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Opinion of the Scientific Committee on Food on the safety assessment of the genetically modified maize line GA21, with tolerance to the herbicide glyphosate

(expressed on 27 February 2002)

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1. TERMS OF REFERENCE

The SCF is asked to assess the safety, from the point of view of consumer health, of the genetically modified maize line GA21, with tolerance to the herbicide glyphosate. The Committee is also invited to focus its deliberations on the issues raised in the comments made by Member States' authorities.

2. BACKGROUND

The Commission has received a petition[1] under Regulation 258/97/EC[2] to place on the market maize grain and derived products from a maize line GA21 that has been genetically modified to express tolerance to the herbicide glyphosate. An opinion is also sought on substantial equivalence for those products which may be considered for notification under Article 5 of the Regulation. Maize line GA21 was produced by the introduction of a modified 5-enolpyruvyl-shikimate-5-phosphate synthase (mEPSPS) gene from maize. EPSPS is an enzyme involved in the shikimic acid pathway for aromatic amino acid biosynthesis in plants and is normally inhibited by glyphosate. Although the mEPSPS shares more than 99.3% homology with the wild type maize EPSPS it is significantly less sensitive to glyphosate. Thus when maize plants having the mEPSPS protein are treated with glyphosate, the plants are unaffected because the new protein continues to supply the plants' needs for aromatic amino acids. The use of such plants therefore allows a greater control of weeds growing within the crop through the application of glyphosate. The value of this genetic modification therefore is entirely agronomic.

The petitioner first submitted in 1998 an application for permission to market these maize products to the Netherlands Competent Authority under the Novel Foods and Novel Food Ingredients Regulation No. 258/97/EC and received a favourable opinion. In accord with the Regulations other Member States were given the opportunity to comment on the initial assessment. A number of Member States raised an objection that the maize line GA21 should not receive clearance for food use ahead of a favourable decision for its Deliberate Release into the Environment under Directive 90/220/EEC. However the Scientific Committee on Plants (SCP) has now delivered a favourable opinion on its environmental release, an opinion adopted by the SCP on 22nd September 2000[3].

Member States have raised other objections to a favourable decision based on the initial safety dossier and the petitioner has produced additional safety information in response. This Committee is requested to focus its deliberations on the issues raised in the comments made by Member States' authorities. In order to do so and to complete the safety assessment it was necessary for the Committee to consider data in the original dossier[1], in the petitioner's response to Member States' objections[4] (listed below), in the Scientific Committee on Plants'

opinion on the safety of maize line GA21[3] and in information submitted in response to queries from the Scientific Committee on Food's Working Group on Novel Foods[5].

- Does the demonstration that the modified EPSPS has no significant sequence homology to known allergens and toxins provide sufficient reassurance as to its safety?

- Data on gastric and post-gastric digestibility studies are used to discount gastrointestinal (GI) allergenicity. Might a molecule such as mEPSPS exert sensitising effects from the oral mucosa as much as from the lower GI tract?

- Data for the variation of levels of p-coumaric acid in sampled control and experimental plants grown at several sites are provided only as average values and do not indicate extreme values.

- A number of questions on the presence/absence of bands on the Southern blots used to derive information on the nature of the DNA insert(s) in GA21 are raised.

- Two open reading frames have been identified in the maize DNA adjoining the insert. Additional evidence is sought that these are not transcribed from an inadvertently inserted truncated rice actin promotor.

- Were the multi-location trials carried out in the USA and Europe assessed in relation to genotypic and/or phenotypic stability?

- Is the intended purpose for use of the novel food to include raw consumption of this product by humans?

- Information is missing on the 5' proximal region of the insert with regard to a possible retroelement.

- In terms of compositional analysis not enough parameters were assayed to establish substantial equivalence and do not include analytical data from glyphosate-treated maize plants.

- With regard to animal feeding studies it was considered desirable that in the mouse toxicity experiments the whole product should have been used as well as the new protein (mEPSPS). Additionally long-term studies were requested e.g. 28 or 90 days, and the animal species used extended to beef cattle, dairy cattle and pigs.

- The labelling of foods produced using maize GA21 should be in accord with current European regulations (258/97/EC, 1139/98/EC and 49/00/EC).

- The company should provide such information (primer sequences) and reference material to enable official testing to be carried out.

- The company should give information on the level of glyphosate and its breakdown products in maize crops treated with glyphosate.

3. EVALUATION

The application presented by the petitioner follows the SCF guidelines expressed on 29th September 1997 and published as Commission Recommendation 97/618/EC[6]. These concern the scientific aspects and the presentation of information necessary to support applications for placing novel foods and novel food ingredients on the market. The GM maize line GA21, the subject of this application, falls into Class 3.1 of these Guidelines dedicated to GM plants and their products. The present evaluation has taken the structured schemes that were previously provided by the SCF as a guide to identify the different aspects required to establish the safety of the novel food.

3.1 Specification of the novel food

The taxonomic position of Maize, *Zea mays* L, is that it belongs to the family Gramineae (grasses). The genus consists of four species *Zea mays*, *Z. diploperennis*, *Z. luxurians* and *Z. perennis*. *Z. mays* includes cultivated maize and teosinte.

Maize, the novel food source, has a long history of safe use. It is one of the few major crops indigenous to the Western Hemisphere and is grown in nearly all areas of the world including the EU[7]. The low price and ready availability of maize has resulted in the development of large volume food and industrial usage. Maize is an excellent raw material for the manufacture of starch. In the USA nearly one quarter of maize starch is sold as starch products; more than three quarters of the starch is converted to a variety of sweetener and fermentation products including high fructose maize syrup and ethanol[8]. Similarly in the EU starch derived from maize is converted into a number of first and second generation products. Additionally maize oil is commercially processed from the germ and accounts for a significant percentage of vegetable oil production. Each of these materials is a component of many foods including bakery and dairy goods, beverages, confectionery and meat products. Maize does not contain toxins or significant anti-nutritional factors[9].

The subject of this application, maize line GA21, was produced by the introduction of a modified 5-enolpyruvyl-shikimate-3-phosphate synthase (mEPSPS) gene from maize (*Zea mays*). Although the mEPSPS protein differs from the wild type maize EPSPS by only three amino acids in a total of 445 it has significantly less affinity for the herbicide glyphosate and so the GA21 plants are tolerant to the herbicide.

On the question of the labelling of foods and food ingredients, the petitioner proposes to take into account the general requirement of Regulation 258/97/EC, the detailed requirements of Regulation 1139/98 and Regulation 49/2000 amending the 1139/98/EC Regulation. This would mean (1) that foodstuffs in which the individual food ingredients do not contain protein or DNA resulting from the genetic modification shall not be subject to specific, additional labelling requirements e.g. starch hydrolysates and maize oil; (2) that foodstuffs in which individual food with a proportion no higher than 1%, provided that this presence is adventitious shall not be subject to additional labelling requirements; (3) that foodstuffs solely comprising maize line GA21, or containing food ingredients derived from maize line GA21, except for those categories in (1) and (2) above would no longer be considered equivalent and should therefore be identified with the words “produced from genetically modified maize” or the abbreviation “genetically modified”.

3.2 Effect of the production process applied to the novel food

The primary use of maize is for animal feed but it is also processed into valuable food products. Of the maize used for food purposes the majority is processed by wet milling to produce starch and sweetener products although some products such as maize flour are produced using dry milling. The wet and dry mill processing of maize into refined derivatives e.g. oils, syrups and starch, involves varying degrees of mechanical, enzymic, heat, acid or pressure treatment or combinations of these[8, 10].

The wet milling process uses mainly shelled field maize. The milling process begins with the maize being steeped to soften the kernel, the steep water is drawn off and the softened kernels passed through a cracking mill to liberate the germs. The germ fraction containing approximately 50% oil on a dry weight basis, is separated by flotation, then washed and dried for oil recovery.

Among the products the primary product of wet milling is starch, the majority of which is converted to various sweeteners while the remainder is consumed directly in foods and used for other industrial purposes. Much of the starch used for food is further chemically modified e.g. using bleaches and acids, and heat-treated to modify the starch properties to meet customer requirements[11]. Syrups derived from maize can be divided into regular corn syrups (e.g. glucose, dextrose), high fructose corn syrups and malto dextrins. A variety of enzymatic and acid-catalysed processes are used for the manufacture of refined sweeteners. Maize syrups are used in a wide variety of foods and drugs to provide sweeteners, viscosity etc. Ethanol is produced from starch by fermentation and may be used in beverages. Maize oil is recovered from maize germ by expelling, solvent extraction or a combination of the two. The resulting crude oil must be further refined, bleached and deodorised to produce a good quality edible oil.

In dry milling the majority of the maize is degermed to give as complete a separation of components as possible in order to recover the maximum number of intact germs, to yield a low-fat, low-fibre product and to retain a maximum amount of horny endosperm as discrete pieces. The rest of the maize is stone-ground in a non-degerming process to produce grits and whole meals rich in bran and germ. The major products of the dry-milling industry are maize germ and bran. Food and food ingredients processed from maize GA21 would not be expected to be different from food and food ingredients derived from non-modified maize.

3.3 History of the organism used as the source of the novel food

Maize, the source of the transgenic variety has a history of safe use. The initial steps in the origin of current cultivars were taken in Mexico and Central America more than 8000 years ago based on teosinte.

Maize is grown all over the world over a range of climatic conditions. In 1996-97 41% of world maize production was grown in the USA and 5.9% (34 million tonnes) in Europe. Two regions in Europe are among the top five maize producing regions in the world. These are the Danube basin from Southwest Germany to the Black Sea and Southern France through to the Po valley of Northern Italy.

Maize use in the EU as in other areas of the world is dominated by the demand for animal feed. In the period 1990-2001 human consumption of maize (excluding alcohol and beer uses) was slightly more than 10% of the total.

3.4 Effect of the genetic modification on the properties of the host organism

Maize line GA21 was generated using particle acceleration technology, also referred to as biolistics or gene gun technology. This line is tolerant to the herbicide glyphosate through the introduction of the gene that codes for the modified form of the EPSPS protein. This trait also provides a positive selection for the transformation event. Plant cells that have acquired and express the gene that codes for the mEPSPS protein grow in the presence of glyphosate; unmodified cells do not survive glyphosate treatment. Consequently, no other marker gene is required to identify those cells that have acquired the new trait as a result of genetic transformation.

The transformation event that led to the generation of line GA21 introduced a 3.4 kb *Not*I restriction endonuclease fragment of the 6.1 kb plasmid pDPG434. First there is a promotor region, r-act. This is a 1.37 kb region comprising the 5' region of the rice actin 1 gene, containing the promoter region and the first intron. Next is a 0.37 kb region encoding an optimised transit peptide. This is based on the chloroplast transit peptide of *Helianthus annuus* (the sunflower) and the ribulose 1,5-bisphosphate carboxylase oxygenase (RuBisCO) gene sequence from *Zea mays*. Its function is to direct the mEPSPS to the chloroplast, the site of aromatic amino acid biosynthesis. There then follows a 1.34 kb region that codes for the mEPSPS protein, which, when expressed, confers resistance to glyphosate. The fusion of the mEPSPS with its optimised transit peptide results in the presence of one extra methionine at the N-terminus of the mature mEPSPS protein. The last functional genetic element is a 0.24 kb region of DNA, comprising the 3' untranslated region of the nopaline synthase gene derived from the Ti plasmid of *Agrobacterium*. Its function is to terminate transcription.

The significant regions of the smaller *Not*I restriction endonuclease fragment of plasmid pDPG434 comprise the ColEl origin of replication, necessary for plasmid maintenance, the *lac*Z gene derived from pBluescript, coding for β-galactosidase and the *bla* gene coding for resistance to β-lactam antibiotics, including ampicillin. To establish that these sequences are not present in the genome of GA21 plants, the applicant has exploited Southern transfer and hybridisation studies. Results have established that plants of the GA21 line do not possess these bacterial sequences. In consequence, there is not even a theoretical risk that these plants will transfer an antibiotic resistance determinant to bacteria with which they come into contact.

Southern transfer and hybridisation was used to establish that plants of the line GA21, in addition to the endogenous gene encoding EPSPS, carry a single insertion of the mEPSPS cassette, located on an *Eco* RV restriction endonuclease digestion fragment of approximately 18.5 kb. Glyphosate tolerance is inherited in a Mendelian fashion, indicating that a gene in a single locus encodes this trait. Detailed molecular analysis, including Southern, Northern and Western blotting, PCR technology and analysis of a λ genomic library have been applied to the mEPSPS cassette of line GA21. These results have established that the following genetic elements have been incorporated into line GA21.

1. A mEPSPS cassette beginning with the last 148 bp of the 3' end of the rice actin promotor sequence plus the complete rice actin intron, followed by the optimised transit peptide, a full-length gene encoding mEPSPS and the nopaline synthase transcription terminator sequence;

2. An estimated three copies (see below) of the complete mEPSPS cassette;

3. A partial mEPSPS cassette comprising the complete promoter sequence and its intron, the optimised transit peptide and a truncated mEPSPS gene containing the first 239 nucleotides, terminating in a stop codon;

4. At the 3' end of the whole cassette is a partial rice actin promoter, terminating before the intron sequence. This is fused with maize genomic DNA.

Downstream of the mEPSPS cassette, nucleotide sequence determination has demonstrated the presence of two putative open reading frames; ORF-1 with the potential to encode 97 amino acids and ORF-2 with the potential to code for 19 amino acids. Northern blot analysis indicates that neither open reading frame is transcribed in plants of line GA21.

The applicants have estimated that there are three complete copies of the internal mEPSPS cassette. This is based upon a direct comparison of the relative signal intensities of DNA bands of different sizes in Southern transfer and hybridisation experiments. This is likely to be a slight underestimate, since it ignores the fact that the larger a DNA fragment is, the more DNA it will contain and the stronger will be its signal. The applicants have made no allowance for this. The actual number of complete internal cassettes is thus likely to be greater than that calculated by the applicant but will not be much greater. This is unlikely to have any significance in the assessment of the safety of this construct.

The possibility that the truncated gene encoding mEPSPS is transcribed or translated was investigated using Northern and Western blots. These experiments did not yield signals consistent with the production of truncated mRNA or protein. This cannot preclude absolutely the possibility that the truncated gene is expressed but the possibility that this is the case will be extremely remote.

The maize line GA21 and its progeny have been field tested at more than 70 sites in the USA since 1994 and eight test sites in Europe since 1996. No differences from unmodified maize plants for the following criteria have been observed; seedling emergence, phenotypic characteristics (ear height, plant height, % of root lodged, % of stalks lodged, % of dropped ears, stay green), growth (seedling vigour, plant height), tasselling, pollen and silk GDU (growing degree units) and yield. The only difference observed has been the tolerance to glyphosate in GA21.

3.5 Genetic stability of the GMO used as novel food source

The analysis of segregation data for six generations of line GA21 progeny is consistent with a single site of insertion of the modified EPSPS genes into the genomic DNA of the maize line GA21 and its inheritance according to Mendelian genetics. The stability of the insert through five generations of crossing and one generation of self pollination has been demonstrated and confirmed by Southern blots on GA21 and its progeny over four generations.

3.6 Specificity of expression of novel genetic material

The expression of the mEPSPS is expected to occur throughout the whole plant since the rice actin promoter has been shown to drive constitutive expression of the encoded protein in GM maize[12]. The expression of the protein determined using an antibody sandwich ELISA has been confirmed in forage and grain. Forage samples (whole maize plant minus the roots) from five US field locations in 1996 gave mean values for wild type and mEPSPS of 118.7 μg/g

fresh weight (range 46.6-210.4) and for grain 3.2 μg/g fresh weight (range 1.4-4.9). Wild type EPSPS was not detectable in the grain from non-transgenic negative segregants while in forage was detectable but non quantifiable. Western blot analysis showed that expression of mEPSPS in young leaves of maize line GA21 was at least one order of magnitude greater than wild type EPSPS of non-transgenic segregants.

3.7 Transfer of genetic material from GMO

The probability of horizontal gene flow from plant material to microorganisms is considered to be vanishingly small. Most concern has been centred on the possible transfer of antibiotic-resistance markers from plant material to microbes in the environment (gut, soil, water and sewage) but molecular characterisation of the insert has demonstrated the absence of the *bla* gene (conferring resistance to beta lactams), the ColE1 origin of replication or the partial *lacZ* sequence present in the plasmid vector pDPG434.

3.8 Ability of the genetically modified microorganism to survive in and colonise the human gut

This section is not relevant to plant-derived novel foods.

3.9 Anticipated intake/extent of use of the novel food

The low price and ready availability of maize has led to the development of large volume food use e.g. as starch, sweeteners, oil, etc. The introduced trait in GA21 confers tolerance to the herbicide glyphosate and is of agronomic value. It would not be expected to affect the anticipated intake or extent of use of the maize products.

3.10 Information from previous human exposure to the novel food or its source

Within the EU France is the largest producer of maize followed by Italy. Imports of maize grain originating from within the EU generally exceeds imports from outside including the USA although the import of maize by-products varies by country and year. Glyphosate tolerant maize has been commercialised in the USA for domestic consumption.

3.11 Nutritional information on the novel food

The glyphosate tolerant maize GA21 and its non-transgenic segregants were grown at five sites in the USA in 1996 to provide samples for compositional analysis. The GA21 maize used in this study had not been treated with the herbicide. Each sample was a pooled sample, one from each of the five sites. The compositional compounds measured in grain included proximate analysis (protein, fat, ash, carbohydrate, moisture, acid detergent fibre and neutral detergent fibre), amino acid and fatty acid profiles, calcium and phosphorus. The comparison of this range of parameters is adequate especially in view of the contribution of maize products to human nutrition.

In grain and forage none of the proximates were statistically significantly different from those for the non-transgenic control line. Similarly none of the fatty acids measured in GA21 grains were statistically different from those of the control. There were, however, two amino acids that were statistically significantly different in GA21, serine and tyrosine. However the observed ranges of both overlapped values for the control and were within the range published in the literature.

An additional study was performed on grain and forage samples from maize GA21, non transgenic controls and other commercial maize lines grown at seven sites in the USA and four in Europe in 1997 and assayed for the same parameters. In these field trials the GA21 maize had been treated with glyphosate.

In these studies, statistically significant differences were found in concentrations of calcium, protein, cystine and histidine in grains of GA21 maize compared with the non-transgenic controls as well as in the concentration of valine compared to other commercial maize lines. The levels of protein, histidine and valine were within the ranges published in the literature and the change in calcium content was at the limit of statistical significance. In addition, each of these variations was found in samples from single sites only. Thus, these statistically significant differences need not be considered as biologically relevant.

At the request of the Netherlands Competent Authority, the applicant provided additional analytical data concerning the secondary plant metabolites furfural, raffinose, phytic acid, p-coumaric acid and ferulic acid. Grain samples were analysed from two transgenic hybrid lines (DK and LH) derived from GA21 maize lines, two corresponding non-transgenic hybrid control lines and non-transgenic commercial maize hybrids, grown at three sites in Europe and three sites in the USA in 1998. The concentration of furfural was below the limit of detection of the method applied (<0.5 ppm) in all samples. There were no statistically significant differences in GA21 grain compared with the non-transgenic controls except for a rise in the concentration of p-coumaric acid in one of the hybrid groups (LH). The change was small and the mean concentration was within the range determined for the commercial maize hybrids. Furthermore there were no differences in the content of ferulic acid which is derived from p-coumaric acid.

As a response to other Member States' objections, additional data were provided concerning the contents of minerals (copper, iron, magnesium, manganese, potassium and zinc), phytic acid, trypsin inhibitor and vitamin E in grain samples from the 1998 field trials in GA21 grain compared with the non-transgenic controls. There were no statistically significant differences except for a lower content of manganese in the LH hybrid group. However the range was within the range determined for the commercial hybrids and those published in the literature.

The data provided allow the conclusion that the composition of maize line GA21 and the two transgenic hybrid lines DK and LH derived from GA21 grown at different sites in the USA and in Europe is substantially equivalent to those of non-transgenic controls and commercial maize varieties.

3.12 Microbiological information on the novel food

Since the composition of GA21 and non-transgenic controls is substantially equivalent, apart from the added trait, there is no reason to believe that the glyphosate tolerant maize would cause the presence of microorganisms to be changed.

3.13 Toxicological information on the novel food

The SCP has expressed an opinion on maize line GA21 (opinion adopted on 22 September 2000)[3]. In this opinion, the residues of glyphosate and the main metabolite aminomethylphosphonic acid in the grain of resistant maize plants were evaluated and it was concluded that the levels found do not raise toxicological concerns given the WHO recommended ADI of 0.3 mg/kg body weight for humans[13].

3.13.1 Toxicological information on the maize line GA21

The mEPSPS gene has been sequenced and the expressed protein has a high amino acid sequence homology to the wild type protein. The gene encodes a 47.4 kD protein consisting of a polypeptide of 445 amino acids which does not share biologically significant homology or have immunologically significant sequence similarities to known toxins or allergens, respectively (PIR, SwissProt, EMBL, GenBank databases).

The EPSPS protein, isolated from leaves of GA21 maize, including mEPSPS (70% of activity), is rapidly degraded *in vitro* in artificial human gastric and intestinal fluids according to Western blot analysis (<15 seconds and <1 minute, respectively). No information is available on whether the protein is degraded to its constituent amino acids or to stable protein fragments. However there is no indication that for this type of protein stable fragments may be formed.

Single doses up to 46 mg/kg bw of bacterially produced mEPSPS protein (40% pure, from *E. coli*) were administered to groups of 10 male and 10 female mice by gavage. No toxic effects were seen and no effects on body weight, body weight gain, food consumption and gross pathology were found. No histopathological investigations were performed and no data on repeated administration of the mEPSPS protein is available. This study is not considered adequate for evaluation because of the low dose used and the low purity of the material tested with no information on the composition of the test material.

Diets containing 11% or 33% of glyphosate treated GA21 maize grains or grains from a non-transgenic parental line were fed to groups (n=20) of male and female Sprague Dawley rats for 90 days. The diets which contained 11% test (GA21) or parental line grain were supplemented with 22% non-transgenic commercial hybrid maize to result in a total maize content of 33%. GA21 and control maize was obtained from maize grown during the same season in a province of Buenos Aires, Argentina in 1998-1999. In addition, 6 non-transgenic commercial hybrids from different locations in the USA grown in 1998 were also tested. There was no mortality and no adverse clinical reactions were observed in the study. Body weights, food consumption, and organ weights were comparable across all groups. No biologically relevant treatment related effects were observed in parameters of clinical chemistry, haematology, urinalyses and in gross- and histopathology.

Seven groups of two day old male and female broiler chickens (Ross X Arbor Acres, n=40) were fed diets containing 50-60% maize line GA21, the parental maize line (DeKalb 580 Hawaii) or five commercial lines of maize for 39 (males) or 41 (females) days. No biologically significant differences in growth, feed efficiency and fat pad weights were observed between the treatment groups. No information on other target animals is available.

In response to the objection on the insufficient analytical data on anti-nutritional compounds and natural toxins, the applicant provided data on phytic acid and trypsin inhibitor concentrations, which did not differ in maize grown at seven European and six US locations. It was clarified that the material of maize line GA21 studied has been treated with glyphosate. It is generally accepted that maize does not contain toxins or significant anti-nutritional factors[9].

4. DISCUSSION

The Committee has assessed the safety from the point of view of consumer health of maize grain and derived products from a maize line GA21 that has been genetically modified to express tolerance to the herbicide glyphosate. The conditions of use of the food or food ingredients are those that apply to conventional maize food products.

Technical information has been identified, according to the SCF recommended guidelines which will assist the Commission in implementing article 7.2 of the Council Regulation (EC) No. 258/97 on novel foods as concerns: the conditions of use of the food or food ingredient, the designation of the food or food ingredient, and its specification as well as the specific labelling requirements as referred to in Article 8 of the Regulation (EC) No. 258/97.

The Committee is satisfied that substantial equivalence apart from its tolerance to glyphosate has been established for maize line GA21 with non-transgenic control plants in regard to phenotypic characteristics, growth criteria and yield. The data on chemical composition of maize line GA21 and the two transgenic hybrid lines LH and DK derived from GA21 allow the Committee to conclude that they are substantially equivalent to non-transgenic controls and commercial maize varieties. The applicant was able to provide data on plant components as required by Member States e.g. p-coumaric acid, which confirmed the conclusion.

The genetic modification results from the introduction of an EPSPS gene from maize that has been modified so that its expressed protein differs in only three amino acids from the 445 amino acids of the wild type enzyme. This allows it to function in the presence of the herbicide glyphosate. In the transgenic plant both the wild type and the modified proteins are produced. No marker genes have been introduced and evidence has been presented to demonstrate the absence of an ampicillin-resistance gene which was present on the plasmid from which the transgenic DNA was cut. The questions raised by Member States on the genetic data have all been answered in Section 3.4 e.g. possible transcription from open reading frames. The evidence presented by the applicant is consistent with the insertion of transgenic DNA at a single site and this insertion has been demonstrated to be stable for several generations under different environmental conditions.

The nutritional evaluation shows that the genetic modification has not changed the nutritional profile of GA21 from that of the conventional maize lines.

Toxicological considerations concentrated on the mEPSPS protein as well as on maize grains. There was absence of amino acid homology with known toxins and allergens and it was readily degraded by simulated gastric and intestinal fluids. An acute toxicity study with the purified mEPSPS protein was submitted but was not considered adequate for evaluation. The applicant submitted data on a 90 day feeding trial of GA21 maize in rats and up to 41 days in broiler chickens, the details of which are in Section 3.13. No biologically relevant treatment related effects were observed. The Committee considered these data as sufficient for evaluation.

5. CONCLUSIONS

Having reviewed all the information provided by the petitioner and in the light of current published scientific information it is concluded that from the point of view of consumer health

maize grain from maize line GA21 and derived products that are the subject of this application are as safe as grain and derived products from conventional maize lines.

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