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Opinion on a request for consent to place on the market a tomato fruit genetically modified to down-regulate the production of polygalacturonase (PG), and solely intended for processing.

(expressed on 23/9/99)

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(Expressed on 23 September 1999)

1. TERMS OF REFERENCE

Within the framework of the Regulation on novel foods a request for consent to place on the market a raw tomato fruit genetically modified to down-regulate the amount of polygalacturonase (PG) produced, has been received by the Commission. The petitioner indicates that the food safety assessment is sought on raw tomato fruit intended solely for processing into non-viable processed products. This tomato fruit is from hybrids and all other breeding material derived from the genetically modified processing tomato inbred line. The Committee is asked to assess the safety from the consumer health point of view of the genetically modified tomato. The Commission also seeks the assistance of the Committee to identify technical information that will assist it to implement Article 7.2 of the Council Regulation (EC) N^{o} 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;
- the specific labelling requirements as referred to in Article 8 of Regulation (EC) N^{o} 258/97.

2. BACKGROUND

The Commission has received a petition to place on the market a tomato fruit that is genetically modified to down-regulate production of polygalacturonase (PG). The tomato fruit is intended solely for processing into non-viable processed products. The genetic modification results in down-regulation of expression of the gene encoding polygalacturonase (PG). This is an enzyme involved in the cleavage of pectin chains in the cell wall of tomato fruits during ripening of the fruit. The result of PG down-regulation is that tomatoes soften less quickly, thus extending the harvest window and conferring better processing properties on the modified fruit. The genetic modification was achieved using *Agrobacterium tumefaciens*-mediated transformation to insert a truncated partial sense PG gene from the tomato variety 'Ailsa Craig'. Additionally, the *npt* II gene was also introduced into the tomato plant. This gene is derived from *Escherichia coli* and is a selectable marker of transformation, conferring resistance to the antibiotic kanamycin.

The petitioner first submitted an application to the UK Advisory Committee on Novel Foods and Processes (ACNFP). This application was made under the Novel Foods and Novel Food Ingredients Regulation N^{o} 258/97. This followed a successful submission, made under the UK's voluntary system, which operated before the introduction of Regulation N^{o} 258/97. Food safety clearance for this product has been obtained from

the Food and Drug Administration in the United States of America, Health Canada and the Mexican Health Authorities.

Following approval by the UK ACNFP, some member states raised concerns about particular aspects of this application. Most Member States have agreed with the safety assessment made by the UK ACNFP. They are content to allow the marketing of tomato products made from these GM plants.

One Member State has suggested that the application should be examined first under Directive N° 90/220 on the Deliberate Release into the Environment. Then, having obtained clearance through that route, the application should be subsequently subject to evaluation under the Novel Foods and Novel Food Ingredients Regulation N° 258/97.

The Scientific Committee on Plants (SCP) has delivered an opinion of this product under directive 90/220/EEC. This was published on 23 June 1998 and is available on-line[1]. The SCP examined the data and information supplied by the petitioner against the background of available knowledge in the areas concerned. The SCP is of the opinion that there is no evidence to indicate that the production of the petitioner's processing tomatoes, with down-regulated polygalacturonase, and the products derived from the tomatoes, are likely to cause adverse effects on human or animal health or the environment.

Another Member State has raised an objection to this submission because the GM tomato plant carries a marker gene that confers resistance to aminoglycosides including kanamycin and neomycin. This objection was on the grounds that this gene could be capable of entering the food chain and there are, as yet, no binding EU proposals on the handling of antibiotic resistance genes in GMOs.

Other concerns pointed out by some Member States were:

- whether the assessment will cover only the processed products or whether it must also cover other uses, including the raw tomato fruit;
- on the possibility of the transfer of the *npt* II gene from the GM plant to bacteria via natural transformation products;
- the potential that the genetic modification could lead to toxic levels of α-tomatine and other glycoalcaloids;
- whether or not the genetic modification results in the production of new proteins or the modification of existing proteins;
- on the potential for allergic reactions, with two issues to be considered in particular: the gastric stability of allergens and the heat processing inactivation of both the DNA and protein expressed in the tomato fruit.

3. EVALUATION

The application presented by the petitioner follows the SCF guidelines expressed on 29 July 1997 and published as Commission Recommendation 97/618/EC[2]. These concern the scientific aspects and the presentation of information necessary to support applications for placing of novel foods and novel food ingredients on the market. The GM tomatoes that are the subject of this application fall 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[2]. In addition to the information submitted by the petitioner[3], the comments of the Member States on the initial assessment report made by the UK ACNFP as summarised above have also been taken into account. The opinion under directive 90/220/EEC expressed by the Scientific Committee on Plants (SCP) published on 23 June 1998 has also been considered[1].

3.I. SPECIFICATION OF THE NF

The specification of the tomato paste produced from modified hybrids will be as specified in the Codex Standard for Processed Tomato Concentrates[4]. The petitioner indicates that there are no specifications for the composition of other peeled and comminuted tomato products (ketchup, pizza sauces, etc.). The petitioner further states that products will be produced in accordance with the existing food hygiene legislation.

Description of the NF

The host plant is TGT7, a commercial variety of tomato (*Lycopersicon esculentum* Mill.) bred for processing. The derivative transgenic, inbred line (a plant line produced by self-pollination over several generations, which is almost genetically uniform) chosen for further development was denominated TGT7F. Tomatoes are members of the family Solanaceae.

The subjects of this application are genetically modified processing tomato hybrids (offspring of a cross between two genetically dissimilar plants of the same species) derived from the genetically modified inbred parental line TGT7F by conventional breeding methods. The petitioner has described different TGT7F-related hybrids. These include, for example, lines that have been denominated 7913F, 11013F and 1401F.

The most relevant parameters to characterise the product include the inserted DNA sequences. The application contains an extensive description of the inserted DNA, together with further appropriate references[3]. In brief, the construct was transformed using *Agrobacterium tumefaciens*-mediated DNA transfer, exploiting the expression vector pJR16S. Plasmid pJR16S contains a truncated copy of the gene that encodes polygalacturonase (PG), isolated from the 'Ailsa Craig' variety of tomato, along with a neomycin phosphotransferase gene (*npt* II), originally located on the bacterial transposon Tn*5* and producing the enzyme aminoglycoside-3'-phosphotransferase II (APH(3')II). The truncated gene encoding PG is in the 'sense' orientation and its expression is controlled by the Cauliflower Mosaic Virus 35S (CaMV 35S) promoter and the nopaline synthase (*nos*) terminator sequences. Expression of the *npt* II gene in plant cells is under the control of the *nos* promoter and terminator sequences. The transformation event that is the subject of this application leads to the down-regulation of the endogenous PG enzyme at the onset of fruit ripening. The reduction of PG expression leads to fruit with the potential to extend the harvest window and with modified processing properties.

Proposed uses

The application under 90/220 addresses this. This application addresses the processing and products derived from the genetically modified inbred parental line TGT7F tomatoes within the Community (258/97) and their eventual use in food. Tomato processing wastes (seed and skins, known as pomace) are sometimes fed to cattle as a proportion of their diet. These wastes, used as animal feeds, are not considered here but have been evaluated by the SCP[1]. Tomatoes that are derived from the parental line TGT7F are thus to be used in the same manner as any other processing tomato.

Labelling

The proposed labelling is: 'produced from genetically modified tomatoes' or 'made from genetically modified tomatoes'. The products will be labelled in accordance with Article 8 of the Regulation N^{o} 258/97 and to any other applicable provision under EU law.

3. II. EFFECT OF THE PRODUCTION PROCESS APPLIED TO THE NF.

Tomatoes for processing generally can be divided into two distinct categories: those intended for products where discrete pieces of tomato are apparent after processing, such as whole canned tomatoes, diced tomatoes, etc., and those without discrete pieces remaining after processing. The latter are also called comminuted products and examples include sauces, juice, puree, etc.

For comminuted products, tomatoes are selected from a harvested crop and are washed. Damaged and discoloured fruits are removed before further processing. The fruits are then chopped and passed through a 'breaking' process where the chopped materials are heated. After 'breaking' the juice can be removed for juice products and the remaining tomato material is further extracted to remove seeds, skin and core. The resulting pulp is then refined in appearance through a second screening and sieving process. To formulate individual products, the pulped and finished material is concentrated by heating in an evaporator at temperatures greater than 93^{o}C for over 20 minutes. The resulting concentrates form the basis for sauces, purees and pastes. Packaging into the end-user package (jar, bottle, can, etc.) then takes place, followed by final heat processing to ensure sterilisation of the product.

Peeled tomato products require the removal of skin. There are three main commercial types of skin removal involving the use of steam blanching, caustic soda or infra-red radiation. Caustic soda peeling is prohibited in Europe. Surface temperatures of 98^{o}C-100^{o}C for between 30 and 60 seconds are used for both steam blanching and caustic soda peeling, whereas infra-red peeling involves surface temperatures greater than 700^{o}C for between 4 and 20 seconds. The peeled or diced tomatoes in tomato juice are packaged and heated to ensure sterilisation of the product. Peeled tomatoes are sold as whole peeled fruit, or as diced or chopped tomatoes and as juices or puree.

The potential of processing to introduce changes in the GM tomato are the same as can be expected for conventional tomatoes. With respect to the new traits of the GM tomato, the resulting effects of the process are:

a) loss of function of the new protein aminoglycoside-3'-phosphotransferase II (APH(3')II) resulting from expression of the introduced *npt* II gene;

b) the degradation of functional DNA corresponding to the two new genes (the truncated PG gene and *npt* II); and

c) the loss of seed germination capacity.

3. III. HISTORY OF THE ORGANISM USED AS THE SOURCE OF THE NF.

The wild *Lycopersicon* species are native to the Andean region from Colombia to Northern Chile, *i.e.* the cultivated tomato, *Lycopersicon esculentum*, is tropical in origin. The wild cherry tomato, *L. esculentum* var. *cerasiforme*, from which the cultivated tomato is thought to have been derived, is known to grow wild as a weed in areas of high rainfall. The natural habitat of the processing tomato is a managed agricultural system. The processing tomato is cultivated outdoors throughout the Southern European Member States, where it has been cultivated for over two centuries. In northern Europe, tomatoes are grown commercially under protection. In the majority of European Member States, home gardeners cultivate tomatoes during the summer months. The largest producers of tomatoes in the EU are Italy, Greece and Spain.

The predominant method of generating processing tomato varieties is by the production of single cross hybrids, allowing the combination of traits from defined inbred parents.

3. IV. EFFECT OF THE GENETIC MODIFICATION ON THE PROPERTIES OF THE HOST ORGANISM.

When focusing on the effects of the genetic modification on the properties of the GMO compared with the unmodified host organism, the intended and the unintended effects can be considered.

Intended effects: Information relating to the inserted DNA.

The DNA insert contains two functional genes: a truncated PG gene inserted in the 'sense' orientation and the *npt* II gene. Other gene fragments have also been inserted into the GM tomatoes. Both the truncated PG gene and the *npt* II selectable marker gene are under the control of constitutive promoters and are, therefore, expressed in all plant tissues.

The inserted DNA present in derivatives of TGT7F has been well characterised. As expected, in addition to the *npt* II gene, the truncated PG gene and their respective regulators, there are other gene fragments present. These comprise part of the origin of replication of bacteriophage M13 and part of gene III from this bacteriophage, two fragments of the *lac* Z gene from *Escherichia coli* and part of the *ocd* gene from *Agrobacterium tumefaciens*. None of these DNA fragments is functional in the tomato

plant. Details of all the inserted DNA fragments have been previously considered by the SCP[1].

The evidence presented by the petitioner is consistent with the insertion of a single DNA cassette at a unique location in the nucleus. The inserted DNA is stable, and is inherited in a Mendelian fashion, in agreement with a single chromosomal location for the inserted DNA. Molecular analysis demonstrates that only DNA lying within the left and right borders of the *Agrobacterium tumefaciens* vector have been incorporated into the transformant. No other plasmid-associated DNA sequences have been detected in transformed tomato plants. Attempts to demonstrate the presence of DNA beyond the left and right border sequences were made using PCR, with primer sets designed to amplify genes associated with plasmid pJR16S.

From an analysis of the open reading frames of the inserted DNA it was concluded that none of the open reading frames except those of the PG and *npt* II genes were associated with potential transcription and translation control sequences. Thus, there is no known way that these accompanying sequences could be transcribed or expressed as proteins that could lead to allergen or toxin production.

The PG gene and its mechanism of action

PG is a key enzyme involved in fruit ripening and is responsible for the breakdown of pectin molecules in the plant cell wall. This results in softening of the ripening fruit. At least three related isozymes (PG1, PG2a and PG2b) are contained in the tomato fruit, the related polypeptides having a molecular weight between 42 and 46 kDa[5]. The introduced PG gene is the first 731bp of a cDNA clone derived from the DNA of the tomato 'Ailsa Craig'[6].

The exact mechanism by which the truncated gene modifies expression is currently under investigation. It is likely, however, that the transcription of the truncated PG gene is necessary to achieve reduction of the mRNA level of the native gene. The accumulation of transcripts in the endogenous gene and the partial gene is reduced in red ripe fruit, presumably due to mutual inhibition[7]. There is little published material to explain gene silencing in transgenic plants but truncated copies of genes in the sense orientation can cause post-transcriptional silencing as effectively as genes in the anti-sense orientation. It is thought that gene silencing acts through modification of messenger RNA[8].

The *npt* II gene

The *npt* II gene allows the selection of modified cells following successful transformation. It is widely used and has been well characterised[9]. The *npt* II gene encodes aminoglycoside-3'-phosphotransferase II (APH(3')II), an aminoglycoside modifying enzyme that inactivates antibiotics including kanamycin and neomycin. This enables the identification of transformed plants on a medium containing small amounts of kanamycin.

Expression of the bacterial *npt* II gene in the plant cells is under the control of the *nos* promoter and terminator sequences. The aminoglycoside-modifying enzyme APH(3')II is the only new protein to be made by the transgenic tomato plants.

Unintended effects of the genetic modification

To evaluate potential unintended effects attention has been paid to potential nutritional, toxicological and microbiological impacts of the novel food, as well as the agronomic aspects, as described later in Sections 3.XI, 3.XII and 3.XIII.

The petitioner has applied the usual techniques in searching for potential unexpected events. A good rationale has been applied for selecting the toxins to be tested and for DNA and compositional analysis.

Additional information on the Line PZ004: a different transformation event.

Information on tomato paste and products manufactured from paste derived from the inbred line PZ004 (alternatively known as UC82B), which represents a different transformation event not related to TGT7F, have also been presented by the petitioner. Two inbred PZ004 lines (E108C29.8 and E109C1.10) were first identified with reduced levels of PG but the original line nomenclature was changed and the distinction between the two lines was abandoned. Therefore, the modified inbred line PZ004 represents a mixture of the two lines identified above. No additional novel proteins have been introduced other than those expressed in TGT7F and the transformation was performed with the same construct, pJR16S. Data on genetic stability, agronomic, toxicological and nutritional data from fresh fruit have been presented and no significant differences have been reported compared with to the unmodified lines used as controls.

3.V. GENETIC STABILITY OF THE GM TOMATO

The petitioner provided information to show the structure of the insert and local maintenance of the introduced genetic material. They also described gene expression in the GM tomato hybrids.

As already pointed out in Section 3.IV, the evidence presented by the petitioner is consistent with the insertion of a single DNA cassette at a unique location in the nucleus. The inserted DNA has been demonstrated to be stable for several generations under different environmental conditions. It is inherited in a Mendelian fashion, in agreement with a unique chromosomal location for the inserted DNA.

To evaluate the agronomic characteristics of the GM inbred and hybrid lines, the petitioners used a number of field trials. These included those in American countries between 1992-1994 and more recently (1996-1997) in European countries (Italy, Spain, France and Greece). No genetic instability has been observed either in the phenotypic effects or in the expression of PG. Other than the intended effects leading to the improved processing characteristics of the GM tomato, as discussed above, no differences were found between GM and unmodified controls, except for a reduced rate of opportunistic fungal infection in the GM line.

All the results presented by the petitioner showed the consistent down-regulation, by about one order of magnitude or higher, of PG enzyme activity. This demonstrates the stability of the introduced, truncated PG gene.

3.VI. SPECIFICITY OF THE EXPRESSION OF THE NOVEL GENETIC MATERIAL.

The expression of the introduced PG gene is under the control of a constitutive promoter and thus the truncated gene is potentially expressed throughout the plant and at all growth stages. Endogenous PG synthesis is, however, '*de novo*' at ripening and thus down-regulation of PG is only seen in the ripening fruit. The expression levels of the *npt* II gene are sufficient to confer resistance to the antibiotic kanamycin in culture. The gene is expressed constitutively throughout the plant.

3.VII. CONSIDERATIONS OF GENE TRANSFER FROM PROCESSED GM TOMATOES.

Although unprocessed GM tomatoes will contain introduced DNA, no functional DNA encoding the aminoglycoside-3'-phosphotransferase II can be detected in the products following food processing of the GM tomatoes. These tomatoes are intended solely for processing. Thus, there is little likelihood of transferring functional DNA from the processed GM tomatoes to other organisms, prokaryotic or eukaryotic. Since some comminuted products may contain seeds, the petitioner investigated the viability of seeds following processing of GM tomatoes. No viable seeds were found following processing of the GM tomatoes.

3. VIII. ABILITY OF THE GMM TO SURVIVE IN AND COLONISE THE HUMAN GUT.

The subject of this application is not a genetically modified microorganism.

3.IX. ANTICIPATED INTAKE/EXTENT OF USE OF THE NF

The cultivated tomato is one of the most popular food crops today. Over 76 million tons of tomatoes are produced each year world-wide. The largest production is in the USA (16%) while within Europe the largest production is in Italy (7% of the world-wide production). There are two somewhat distinct tomato industries or sectors; one based on fresh fruit, as used for salads, etc.: the other is based around processing tomatoes. The tomato is consumed in many different forms; eaten raw, cooked in a variety of ways, or in one of many processed food products such as soups, preserves, ketchup, paste, pickles, sauces and ready cooked meals. Processing tomatoes are claimed to be unpalatable when eaten raw.

The petitioner cites an average consumption of processed tomato products within the EU has been estimated at 14 kg per person per year[11]. It is not envisaged that the introduction of tomato products made from GM tomatoes will lead to an overall increase in tomato consumption, neither can any new uses or markets be anticipated. GM tomato products are expected to replace those from conventional tomatoes.

3.X. INFORMATION FROM PREVIOUS HUMAN EXPOSURE TO THE NF OR ITS SOURCE.

Canned tomato paste, clearly labelled as being derived from GM plants and produced from hybrids derived from the inbred line TGT7F, has been on sale in the UK since

February 1996. Sales of about 800000 cans per year have been achieved. So far, no problems related to toxicity or allergenicity have been reported.

3. XI. NUTRITIONAL EVALUATION

Processed tomato products are rarely consumed on their own. It is not anticipated that the introduction into the market of processed tomato products made from GM tomatoes will lead to an overall increase in consumption. Products from processing tomatoes are often consumed as an accompaniment to other food ingredients (*e.g.* pizza sauce, ketchup, etc.) in a proportion that is usually less than 25% of the total ingredients. Processed tomato products do, however, supply some important nutritional components to the diet, namely vitamins.

The fresh fruit was analysed for key nutritional components to demonstrate that, apart from the intended specific effects of the introduced genes, there is no significant difference between the modified tomato hybrids (e.g. 11013F, 7913F) and their corresponding unmodified controls. The following components were analysed: moisture, ash, fat, total carbohydrate, available carbohydrate, dietary fibre, total sugars, protein, energy value, vitamins A (as β-carotene), B_1, B_2, B_6, C and E, nicotinic acid, pantothenic acid, folic acid, biotin, malic and citric acids, and lycopene. The results show that nutritional values of the modified fresh tomatoes fall within the range of unmodified control fruit, indicating that the genetic modification has not altered the nutritional profile of the fresh tomato.

The nutritional assessment of peeled tomato products (from hybrids 11013F, 7913F) was also considered. This was achieved by comparing products with unmodified controls that were grown under the same agronomic conditions on the same site and that were harvested and processed in the same way. Furthermore, two commercially available products were analysed for comparison. Diced or chopped tomato, together with tomato juice, were analysed for the following components: moisture, ash, fat, total carbohydrate, available carbohydrate, dietary fibre (soluble and insoluble), cellulose, hemicellulose, pectins, total sugars, protein, energy, vitamins A (as β-carotene, B_1, B_2, B_6, C and E, nicotinic acid, pantothenic acid, folic acid, biotin, malic and citric acids, and lycopene. Results showed that the genetic modification has not changed the nutritional profile of the peeled tomato product.

In conclusion, the nutritional assessment showed that the genetic modification has not changed the nutritional profile of peeled tomato products.

3. XII. MICROBIOLOGICAL INFORMATION

Data has been presented to show that the genetic modification has not led to changes in the agronomic performance of the tomato lines. It is not likely that the genetic modification and its effects will change the composition of the epiphytic flora compared with that of conventional tomato plants. The delay in softening of fruit during ripening resulting from the genetic modification event offers fewer opportunities for opportunistic infection of the fruit.

3. XIII. TOXICOLOGICAL INFORMATION

The establishment of substantial equivalence is one of the key issues for the scientific assessment of degree of safety of GM food, although not being a safety assessment in

itself. No toxicological studies have been performed by the applicant. The present application does, however, correspond to a GM food for which substantial equivalence to its conventional counterpart can be demonstrated with regard to the genetic, agronomic, nutritional and compositional characteristics of the GMO, with the differences being those triggered by the insertion of specific DNA. This matter has been addressed in section 3.II.

Traditionally, plant breeders have selected new varieties of food plants by comparison with existing commercial lines, mainly based on yield, disease resistance, taste or external appearance. Frequently, the nutritional characteristics or the levels of specific toxicants have been omitted in the assessment of the products of traditional breeding. The safety of new varieties has usually been presumed from the known safe food use of the parental lines.

The scope of the evaluation will depend on the nature of perceived concerns. In the present case, it is reasonable to address the potential for accumulating naturally occurring toxicants and toxic metals and the potential to elicit allergenic responses.

Naturally occurring toxins and toxic metals

The tomato, in common with other members of the family Solanaceae, is known to have the potential to accumulate naturally occurring toxins known as glycoalkaloids. Tests for toxins were conducted using conventional fresh fruit, commercially available paste samples and non-GM paste as controls.

The principal toxin of tomatoes is α-tomatine and it has been analysed in the hybrids 11013F and 7913F. The results show that the levels were below the level of detection of 15 mg/kg in both the modified and control fresh fruit samples. The two other naturally occurring glycoalkaloids in the tomato, solanine and chaconine, were analysed in the inbred lines and both were found to be below the level of detection of 5 mg/kg. Similarly, other naturally occurring compounds (tyramine, tryptamine, serotonin, histamine, nicotine and lectins) were found to occur at sufficiently low levels in the inbred and the hybrids H282F and 1401F to be regarded as safe. The levels of these compounds were often below the limit of detection of the tests used. The levels of α-tomatine, chaconine, solanine and nicotine were all below the level of detection in the peeled products in both the modified and control lines 1401F and 11013F. The paste produced from the TGT7F inbred line had detectable levels of α-tomatine (58 mg/kg) although this was below that of the non-GM TGT7 control (74 mg/kg).

The analysis of toxic metals, namely mercury, cadmium, arsenic and lead, has been carried out on the inbred and hybrids H282F and 1401F. These studies show that the levels of these elements were well within the range of values obtained from unmodified and commercial control fresh fruits and paste.

There is no evidence to suggest that a different trend would be expected for the levels of any of the toxicants in varieties other than those that have been already tested by the petitioner. The method used was not able to determine the levels of α-tomatine in either the modified or the unmodified fruits (except for tomato paste). This issue could have been tentatively addressed by using a more powerful methodology (lowering the detection threshold of 15 mg/kg) and/or by measuring toxin levels, not only in ripe tomatoes but also in unripe fruits, where toxicants occur at higher levels. Measuring levels of α-tomatine in unripe fruit would, however, have no relevance for the assessment of levels found in food products.

From the available data it is reasonable to conclude that neither the growing environment nor the genetic modification had affected significantly either the levels of or other naturally occurring toxins. The levels of toxic metals tested in the fresh fruit samples have been found not to differ from those seen in the modified fruit.

Allergenicity

No allergenic consequences are expected from the reduction of the PG levels resulting from the genetic modification.

The APH(3')II protein has not been detected in the processed products. It has been reported that this protein is rapidly degraded in simulated gastric fluid and therefore there is little potential for it to reach the intestinal mucosa and elicit an allergenic response[10].

The native APH(3')II can be found associated with the microbial bowel flora of people colonised with resistant bacteria. This has not led to recognised problems. The protein lacks homology at the amino acid level with known allergens.

4. CONCLUSIONS

The Committee has assessed the safety of tomato fruit, genetically modified to down-regulate the production of polygalacturonase, from the point of view of consumer health. These tomatoes are intended solely for processing into non-viable processed products. The assessment has been made within the framework of the regulation on novel foods, for tomato hybrids and all other breeding material derived from the genetically modified processing tomato of the inbred line TGT7F.

Technical information has been identified, according to the SCF recommended guidelines, which will assist the Commission to implement article 7.2 of the Council Regulation (EC) N^{o} 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 Regulation (EC) N^{o} 258/97.

The present assessment does not cover raw tomato fruit as a novel food or food ingredient. The only tomato products that can obtain clearance from this assessment are those from the hybrids derived from the TGT7F inbred line that have been processed, and that are subject to a heat treatment. This heat treatment causes biological inactivation of the APH(3')II protein and of the *npt* II and truncated PG genes. The products will be labelled in accordance to article 8 of the Regulation 258/97 and to any other applicable provision in EU law. This would facilitate any epidemiological studies which might be undertaken in the future.

The conditions of use of the food or food ingredients are those that apply to the conventional unmodified processing tomato products. The specification of the tomato paste produced from modified hybrids will be as specified in the Codex Standard 57-1981 for processed tomato concentrates[4]. The other peeled and comminuted tomato products (ketchup, pizza sauces, etc.) will be produced in accordance with the existing food hygiene legislation.

It can be concluded that the Substantial Equivalence to the unmodified and conventional counterparts has been established for the GM tomato raw fruit except for the specified traits, as well as for processed products. The detected differences between modified and unmodified tomatoes are only those triggered by genetic modification, which produced the down-regulation of the PG gene. This leads to a modified phenotype of the fruit tomato with improved processing characteristics.

The genetic modification results in the presence of one foreign protein, encoded by the *npt* II gene. No other protein changes are expected from the reported data. However, the question whether genetic modification results in modifications of the existing proteins cannot be totally answered. This question would apply equally to other GM foods as well as to new strains developed by traditional crosses not involving GM technology.

The evidence presented by the petitioner is consistent with the insertion of a single DNA cassette at a unique location in the nucleus. The inserted DNA has been demonstrated to be stable for several generations under different environmental conditions. It is inherited in a Mendelian fashion, in agreement with a unique chromosomal location for the inserted DNA.

The genetic modification has been well characterised, showing only the expected two new functional genes: the truncated PG gene and the *npt* II gene. Processing ensures the degradation of the introduced DNA and denaturation of the protein encoded thereon. The possibility of the transfer of the *npt* II gene from the GM plant to bacteria via natural transformation processes is considered to be remote. The potential for occurrence of allergic reactions resulting from the consumption of this product appears not to differ from the unmodified conventional counterpart.

The nutritional evaluation showed that the genetic modification has not changed the nutritional profile of the conventional tomato counterparts; neither have the levels of natural toxicants nor toxic metals been altered as a consequence of the genetic modification event.

Having reviewed all the information provided by the petitioner, and in the light of current published scientific information, it can be concluded that, from the consumer health point of view, processed foods derived from GM tomatoes that are the subject of this application are as safe as products from conventional fruit.

6. REFERENCES

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   http://europa.eu.int/comm/dg24/health/sc/scp/out19_en.html
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