mg/kg body wt./day was retained.

Based on data showing current admixed concentrations of hydrazine in the additive polyvinylpyrrolidone to be no greater than 1 mg/kg, the ADI for additive polyvinylpyrrolidone was established at 0 to 50 mg/kg body wt./day at the 30th Assembly (1986).

5. Physicochemical properties

(1) structural formula, (2) manufacturing method, (3) specifications*1, (4) food additive stability, and (5) analytical methods of the food additive in food products should be provided.

(1) Structural formula

① Structural or rational formula

In the case of organic compounds, the *Japan's Specifications and Standards for Food Additives* should be referred.

② Molecular or compositional formula, and molecular weight

Describe in conformance to the rules of *the Japan's Specifications and Standards for Food Additives*. For mixtures, the molecular formulas and molecular weights of the respective contents should be provided.

(2) Manufacturing methods

The manufacturing process with a flow chart or the like should be briefly described.

The removal process of harmful factors should also be noted.

(3) Specifications

Required items to ensure constant quality with respect to the safety and effectiveness of the subject food additive should be established.

① Draft specifications

In draft specifications, the name of the food additives, content (purity), chemical and physical properties (identification, Specific properties), permitted levels of impurities, and purity analysis methods of the additive should be presented.

For explanations of each item, refer to iv. Draft specifications.

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*1 Specifications includes ① draft specifications, ② comparison table of draft specifications and existing specifications (specifications established by international institution, specifications of other foreign countries, pharmaceutical specifications), ③ grounds for establishing the draft specifications and overview of testing method study, and ④ verification data of test methods and test results.

Notes

· The JECFA Combined Compendium of Food Additive Specifications, US Food Chemical Codex (FCC), and EU laws in a proper manner should be cited.

· If the Japanese Pharmacopoeia establishes the specifications, the citation should be provided as necessary.

· If no specifications exist, new draft specifications for the subject food additive should be established.

· Any laws referenced should be indicated by Ref Std. number in the tables. The relevant parts should be attached as Reference.

· As a general rule, test methods established as GENERAL TESTS in *Japan's Specifications and Standards for Food Additives* should be used.

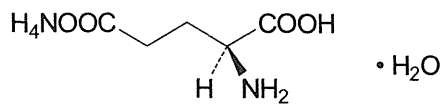
The following websites enable the availability of specifications of JECFA and the EU and FCC specifications.

JECFA: http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/

EU: http://ec.europa.eu/food/food/fAEF/additives/specifications_en.htm

FCC: http://www.usp.org/store/products-services/food-chemicals-codex-fcc (payment required)

(Example of description)

Item[a)]	Draft Specifications	Ref. Std.
① Japanese Name	L－グルタミン酸アンモニウム	
② English Name	Monoammonium L-Glutamate	1
Other English Name	--	—
③ Other Japanese Name	--	—
④ Structural or Rational Formula		1, 2
⑤ Molecular or Compositional Formula	$C_5H_{12}N_2O_4 \cdot H_2O$	1
Molecular or Formula Weight	182.18	1
⑥ Chemical Name	Monoammonium monohydrogen (2*S*) - 2 -aminopentanedioate monohydrate	3
⑦ CAS Registry	[139883 - 82 - 2]	3

Number			
⑧ Definition[b)]		--	
⑨ Content (Assay)[c)]		Contains not less than 99.0% of monoammonium L-glutamate monohydrate ($C_5H_{12}N_2O_4 \cdot H_2O$) on the dried basis.	1
⑩ Description		Monoammonium L-Glutamate occurs as colorless to white crystals or white crystalline powder.	1
⑪ Identification	(1)	Use an aqueous solution (1 in 200) of Monoammonium L-Glutamate as the test solution and a solution (1 in 200) of monosodium L-glutamate monohydrate as the control solution. …	1
	(2)	Monoammonium L-Glutamate responds to the test for the ammonium salt.	1, 2
⑫ Specific Rotation[c)]		$[\alpha]^{20}_D$ = +25.4 to +26.4° (10 g, hydrochloric acid (1 → 6), 100 mL, on the dried basis)	1
pH		6.0 to 7.0 (1.0 g, 20 mL water)	1
⑬ Purity	(1)	Lead: Not more than 1 μg/g as Pb (4.0 g, Method 1, Control solution Lead Standard Solution 4.0 mL, frame method)	1, 2
	(2)	Arsenic: Not more than 3 μg/g as As (0.50 g, Method 1, Standard color Arsenic Standard Solution 3.0 mL, Apparatus B)	2
	(3)	Pyrrolidone carboxylic acid: Weigh 0.50 g of Monoammonium L-Glutamate and dissolve in water to prepare 100 mL of test solution. Separately, weigh 0.50 g of monosodium L-glutamate monohydrate and 2.5 mg of DL-2-pyrrolidone-5-carboxylic acid, and dissolve them in water to make exactly 100 mL of reference solution. Measure 2 μL each of the test solution and thr controlsolution, …a 2:1:1 mixture of 1-butanol/water/acetic acid …	1, 2, 4
⑭ Loss on Drying[c)]		Not more than 0.5% (50°C, 4 h)	1, 2
⑮ Residue on Ignition[c)]		Not more than 0.1% (800°C, 15 m)	1, 2
⑯ Microbial Limit		--	—
⑰ Assay (Method of Assay)[c)]		Weigh accurately about 0.15 g of Monoammonium L-Glutamate, add 3 mL of formic acid to dissolve, and then add 50 mL of acetic acid. Titrate the resulting solution with 0.1 mol/L perchloric acid. Confirm the end point …	1, 2
⑱ Storage Standards		--	—

Reference specifications
1: JECFA Combined Compendium of Food Additive Specifications (Ref. X)
2: *Japan's Specifications and Standards for Food Additives, 8th Edition* (Ref. X)
3: Food Chemical Codex Ninth Edition (Ref. X)
4: Japanese Standards of Quasi-Drug Ingredients 2006 (Ref. X)

[a] For the items given in ① to ⑱, requirements to assure a certain level of quality concerning safety and effectiveness of the subject food additive should be established (see iv. Draft specifications).

[b] If the subject additive originates in extract of animals, plants, or microorganisms, originates from minerals, or the like, the definition should include information on the origin, preparation method, nature, and impurities.

Example of ⑧ Definition: Dunaliela Carotene is obtained from the entire part of the alga *Dunaliella bardawil* or *Dunaliella salina* and consists mainly of b-carotene. It may contain edible fats or oils. Reference specification: JECFA monograph Carotenes (Algae). Grounds for scientific names: NCBI Taxonomy.

[c] The items to be set in ⑨, ⑫, ⑭, ⑮, and ⑰ should be entered.

② Comparison table of draft specifications and existing specifications

A comparison table showing the specifications established by an international institution and foreign countries, and pharmaceutical specifications, etc. should be attached.

(Example of description)

Comparison Table

	Draft Specifications	JECFA	FCC	EU
Content (Assay)	Not less than 99.0% (dried basis)	Not less than 99.0% (dried basis)	98.5%–101.5% (drid basis)	99.0%–101.0% (anhydrous basis)
Description	Colorless to white crystals or white crystalline powder	White, practically odorless crystals or crystalline powder	White, free flowing crystalline powder	White, almost odorless crystals or crystalline powder
Identification tests				
Test for ・・・	Positive (TLC: ninhydrin coloration)	Positive (TLC: ninhydrin coloration)	--	Positive (TLC)
Test for ・・・	Positive	Positive	--	Positive
Solubility	Not established	Freely soluble in water	--	--
Infrared Spectrum	Not established	--	Matches reference spectra	--
(Specific properties)				

Specific Rotation $[\alpha]^{20}_{D}$ (dried basis)	+25.4 – +26.4° (10 w/v%, hydrochloric acid (1→6))	+25.4 – +26.4° (10 w/v%, 2N HCl)	+25.4 – +26.4° (10 w/v%, 2N HCl)	+25.4 – +26.4° (10% soln., 2N HCl) (Identification)
pH	pH 6.0–7.0 (1.0 g, water 20 mL)	pH 6.0–7.0 (1 in 20)	pH 6.0–7.0 (1:20) (Description)	pH 6.0–7.0 (5% solution) (Identification)
Purity tests				
Lead (Pb)	Not more than 2 μg/g	Not more than 1 mg/kg	Not more than 5 mg/kg	Not more than 2 mg/kg
Arsenic (As)	Not more than 3 μg/g	--	--	--
____ acid	Negative (TLC)	Negative (TLC)	--	Not more than 0.2%
Loss on Drying	Not more than 0.5% (50°C, 4 h)	Not more than 0.5% (50°C, 4 h)	Not more than 0.5% (50°C, 4 h)	Not more than 0.5% (50°C, 4 h)
Residue on Ignition	Not more than 0.1% (800°C, 15 min)	Not more than 0.1% (800°C, 15 min)	Not more than 0.1% (800°C, 15 min)	Not more than 0.1%
Assay (Method of Assay)	Non-aqueous titration, sample mass 0.15 g, 0.1 mol/L perchloric acid	Non-aqueous titration, sample mass 200 mg, 0.1N perchloric acid	Non-aqueous titration, sample mass 250 mg, 0.1N perchloric acid	No procedure listed

③ Grounds for establishing the draft specifications

The grounds (reason for setting the item, source, reaction principle, etc.) and an overview of the review of testing method in sequence of the item numbers in the draft specifications should be shown.

④Validation data of test methods and test results

The Validation data of test methods and test results should be shown. Conformity to specification values established for the specifications with respect to amount contained (purity), chemical and physical properties (identification, specific properties), permitted impurity levels, etc. should also be explained.

Notes

- To show appropriateness for test methods established, verification data of testing methods (e.g., recovery test) should be provided.
- To show that the subject food additive conforms to the specifications established in the draft specifications, analytical results of an appropriate quantity of lots (e.g., 3 lots per product, measured 3 times respectively) should be provided.

(4) Stability of Food Additive

The stability of the food additive including a search for decomposition products should be reviewed.

(5) Analytical Methods of Food Additive in Food Products

Basically, analytical methods should be established for foods in which the food additive is likely to be used at high possibility. They should be methods to identify the addition of the food additive quantitatively and qualitatively by chemically analyzing target foods. If the use standard does not need to be established, or if there is no residue in the food product, the assay may be omitted from the analytical methods of the food additive in food products.

Notes
· In case the use standard is established, it must be denoted as a general rule.
· A quantitative assay to separate the subject additive from other food additives with a similar purpose should be considered.

6. Draft of use standards

Study the needs for establishing draft of use standards upon comprehensive review of the safety, effectiveness, and estimated intake of the subject food additive, and the Codex standards, use standards in other countries, etc.

Notes
· Even if codex standards or other countries' standards of are proposed, the draft of use standards must be prepared with reference to use standards for other food additives already established.
·For the draft of use standards, tables should be prepared as needed.
· Any revisions to use standards should be marked by underscoring and crossing out.

(1) Draft of use standards

Comprehensively review food additive safety and effectiveness. If the establishment of a use standard is determined necessary, describe the draft of use standards.

Notes
The draft of use standards must be prepared with reference to use standards for other food additives already established.

(2) Grounds for establishing draft of use standards

Provide the grounds for establishing the draft of use standards based on use status in foreign countries and materials related to effectiveness and safety, etc. As "Reference," submit the materials quoted as the grounds for establishment.

Notes

· Even if codex standards or standards of other countries are proposed, applicants should discuss whether there are any issues of safety with reference to safety test results and intake estimate results.

7. Other

Describe any other necessary matters.

ii Findings regarding effectiveness

It should be proven or confirmed that the use of the food additive comes under one or more of the purpose set out in (1) to (4) below. However, where the manufacturing or processing method for a target food can be improved or modified at comparatively low cost, and the improved or modified method does not require the food additive for the manufacture or processing of the food, the use of the food additive is not justified.

(1) To preserve the nutritional quality of the food.
An intentional reduction in the nutritional quality of a food would be justified in the circumstances dealt with in section (2) below and also in other circumstances where the food does not constitute a significant item in a normal diet.

(2) To provide necessary ingredients or constitutions for food manufactured for consumers who have special dietary need, provided that the food additive is not intended to provide medical effects, such as prevention or treatments of certain disease.

(3) To enhance the keeping quality or stability of a food or to improve its organoleptic properties, provided that this does not so change the nature, substance, or quality of the food as to deceive the consumer.

(4) To provide aids in the manufacture, processing, preparation, treatment, packing, transport, or storage of food, provided that the food additive is not used to disguise the effects of the use of faulty raw materials or of undesirable (including unhygienic) practices or techniques during the course of any of these activities.

Documents on effectiveness

(1) Studies concerning effectiveness should be conducted to establish that the food additive has expected effects, according to its purposes. For example, the studies to clarify the correlation between the effect of the antioxidant for the target foods and the added amount, and/or the time-course after the addition of the antioxidant. For preservative, the studies to clarify the improved effect of shelf life time induced by the preservative property should be conducted.

(2) Comparisons in effects with a widely used food additive, which has already been approved for the same use, are desirable.

(3) Studies on the stability of the food additive in foods should be conducted. For unstable food additives, breakdown products should be examined on their kinds and extent.

(4) Effects of the food additive on main nutrients in foods should be also examined.

The points of assay methods of effective data demonstrating effectiveness and the points of its submission

- Evidence from well-designed study is required to be submitted to demonstrate that the food additive indeed fulfills the intended effect and to support utilization purpose of the food additive.
- Where possible, these studies should be conducted using graded levels of the additive in the food and the effects should be noted. The effects should be compared with controls containing no additive.
- For test results, appropriate statistical treatment of the results should be undertaken, including application of tests of significance. These data should be used not only to demonstrate effectiveness, but also to establish the minimum effective use level.
- Presentation of the results in tabular and graphical form is desirable and helps to facilitate the interpretation of the results. For example, a graphical representation of effects at various food additive use levels allows quick visualization of minimum levels of efficacious use of a food additive.
- Where possible, the data demonstrating effectiveness should have been accepted and listed in a scientific article and evaluated objectively.

Notes

- There is often the case that attached data is only for some part of foods which intended to use according to the proposed use standards. It has no explanation for reason of abbreviation of data on other foods. Explanation should be described if the data for some foods is abbreviated and regarded the limited data demonstrates the intended effectiveness by the applicant.
- The attachment of minimum and basic safety data demonstrate effectiveness is desirable, not only describing the proposed additive is widely used overseas.
- Description of difference (advantage) compared with other food additives which already approved and distributed for the same intended use is desirable.
- Concrete explanation of the usage with mechanism, reaction mechanism, data or the like is desirable.

Below are five examples from information which released to the public in Japan, EU, Australia and New Zealand.

Documents for food additives already assessed in japan are released to the public at "Reports on approval of new designations by food additives unit of food sanitation section meeting of pharmaceutical affairs and food sanitation council" in the website of MHLW. Regarding Australia and New Zealand, documents submitted are released as "Approval Report" in the website of FSANZ. Documents submitted in EU are also released as "Scientific Opinion on safety evaluation of food additives" in the website of EFSA.

(Examples of Actual Cases and examples of description)

Example 1. Excerpt from Additive Subgroup Report Concerning Food Additive Designation of Polysorbate (Japan)

(1) Characteristics as an Emulsifier

Emulsifiers are substances that have a hydrophilic group and lipophilic group in each molecule. Arrayed between water and oil or between water and air, they facilitate emulsification and stabilize mixtures. Emulsifiers may be the O/W type with oil droplets in water, or the W/O type with water droplets in oil. As O/W emulsifiers, polysorbates are strongly hydrophilic and have an HLB[*1], the index of the balance between hydrophilic and lipophilic groups, ranging from 10 to 17. Many conventional emulsifiers have a low or medium HLB with high lipophilicity. Sucrose fatty acid esters and glycerin fatty acid esters can be used to prepare emulsifiers with a wide HLB range by respectively varying their degree of esterification or glycerin polymerization, and the type of fatty acid. Nonetheless, it is thought to be difficult to obtain an HLB as high as a polysorbate. HLBs for polysorbates and other emulsifiers are compiled in the following table. (Ref. X)

Name	HLB
Polysorbates	10 -17[a)]
Fatty acid monoglyceride	3 - 4
Sucrose fatty acid esters	3 - 15
Sorbian fatty acid ester	2 - 8
propylene glycol fatty acid ester	3 - 4
Vegetable lecithin	-

[a)] Polysorbate 20: 16.7; Polysorbate 60: 14.9;
Polysorbate 65: 10.5; Polysorbate 80: 15.0

(2) Emulsifying Power Test for O/W Systems

For a blend of 50 g soy oil and 450 g tap water with no emulsifier as control segment, test segments were prepared by adding 5 g each of the emulsifiers provided in the table, such as polysorbate 60 or glycerin fatty acid ester, to either soy oil or tap water. Soy oil, water, and emulsifier (test segment) were then emulsified with a TK Homo Mixer at 60°C, 10,000 rpm for 5 minutes. The emulsion was transferred to an emulsion test tube and left to stand at room temperature. The amount of separation to the oil layer was measured over time. The test segment employing polysorbate 60 did not result in observation of any oil flotation after 24 hours; however, glycerin fatty acid ester and lecithin caused gelation and uneven emulsification, while sorbitan fatty acid ester and propylene glycol fatty acid ester resulted in 100% oil flotation after 24 hours. Oil droplets were present after 24 hours for sucrose fatty acid ester, demonstrating insufficient emulsifying power. (Ref. X)

[*1] HLB (Hydrophlic Lipophilic Balance) : The Value shows the degree of affinity to oil and water and takes 0 to 20. Lipophilic property becomes higher as it approaches 0 and hydrophlic property becomes higher as it approaches 20.

Emulsifier	The amount of separation to the oil layer				Addition method	HLB
	0.5h	1h	2h	24h		
None	100%	100%	100%	100%	-	-
Polysorbate 60	0%	0%	0%	0%	Add to soy oil	14.9
Glycerin fatty acid ester	Gelatinization	Gelatinization	Gelatinization	Gelatinization	Add to soy oil	3.8
Sucrose fatty acid esters	0%	0%	0%	0%[a)]	Add to water	11
Sorbian fatty acid ester	100%	100%	100%	100%	Add to soy oil	4.7
propylene glycol fatty acid ester	10%	40%	60%	100%	Add to soy oil	3.4
Lecithin	Gelatinization	Gelatinization	Gelatinization	Gelatinization	Add to soy oil	-

[a)] Oil droplets on its surface

Example 2. Excerpt from Additive Subgroup Report Concerning Food Additive Designation of Calcium Silicate (Japan)

(1) Fundamental Properties

a. Formability

A mixture (400 mg) of aspirin granules with enteric coating, excipient, and disintegrator at a weight ratio of 1:2:1 was made into a tablet (tableting pressure 100 MPa) to measure the tableting pressure necessary for obtaining a tablet with a hardness of approximately 5 kgf. Consequently, the use of calcium silicate as excipient was found to afford the lowest tableting pressure and to exhibit favorable formability. (Ref. X)

Excipient	Hardness (kgf)	Tableting pressure (MPa)
Calcium silicate	5.9±0.17	6.8±0.07
Synthetic hydrotalcite	6.0±0.28	46.9±0.06
Crystalline cellulose	5.2±0.21	49.9±0.05
Magnesium aluminometasilicate	5.4±0.14	56.2±0.12
Dried aluminum hydroxide gel	5.5±0.32	74.7±0.23
Cornstarch	5.0±0.58	100.5±0.05

Table 1. The tableting pressure necessary for obtaining a tablet with a hardness of approximately 5 kgf.

b. Liquid absorption

Dibutyl phthalate was used as oily substance in the measurement of liquid absorption volume of calcium silicate and other excipients (three kinds of silicate, crystalline cellulose, corn starch, and calcium monohydrogen phosphate) according to the method provided by JIS K-6220, 26 (1977). The liquid absorption volume of calcium silicate was approximately 7 times its own weight and exhibited liquid retention capacity of approximately 4 to 14 times more than the other excipients, except for light anhydrous silicic acid. (Ref. X)

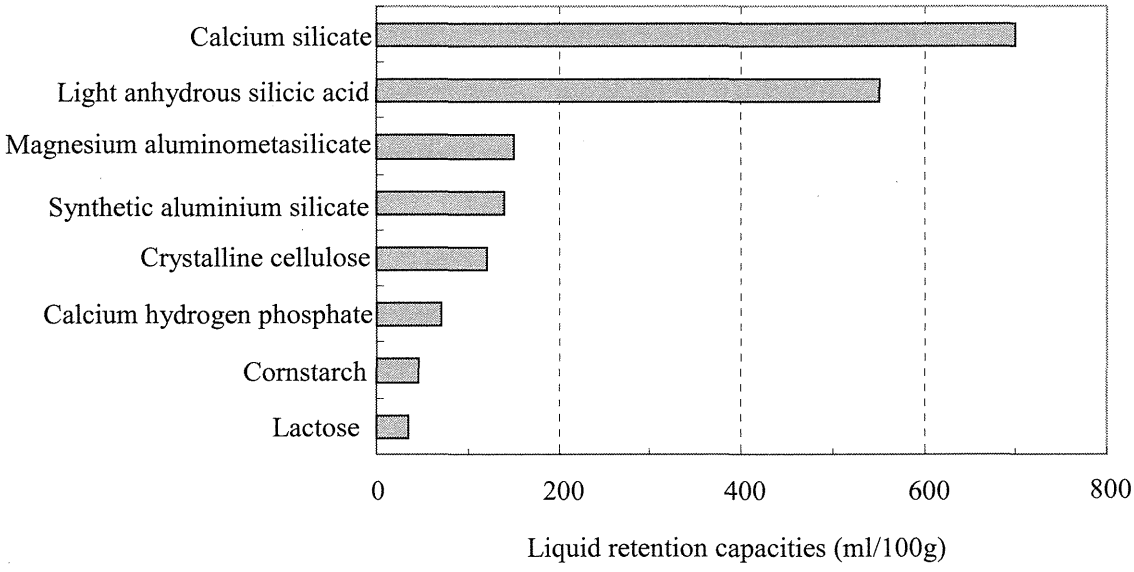


Figure 1. Liquid retention capacities of calcium silicate and the other excipients

(2) Actual Usage in Food Products

In the U.S., the product is employed as an anti-caking agent in powdered drinks such as iced tea, creamed soup, and cocoa, flavorings such as pork spice, cinnamon, and pork gravy, and sweeteners such as cane sugar and aspartame (Ref. X). Its properties of oil absorption and formability lend the product to usage as an excipient for formulations of vitamin E (which is fat-soluble) as powders, granules, or tablets in the field of pharmaceuticals—also in Japan (Ref. X).

Example 3. Excerpt from Additive Subgroup Report Concerning Food Additive Designation of Neotame (Japan)

(1) Sweetness

The sweetness of neotame was assessed by sugar-equivalent sweetness (Reference 1). Respective concentrations (2, 4, 9, 20, 40 ppm) of aqueous neotame solutions were prepared. Sweetness was assessed according to organoleptic testing, and represented by sugar solution concentrations (sugar-equivalent sweetness: %SE) offering comparable sweetness.

The results are shown in Figure 1 as a sugar-equivalent sweetness curve plotted against neotame concentration. According to the fitted curve, the concentration of neotame that provided the same sweetness as 8% sugar (8% SE) was 10.3 ppm.

Comparison of the sweetness between neotame and sugar (Table 1) revealed that the sweetness of neotame was approximately 7,000 to 13,000 times greater than that of sugar.

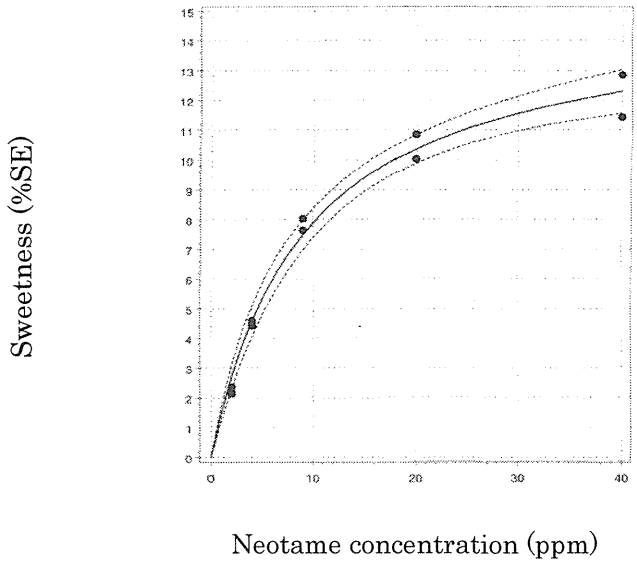


Figure 1. The sugar-equivalent sweetness curve of neotame

● : Measured values —— : A fitted curve --- : 95% confidence limits

The fitted curve:

$$\text{Sweetness (\%SE)} = \frac{\text{Rmax}}{1/K \times 1/C + 1} = \frac{15.1}{9.18 \times 1/C + 1}$$

Rmax : maximum sweetness (%SE), 1/K : The concentration provided the degree of one half of the maximum sweetness (ppm), C : Concentration (ppm)

Table 1. Comparison of the sweetness between neotame and sugar

Sweetness (%SE)	Sweetness magnification (Sugar / Neotame)
3	13181
4	12092
5	11002
6	9913
7	8824
8	7734
9	6645

(2) Stability

With respect to the stability of neotame, hardly any change was observed under long-term storage testing (25°C, 60% RH) across 260 weeks for the measured items, such as properties, content, and the like (Reference 2).

The stability of neotame in solution sustains the effects of pH and temperature. Neotame is relatively stable between the pH range of 3 to 5.5, but becomes more susceptible to hydrolysis at pH3 and below and at 5.5 and

above as the temperature rises (Reference 6). The half-life of neotame at pH 4.5 was about 30 weeks at 25°C, about 45 days at 40°C, and about 40 hours at 80°C. At pH 7, the half-life was about 2 weeks at 25°C, about 3 days at 40°C, and about 4 hours at 80°C.

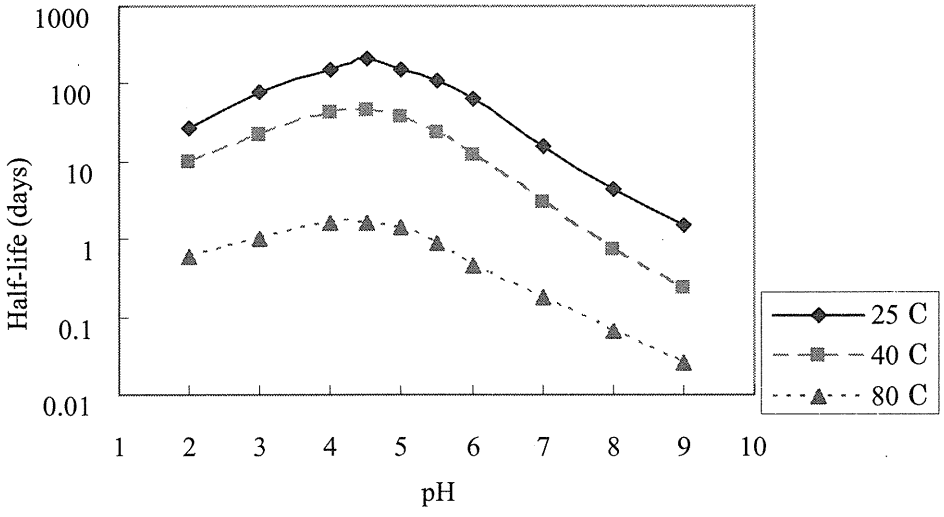


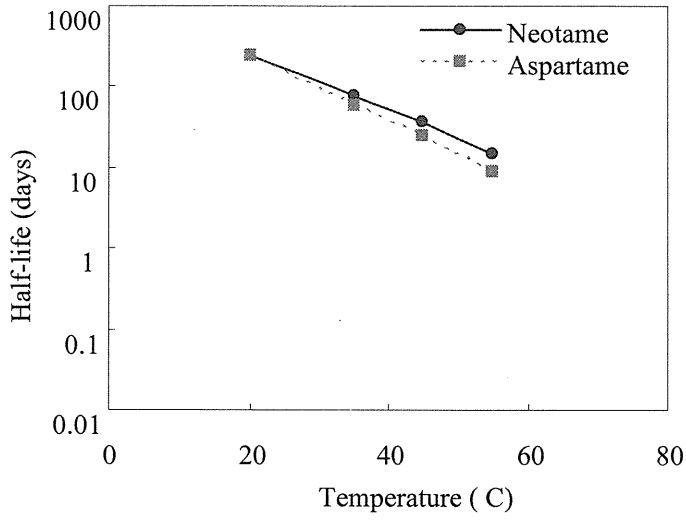
Figure 2. the effects of pH and temperature on the stability of neotame

The report regarding neotame stability compared to aspartame and regarding stability in food products was as follows.

1) Stability Comparison to Aspartame

The comparison of half-life between neotame and aspartame at pH 3.2 and pH 7 is shown below. Under the described conditions, the half-life of neotame was longer. Neotame can be considered as or more stable than aspartame.

(a) pH3.2



(b) pH7

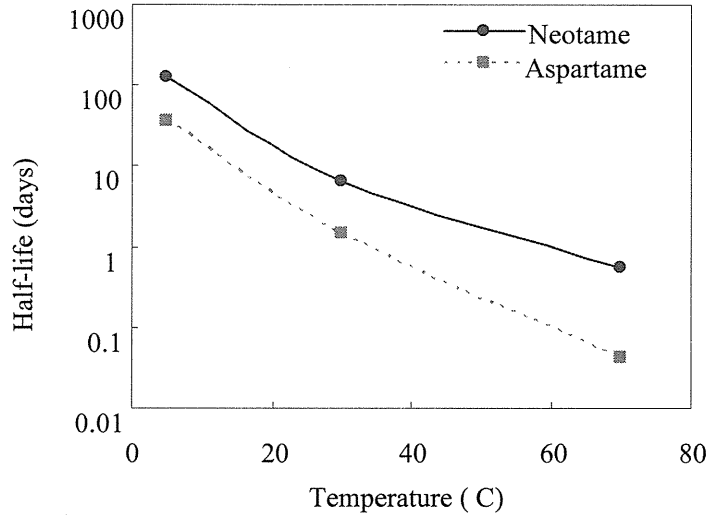


Figure 3 The comparison of half-life between neotame and aspartame

① Thermal stability

Neotame (25 ppm) and aspartame (500 ppm) were respectively added to milk (1% fat, pH 6.5). After the respective mixtures were homogenized, they were subjected to UHT[*1] processing for 8 seconds at 142°C. The sweetener content both before and after UHT processing was analyzed to study the impact of UHT processing of milk on neotame stability. The residual ratios of neotame and aspartame after UHT processing were 91.0% and 69.0%, respectively (Reference 3).

The stability of neotame (25 ppm) and aspartame (525 ppm) after HTST[*2]

[*1] UHT: Ultra-high temperature pasteurization (Ministerial ordinance on Milk and Milk products Concerning Compositional Standards, etc sets this method of pasteurizing more than one second and less than three seconds between 120 C and 150 C using continuous ultrahigh-temperature sterilizer with automatic control device.)

[*2] HTST: High-temperature short-time pasteurization (Ministerial ordinance on Milk and Milk products Concerning Compositional Standards, etc sets this method of pasteurizing 15 seconds or more at 72 C or more using continuous ultrahigh-temperature and short-time sterilizer with automatic control device.)

processing for 40 seconds at 85 C was also compared during yogurt manufacture operation. The residual ratios of neotame and aspartame after HTST processing were 98.7% and 89.5%, respectively (Reference 4).

The heat resistance of neotame (35 ppm) and aspartame (about 2,700 ppm) was also compared during a baking process of yellow cake. The residual ratios of neotame and aspartame were 85.1% and 59.3%, respectively (Reference 5).

② Resistance property for fermentation

The stability of neotame and aspartame was compared during a fermentation process of yogurt (foı 6 hours at 40 C). The residual ratios of neotame and aspartame during the fermentation process were 87.9% and56.0%, respectively (Reference 4).

③ Preservation stability

After refrigerating 8 weeks of yogurt, the stability of neotame and aspartame was favorable without decrease (Reference 3).

After 5 days storage of yellowcake at 25 C and 60% RH, the residual ratios of neotame and aspartame were 94.6% and 83.9%, respectively (Reference 5).

Production / storage	Food	sweetener	pH	temperature	Relative humidity	time	Concentration at early phase		Concentration after processing		Residue ratio of sweetness[b] (%)
							ppm	%SE[a]	ppm	%SE[a]	
UHT processing	Milk[c] (1%fat)	Neotame	6.5	142 C	-	8 seconds	25.0	11.0	22.8	10.8	97.4
		Aspartame	6.5	142 C	-	8 seconds	500.0	7.7	345.0	6.1	80.2
HTST processing	Yogurt[d] (milk)	Neotame	6.5	85 C	-	40 seconds	24.0	10.9	23.7	10.9	99.6
		Aspartame	6.5	85 C	-	40 seconds	519.0	7.8	464.5	7.3	94.0
baking	Yellow cake[e]	Neotame	-	177 C	-	30 minutes	35.1	12.0	29.9	11.5	96.5
		Aspartame	-	177 C	-	30 minutes	2624.7	13.8	1556.1	12.2	88.5
fermentation	Yogurt[c]	Neotame	-	40 C	-	6 hours	23.7	10.9	20.8	10.5	96.3
		Aspartame	-	40 C	-	6 hours	464.5	7.3	260.3	5.1	69.2
storage	Yellow cake[e]	Neotame	-	25 C	60%	5 days	29.9	11.5	28.3	11.4	98.7
		Aspartame	-	25 C	60%	5 days	1556.1	12.2	1306.0	11.6	94.9
storage	Yogurt[d]	Neotame	4.4	5 C	-	8 weeks	20.8	10.5	20.8	10.5	100.0
		Aspartame	4.4	5 C	-	8 weeks	260.3	5.1	254.0	5.0	98.3

[a] The values were calculated using the concentration of neotame or aspartame (A ppm) and the following formula (sugar-equivalent sweetness curve (Reference 2)).

$$\text{Sugar-equivalent sweetness of neotame (\%SE)} = \frac{15.1}{9.18 \times 1/A+1}$$

$$\text{Sugar-equivalent sweetness of aspartame (\%SE)} = \frac{17.1}{610 \times 1/A+1}$$

[b] Residual ratio of sweetness (%) = the sweetness after processing (%SE) / the sweetness at early phase (%SE) x 100

[c] Reference 5

[d] Reference 6

[e] Reference 7

Above results actually applied to foods indicates that neotame can be considered as or more stable than aspartame, analogical sweetener.

2) The stability and chronological change of sweetness in carbonated drink

A carbonated drink similar to Coca-Cola added 17 ppm of neotame (approximately pH3.2) was prepared and stored 26 weeks at 25±2 C. The change of neotame content during preservation period was measured. The chronological change of sweetness was also evaluated using organoleptic test (Reference 7).

The residual concentration after 8weeks was 12.2 ppm (72% of early phase), and 5.9 ppm (35%) after 26 weeks. The sweetness was maintained through 22 weeks (the final residual concentration of neotame was 41% of early phase).

Resolvents from a carbonated drink (200 ppm) after preservation for 8 weeks at 20 C were N-[N-(3,3-dimethylbutyl)-L-α-aspartyl]-L-phenylalanine(NC-00751), N-[N-(3,3-dimethylbutyl)-L-β-aspartyl]-L- phenylalanine 1-methyl ester (NC-00764), N-[N-(3,3-dimethylbutyl)-L-aspartimide]-L-phenylalanine 1-methyl ester (NC-00777) and N-[N-(3,3-dimethylbutyl)-L- aspartimide]-L- phenylalanine (NC-00779) .

3) The stability and chronological change of sweetness in English tea

English tea added 8 ppm of neotame (approximately pH3.2) was prepared and stored 26 weeks at 25±2 C. The change of neotame content during preservation period was measured. The chronological change of sweetness was also evaluated using organoleptic test (Reference 8).

The residual concentration after 8weeks was 6.14 ppm (77% of early phase), and 4.09 ppm (52%) after 26 weeks. The half-life period was estimated to be week 31. At sweetness judgment after 26 weeks storage, 71% of inspectors judged the sweetness was weak or not enough. The sweetness was maintained until approximately week 25.

4) The stability and chronological change of sweetness in chewing gum

A chewing gum added 250 ppm of neotame was prepared and stored 26 weeks at 25±2 C and 60±5% RH. The change of neotame content in week 0, 4, 8, 16 and 26, respectively, was measured. The chronological change of sweetness was also evaluated using organoleptic test (Reference 9). (Table 2)

The residual ratio after 26 weeks was 43% of early phase. The half-life period of neotame in chewing gum

was estimated to be week 21.3. At organoleptic test after 26 weeks storage, 80% of inspectors judged the chewing gum has enough sweetness.

Table 2 Chronological change of amount of neotame in chewing gum (0 ~ 26 weeks storage)

	0 week	4 weeks	8 weeks	16 weeks	26 weeks
Neotame (ppm)	242.7[a)]	222.2[b)]	192.0[b)]	149.9[b)]	103.5[b)]
Residual ratio of neotame (%)	100	92	79	62	43
Sweetness equivalence to sugar (% SE)	14.5	14.5	14.4	14.2	13.9

[a)] Average of repeated 18 times storage [b)] Average of repeated 6 times storage

With above results, it is reported that neotame retains its sweetness for certain period although influenced from pH and temperature and resolves over time.

Example 4. Excerpt from safety evaluation of sodium carboxymethylcellulose (Australia and New Zealand, FSANZ)

3.1 Technological justification

3.1.1 Use of the additive in wine and sparkling wine

The Application requests an extension of use of CMC to enable it to be used in wine and sparkling wine production as an additional tool for preventing clouding and sediment formation resulting from the precipitation of tartrate crystals during storage. Tartrate occurs naturally in wine and is mainly in the potassium form however calcium tartrate can also be present. As a result of change in storage temperature during transport tartrate can crystallize in wine resulting in cloudy wine with sediment which is undesirable to many consumers. Current methods used in Australia to control tartrate crystallization in wine can be divided into two categories: 1) encouraging and accelerating crystal growth followed by removing the crystals by filtering 2) inhibiting crystal precipitation.

The Application explains that the additive works by inhibiting crystal growth in wine. The additive acts as a protective colloid which prevents tartrate crystals seeding and subsequently precipitating. CMC is added to the wine towards the end of the production process unlike other existing tartrate crystal control methods chilling or filtration steps are not required.

Information provided by the applicant states that in contrast to metatartaric acid the effectiveness of this additive is temperature insensitive and thus crystal stability is obtained even with temperature fluctuations, such as those

which occur during storage and transport. However other currently available methods for tartrate crystal control need to be retained as under certain circumstances e.g. for high quality wine, wine which is strongly saturated with tartrate or wines with high levels of calcium tartrate the existing methods may be more suitable.

A maximum use level of 100 mg/L is proposed in the application. Information provided with the application, namely results of tests to investigate the degree of tartrate crystal precipitation overtime is deemed sufficient by FSANZ to demonstrate that the use of CMC at this proposed level is effective.

3.1.2 Evidence of the effectiveness of the additive in wine

The Applicant stated that the additive has been trialled by several major companies, including in Australia, and has provided information to show increased stability of wines treated with CMC compared with untreated or metatartic acid treated wine.

Storage of additive treated wine at 17^0C for 10 months followed by storage at -4^0C for 8 days did not result in visual evidence of crystal precipitation. This test is an OIV accepted method to test the stability of tartrate crystals. In addition storage of additive treated wine at 17^0C for 10 months followed by checking the difference in conductivity by means of the minicontact process, showed the additive treated wine had a low difference in conductivity compared with untreated (Control) or metatartaric acid treated wine. The Applicant provided a paper which stated that low difference in conductivity means high stability with respect to tartrate. This information was provided by the Applicant to demonstrate stability of the wine treated with additive over time.

3.1.3 Cost and environmental advantages

As indicated in Section 3.1.1 above use of CMC for tartrate crystal control does not involve chilling or filtration step, both of which are energy dependent. The Applicant explains that the absence of these steps in wine production utilising CMC results in a more cost effective process with environmental advantages over other existing methods of control.

Example 5. Excerpt from Scientific Opinion on the safety of advantame (EU, EFSA)

Advantame is a high-intensity sweetener enables to add to food categories which allowed to use of high-intensity sweeteners set by EU law. A report estimating degree of sweetness shows advantame is approximately 37,000 times sweeter than sucrose. The food categories and the use level allows addition of advantame are listed in table 2.

Table 2: Food uses and maximum use level for advantame proposed by the applicant (abstract)