

ApplicationTesting and Analysis of Genetically Modified FoodNote– Application of MultiNA –

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No.15



(Photo Above: Natural product, unrelated to text contents)

1. Introduction

Genetically modified organism (GMO) has burgeoned over the years in order to satiate the global appetite or to add value to natural agriculture products. Technology to increase crop yields has been a constant demand, and the introduction and success of increased agricultural yield by using gene recombinant technology has indeed increased productivity in crop yields. On the other hand, the question arises as to whether these genetically modified food sources safe to eat, and nutritionally beneficial compared to natural products? The necessity to protect consumers while assisting agricultural food producers is a challenge for regulatory agencies globally, requiring that they keep up with quickly evolving technology and increasing genetically modified foods. In this environment, various regulations are conducted in many countries. For example, in Japan, only genetically modified foods that have received approval through safety assessment are permitted to be circulated in the domestic food market.

Domestic consumers tend to avoid such genetically modified foods though many GMO food have been approved by the safety assessment, the cultivation and circulation of foods developed using gene recombinant technology are currently rare in Japan. However, genetically modified organisms are actively cultivated globally, and large quantities of genetically modified organisms and their processed foods spread all over the world. Thus, genetically modified may penetrate gradually into the Japanese market in future.

2. Genetically Modified Organism (GMO)

Genetically modified organisms are farm products that breed improvement is introduced by gene recombinant technology. Comparing to conventional methods of hybridization and artificial mutation, the gene recombinant technology transforms plants artificially and enables the introduction of genes from other species and a wider variety of breed improvements in a much shorter period of time.

Various characteristic forms including insect resistance, virus resistance and herbicide tolerance for the improvement of cultivation, high lysine for the increment of nutritive value and high oleic for health promotion are introduced to genetically modified organisms distributed globally.

According to ISAAA¹⁾ 2009 statistics, the cultivation area for genetically modified organisms has reached as much as 134 million hectares. The proportion of genetically modified organisms to whole organisms has reached 77 % for soybeans, 26 % for corn, 21 % for rapeseed, and 49 % for cotton respectively. Genetically modified organisms and their processed food are referred to as genetically modified food. According to the Food Sanitation Act in Japan, the safety assessment of genetically modified foods is mandatory and only foods approved in the assessment are permitted to be imported and circulated.

As of July 2010, genetically modified foods corresponding to 126 varieties of genetically modified organisms have been approved through safety assessments. These include 8 varieties of potatoes, 7 varieties of soybeans, 3 varieties of sugar beets, 70 varieties of corn, 15 varieties of rapeseed, 20 varieties of cotton, and 3 varieties of alfalfa².

3. Labeling of Genetically Modified Foods in Japan

According to Food Sanitation Act and Japanese Agricultural Standard (JAS) Law^{2), 3)} (Law Concerning Standardization and Proper Labeling of Agricultural and Forestry Products ~ Law No. 175, 1950), the genetically modified foods which are specified to be labeled as such are shown in Table 1^{2), 3)}. The items for which food labeling is obligatory include the 7 types of agricultural products along with the 32 types of processed foods containing those products listed in (1) of 1 of Table 1, as well as high oleic sovbean and high lysine corn of category 2 in Table 1. The labeling of processed foods (corresponding to (2) of 1 in Table 1) in which genetically modified DNA or resulting protein does not remain after processing, is voluntary. The main raw ingredients of processed foods (those among the top 3 ingredients in terms of weight ratio of all ingredients, and where the weight ratio is at least 5 %) must be included in the label. The labeling of genetically modified foods is summarized in Table 2^{2), 3)}.

The segregation of genetically modified and non-genetically modified agricultural products (foods) is extremely important for labeling of genetically modified products . Whether or not identity preserved handling (IP) has been conducted is specified on the label.

Identity preserved handling refers to the management system in which genetically modified and non-genetically modified foods are segregated through every stage including production, distribution (truck, silo, container ship, etc.), and processing (at processing companies) under the greatest care. Further, its strict management should be confirmed by documents.

The implementation of Identity preserved handling cannot necessarily prevent the mixing of genetically modified foods into non-genetically modified foods.

If Identity preserved handling for soybean or corn is conducted and its mixing rate of genetically modified organism into non-genetically modified organism (GMO content) is less than 5 %, this Identity preserved handling is regarded as proper. The subject of the GMO content is described further on page 7.

[References]

2) Department of Food Safety, The Ministry of Health, Labour and Welfare, Japan, http://www.mhlw.go.jp/english/topics/foodsafety/dna/index.html 3) Ministry of Agriculture, Forestry and Fisheries, Japan, "Food Labeling for Processed Foods", http://www.maff.go.jp/e/jas/labeling/modified.html

¹⁾ ISAAA (International Service for the Acquisition of Agri-biotech Applications), http://www.isaaa.org

1	Produce whose composition and nutritional value are similar to that of conventional produce					
	1) Agricultural products and processed foods containing genetically modified DNA or protein even after processing					
	Agricultural Products	ricultural Products Soybean (including green soybeans and soybean sprouts), Corn, Potato, Rapeseed, Cottonseed, Alfalfa, and Sugar beet				
	Processed Foods	Items subject to labeling	Ingredient to be labeled			
		1. <i>Tofu</i> (soybean curd) and fried <i>tofu</i>	Soybean			
		2. Dried soybean curd, soybean refuse, yuba				
		3. Natto (fermented soy beans)				
		4. <i>To-nyu</i> (Soy milk)				
		5. <i>Miso</i> (soybean paste)				
		6. Cooked soy bean				
		7. Canned or bottled soybean				
		8. Kinako (roasted soybean fluor)				
		9. Roasted soybean	-			
		10. Item containing food of items 1 to 9 as a main ingredient				
		11. Item containing soybeans (for cooking) as a main ingredient				
		12. Item containing soybean flour as a main ingredient				
		13. Item containing soybean protein as a main ingredient				
		14. Item containing edamame (green soybean) as a main ingredient	Edamame			
		15. Item containing soybean sprouts as a main ingredient	Soybean sprouts			
		16. Corn snacks	Corn			
		17. Corn starch				
		18. Popcorn				
		19. Frozen corn				
		20. Canned corn or bottled corn				
		21. Item containing corn flour as a main ingredient				
		22. Item containing corn grits as a main ingredient (except corn flakes)				
		23. Item containing corn (for cooking) as a main ingredient				
		24. Item containing food of items 16 to 20 as a main ingredient				
		25. Frozen potato	Potato			
		26. Dried potato				
		27. Potato starch				
		28. Potato snacks	_			
		29. Item containing food of items 25 to 28 as a main ingredient				
		30. Item containing potatoes (for cooking) as a main ingredient				
		31. Item containing alfalfa as a main ingredient	Alfalfa			
		32. Item containing sugar beet as a main ingredient	Sugar beet			
	(2) Processed foods in which genetically modified DNA or resulting protein does not remain after processing (e.g., soybean oil, soy source, corn oil, isomerized liquid sugar)					
2	Produce whose composition or nutritional value is markedly different from that of conventional produce (high oleic acid soybeans, high lysine corn)					

Table 1 Foods to Be Labeled as Genetically Modified Food in Japan

	Class	fication	Labeling Example	Labeling	
1 Produce whose composition and nutritional value are similar to that of conventional produce					
	(1) Agricultural products and processed foods containing genetically modified DNA or resulting protein even after processing (corresponding to 7 agricultural products and 32 processed food categories in Table 1)	GM agricultural products under the identity preserved handling or processed foods made form those	"GMO segregated from non- GMO", "GMO"	Mandatory	
		Agricultural products, not segregated GM products and non- GM products, or processed foods made from those the identity preserved handling2 or processed foods made form those	"Not segregated from GMO"	Mandatory	
		non-GM agricultural products under the identity preserved handling or processed foods made from those	"Non-GMO segregated from GMO", "Non-GMO"	Voluntary	
	(2) Processed foods in which genet protein does not remain after p source, corn oil, isomerized liqu	ically modified DNA or resulting rocessing (e.g., soybean oil, soy id sugar)	"Non-GMO segregated from GMO", "Non-GMO"	Voluntary	
2	2 Produce whose composition or nutritional value is markedly different from that of conventional produce(high oleic acid soybeans, high lysine corn)		"soybeans (high oleic, genetically modified)"	Mandatory	

Table 2 Labeling of Genetically Modified Foods in Japan

4. Testing and Analysis of Genetically Modified Foods in Japan

The standard tests and methods used for analysis of genetically modified foods are specified in "Testing for Foods Produced by Recombinant DNA Techniques^{" 1)}, notifications concerning inspection and guidance of imported foods $^{2)-5}$ by The Ministry of Health, Labour and Welfare, and "JAS analytical test handbook "6) by Food and Agricultural Materials Inspection Center.

Table 3 shows the genetically modified foods that are subject to testing, and test methods to be used. Both approved and unapproved genetically modified foods based on safety assessment are subject to the testing.

As of July, 2010, papaya (55-1), corn (CBH351), corn (Bt10),

corn (DAS59132), rice (LLRICE601), rice (Bt), and rapeseed (RT73 B.rapa) have not been unapproved by the safety assessment

The tests can be classified to gualitative testing to determine the presence or absence of genetically modified organisms (GMO) and quantitative testing to determine the ratio of genetically modified organisms to non-genetically modified organisms (GMO content). The methods adopted for gualitative testing include lateral flow immunoassay, qualitative PCR, and the GUS gene test, while quantitative PCR and ELISA (enzyme-linked immunosorbent assay) are adopted for quantitative testing.

Food Product	Genetically Modified Gene	Test Type	Test Method	References
Papaya (raw or processed)	Рарауа (55-1)		Qualitative PCR, GUS gene test	
Corn (grain)			Lateral flow immunoassay	
Corn (partially processed)	Corn (CBH351)		Lateral flow immunoassay, Qualitative PCR	
Corn (processed)		Qualitative test		1)
Corn (grain)				
Corn (partially processed)	Corn (Bt10)		Qualitative PCR	
Corn (grain)	Corn (DAS59132)			
	Corn (GA21)			1) 6)
	Corn (Event176)		Quantitative PCR Qualitative PCR / Quantitative PCR	
Corn	Corn (Bt11)	Quantitative test or Qualitative test / Quantitative test		
	Corn (T25)			
	Corn (Mon810)			
Soybean	Soybean (Roundup Ready Soybean)	Quantitative test or Qualitative test / Quantitative test	Quantitative PCR Qualitative PCR / Quantitative PCR	1) 6)
Soybean	CP4EPSPS protein	Quantitative test	ELISA	1)
Rice	Rice (LLRICE601)			3)
Rice	Rice (Bt)			4)
Rapeseed	Rapeseed (RT73 B.rapa)	Qualitative test	Qualitative PCR	5)
Dotato	Potato (New Leaf)			6)
Γυιαίυ	Potato (New Leaf Plus)			0)

Table 3 Testing Methods for Genetically Modified Foods in Japan

[References]

¹⁾ The Ministry of Health, Labour and Welfare, Japan, "Testing for Foods Produced by Recombinant DNA Techniques",

http://www.mhlw.go.jp/english/topics/food/sec05-1a.html

²⁾ http://www.mhlw.go.jp/english/topics/importedfoods/index.html

a) Department of Food Safety, The Ministry of Health, Labour and Welfare, Japan, Notification No. 0915002, September 15, 2006.
b) Department of Food Safety, The Ministry of Health, Labour and Welfare, Japan, Notification No. 0220002, February 20, 2007.

⁵⁾ Department of Food Safety, The Ministry of Health, Labour and Welfare, Japan Notification No. 0914 -5, September 14, 2009.

^{6) &}quot;Japanese Agricultural Standard (JAS) analytical test handbook:

genetically modified food quality, labeling analysis manual for individual products, 2nd revision (2002)", Food and Agricultural Materials Inspection Center, Japan.

Table 4 presents an overview of analysis methods for testing genetically modified foods. Since the ELISA and lateral flow immunoassay methods are based on antigen-antibody reactions, they are not applicable to testing for processed foods because antigenicity is lost due to protein denaturation during heat processing, etc. DNA exhibits superior stability to protein because DNA has better thermal stability and is more tolerant to decomposition and denaturation upon heating or other processes. On the other hand, qualitative PCR is applicable for testing of both agricultural products and processed foods due to the high possibility of target gene amplification by PCR. However, quantitative PCR cannot be applied to determination of recombinant gene content in processed foods, as discussed later in this document.

Table 4 Analysis Methods Used for Testing Genetically Modified Foods

Analysis Method	Overview
ELISA (Enzyme-Linked Immunosorbent Assay)	It is used for quantitative analysis or qualitative analysis (detection) of antigens and antibodies in a sample. It utilizes the high specificity of the antigen-antibody reaction and the high sensitivity of enzymatic reactions.
Lateral Flow Immunoassay	This is one type of immunochromatography that uses the antigen-antibody reaction as in the ELISA method. Here, a drop of sample is applied to a test strip, and as it migrates along the strip by capillary action, the presence or absence of an antigen in the sample is determined based on comparison of the color patterns in the test line and a control line. When the a sample including the target antigen passes through a zone including dyed antigen-specific antibodies, complex between antigen in the sample and dyed antibody (antigen- dyed antibody complex) is formed. Antigen-specific antibody is fixed in the test line zone, and it binds to the antigen- dyed antibody complex. The control line includes an antibody that binds dyed-antibody. If antigen is present in the sample, both the test line and control line are colored. If there are no antigens present in the sample, only the control line is colored.
GUS Gene Test	A β -glucuronidase (GUS) gene might be introduced along with an exogenous gene for use as an indicator (reporter) of genetic recombination. In this type of gene recombination, the GUS gene is expressed along with the recombinant gene, making it possible to confirm the success of recombination process based on the presence or absence of GUS activity. In the GUS gene test, the reagent containing the substrate 5-bromo-4-chloro-3-indolyl- β -D-glucuronide (X-Gluc) is added, and GUS activity is confirmed by the appearance of blue coloring.
Qualitative PCR	PCR (Polymerase Chain Reaction) is a technique in which a specific region of a DNA from template DNA is selectively amplified. In PCR, two single chain DNA fragments (primer pair) which are complimentary to both ends of the specific region to be amplified are used. An enzyme for DNA synthesis (DNA polymerase) is also added to reaction tube and a cycle reaction (dissociation of double-strand DNA to single-strand DNA (Denaturation) \rightarrow primers binding to each strand (Annealing) \rightarrow DNA synthesis (Elongation) is repeated to amplify the specific gene region selectively. Thus, in principle, the specific gene region is amplified by a factor of 2 during each reaction cycle. In qualitative PCR, PCR is conducted to detect a target gene region included in a DNA template extracted from the sample, and the obtained amplification product (PCR product) is subjected to electrophoretic analysis. If the target gene region is included in the extracted DNA, the PCR product corresponding to the target gene region will be detected.
Quantitative PCR	In quantitative PCR, PCR is conducted to amplify the specific gene region using a template DNA extracted from a sample and its amplification process is monitored just-timely. A fluorescent compound (intercalator) which can bind with double-stranded DNA, or a fluorescent marker probe to enable recognition of a specific part of the amplification region is added to allow monitoring of the amplification products at each cycle. Analysis of the obtained amplification curve allows determination of the quantity (number of copies) of the target genes.

Fig. 1 shows an example of the procedure used for analysis of genetically modified food using qualitative PCR. The sample is pulverized, and the DNA is extracted using an extraction kit. The DNA concentration of the extracted DNA is determined using the BioSpec-nano Ultraviolet-Visible spectrophotometer for life sciences, and PCR is conducted using a specified quantity of extracted DNA as the template. Electrophoretic analysis of the obtained PCR products is conducted using the 'MCE-202' MultiNA microchip electrophoresis system, and the presence or absence of PCR products corresponding to the target region is confirmed.



Due to extremely high analysis sensitivity, qualitative PCR can detect even minute levels of modified genes in extracted DNA.When Identity preserved handling is implemented, the permissible genetically modified organism (GMO) content to non-GMO is 5 %.

However, recombinant gene is often detected even though the GMO content is below 5 %. When recombinant DNA is detected by qualitative PCR, quantitative PCR testing will be conducted to determine the GMO content. DNA extracted from the sample is used as the template in quantitative PCR, and PCR is conducted using a primer to detect recombinant and endogenous genes.

The number of copies of recombinant and endogenous genes in the extracted DNA can be determined by analysis of the quantitative PCR amplification curve. The GMO content and internal standard ratio are defined according to Equation 1 and 2, respectively. When the content of genetically modified species exceeds 5 % in identity preserved handling foods labeled as "non-GM (non-Genetically Modified)" or "Non-GM segregated from GM", a close inspection of the identity preserved handling is necessary. It should be mentioned that since the degradation rates of recombinant genes and endogenous genes are not necessarily same in processed food, obtaining the GMO content accurately by quantitative PCR method is impossible.

Fig. 1 Example of Procedure for Analysis of Genetically Modified Food by Qualitative PCR

GMO content (%) = {(number of copies of the recombinant gene) / (number of copies of internal standard genes)} × (1 / Internal standard ratio) × 100	(Equation 1)
Internal standard ratio = (Number of recombinant gene in pure genetically modified agriculture product) / (Number of internal gene in pure genetically modified agriculture product)	(Equation 2)

[Reference]

"Japanese Agricultural Standard (JAS) analytical test handbook:

genetically modified food quality, labeling analysis manual for individual products, 2nd revision (2002)", Food and Agricultural Materials Inspection Center, Japan.

5. Introduction of Tools for Optimizing Inspection and Analysis of Foods by Qualitative PCR

MCE-202 MultiNA Microchip Electrophoresis System

Agarose gel electrophoretic analysis requires a great deal of time and effort to conduct a series of operations including the mixing of reagents, preparing the gel, conducting electrophoresis, acquiring an image of the results, and postcleanup. In addition, its data has a tendency to show inferior sensitivity, resolution and quantitation performance.

The MCE-202 MultiNA microchip electrophoresis system solves these problems of agarose gel electrophoresis all at once since the system is based on brand-new, superior platform and fully automated.



Fig. 2 MultiNA

High Analysis Performance Compared with agarose gel electrophoresis, the microchip electrophoretic analysis with the MultiNA delivers excellent sensitivity, separation, repeatability and guantitation performance.

Automated Operation for up to 120 Analyses

Simply set up the samples and the separation buffer for automated analysis of up to 120 analyses. The parallel processing for analysis pretreatment and electrophoresis permits a processing speed of just 80 seconds per analysis.¹⁾

MultiNA Features

Maximum Ease of Use

Analysis operation with the MultiNA is extremely simple. Just set up the analysis schedule, and then simply load the reagents and samples and click the [Start] button.

Reduce Analysis Costs

The reusable, high-performance microchip achieves lower running costs per analysis than agarose gel electrophoresis.

¹⁾ When 4 microchips are used in DNA standard analysis (for example, DNA-1000 Kit / Premix mode), this does not include the time required for the initial rinse and final rinse, and the initial analysis.

BioSpec-nano UV-VIS Spectrophotometer for Life Sciences

To successfully guide the PCR reaction to completion, confirming the DNA concentration of the extracted DNA and checking of DNA purity using OD ratio (OD260/280) are indispensable. Conducting analysis with UV-VIS spectrophotometers which use conventional cuvettes is both labor intensive and time consuming due to the required rinsing and drying of the cuvettes.

The BioSpec-nano, which incorporates a cuvette-free optical system, an innovative, automatic mounting mechanism, and an automatic wiping mechanism, offers simple fast and simple nucleic acid analysis of 1 to 2 μ L samples. High throughput analysis is achieved, requiring a mere 15 seconds to complete one analysis.



Fig. 3 BioSpec-nano

BioSpec-nano Features

Drop and Click Analysis

DNA concentration and purity can be checked by just dropping the sample on the target, and clicking the button. Measurement and wiping are both handled automatically by the instrument.

Nucleic Acid Quantitation of 1 to 2 µL Samples

Sample volumes of 1 μL (0.2 mm optical path length) and 2 μL (0.7 mm optical path length) can be measured.

Simple and Quick Analysis

Blank measurement, sample measurement, report output in PDF or CSV format, and other basic operations are conducted simply and quickly just by clicking a button.

Support for Wide Range of Analyses

Nucleic acid quantitation, quantitation of nucleic acid labeled for micro-array, protein quantitation by OD280, and labeled protein quantitation are all supported.

6. Examples of Qualitative PCR Analysis of Genetically Modified Foods Using the MultiNA 6.1 Analysis of Genetically Modified Corn (MON810)

Here we introduce an analysis of genetically modified corn (MON810) as an example of genetically modified food analysis. After extracting DNA from 3 powdered samples consisting of genetically modified corn (MON810) having GMO content of 0 %, 1 % and 5 %, respectively, the extracted DNA from each of the samples was used as a template. PCR was then conducted using a primer for endogenous gene *SSIIb*-3 detection²⁾ and a primer for the genetically modified MON810 detection³⁾. The electrophoretic analysis of PCR product using the MultiNA are shown in Fig. 4. In analysis of the PCR products using the primer for the endogenous gene *SSIIb*-3 detection, the PCR product (114)

bp) corresponding to *SSIIb*-3 was detected in all of the samples except for the negative control. The endogenous gene *SSIIb*-3 is a gene that is specific to corn, and detection of the endogenous gene in a sample means PCR testing of the recombinant gene in that sample is effective. On the other hand, in analysis of the PCR products using the primer for the genetically modified MON810 detection, the PCR product (113 bp) corresponding to MON810 was detected in the 1 % and 5 % GMO content samples, as well as in the positive control sample.

Gel Image



Fig. 4 Analysis of Genetically Modified Corn (MON810) Using MultiNA

[References]

- 1) Shimadzu Application News No. B29, Qualitative Analysis of Genetically Modified Corn by Standard Method with MCE-202 "MultiNA"
- 2) The Ministry of Health, Labour and Welfare, Japan, "Testing for Foods Produced by Recombinant DNA Techniques",
- http://www.mhlw.go.jp/english/topics/food/sec05-1a.html
- 3) "Japanese Agricultural Standard (JAS) analytical test handbook:

genetically modified food quality, labeling analysis manual for individual products, 2nd revision (2002)", Food and Agricultural Materials Inspection Center, Japan.

6.2 Detection of Genetically Modified DNA (GA21) in Processed Corn

Here we introduce an example of analysis of genetically modified DNA in processed corn using qualitative PCR. DNA was extracted from 4 types of processed corn products (2 types of canned corn, 1 type of popcorn, 1 type of corn starch), and the DNA extracted from each of the samples was used as a template. PCR was conducted using a primer for the endogenous gene *SSIIb* detection and a primer for the genetically modified GA21 detection. Next, the obtained PCR products were analyzed using the MultiNA. The analysis results are shown in Fig. 5. In PCR using the primer for the endogenous gene *SSIIb* detection, the PCR product (151 bp) corresponding to *SSIIb* was detected in all of the processed food samples and in the positive control plasmid. If damage to DNA derived from processed food is considerable due to heating during processing, the endogenous genes will not be detected. In samples where the endogenous gene is not detected, qualitative testing for genetically modified genes in these samples is regarded as invalid. On the other hand, in analysis of the PCR products using the primer for the genetically modified GA21 detection, the PCR product (133 bp) corresponding to GA21 was detected only in the positive control plasmid, and was not detected in the 4 types of processed food samples, which were labeled as " Non-GMO"

As shown in the electropherograms of the negative and positive controls, the *SSIIb* gene (151 bp) and GA21 gene (133 bp) are clearly detected using only 20 copies of the positive control plasmid. Thus, high-sensitivity qualitative PCR analysis of genetically modified food is clearly achieved using the MultiNA.



Fig. 5 Analysis of Genetically Modified Gene (GA21) in Processed Corn Food Products Using MultiNA

[Reference]

"Japanese Agricultural Standard (JAS) analytical test handbook:

genetically modified food quality, labeling analysis manual for individual products, 2nd revision (2002)", Food and Agricultural Materials Inspection Center, Japan.

6.3 Analysis of Genetically Modified Foods Unapproved by Safety Assessment in Japan

Some genetically modified foods that are unapproved by Japanese safety assessment, are permitted to be circulated in global market.

These particular foods are subject to qualitative inspection in Japan (Table 3). Positive control plasmids and primers according to official inspection methods are commercially available, making it possible to conduct analysis for modified DNA in these foods by the qualitative PCR method. Examples of analysis of 3 types of modified DNA that were unapproved by the safety inspection as of July, 2010, including corn (CBH351)¹⁾, papaya (55-1)¹⁾, and rice (Bt)²⁾, are shown below. PCR was conducted using the respective positive control plasmids as templates, and the primers specified in the respective test methods for detection and identification. The obtained PCR products were analyzed using the MultiNA, and the results shown in Fig. 6 were obtained. The PCR products corresponding to the respective target genes and the primers can be verified.





Fig. 6 Analysis of Genetically Modified Corn (CBH351), Papaya (55-1), Rice (Bt) using MultiNA

[References]

1) The Ministry of Health, Labour and Welfare, Japan, "Testing for Foods Produced by Recombinant DNA Techniques",

http://www.mhlw.go.jp/english/topics/food/sec05-1a.html

2) Department of Food Safety, The Ministry of Health, Labour and Welfare, Japan, Notification No. 0220002 of February 20, 2007.

Application No. 15 Note

> MCE®-202 MultiNA is not available in the United States. *This document is based on information valid at the time of publication. It may be changed without notice.





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