Tentative Translation

Safety Assessment of Genetically Modified Food

Maize line MON88017 tolerant to the herbicide glyphosate and resistant to coleopteran pests

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Food Safety Commission

Contents

〈Process of Deliberations〉

December 6, 2004	Food safety assessment of genetically modified Maize Line MON88017 was requested by the Minister of Health, Labour and Welfare (MHLW)
December 9, 2004	The 73rd Commissioners Meeting (explanation of the request from MHLW)
January 24, 2005	The 21st Meeting of the Genetically Modified Foods Expert Committee (GMF-EC)
April 25, 2005	The 26th Meeting of GMF-EC
June 17, 2005	The 28th Meeting of GMF-EC
August 1, 2005	The 30th Meeting of GMF-EC
August 18, 2005	The 107th Commissioners Meeting (draft report on the safety assessment)
August 18 to September 14, 2005	Collection of public comments
September 30, 2005	Final report to Head Commissioner from GMF-EC
October 6, 2005	The 114th Commissioners Meeting (final decision) Notification of the opinion on the safety assessment to MHLW

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Report on Safety Assessment of Maize Line MON88017 Tolerant to the Herbicide Glyphosate and Resistant to Coleopteran Pests as Food

Ⅰ Introduction

The Food Safety Commission received a request from the Ministry of Health, Labour and Welfare in accordance with the Food Safety Basic Law to provide its opinion on safety assessment of foods derived from maize line MON88017 tolerant to the herbicide glyphosate and resistant to coleopteran pests. (Relevant documents were received on December 6, 2004.)

Ⅱ Outline of the food to be assessed

Name	:	Maize line MON88017 tolerant to the herbicide glyphosate and resistant to coleopteran pests
Properties	:	Glyphosate-tolerance and coleopteran pest-resistance
Applicant	:	Monsanto Japan Limited.
Developer	:	Monsanto Company (USA)

Genetically modified maize line MON88017 tolerant to the herbicide glyphosate and resistant to coleopteran pests (hereinafter MON88017) was produced by introducing a modified *cp4 epsps* (*aroA*) gene derived from *Agrobacterium* sp. CP4 strain and a modified *cry3Bb1* gene derived from the gram-positive bacterium *Bacillus thuringiensis* ssp. *kumamotoensis*.

The host of this line, dent maize is mainly used as feed, but also used as materials for corn oil, starch and other foods.

Ⅲ Safety assessment of the genetically modified food

Section 1 Properties of the host used as a counterpart for comparison (or other comparator) in safety assessment and its differences from the recombinant plant

1 Host and introduced DNA

(1) Species and origin of the host

The host used is dent maize (*Zea mays*), which belongs to Poaceae.

(2) Species and origin of the donor

The modified *cp4 epsps* and modified *cry3Bb1* genes were originated from the *epsps* gene isolated from *Agrobacterium* sp. CP4 strain and the *cry3Bb1* gene isolated from *B. thuringiensis* ssp. *kumamotoensis*, respectively.

(3) Properties of the introduced DNA and methods for DNA transfer

The modified *cp4 epsps* and modified *cry3Bb1* genes introduced into the genome of maize express the proteins that confer herbicide glyphosate tolerance and insecticidal activity against Coleoptera (corn

rootworms). The genes were introduced into the genome of a hybrid dent maize by the *Agrobacterium*-mediated gene transfer method using a plasmid PV-ZMIR39 containing the modified *epsps* and modified *cry3Bb1* genes.

2 History of utilization of the host as food

The host, maize, is one of the major cereal crops along with wheat and rice. The grain of maize, e.g., corn, has been consumed as food since B.C., so that maize has been cultivated as one of the major crop plants in the world (Reference 1). The world production of corn in 2000 was about 590 million tons (Reference 2).

3 Components of the food derived from the host

(1) Outline of the types and amounts of major nutrients (proteins, lipids, etc.) contained in the edible parts of the host

It has been reported that major nutrients in the kernels of dent maize consist of protein (6-16.1%), fat (2.48-5.7%), fiber (10.99-11.41%), ash (0.89-6.28%), and carbohydrate (77.4-88.1%) (literature values).

(2) Outline of the types and amounts of toxic constituents and anti-nutrients

There have been no reports that dent maize produces toxic constituents and anti-nutrients that cause adverse effects on human health (Reference 3).

4 Usages of the host and recombinant plants as food and their differences

(1) Harvesting time and storage method

The harvesting time and storage methods for MON88017 are the same as those for conventional maize strains.

(2) Consumable (edible) parts

The edible parts of MON88017 are the same as those of conventional maize strains.

(3) Consumption volume

The consumption of MON88017 is estimated to be comparable to that of conventional maize.

(4) Cooking and processing methods

The cooking and processing methods for corns of MON88017 are the same as those of conventional maize strains.

5 Reasons for using any plant/product in addition to the host as a comparator and its properties as food

No other plant/product than the host is used as a comparator.

6 Differences that need to be assessed for safety

In MON88017, modified CP4 EPSPS and modified Cry3Bb1 proteins are produced by the inserted DNA cassettes containing the modified *cp4 epsps* and modified *cry3Bb1* genes. These are the only differences from the host.

Based on the items 1 to 6 stated above, it has been concluded that existing maize can be used as a comparator to assess the safety of the MON88017 line .

Section 2 Purposes and usages of the recombinant plant

The modified *cp4 epsps* gene inserted into the genome of MON88017 encodes modified CP4 EPSPS protein that inactivates the herbicide glyphosate, preventing the plants from withering or dying (herbicidal activity). This allows the genetically modified plants to continue growing irrespective of glyphosate applications during their cultivation, while ordinary intolerant weeds do not survive.

The modified *cry3Bb1* gene in MON88017 encodes the modified Cry3Bb1 protein and endows the recombinants with resistance to corn rootworms (Coleoptera, *Diabrotica* sp.), protecting them from the pest insects.

Section 3 Host

1 Taxonomic status (species, variety and strain)

The maize (*Zea mays*) used as the host plant was a hybrid of dent maize.

2 Genetic ancestry and breeding history

Maize is considered to have been originated from Mexico or Guatemala though there is no decisive evidence. The most convincing hypothesis is that it was derived from teosinte (*Zea mexicana*) in the process of breeding. (References 4, 5 and 6)

3 Production of harmful physiological substances

There have been no reports on the productivity of harmful physiological substances in maize. (Reference 3)

4 Allergenicity

Maize is not regarded as a major allergy-inducing food (Reference 7) with a few reports of allergy cases. In the rare cases reported as anaphylaxis (References 8 and 9), no allergen has been identified.

Recently, Pasterollo et al. have reported that lipid transfer protein (LTP) serves as a major allergen of maize (References 10 and 11). The sensitization to this allergen is mainly observed in Southern Europe. It has been suggested that patients sensitized to maize LTP might elicit allergic reactions to LTP of other vegetables.

5 Foreign pathogenic factors (e.g. viruses)

While many diseases in maize have been known simlar to those in many other plants, they are not reported to be infectious to human and other animals.

6 Safe consumption

Maize is one of the major cereal crops in the world along with rice and wheat and has been consumed since ancient times. In 2003, Japan imported about 3,590,000 tons of maize grains for starch production

and 830,000 tons for other food ingredients. (Reference 12)

As for feeds, about 11,860,000 tons were used as an ingredient for mixed feeds in 2003. The imported amount in 2003 was about 12,390,000 tons, about 93% of which was imported from the USA. (References 12 and 13)

7 Close relatives of the host

The *Tripsacum* genus and teosinte of the *Zea* genus are close relatives to maize, but teosinte is the only species that can be naturally cross-fertilized with maize. Natural cross-fertilization with *Tripsacum* genus plants has not been known (Reference 7). In Japan, wild species of the *Tripsacum* genus and teosinte have not been reported (References 14 and 15).

Section 4 Vector

1 Name and origin

The plasmid PV-ZMIR39 used to produce the MON88017 line was constructed from the intermediate plasmids A to D.

All these plasmids were constructed from plasmids derived from *Rhizobium radiobacter* (*Agrobacterium tumefaciens*) or nonpathogenic *Escherichia coli*.

2 Properties

The recognition sites of restriction endonucleases in the intermediate plasmids A to D have been identified. The functions of all the components of these plasmids used for construction of the plasmid PV-ZMIR39 have also been clarified .

Section 5 Inserted DNA, gene products, and expression vector construction

1 Donor of the inserted DNA

(1) Name, origin and taxonomy

Of the genes inserted into MON88017, the modified *cp4 epsps* gene is derived from *Agrobacterium* sp. CP4 strain, and the modified *cry3Bb1* gene is derived from *B. thuringiensis* ssp. *kumamotoensis*.

(2) Safety

Agrobacterium sp. from which the modified *cp4 epsps* gene was derived is a gram-negative bacterium existing in soil and rhizospheres of plants. No pathogenic and other problems associated with *Rhizobium* (*Agrobacterium*) in humans and livestock have been reported.

B. thuringiensis ssp. *kumamotoensis* from which the modified *cry3Bb1* gene was derived is a gram-positive bacterium commonly found in soil. No pathogenic and other problems associated with *B. thuringiensis* ssp. *kumamotoensis* in humans and livestock have been reported.

2 Properties of the inserted DNA or genes (including the drug resistance gene) and their gene products

The *cp4 epsps* (*aroA*) gene cloned from *Agrobacterium* sp. CP4 strain was modified to enhance the expression of the gene product in plants. The *cry3Bb1* gene cloned from *B. thuringiensis* ssp. *kumamotoensis* was modified to enhance the insecticidal activity of the gene product. The genetic components of the inserted DNA are shown in the table below. Their recognition sites of restriction endonucleases and functions have been identified.

3 Regulatory regions involved in the expression of the inserted genes (including the drug-resistance gene)

(1) Promoter

In the two gene expression cassettes of the plasmid PV-ZMIR39, the promoter for the modified *cp4 epsps* gene is P-ract1 of the actin 1 gene derived from rice (rice actin 1 promoter) (Reference 16), and the promoter for the modified *cry3Bb1* gene is P-e35S (e35S promoter) derived from cauliflower mosaic virus (CaMV) (Reference 17).

(2) Terminator

In the two gene expression cassettes of the plasmid PV-ZMIR39, the terminator for the modified *cp4 epsps* gene is NOS 3', the 3' untranslated region of the nopaline synthetic gene derived from *Rhizobium radiobacter* (*Agrobacterium tumefaciens*), and the terminator for the modified *cry3Bb1* gene is tahsp 17 3', the 3' untranslated region of heat shock protein 17.3 derived from wheat.

(3) Others

DNA sequences known to be harmful to humans and livestock are not present in the plasmid.

4 Methods for construction of the expression vector with foreign DNA inserts

The plasmid PV-ZMIR39, which was used for the production of MON88017, was constructed as follows: the modified *cry3Bb1* gene cassette, which was first constructed in a pUC119-derived expression vector, was inserted in a pUC119-derived vector with a kanamycin-resistance gene, and then the modified *cry3Bb1* gene cassette was connected with a pBR322-derived vector containing the modified *cp4 epsps* gene cassette.

5 Expression vector constructed

- MON88017 was developed using the plasmid PV-ZMIR39.
- The size of PV-ZMIR39 is 12,368 bp, and the nucleotide sequence of the plasmid and the recognition sites of restriction endonucleases have been determined.
- The function of each component element of PV-ZMIR39 has already been clarified. No known harmful nucleotide sequence is included.
- The intended region of the vector to be inserted into the host genome is from the left border region to the right border region in the clockwise direction.
- The sizes, origins and nucleotide sequences of the genes to be inserted have been identified.

・DNAs inserted into MON88017

Component elements	Function
Modified *cp4 epsps* gene cassette	
P-ract	Promoter region of the actin 1 gene derived from rice
ract1 intron	Intron of the rice actin gene
CTP2	Chloroplast transit peptide sequence derived from the *Arabidopsis epsps* gene, connected to the N-terminal of the *cp4 epsps* gene
Modified *cp4 epsps*	Modified 5-enol-pyruvylshikimate-3-phosphate synthase (EPSPS) gene from *Agrobacterium* sp. CP4 strain
NOS3'	Terminator region of the nopaline synthase (NOS) gene derived from T-DNA of *R. radiobacter* (*Agrobacterium tumefaciens*)
Modified *cry3Bb1* gene cassette	
P-e35S	Promoter region of cauliflower mosaic virus (CaMV)
wt CAB leader	5' untranslated region of the wheat chlorophyll a/b binding protein gene
ract1 intron	Intron of the rice actin gene
Modified *cry3Bb1*	Modified *cry3Bb1* gene derived from *B. thuringiensis*
tahsp17 3'	3' untranslated terminator region of wheat heat shock protein17.3

6 Methods for DNA transfer into the host and subsequent breeding

The T-DNA region of the plasmid PV-ZMIR39 was introduced to the host by the *Agrobacterium*-mediated method.

After the transformation, individual plants were regenerated by selecting transformed callus on culture media containing glyphosate. From these plants, further selection was carried out by determining the expression levels of modified Cry3Bb1 protein by ELISA to select strains with glyphosate tolerance and Coleoptera resistance.

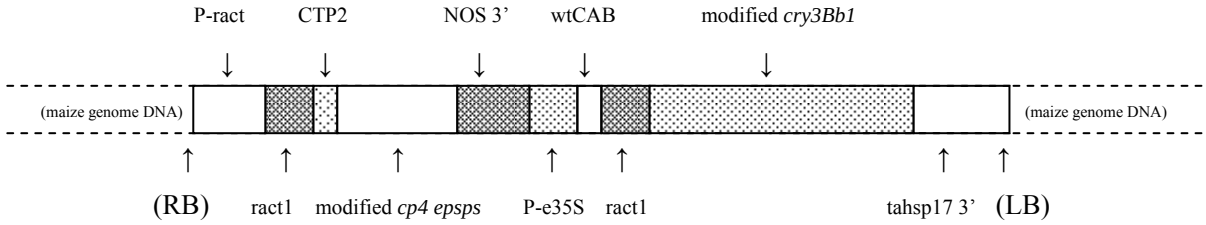
Section 6 Recombinant plant

1 Inserted genes

(1) Copy number and flanking sequences of the host genome

Southern blot analysis was conducted in order to examine the number of sites where the modified *cp4 epsps* and modified *cry3Bb1* genes were inserted, their copy numbers, and integrity of the expression casettes including the presence or absence of external plasmid sequences in the genome of MON88017 line. As a result, it was confirmed that one copy of the intended T-DNA region containing the two gene expression cassettes had been successfully introduced in a perfect form. No external skeleton of the plasmid used was detected. The nucleotide sequences of the flanking regions in the genome of MON88017 have been also determined.

・DNA introduced into the genetically modified maize line MON88017 (schematic diagram)



(2) Presence of open reading frames and the possibility of their transcription and expression

Southern blotting and PCR analysis confirmed that only a single copy of the T-DNA region of the plasmid PV-ZMIR39, containing the modified *cp4 epsps* and modified *cry3Bb1* gene cassettes, was introduced into MON88017, and that no other gene fragments were introduced. Based on these findings, it was considered that no open reading frame that could express an unintended protein was contained. However, it was revealed that 19 and 1 bp sequences inconsistent with the DNA sequence of the PCR products were located adjacent to the 5' and 3' ends of the inserted DNA in MON88017, respectively.

In order to exclude a possibility of the presence of open reading frames capable of expressing an unintended protein, the GenBank database including DDBJ data was searched for the DNA sequences (5' 103 bp and 3' 221 bp sequences) adjacent to the inserted DNA by the program BLAST (blastn). When compared with the sequences expected to have known transcripts or functions, there were no sequences with high homology at or below 1e-30 of e values, indicating that the possibility was very low that the inserted DNA disrupted the gene present in the maize genome. In another comparison with the sequences whose functions were neither known nor expected to have any function at the time of the comparison, the following sequences were found to have high homology at or below 1e-30 of e values: 30 sequences in the 5' flanking region and 10 in the 3' flanking region. On the assumption that the regions containing these sequences could be translated, and also considering the expected frameshifts, similarity of the assumed open reading frames with the sequences of known allergens and toxins were compared. However, it was confirmed that no significantly similar sequence was found.

2 Spatial and temporal expression levels of the gene product in the recombinant plant

The levels of expressions of modified CP4 EPSPS and modified Cry3Bb1 proteins in the recombinant and non-recombinant plants were determined.

In a cultivation study conducted in 2000, four samples each were collected from three different fields. Expression levels of the modified CP4 EPSPS and modified Cry3Bb1 proteins were determined by ELISA methods (Reference 18) in the pollen, silk, stems and leaves, kernels, and stover of the MON88017 and non-recombinant control maize plants.

Mean levels of modified CP4 EPSPS in MON88017 were 220 μg/g (fresh weight; FW) in pollens, 16 μg/g (FW) in stems and leaves, and 5.1 μg/g (FW) in kernels.

Mean levels of modified Cry3Bb1 in MON88017 were 14 μg/g (FW) in pollen, 37 μg/g (FW) in silk, 27 μg/g (FW) in stems and leaves, 13 μg/g (FW) in kernels, and 30 μg/g (FW) in stover.

3 Daily intake of the gene product (protein) and its significance

・Modified CP4 EPSPS protein

The maximum level of modified CP4 EPSPS in the kernels of MON88017 harvested in the field was 6.3 μg/g (FW).

The average daily intake of "maize grains and/or processed food thereof" in Japanese is 0.4 g (Reference 19). On the assumption that all the consumed maize grains are derived from MON88017, the maximal daily intake of the modified CP4 EPSPS protein would be expected to be 2.52 μg.

Since the average intake of protein is 71.5 g (Reference 20), the percentage of modified CP4 EPSPS protein to the total protein is calculated to be 3.5×10^{-6}%.

・Modified Cry3Bb1 protein

The maximum level of Cry3Bb1 protein in the kernels of MON88017 harvested in the field was 19 μg/g (FW).

The average daily intake of maize grains in Japanese is 0.4 g (Reference 19). On the assumption that all the consumed maize grains are derived from MON88017 maize, the maximal daily intake of the modified Cry3Bb1 protein would be expected to be 7.6 μg.

Therefore, the percentage of modified Cry3Bb1 protein to the total protein is calculated to be 1.06×10^{-5}%.

4 Allergenicity of the gene product (protein)

(1) Allergenicity of the donor of the introduced gene

Allergenicity of *Rhizobium* (*Agrobacterium*) to humans has not been reported. The CP4 strain, the donor of the modified *epsps* gene, belongs to *Rhizobium*.

Allergenicity of *B. thuringiensis* ssp. *kumamotoensis*, the donor of the modified *cry3Bb1* gene, to humans has not been reported.

(2) Allergenicity of the gene product (protein)

There are no findings indicating that either modified CP4 EPSPS or modified Cry3Bb1 protein has allergenicity.

(3) Sensitivity of the gene product (protein) to physicochemical treatments

1) Sensitivity to artificial gastric fluid

Modified CP4 EPSPS protein and modified Cry3Bb1 protein produced by *E. coli* were treated with artificial gastric fluid and then analyzed by Western blotting. Both proteins were digested below the lower limit of immunochemical detection within 15 seconds.

The artificial gastric fluid was prepared according to the United States Pharmacopeia.

2) Sensitivity to artificial intestinal fluid

The modified CP4 EPSPS protein produced by *E. coli* was treated with the artificial intestinal fluid and then analyzed by Western blotting. In the artificial intestinal fluid, most of immunoreactivity of the modified CP4 EPSPS protein disappeared in 10 minutes and completely after 100 minutes.

The modified Cry3Bb1 protein produced by *E. coli* was treated with artificial intestinal fluid and then analyzed by Western blotting. In the artificial intestinal fluid, the trypsin tolerant core protein of 59 kDa remained even 24 hours later.

3) Sensitivity to heat treatment

In a heating test, where defatted Roundup Ready soybeans containing the modified CP4 EPSPS protein were used, ELISA analysis confirmed that 99% or more of immunoreactivity of the protein was lost after heat treatment at 100 °C for 38 minutes (References 21 and 22).

After kernels of MON88017 were heated under standard corn processing conditions (about 206 °C for 20 minutes), proteins were extracted and analyzed by Western blotting. Immunoreactivity of the modified Cry3Bb1 protein was below the lower limit of detection.

(4) Similarity of amino acid sequence of the gene product (protein) with known allergens (including the proteins involved in gluten-sensitive enteropathy)

To examine the similarity of amino acid sequence of the modified CP4 EPSPS and modified Cry3Bb1 proteins with known allergens, homology searches were conducted using a database of 752 known allergens and gliadins. FASTA, the standard tool for database search, was used to find homologous allergens (References 23, 24, 25, 26 and 27). In addition, homology searches using eight consecutive amino acid residues of the modified CP4 EPSPS and modified Cry3Bb1 proteins were performed to identify a possible antigenic determinant.

In all searches, modified CP4 EPSPS and modified Cry3Bb1 proteins had no similarity of amino acid sequence with known protein allergens and gluten-sensitive enteropathy-related proteins.

As a result of the comprehensive reviews of (1) to (4) and 3 of the previous section, it was confirmed that there were no data indicating the allergenicity of modified CP4 EPSPS protein and modified Cry3Bb1 protein.

5 Stability of the gene introduced into the recombinant plant

Segregation ratios in 10 generations of MON88017 line were assessed using the expression of modified Cry3Bb1 protein as a marker. The result showed no statistically significant difference (chi-square test) between observed and expected values of all but one generation. In the generation where a significant difference was observed, the observed value exceeded the expected value. A possible reason is as follows: a high concentration of glyphosate was applied to the immediately preceding generation that was heterozygous for the inserted gene; only the pollen carrying the modified *cp4 epsps* gene survived and intercrossed; and thus no segregation occurred in this generation.

To confirm the stability of the introduced gene of MON88017 in later generations, Southern blot analysis was conducted for genomic DNAs obtained from multiple generations. In this analysis, the DNAs were digested with restriction enzymes that cleave the T-DNA region of the expression vector at one site, and four probes that cover the T-DNA region were used. As a result, the identical band profiles were onfirmed in all the generations.

To confirm the stability of expression of modified Cry3Bb1 protein in MON88017, Western blot analysis was conducted using powdered kernels obtained from multiple generations. As a result, the presence of a band consistent with the molecular weights of modified Cry3Bb1 protein was confirmed in all the generations.

The stability of expression of modified CP4 EPSPS protein in MON88017 was confirmed by applying glyphosate in multiple generations.

From these results, it was confirmed that the genes introduced in MON88017 were stably inherited as single dominant genes according to Mendel's laws.

6 Effect of the expressed gene product (protein) on the metabolic pathways

The EPSPS protein catalyzes a step in the shikimate pathway, an aromatic amino acid biosynthetic pathway. It is known that the synthetic step from 3-deoxy-D-arabino-heptulosonate-7-phosphate to chorismic acid, which is known to be important in this metabolic pathway, is rarely inhibited or regulated by intermediates or end products (References 28 and 29). This suggests that EPSPS protein does not play an important role in this pathway as a rate-limiting enzyme.

It is also known that EPSPS protein reacts specifically with phosphoenolpyruvic acid and shikimate -3-phosphate (S3P) (Reference 30). In addition, only shikimic acid, structurally similar to S3P, is known to react with EPSPS, but the reactivity of EPSPS with shikimic acid is merely about one two-millionth of that with S3P. Therefore, it is unlikely that EPSPS reacts with shikimic acid *in planta*.

Modified Cry3Bb1 protein does not possess enzymatic activity and therefore is not considered to affect the metabolic pathway *in planta*.

These findings suggest that it is very unlikely that these gene products can affect metabolic pathways of the host maize.

7 Differences from the host

Major components, fibers, fatty acid composition, amino acid composition, inorganics, vitamins, antinutrients, and secondary metabolites in stems, leaves and kernels were analyzed and compared among MON88017, a non-recombinant control maize, and 12 commercialized non-recombinant maize varieties.

Measurements of major components (ash, carbohydrate, water, protein and total lipid), fibers (acid detergent fiber and neutral detergent fiber), and inorganics (calcium and phosphate) in stems and leaves showed no statistically significant differences between MON88017 and non-recombinant varieties.

Eighteen amino acids, nine fatty acids, inorganics (calcium, copper, iron, magnesium, manganese, phosphate, potassium and zinc), major components (ash, carbohydrate, water, protein and total lipid), fibers (acid detergent fiber, neutral detergent fiber and total dietary fiber), vitamins (folic acid, niacin, vitamin B1, vitamin B2, vitamin B6 and vitamin E), secondary metabolites (ferulic acid and *p*-coumaric acid), and antinutrients (phytic acid and raffinose) in kernels were also analyzed. As a result, statistically significant differences were observed in 18:2 linoleic acid, 20:0 arachic acid and vitamin B1 between MON88017 and non-recombinant varieties. However, the average values were within analytical values of commercialized non-recombinant varieties. Therefore, it was considered that these statistically significant differences were not biologically significant.

8 Approval and usage of the recombinant plant as food in other countries

In the USA, an application for safety review of MON88017 as food and feed was filed with the Food and Drug Administration (FDA) in March 2004. It was approved in January 2005. In January 2004, an application for exemption from the establishment of a residue standard for the modified Cry3Bb1 protein was filed with the Environmental Protection Agency (EPA). In April 2004, an application for

non-regulated status (commercial scale production) was filed with the United States Department of Agriculture (USDA).

In Canada, an application for safety review as food was filed with the Health Canada in May 2004, and an application for safety on environment and feed was filed with the Canadian Food Inspection Agency (CFIA) also in May 2004.

In Australia and New Zealand, an application for safety review as food and feed was filed with the Food Standards Australia New Zealand (FSANZ) in October 2004.

9 Methods for cultivation

The cultivation methods for MON88017 line differs from conventional methods for non-recombinant maize varieties only in the following points: herbicide glyphosate can be used throughout its growing period, and it shows resistance to corn rootworms.

10 Methods for seed production and management

Methods for production and management of MON88017 seeds are the same as those of conventional maize varieties.

Section 7 Studies required additionally when safety cannot be confirmed based on Sections 2 to 6

Substantial findings on the safety have been obtained from Sections 2 to 6, and therefore the Commision do not think it necessary to conduct the following studies. The applicant submitted data from acute toxicity studies, which were also reviewd to acertain the safety.

1. Acute toxicity study
2. Subacute toxicity study
3. Chronic toxicity study
4. Reproduction study
5. Mutagenicity study
6. Carcinogenicity study
7. Other required studies (e.g. intestinal toxicity, immunotoxicity, neurotoxicity, or nutritional assessment studies)

1. Acute toxicity study

Acute toxicity studies were conducted in mice, where modified CP4 EPSPS protein or modified Cry3Bb1 protein produced by *E. coli* was administered by gavage. In the studies, no harmful effect was observed in mice receiving the highest dose of either protein.

Ⅳ Conclusion

As a result of the safety assessment of the genetically modified MON88017 tolerant to the herbicide glyphosate and resistant to coleopteran pests based on the “Standards for the Safety Assessment of Genetically

Modified Foods (Seed Plants) ", any risk that the use of MON88017 line as food causes any adverse effect on human health has not been identified.

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