1991 Act No. 118 of 1991 as amended

5 *Major procedure (12 months to complete assessment)* Applies to the development of a new food standard or a major variation to a food regulatory measure involving considerable scientific or technical complexity.

6 Interim report of the Technical Expert Committee, 17/10/2012, Supreme Court of India D.NO. 1944/2005/Sc/PIL

As the consumer information on FSANZ website says:

> *Where possible, submissions should contain scientific evidence rather than conjecture to back up any assertions as FSANZ is required to use the best scientific evidence available in its decision-making processes.*[7]

Yet FSANZ, an expert government food assessment body has requested the public to provide informed submissions on something without any pertinent food safety data.

We would like to reiterate that there has been no scientific information on the most important part of risk assessment: feeding data on any potentially adverse effects that might arise out of eating this soybean. In this regard, FSANZ has not followed its own protocols. We would like to submit our review of valid, peer-reviewed scientific information from publications that demand consideration above the industry assurance of safety. It is not acceptable that FSANZ requires scientific data from submitters yet its experts rely on industry assurances without any scientific proof.

This is especially relevant due to the comprehensive feeding trials (Seralini, 2012) that were published in the Journal Food and Chemical Toxicity 2012 documenting the lifetime feeding of rats and the severe adverse effects and deaths that were recorded in the rats fed transgenic product. GE Free NZ and others presented the studies and concerns in a document called"Fed Up with FSANZ". The study found that when GE foods associated with glyphosate applications were fed to animals over their lifetime, those animals developed serious health problems in the livers, kidneys and developed endocrine related testicular, uterine and mammary tumours leading to death or requiring euthanasia.[8]

Irrespective of FSANZ interpretation of these results, DAS 44406-6 is an untested, new food, using novel stacked genes and herbicide formulations, that has never entered the food chain before. Unless approval is halted until proper scientific evidence can demonstrate its safety, court action will be considered.

We are writing this noting that many of the references FSANZ is guided by for food safety are taken from the OECD and EFSA guidelines on GM Foods. We presume that the harmonization and default position is to these bodies when assessing food safety. We are of the understanding that feeding studies are to be part of the review process in major applications.

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[7] Information for Submitters http://www.foodstandards.govt.nz/foodstandards/changingthecode/informationforsubmit1129.cfm

[8] Seralini. G-E., Clair. E., Mesnage. R., Gress. S., Defarge. N., Malatesta. M,. Hennequin. D. and de Vendomois. JS. (2012) Long term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Food and Chemical Toxicity. Vol: 50, (11) 4221–4231http://dx.doi.org/10.1016/j.fct.2012.08.005

Does FSANZ follow the OECD guidelines for GE foods safety? If so, the FSANZ Act requires that a major new application such as that for DAS 44406-6 has a proper scientific assessment.

For submitters, the most crucial information about the new product is how it will affect them when they eat it, and what adverse effects people can expect from eating the whole food. Consumers cannot make informed comment when the information that would relate to potential impact on their health is unavailable. The assessment report provided is highly misleading since there is in fact, no data on the health effects of eating this whole soybean food.

GE Free NZ would like this application to be immediately recalled and the clock stopped until feeding studies are conducted. This is an untested and potentially dangerous food with significant public health implications.

We outline our concerns in this matter:

1. <u>Compositional equivalence –</u>

There are many concerns about the evaluation that FSANZ has made. When GE Free NZ asked for the animals feeding studies they received this reply - Correspondence with FSANZ stated

> *Where a GM food has been shown to be compositionally equivalent to conventional varieties, as is the case for soybean line 44406, the evidence to date indicates that feeding studies using target livestock species will add little value to the safety assessment and generally are not warranted (OECD, 2003; EFSA, 2008).*

This application shows that the DAS 44406-6 is not"Compositionally equivalent" to its conventional control. As set out in the applicant's information below:

<u>Alteration of nutritional parameters</u>

"Soybean 44406 is the result of a simple genetic modification to confer herbicide tolerance with no intention to significantly alter nutritional parameters in the food. In addition, the extensive compositional analyses of seed that have been undertaken to demonstrate the nutritional adequacy of line 44406, indicate it is equivalent in composition to conventional soybean cultivars. The introduction of soybean line DAS-44406-6 into the food supply is therefore expected to have little nutritional impact" p.38

GE Free NZ believes that even though there was no intention to alter the nutritional parameters, the act of engineering new genes and production requiring specific commercial sprays significantly alters vital parameters in the DAS 44406-6 soybean, including its chemical composition.

In support of this belief, the Dow compositional analysis document of evidence provided shows that the event DAS-444Ø6-6 sprayed with three herbicides has shown significant differences between the control and the transgenic soybean event in all the categories tested.

The fact that this application event DAS-444Ø6-6 contains three novel genes AAD-12, 2mEPSPS, or PAT proteins to enable the soy plant to withstand three different herbicides Weedar64 (2,4-D) Liberty (Glufosinate ammonium) Durango DMA (glyphosate), sprayed with three applications of each herbicide over the plants growing season, in itself makes the soybean compositional characteristics different from its non transgenic control. To refresh the reviewer's memory of this fact, we outline the relevant places where the significant differences are detailed in the Dow compositional analysis report[9].

Proximate and Fiber Analysis of Seed (p27)

Statistically significant overall treatment effects were found for protein and carbohydrates, where some DAS-444Ø6-6 entries contained more protein and less carbohydrate than the control. See Table 12 (p28)

Mineral Analysis of Seed

Statistically significant differences were observed for calcium, potassium, and zinc for some DAS-444Ø6-6 entries compared with the control. (p.31)

Amino Acid Analysis of Seed

Statistically significant differences were observed for cystine, histidine, lysine, tryptophan, and tyrosine for some DAS-444Ø6-6 entries compared with the control, where mean differences were negligible and not biologically meaningful as means were within literature ranges and within ranges for reference lines included in the study. (p.37)

"Biologically meaningful"is a particular term that has not been used before in FSANZ assessments that rely on scientific proof. Specifically, if there are no feeding studies conducted how did FSANZ deduce that there were no effects that were "biologically meaningful"

Bioactive Analysis of Seed (p.58)

Statistically significant differences were observed for lectin, raffinose, trypsin

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[9] Nutrient Composition of a Transformed Soybean Cultivar Containing Aryloxyalkanoate Dioxygenase-12 (AAD-12), Double Mutant Maize EPSPS Gene (2mEPSPS), and Phosphinothricin Acetyltransferase (PAT) - Event DAS-444Ø6-6

inhibitor, total daidzein equivalent, and total genistein equivalent for some DAS-444Ø6-6 entries compared with the control.

There are statistical differences between the control and the soybean DAS 44406-6 event in all the sections tested. This means that under OECD, 2003; EFSA, 2008 long term animal feeding tests are triggered and must be conducted on the whole soybean.

2. <u>Immune reactivity</u>

Application A1073 details how researchers discriminated between the control and the transgenic "as the non-transgenic extracts of Maverick did not contain detectable amounts immunoreactive protein". They documented that fact that after 30 minutes of cooking at temperature of 95C the 2mEPSPS enzyme activity was reduced with up to 73% and 90% of its immunoreactivity lost. Showing that heating would "significantly degrade the tertiary structure of the 2mEPSPS protein, reduce its immunoreactivity, and significantly diminish its enzymatic activity" (p.8)

An immune reactive protein is a foreign substance (antigen) that causes the body to mount a defense reaction producing antibodies against it. This can cause reactions like tissue inflammation that can be life threatening as in anaphylaxis and for those who experience chronic reaction they could have allergies and autoimmune diseases. We have no information that this process is not initiated by the amount of protein remaining in the product after cooking, or for consumers who prefer consuming soy products in their uncooked state.

There are no diagnostic tools to detect immune reaction to these proteins unless testing is conducted. Public health implications arising from adverse immune reactivity arising from ingestion of soybean DAS-444Ø6-6 therefore remain significant but unaddressed.

3. <u>OECD, Codex Alimentarius, EFSA.</u>

The three transgenic proteins in soybean DAS-444Ø6-6 have never been used in combination before, nor have the levels of herbicide applied been used in the growing of these foods. Under the EFSA and OECD guidelines, this constitutes a need to demonstrate that these newly expressed proteins and accompanied herbicide residue should undergo animal feeding studies to show they will not adversely affect human health. According to the European Food Safety Authority in 2011[10] the applicant should provide in relation to the

[10] EFSA Panel on Genetically Modified Organisms (GMO); Scientific Opinion on Guidance for risk assessment of food and feed from genetically modified plants. EFSA Journal 2011; 9(5): 2150. [37 pp.] doi:10.2903/j.efsa.2011.2150. Available online:

safety of newly expressed proteins,

> *e) repeated dose toxicity studies using laboratory animals, unless reliable information demonstrating the safety of the newly expressed protein (including its mode of action) can be provided, and it is demonstrated that the protein is not structurally and functionally related to proteins adversely affecting human or animal health. The repeated dose 28-day oral toxicity study in rodents with the newly expressed protein should be performed according to OECD guideline 407 (Table 2). It is recommended to use a sufficient number of animals per group e.g. 10/sex in order to obtain an adequate statistical power. Depending on the outcome of the 28-day toxicity study, further targeted investigations may be required.*

Under clause 3.3.2 of the EFSA guidance for risk assessment for food from GM plants[11], toxicological assessment tests should be conducted to show any toxicological effects such as

- dose response relationships
- threshold levels
- delayed onset of adverse effects
- risks for certain groups in the population
- use of uncertainty factors in extrapolating from animal data to humans

It is known that soybean has naturally occurring toxins. Relative concentrations of these could be altered by the engineered event. Though temperature studies have been conducted there is no data to elucidate whether the intact DNA survived heating, or if the foreign DNA could pose a more significant immunological reaction if it enters the blood stream. Until scientific feeding tests are conducted, none of these major effects can be assessed.

The following clause 3.3.3, (Guidance for risk assessment, EFSA (2011) states

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www.efsa.europa.eu/efsajournal.htm

[11] Guidance for risk assessment of food and feed from genetically modified plants. EFSA Panel on Genetically Modified Organisms (GMO) European Food Safety Authority (EFSA), Parma, Italy, EFSA Journal 2011; 9(5):2150

"the applicant should ensure that the final risk characterisation clearly demonstrates that:

. a) consumption of food and feed derived from GM plants is as safe as the respective comparators;

. b) the food derived from a GM plant is not nutritionally disadvantageous for the consumer compared to the food which is intended to replace;

. c) the feed derived from a GM plant feed is not nutritionally disadvantageous for animals compared to the feed which is intended to replace;

. d) the feed derived from a GM plant does not harm or mislead the consumer by impairing distinctive features of the animal products compared to conventionally produced feed.

The applicant has not been able to demonstrate that the DAS444406-6 event is safe in respect to any of these points as there are no feeding studies to look at adverse effects.

In prior correspondence Dow AgroSciences misled FSANZ, who should not be reliant on industry interpretation of legislation, by telling FSANZ that the EFSA stance on animal feeding studies is that animal feeding studies should only be carried out for "…traits that have an intentionally modified nutrient composition"[12].

This industry interpretation of legislation contradicts the Codex Alimentarius Foods derived from modern biotechnology on unintended effects that have not been considered that states-

> *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. (*point 15 & 16, p.2) [13]

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12 Paul Brent correspondence to GE Free NZ under Freedom of Information request, 7/3/2012. (email from Dow to FSANZ, Re role of animal feeding trials (EFSA, Food Chem tox, 2008).pdf

13 Guideline For The Conduct Of Food Safety Assessment Of Foods Derived From Recombinant-Dna Plants *CAC/GL 45-2003*
http://ec.europa.eu/food/food/biotechnology/qanda/i2_en.print.htm

As acknowledged by the applicant, there were unexpected alterations. Dow's compositional analysis of seed showed a significant difference between anti nutrient, proteins, mineral and vitamin composition. Codex says:

> *In the case of proteins, the assessment of potential toxicity should focus on amino acid sequence similarity between the protein and known protein toxins and anti-nutrients (e.g. protease inhibitors, lectins) as well as stability to heat or processing and to degradation in appropriate representative gastric and intestinal model systems. Appropriate oral toxicity studies may need to be carried out in cases where the protein present in the food is not similar to proteins that have previously been consumed safely in food, and taking into account its biological function in the plant where known. (point 38, p.6)*

It goes on to say:

> *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 bio-availabilities of nutrients are expected or if the composition is not comparable to conventional foods. In addition, 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. (Codex Alimentarius, p.17)*

> **Potential accumulation of substances significant to human health**

> *54 Some recombinant-DNA plants may exhibit traits (e.g. herbicide tolerance) that may indirectly result in the potential for accumulation of pesticide residues, altered metabolites of such residues, toxic metabolites, contaminants, or other substances that may be relevant to human health. The safety assessment should take this potential for accumulation into account. Conventional procedures for establishing the safety of such compounds (e.g. procedures for assessing the human safety of chemicals) should be applied. (Codex Alimentarius p.18)*

Significant differences were shown between the control soybean and the GE soybean DAS 44406-6. These differences are expressed by three novel genes inserted into the plant DNA and the possible interaction between the product-required herbicides used to produce the soybean, and the metabolites produced by the recombinant DNA in transgenic soybean plants.

In accordance with Codex Alimentarius, animal feeding studies must be conducted with adequate immunoresponse testing to ensure that the allergenic potential of the immunoreactive proteins in both cooked and uncooked soy DAS 44406-6 do not

cause allergic reactions in laboratory animals (Section 4 - Codex Alimentarius, p.22). We also consider it vital that the bioavailability of nutrients, introduced foreign proteins and foreign DNA be assessed and the significance of nutrient alteration tested, as significant compositional changes in soybean DAS 44406-6 have been demonstrated (Section3 Codex Alimentarius, p.25).

Even though GE Free NZ received 30,000 pages of applicant's information, none of it is directly relevant to public health. It is only relevant to patent legislation and commercial sensitivity. Until there are comprehensive Codex approved feeding studies conducted on DAS 44406-6 (A1073) there is no protection for public health, which FSANZ is charged with under legislation.

Summary –

1. The new food soybean DAS 44406-6 has not been found safe for human consumption.

2. This application A1073 does not follow Codex Alimentarius protocols on GE food assessments.

3. FSANZ has misled the public in its finding on A1073 safety for public consumption as there are no safety studies to evaluate.

4. This application has disregarded the statistical differences between the composition of GE food DAS-44406-6 and normal soybeans.

5. This application must have the clock stopped until long term feeding studies are conducted and independently assessed.

GE Free recommends that this application is not approved due to absence of required data. The application should not proceed and information from long term feeding studies is required. Once these studies are completed the application must be re-submitted for public comment.

Yours sincerely,

Jon Muller
Secretary of GE Free (NZ) in Food and Environment.