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MHLW Seeks Comments on Proposed new Food Additives: Azoxystrobin and Chlorous Acid Water

Report Categories:
Sanitary/Phytosanitary/Food Safety

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Report Highlights:
On July 30, 2012, the Japanese Government announced its intention to approve two new food additives: 'Azoxystrobin' and 'Chlorous Acid Water'. The domestic comment period will close on August 13, 2012. However, MHLW will also notify these proposed changes to the WTO/SPS committee, which will provide another chance for public comments to be submitted on this subject.

General Information:
On July 30, 2012, the Government of Japan (GOJ) announced plans to designate two new food additives, azoxystrobin and chlorous acid water. The domestic comment period will close on August 13, 2012. However MHLW will also notify these proposed changes to the WTO/SPS committee, which will provide another chance for public comments to be submitted on this subject.

The actual WTO-SPS notifications can be found at the site below.
http://www.wto.org/english/tratop_e/sps_e/work_and_doc_e.htm

After the closing of the WTO comment period, a final report will be made based on the conclusions reached at a session of the Pharmaceutical Affairs and Food Sanitation Council slated to be held at a later date. This will then constitute the final decision.

Parties interested in providing comments to the GOJ can do so in either Japanese or English. The GOJ point of contact for the comment for this particular announcement is indicated below.
If you have comments, please send them directly to the Japanese Government at:

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Please also consider copying the U.S. Embassy, Tokyo at agtokyo@usda.gov on your comments in order for them to be considered as part of the official U.S. Government comments to the WTO.

Designation of Food Additives

Japan is going to designate Azoxystrobin and Chlorous Acid Water as authorized additives.

Under Article 10 of the Food Sanitation Law, food additives shall not be used or marketed without authorization by the Minister of Health, Labour and Welfare. When compositional specifications or standards for use or manufacturing are established for food additives based on Article 11 of the law, those additives shall not be used or marketed unless they meet the standards or specifications.

In response to a request from the Minister, the Committee on Food Additives of the Food Sanitation Council that is established under the Pharmaceutical Affairs and Food Sanitation Council has discussed the adequacy of the designation of Azoxystrobin (CAS No. 131860-33-8) and Chlorous Acid Water* as food additives. The conclusion of the committee is outlined below.

Azoxystrobin is registered as a pesticide in more than 50 countries. It is generally used as fungicide for

various crops, like rice, wheat, legumes, and grapes. It was registered in Japan on April 24, 1998. Chlorous Acid Water is generally used as sterilizer.

* Note) Chlorous Acid Water is defined as below in the compositional specifications based on the Food Additive Act of Japan.

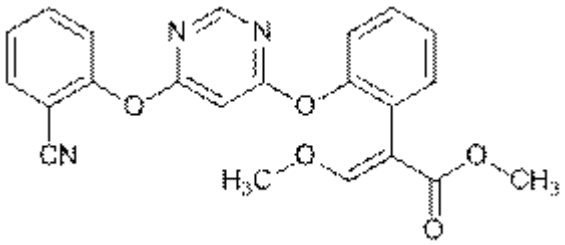
Saturated sodium chloride solution with hydrochloric acid is electrolyzed under acidic condition in an electrolytic cell without a septum ("electrolytic cell without a septum" refers to a cell consisting of an anode and a cathode not separated by a septum) to obtain an aqueous solution. The resulting solution is strongly acidified with sulfuric acid to generate chloric acid, which is converted into chlorous acid water with addition of hydrogen peroxide water.

Outline of conclusion

The Minister should, based on Article 10 of the Food Sanitation Law, designate Azoxystrobin and Chlorous Acid Water as food additives unlikely to harm human health, and establish compositional specifications and use standards for these substances based on Article 11 of the law. See Attachment 2-1 and 2-2.

Attachment 2-1

Azoxystrobin
アゾキシストロビン



Standard for use

Azoxystrobin can be used in citrus fruits (excluding *unshū* oranges) only.
It shall not remain more than 0.010 g/kg as azoxystrobin.

Compositional specifications

Substance name Azoxystrobin
Molecular formula $C_{22}H_{17}N_3O_5$
Mol. Weight 403.39
hemical name [CAS number]
Methyl (*E*)-2-{2-[6-(2-cyanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate
[131860-33-8]
Content Azoxystrobin contains not less than 95.0% of azoxystrobin ($C_{22}H_{17}N_3O_5$).

Description Azoxystrobin occurs as a white to yellow-red, odorless powder.

Identification

Determine the infrared absorption spectrum of Azoxystrobin as directed in the Paste Method under Infrared Spectrophotometry. It exhibits absorption bands at wavenumbers of about 2230 cm^{-1}, 1625 cm^{-1}, 1587 cm^{-1}, 1201 cm^{-1}, 1155 cm^{-1}, 840 cm^{-1}.

Purity

(1) Melting point 114–119°C.

(2) Lead Not more than 2.0 μg/g as Pb.

Test Solution Weigh 2.0 g of Azoxystrobin, and transfer it into a platinum, quartz, or porcelain crucible; or a quartz beaker. Add diluted sulfuric acid (1 in 4) to moist the whole of it, and heat on a hot plate while gradually increasing temperature until white fumes are no longer emit evolved. Add diluted sulfuric acid (1 in 4) again if necessary, and heat until the sample is carbonized. Place a lid on the crucible (or beaker), and heat in an electric furnace while gradually increasing temperature, and ignite at 500–600°C until the content is incinerated. Add 10 ml of diluted hydrochloric acid (1 in 4) to the residue, and evaporate on a water bath to dryness. Add a small amount of diluted nitric acid (1 in 100), heat to dissolve it, and cool. Add diluted nitric acid (1 in 100) to make exactly 100 ml.

Control Solution Measure exactly 1 ml of Lead Standard Solution, and add water to make exactly 100 ml. Measure exactly 4 ml of this solution, and add diluted nitric acid (1 in 100) to make exactly 100 ml.

Procedure Proceed as directed in Method 1 in the Lead Limit Test.

Water Content Not more than 0.50% (2.0 g, Direct Titration).

Assay Weigh accurately about 0.05 g each of Azoxystrobin and azoxystrobin for assay. Dissolve each in acetonitrile to make exactly 100 ml. Use them as test solution and standard solution respectively. Aanalyze 10 μl portions of the test solution and the standard solution by liquid chromatography using the operating conditions given below. Measure the peak areas (A_T and A_S) of azoxystrobin for the test solution and the standard solution. Calculate the azoxystrobin content by the formula:

$$\text{Content (\%) of azoxystrobin } (C_{22}H_{17}N_3O_5) = \frac{\text{ight (g) of azoxystrobin for assay}}{\text{Weight (g) of the sample}} \times \frac{A_T}{A_S} \times 100$$

ating conditions

tor: Ultraviolet spectrophotometer.

nn: A stainless steel tube of 4.6 mm internal diameter and 15 cm length.

lumn packing material: 5-μm octadecyl silanized silica gel for liquidchromatography.

nn temperature: 40°C.

e phase: A 9:11 mixture of acetonitrile/water.

rate: Adjust so that the retention time of azoxystrobin is about 15 minutes.

Regents and Solutions

1,4-BTMSB-*d*4 $C_{12}H_{18}D_4Si_2$ Deuterated 1,4-bis(trimethylsilyl)benzene whose traceability to the International System of Units is ensured.

Azoxystrobin for Assay $C_{22}H_{17}N_3O_5$ A white powder.

Content Not less than 99% of azoxystrobin ($C_{22}H_{17}N_3O_5$).

Identification Determine the infrared absorption spectrum of Azoxystrobin as directed in the Paste Method or Potassium Bromide Disk Method under Infrared Spectrophotometry. It exhibits absorption bands at about 2230 cm^{-1},

1625 cm^{-1}, 1587 cm^{-1}, 1201 cm^{-1}, 1155 cm^{-1}, 840 cm^{-1}.

Melting point 115–119°C.

Assay Weigh accurately about 20 mg of Azoxystrobin for Assay and about 4 mg of 1,4-BTMSB-d_4, and add 2 ml of deuterated acetonitrile to dissolve them together. Transfer the resulting solution to an NMR tube of 5 mm in external diameter, stopper tightly, and measure ^{1}HNMR spectra using a spectrometer at a proton resonance frequency of 400 MHz or more. Assuming the signal of 1,4-BTMSB-d_4 as δ 0.23 ppm, when the signal intensities around δ 3.40–3.80 ppm, δ 6.43 ppm, and δ 8.28 ppm are designated as A_1 (corresponding to 6 hydrogens), A_2 (corresponding to 1 hydrogen), and A_3 (corresponding to 1 hydrogen), respectively, confirm that each of $(A_1/6)/A_2$, $(A_1/6)/A_3$, and A_2/A_3 is 1.0. Then, assuming the signal intensity of 1,4-BTMSB-d_4 as 18.00, when the sum of A_1, A_2, and A_3, the sum of the number of hydrogens, and the purity of 1,4-BTMSB-d_4 are designated as I, N, and P(%), respectively, determine the content of azoxystrobin by the following formula. If the signal from Azoxystrobin for Assay is overlapped with the signal from a contaminant, do not use its signal area intensity for the assay.

$$\text{Content (\%) of azoxystrobin } (C_{22}H_{17}N_3O_5) = \frac{\text{Weight (mg) of 1,4-BTMSB-}d_4 \times I \times P}{\text{Weight (mg) of the sample} \times N} \times 1.781$$

Operating conditions

Spinning: Off.

^{13}C decoupling: Present.

Acquisition time: 4 seconds.

Spectral range: At least 20 ppm including between −5 ppm and 15 ppm.

Flip angle: 90°.

Delay time: 64 seconds.

Dummy scans: Not less than 1.

Number of accumulation: Not less than 8.

Deuterated acetonitrile C_2D_3N Use deuterated acetonitrile produced exclusively for NMR spectral measurement.

Attachment 2-2

Chlorous Acid Water

Standard for use

Chlorous Acid Water can be used in polished rice, legumes/pulses, vegetables (excluding mushrooms), fruits, seaweeds, fish and shellfish (including whale meat), and meats (livestock and poultry including wild animals). The maximum use amount shall be 0.40 g/kg of water for dipping or spraying of each commodity (for rice, 0.40 g/kg of water for dipping). The Chlorous Acid Water used shall be decomposed or removed before the completion of the final food. Please note that the 'final food' means

food products being distributed, sold and served to consumers in general.

Standard for manufacturing
Sodium chloride used as a manufacturing material shall be sodium chloride specified in the Japanese Pharmacopoeia. Please note that sodium chloride without Japanese Pharmacopoeia specification does not meet manufacturing standard. The information of Japanese Pharmacopoeia can be found below.

Japanese Pharmacopoeia
http://www.mhlw.go.jp/topics/bukyoku/iyaku/yakkyoku/english.html

Compositional specifications

Substance name: Chlorous Acid Water

Definition: Saturated sodium chloride solution with hydrochloric acid is electrolyzed under acidic condition in an electrolytic cell without a septum ("electrolytic cell without a septum" refers to a cell consisting of an anode and a cathode not separated by a septum) to obtain an aqueous solution. The resulting solution is strongly acidified with sulfuric acid to generate chloric acid, which is converted into chlorous acid water with addition of hydrogen peroxide water.

Content: Chlorous Acid Water contains not less than 4.0–6.0% of chlorous acid ($HClO_2$ = 68.46).

Description: Chlorous Acid Water occurs as a light yellow-green to yellow-red transparent liquid having a chlorine odor.

Identification:
(1) To 5 mL of a solution of Hypochlorous Acid Water (1 in 20), add 0.1 mL of potassium permanganate solution (1 in 300). A red-purple color is produced, which changes to light yellow on the addition of 1 mL of diluted sulfuric acid (1 in 20).
(2) A solution of Chlorous Acid Water (1 in 20) exhibits absorption maxima at wavelengths of 258–262 nm and 346–361 nm.
(3) The color of potassium iodide-starch paper changes to blue in Chlorous Acid Water and then fades.

Purity:
(1) Lead Not more than 1.0 μg/g as Pb.
Test Solution To 5.0 g of Chlorous Acid Water, add 2 mL of nitric acid ad 20 mL of hydrochloric acid, and evaporate on a water bath to dryness. To the residue, add diluted nitric acid (1 in 150) to make 10 ml.
Control Solution Dilute 1.0 mL of Lead Standard Solution with diluted nitric acid (1 in 150) up to 20 mL.
Procedure Proceed as directed in Method 1 in the Lead Limit Test.
(2) Arsenic No more than 1.0 μg/g as As_2O_3 (2.0 g, Medthod 2, Apparatus B).

Assay:
Sample Solution Weigh accurately about 5 g of Chlorous Acid Water, and add water to make

exactly 100 mL. Transfer the resulting solution into a gas washing bottle, and blow nitrogen gas into the bottle until the solution is colorless. Use this as the sample solution. Place exactly 20 mL of the sample solution in an iodine-flask, add 10 mL of diluted sulfuric acid (1 in 10), and then add 1 g of potassium iodide. Immediately put a stopper tightly on the flask, and shake well. Pour 5 mL of potassium iodide TS in the upper part of the flask without removing the stopper, and allow to stand for 15 minutes in a dark place. Loosen the stopper to pour potassium iodide TS into the flask, immediately stopper tightly, and shake well. Titrate free iodine with 0.1 mol/L sodium thiosulfate. Add 5 mL of starch TS as the indicator when the color of the solution changes to light yellow. Perform a blank test to make a necessary correction.

Each mL of 0.1 mol/L sodium thiosulfate =1.711 mg of $HCLO_2$