SYNTHETIC L-METHIONINE FROM JAPAN

Determination of the Commission in Investigation No. 751-TA-4 Under Section 751 of the Tariff Act of 1930, Together With the Information Obtained in the Investigation

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UNITED STATES INTERNATIONAL TRADE COMMISSION

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CONTENTS

Tables

Note.--Information which would disclose confidential operations of individual concerns may not be published and, therefore, has been deleted from this report. Deletions are indicated by asterisks.

UNITED STATES INTERNATIONAL TRADE COMMISSION
Washington, D.C. 20436

Investigation No. 751-TA-4

SYNTHETIC L-METHIONINE FROM JAPAN

Determination

On the basis of the record 1/ developed in investigation No. 751-TA-4, the Commission unanimously determines, pursuant to section 751 of the Tariff Act of 1930, that no industry in the United States would be materially injured or threatened with material injury, nor would the establishment of an industry in the United States be materially retarded, by reason of imports of synthetic L-methionine from Japan covered by antidumping order T.D. 73-188, if the order were modified to exclude synthetic L-methionine.

Background

This is a section 751 review of a prior Commission determination. On May 14, 1973, in Synthetic Methionine from Japan, Inv. No. AA1921-115, T.C. Pub. No. 578 (May 1973) the Commission determined, pursuant to the Antidumping Act, 1921, that an industry in the United States was being injured by reason of imports of synthetic methionine from Japan determined by the Secretary of the Treasury to be sold, or likely to be sold at less than fair value. The Department of the Treasury published its finding of dumping in the Federal Register on July 3, 1973 (38 F.R. 18382).

On December 15, 1980, the Commission received a request to review its determination of injury in investigation No. AA1921-115 with respect to synthetic L-methionine. The request was filed by Kyowa Hakko U.S.A., Inc., an importer of synthetic L-methionine from Japan.

1/ The "record" is defined in sec. 207.2(j) of the Commission's Rules of Practice and Procedure (19 CFR 207.2(j)).

On April 15, 1981, the Commission published notice in the Federal Register of the proposed institution of a section 751 review investigation regarding synthetic L-methionine from Japan (46 F.R. 22087). Interested persons were given 30 days in which to comment. No comments adverse to institution of the investigation were received.

The Commission instituted review investigation No. 751-TA-4 on May 28, 1981. The purpose of the investigation was to determine whether an industry in the United States would be materially injured or threatened with material injury, or the establishment of an industry in the United States would be materially retarded, if the antidumping order regarding synthetic methionine from Japan were modified to exclude synthetic L-methionine.

Notice of the institution of the Commission's investigation was published in the Federal Register on June 5, 1981 (46 F.R. 30216). The notice gave interested persons 14 days in which to request a public hearing. No such request was made and no public hearing was held. The Commission vote on this investigation was held in publ c session on July 14, 1981.

VIEWS OF THE COMMISSION

Determination

On the basis of the record in investigation No. 751-TA-4, we determine, pursuant to section 751(b) of the Tariff Act of 1930 (19 U.S.C. § 1675(b)), that no industry in the United States would be materially injured or threatened with material injury, nor would the establishment of an industry in the United States be materially retarded, by reason of imports of synthetic L-methionine from Japan covered by antidumping duty order T.D. 73-188, if the order were modified to exclude synthetic L-methionine. 1/

Background

On July 27, 1972, the Treasury Department received a complaint from Monsanto Commercial Products Co. alleging that synthetic methionine from Japan was being imported into the United States in violation of the Antidumping Act, 1921. Monsanto, which was, and still is, a producer of calcium salt of methionine hydroxy analogue (MHA), included specific information concerning DL-methionine imports only. 2/ On the basis of the Monsanto complaint, Treasury began an antidumping proceeding on August 25, 1972. 3/

Treasury's determination of sales at less than fair value was made on February 12, 1973. 4/ Then, on May 14, 1973, the Commission determined that

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1/ Classified under item 425.0420 of the Tariff Schedules of the United States (TSUS). That TSUS item includes all methionines and is a statistical annotation under item 425.04, amino acids.

2/ Letter from D. A. MacDonald, Director of Sales, Monsanto, to R. J. Giadonato (July 24, 1972).

3/ Antidumping Proceeding Notice, Federal Register on August 31, 1972 (37 F.R. 17768).

4/ 38 F.R. 4524 (February 15, 1981).

an industry was being injured by the importation of synthetic methionine from Japan. 5/ The Treasury Department published its finding of dumping in the Federal Register on July 3, 1973 (37 F.R. 18382). The scope of the Commission's determination remains unclear, specifically as to whether the determination was intended to include synthetic L-methionine. 6/ Treasury interpreted the finding as encompassing all synthetic methionine from Japan, including synthetic L-methionine. 7/

On December 15, 1980, Kyowa Hakko U.S.A., Inc., an importer of synthetic L-methionine from Japan, filed a request with the Commission for review of its determination of injury in Inv. No. AA1921-115, with respect to synthetic L-methionine. 8/

Following a request for public comments, the Commission voted to institute investigation No. 751-TA-4 on May 28, 1981. 9/ The notice of

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5/ Synthetic Methionine from Japan, Inv. No. AA1921-115, T.C. Pub. 578 (May 1973).

6/ The "Statement of Reasons" accompanying the determination focuses on the injury caused by synthetic methionine sold in the animal feed market, i.e., by DL-methionine. The discussion about whether a distinction should be made on the basis of use at 3-4, n.3, is directed solely at DL-methionine.

The Commission staff defined "synthetic methionine" to include only DL-methionine; it defined L-methionine as "natural methionine." These definitions appeared in both the questionnaires and the staff report. Staff report on investigation No. AA1921-115 at 3,4,50, and 69; Questionnaires sent to purchasers, importers, and U.S. producers in investigation No. AA1921-115.

7/ Letter from Edward L. Morgan, Ass't Secretary of the Treasury, to H. William Tanaka (July 3, 1973).

8/ Letter from Kohta Fujiwara, Marketing Manager, Kyowa Hakko U.S.A., Inc., to the Secretary of the Commission (December 10, 1980).

9/ This proceeding has been styled as a section 751(b) investigation rather than a proceeding under section 207.46 of the Commission's Rules of Practice and Procedure (19 CFR § 207.46 (1980)). Section 207.46 provides for the modification or clarification of a determination, but limits such clarifications to those made "within a reasonable time." Eight years have elapsed since the determination in investigation No. AA1921-115. No importer of L-methionine from Japan or government agency sought such clarification (footnote continued)

institution was published in the Federal Register on June 5, 1981 (46 F.R. 30216).

The Domestic Industry

The domestic industry consists of all domestic producers of a like product or those producers whose total output of the like product constitutes a major portion of domestic production of that product. 10/ A like product is a product which is like, or in the absence of like, most similar in characteristics and uses with, the imported product which is the subject of the investigation. 11/

We find that there is no domestic product which is "like" synthetic L-methionine, the imported product under review. The "like product", therefore, consists of those forms of synthetic methionine produced in the United States, which are most similar in characteristics and uses to synthetic L-methionine.

Methionine can occur naturally or be synthesized chemically. 12/ It is an amino acid and, thus, is one of the chief constituents of protein. As methionine cannot be synthesized by the human body, it must be obtained through the diet. Normally, people obtain all the methionine they need from

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9/ (footnote continued) during that period. Since review under section 207.46 of the rules is foreclosed by the passage of time, we have turned to section 751(b) as the appropriate means for review. We have, in addition, provided Commerce with an advisory recommendation under section 751(c) regarding unliquidated duties. See fn. 35, infra.

10/ Section 771(4)(A) of the Tariff Act of 1930 (19 U.S.C. §1677(4)(A)).

11/ Section 771(10) of the Tariff Act of 1930 (19 U.S.C. §1677(10)).

12/ There is no known commercial method for extracting L-methionine from natural sources.

sources such as meat, eggs, and milk. The methionine form present in these foods, and the only form to occur in nature, is L-methionine. 13/ Synthetic L-methionine thus serves as a source of methionine for those who cannot obtain the required amounts from foodstuffs because of illness or allergies.

There are five types of synthetically produced methionine: L-methionine, DL-methionine feed grade, DL-methionine U.S.P. (or N.F.) grade, D-methionine, and calcium salt of methionine hydroxy analogue (MHA). Of the five, only DL-methionine feed grade and MHA are produced in the United States. Both of these types differ significantly from L-methionine in physical properties, production processes, costs, and uses.

Synthetic L-methionine is a chemical compound synthesized from two petrochemicals, acrolein and methyl mercaptan. These two chemicals are put through a series of reactions to yield DL-methionine, from which L-methionine can be derived through further processes. In appearance, synthetic L-methionine is a white crystalline powder.

There are two principal uses for synthetic L-methionine. One is to enrich soy-based infant formulas for babies who are allergic to milk protein. The other is in intravenous feedings of hospitalized people. All U.S. consumption of synthetic L-methionine is supplied by imports.

DL-methionine is a mixture of equal amounts of D- and L-methionine. 14/

13/ Because a solution of L-methionine rotates polarized light to the left, this form of methionine is said to be levorotatory, or "L-". See Staff report at A-2.

14/ In solution, D-methionine rotates polarized light to the right, i.e., is dextrorotatory or "D-". It counteracts the leftward effect of the L-methionine and leaves the DL form optically inactive. Thus, a solution of DL-methionine does not rotate polarized light at all. See Staff report at A-3.

DL-methionine feed grade is slightly yellowish in color. 15/ As a prior stage in the synthesis of L-methionine, DL-methionine necessarily is less costly to produce. 16/

The major use of DL-methionine feed grade is as a nutrient added to the feed rations of poultry and swine. A tiny percentage of U.S. purchases of DL-methionine is for use in the production of cephalosporin antibiotics. In this use, DL-methionine is an intermediate in a manufacturing process of which the end product is for human consumption. 17/ Together, these two uses account for nearly 100 percent of U.S. consumption of DL-methionine feed grade.

Calcium salt of methionine hydroxy analogue, or MHA, is the one synthetic methionine form to be produced only in the United States. It has a chemical formula distinct from that of the other methionine forms. MHA is not an amino acid and cannot supply people with their methionine requirement. The only commercial use of MHA is as a dietary supplement in animal feed. Production of MHA begins with the same two petrochemicals with which DL-methionine production begins. The two manufacturing processes are substantially

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15/ In contrast, DL-methionine U.S.P. (or N.F.) grade is whiter in color. DL-methionine feed grade changes color as it is refined into U.S.P. grade. Both grades, however, are of the same methionine form and therefore have the same chemical formula, are optically inactive, and represent the same mixture of D- and L-methionine. The only significant differences are in the higher purity level of the U.S.P. grade and in its higher cost due to the additional purification processes. See Staff report at A-3.

16/ D-methionine is merely a by-product of the isolation of L-methionine; it currently has no commercial use.

17/ Food and Drug Administration regulations relating to amino acids in special dietary and nutritional additives permit the use of DL-methionine in all non-infant products. 21 CFR § 172.320 (1980). However, nearly all therapeutic nutrients for humans now contain only synthetic L-methionine.

similar and cost-competitive. 18/

Neither of the two domestically produced types qualifies as a product "like" synthetic L-methionine. MHA has a chemical formula different from that of synthetic L-methionine and is not an amino acid; DL-methionine feed grade has physical properties different from L-methionine (optical inactivity and a yellowish color) though it shares the L form's chemical formula. Synthetic L-methionine's commercial uses are exclusively in human nutrient markets; MHA's are exclusively in animal feed markets. DL-methionine is used primarily in animal feed and its one pharmaceutical use is one in which L-methionine is not used. Therefore, we find that there is no product manufactured in the United States which is "like" synthetic L-methionine within the meaning of section 771(10) of the Tariff Act of 1930 (19 U.S.C. 1677(10)).

In the absence of such a product, we now turn to a determination of which domestic product is most similar in characteristics and uses to the article under review. The domestically produced good which is "most similar" to the imported product is synthetic methionine of the DL and MHA forms. The slight difference in the chemical formulas of DL-methionine and MHA is not a determining factor in the marketplace. They are commercially fungible as forms of synthetic methionine used in animal feed additives, .

We find, therefore, that the appropriate industry for the purposes of

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18/ Staff report at A-5 and A-7.

this investigation is the domestic producers of DL-methionine and MHA. 19/ Degussa Corp. is the only producer of DL-methionine located in the United States. Monsanto and duPont are the two companies which produce MHA domestically.

Material injury or threat of material injury

We conclude that modification of the synthetic methionine antidumping order 20/ to exclude synthetic L-methionine will not result in material injury or the threat thereof to a domestic industry. Sales of imported synthetic L-methionine have no impact on domestically produced DL-methionine or MHA.

L-methionine occupies a distinct segment of the methionine market. The major market for L-methionine is in soy-based infant formulas for babies allergic to the protein in cow's milk. Infant formula manufacturers account for more than three-quarters of U.S. purchases of L-methionine. The Food and Drug Administration (FDA) does not permit the use of either MHA or DL-methionine as a food additive in infant formulas, 21/ so neither of these products could compete with L-methionine in its major market.

The other commercial markets for L-methionine are in the production of intravenous solutions and infant food additives. 22/ In these markets, MHA

19/ Chairman Alberger notes that the above analysis of "domestic industry" and "like product" is technically correct, but may be overly tedious. In his view, the overriding objective here is to find whether any relevant industry is injured by the imports in question. The industry worthy of analysis clearly is the producers of methionine products, and they really do not compete with the imports in question. Thus, the case is quite easy and need not be complicated by extensive analysis.

20/ T.D. 73-188.

21/ 21 CFR § 172.320(a) (1980); Staff report at A-3,8.

22/ Staff report at A-7-8.

would be unacceptable because it is not an amino acid and cannot supply people with their methionine requirement. FDA regulations, therefore, do not permit its use as a special dietary or nutritional additive in foods intended for human consumption. 23/ Although FDA regulations permit the use of DL-methionine in non-infant nutritional preparations, recent studies of DL-methionine utilization in human beings have shown that D-methionine is poorly utilized by the human body. 24/ When human beings consume DL-methionine, large amounts of D-methionine are not metabolized and are excreted in the urine. 25/ The use of DL-methionine in therapeutic nutrient products has virtually disappeared. Most, if not all, manufacturers of intravenous solutions and non-infant nutritional preparations use only L-methionine. 26/ Neither domestically produced DL-methionine nor MHA would be a satisfactory substitute for L-methionine in nutritional preparations. Sales of imported L-methionine from Japan in the therapeutic nutrient market do not represent a loss to a U.S. industry.

Conversely, imported synthetic L-methionine could not penetrate markets currently held by domestic DL-methionine feed grade or MHA. Almost all U.S.-produced DL-methionine and MHA is used as a supplement in animal and poultry feeds. 27/ Although it is theoretically possible to use L-methionine

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23/ 21 CFR § 172.320 (1980). Animals, unlike humans, can convert MHA into methionine amino acid in their bodies. Consequently, MHA's commercial use is as a dietary supplement in animal feed. FDA regulations list MHA as a suitable dietary supplement for animals. 21 CFR § 582.5477 (1980).

24/ See, generally, the articles cited in Staff report at A-8, fn. 1 & 2.

25/ Staff report at A-8.

26/ Id.

27/ DL-methionine feed grade competes with MHA in the animal feed market. DL-methionine is slightly more efficient than MHA, such that 1 pound of DL-methionine is equivalent to 1.2 pounds of MHA. The two are, however, competitively priced. Staff report at A-6-7.

in animal feed, as a practical matter, this is never done. Poultry, swine, and certain other animals can metabolize both D-methionine and L-methionine. DL-methionine, therefore, is nearly as efficient as L-methionine and a good deal cheaper, since the extra production processes required to separate and purify L-methionine greatly increase its cost. 28/ The average per unit value of DL-methionine feed grade was $1.14 per pound in 1979, while that of L-methionine was approximately $15.00 per pound. 29/ Similarly, while MHA is slightly less efficient than DL-methionine, it is competitively priced, and shares DL-methionine's cost advantage over L-methionine.

A small percentage of DL-methionine has been consumed in the production of cephalosporin antibiotics. 30/ These antibiotics are fermented from a mold, celphalosporin acremonium, which requires methionine in its diet. DL-methionine satisfies the mold's methionine needs and, in addition, is a source of sulphur. 31/ Hence, L-methionine has no inherent advantage over DL-methionine and may even be at a disadvantage. In view of the wide disparity in the prices of L-methionine and DL-methionine and the absence of any advantage from using L-methionine, there is no reason for an antibiotic producer to switch.

28/ Staff report at A-4.

29/ Staff report at Table 1, p. A-45. This disparity has existed for some time. In 1963, the per unit values of DL-methionine and L-methionine from Japan were $1.46 per pound and $5.45 per pound respectively; the per unit values of German DL-methionine and L-methionine were $.90 and $10.62 respectively. Staff report on Investigation No. AA-1921-115, at Table 5, p. 50.

30/ Staff report at A-8.

31/ Letter from C. Harvey Bradley, Jr., General Counsel of Eli Lilly and Co., to the Secretary of the Tariff Commission (February 26, 1973) (Exhibit B of attached letter).

We conclude that imported L-methionine from Japan does not compete with domestically produced varieties of synthetic methionine. Synthetic L-methionine occupies a discrete and insular section of the methionine market. Under current market conditions, DL-methionine or MHA could not or would not be used in place of L-methionine or vice versa.

Material retardation of the establishment of a domestic industry

Modification of the synthetic methionine dumping order will not materially retard the establishment of a synthetic L-methionine industry. During the period covered by the dumping order, there were no attempts to begin production of synthetic L-methionine in the United States. 32/ The staff was unable to uncover any indication that any firm considered commencing production of L-methionine in the United States, or that any firm decided to forego such production for reasons related to the importation of synthetic L-methionine from Japan. 33/

No company reported plans to commence L-methionine production in the future. 34/ The unsubstantiated possibility that modification of the antidumping order to exclude methionine will materially retard the establishment of a domestic industry is pure speculation and an insufficient basis for retaining the dumping order.

32/ The issue of material retardation relates to the establishment of an industry producing a "like" product, i.e., synthetic L-methionine.
33/ Staff report at A-6.
34/ Id.

Conclusion

After review of the information developed in the course of this investigation, we determine that the antidumping order, T.D. 73-188, should be modified to exclude synthetic L-methionine from Japan. 35/

35/ The Department of Commerce has asked us to recommend a date as of which the dumping order should be revoked pursuant to section 751(c) of the Tariff Act of 1930. There has been a good deal of confusion concerning the application of the Commission's determination in AA1921-115 to synthetic L-methionine. Our review of the record in our earlier investigation has convinced us that synthetic L-methionine was not within the scope of the Commission's investigation. See fn. 5, supra. As the Commerce Department has requested our recommendation, we recommend that the dumping order be retroactively revoked as to unliquidated entries of synthetic L-methionine entered, or withdrawn from the warehouse for consumption, on or after July 3, 1973.

INFORMATION OBTAINED IN THE INVESTIGATION

Introduction

On May 28, 1981, the U.S. International Trade Commission instituted review investigation No. 751-TA-4 under section 751(b) of the Tariff Act of 1930, 19 U.S.C., 1675(b). Notice of the Commission's investigation was published in the Federal Register of June 5, 1981 (46 F.R. 30216). 1/ The purpose of the investigation is to determine whether an industry in the United States would be materially injured, or would be threatened with material injury, or the establishment of an industry in the United States would be materially retarded, if the antidumping order regarding synthetic methionine from Japan were to be modified or revoked with respect to synthetic L-methionine, provided for in item 425.04 of the Tariff Schedules of the United States (TSUS).

On May 14, 1973, the Commission determined that an industry in the United States was injured within the meaning of the Antidumping Act, 1921, by reason of imports of synthetic methionine from Japan determined by the Secretary of the Treasury to be sold, or likely to be sold, at less than fair value (LTFV) within the meaning of the Antidumping Act, 1921. On July 3, 1973, the Department of the Treasury issued a finding of dumping, which was published in the Federal Register of July 10, 1973 (38 F.R. 18382).

On December 15, 1980, the Commission received a request to review its affirmative determination in investigation No. AA1921-115, synthetic methionine from Japan, with respect to synthetic L-methionine. The request was filed by Kyowa Hakko U.S.A., Inc., an importer of synthetic L-methionine from Japan.

The Commission requested comments from the public regarding the proposed institution of a review investigation in a notice published in the Federal Register on April 15, 1981 (46 F.R. 22087). 1/ No comments adverse to institution were received. Accordingly, on the basis of the Kyowa Hakko request and other information, the Commission, on May 28, 1981, voted to institute investigation No. 751-TA-4. The notice of institution of the investigation was published in the Federal Register of June 5, 1981 (46 F.R. 30216) and gave interested persons 14 days after publication of the notice in which to request that a public hearing be held.

No public hearing was requested and no public hearing was held. Pursuant to section 207.45(b) of the Commission's Rules of Practice and Procedure, published in the Federal Register of March 23, 1981 (46 F.R. 10823), the

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1/ Copies of the Commission's notices related to this investigation are presented in app. A.

Commission is required to complete its investigation within 120 days of the institution of the investigation, or by September 26, 1981. However, the Commission has indicated that it wishes to expedite the conduct of this investigation and currently is scheduled to report its determination to the Department of Commerce by July 22, 1981.

Description and Uses

Synthetic L-methionine

The imported article under investigation is synthetic L-methionine, a form of synthetic methionine. Methionine is an amino acid with the chemical name of 2-amino-4-(methylthio)butyric acid. Methionine is one of the essential amino acids that must be supplied in the diets of humans and animals. Humans, under usual conditions, obtain required amino acids, such as methionine, from proteins in their diets. Proteins found in eggs, beef, and milk are sources of amino acids, including methionine, for humans. Under certain special conditions, usually medically related, a methionine deficiency may occur.

The different forms of methionine can be distinguished in terms of their optical activity. Methionine exists as two optically active isomers, or as a mixture of the two isomers. Optical isomers differ from one another in the way the atoms, or groups of atoms, of the chemical molecule are arranged in space. The molecular formulas and the molecular weights of the isomers are identical. It is not unusual, however, for the optical isomers to have significantly different physiological properties. The isomers are called optically active because when polarized light is passed through a medium containing one type of isomer, the plane of polarization is rotated. If the isomer rotates the polarized light to the right, it is known as dextrorotatory (D), and if the polarized light is rotated to the left, the isomer is called levorotatory (L). If the D and the L isomers are mixed in equal portions, then the mixture is not optically active, and the mixture is called racemic (DL). In this report, capital letters are used to abbreviate the isomers to avoid confusing a lowercase letter with an Arabic numeral.

All of the amino acids that occur naturally in food proteins are present as the optically active L-isomers. Thus, naturally occurring methionine obtained from food is L-methionine. However, any synthetic process which produces optically active amino acids yields a racemic mixture. Thus, synthetic processes for producing methionine yield DL-methionine that is a racemic mixture, half of which is D-methionine and half, L-methionine. Procedures to separate racemic mixtures of methionine into L-methionine and D-methionine are complex and costly. Synthetic L-methionine is, therefore, a more advanced and costly product than DL-methionine, and L-methionine sells for more than 10 times the price of animal-feed-grade DL-methionine.

The article considered in this investigation is synthetic L-methionine, as opposed to D-methionine or DL-methionine. Synthetic L-methionine is a white crystalline powder with a slight characteristic odor. It is optically active, and a solution containing L-methionine rotates polarized light to the left, thus providing a simple method of distinguishing synthetic L-methionine from other forms of synthetic methionine.

The major end use for L-methionine is in certain formulas having a soy-protein base for infants that are allergic to protein from cow's milk. Food and Drug Administration (FDA) regulations prohibit the use of DL-methionine in infant foods, so only L-methionine can be used in these products. 1/ A wide range of therapeutic nutrient preparations are available for infants and for oral and tube feeding of children and adults. Many of these products contain added synthetic L-methionine to bring methionine levels up to required nutritional standards. According to FDA regulations, all food additive chemicals must meet the specifications as published in the Food Chemicals Codex. 2/

The other principal end use for L-methionine is in amino acid solutions for intravenous feeding of hospitalized humans. These intravenous amino acid solutions are often mixtures of 10 to 15 amino acids. Synthetic L-methionine is one of the amino acids used to make these solutions. These therapeutic amino acid solutions are used when there is interference with ingestion, digestion, or absorption of protein for long periods, or when intravenous supplementation of oral protein intake is required. These amino acid solutions must be pathogen free so great care must be exercised in their production.

DL-methionine

It is important to distinguish DL-methionine from L-methionine. DL-methionine is a mixture of D-methionine and L-methionine. The mixture is not optically active, and is marketed in two grades--animal-feed grade and United States Pharmacopeia (U.S.P.) or National Formulary (N.F.) grade. The U.S.P. or N.F. grade is identical and conforms to the Food Chemicals Codex specifications. 3/ The U.S.P. or N.F. grade of DL-methionine (racemethionine) differs from animal-feed-grade DL-methionine only in purity, and it can be produced from feed-grade material by certain chemical purification processes. The purification processes increase the cost of U.S.P. grade, and U.S.P.-grade DL-methionine sells for about two times the price of animal-feed-grade DL-methionine. The principal use of DL-methionine is as an animal-feed supplement, mostly in poultry and swine feeds. Small quantities of DL-methionine are used in pharmaceutical preparations and in the production of certain antibiotics.

The calcium salt of the hydroxy analog of methionine

There is a chemical related to methionine which has been produced in the United States. The related chemical, DL-2-hydroxy-4-(methylthiobutyrate)Ca, is the calcium salt of the hydroxy analog of methionine. The chemical differs from DL-methionine in that the amino group of the chemical molecule has been

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1/ Relevant FDA regulations on amino acids, including methionine, are reproduced in app. B.

2/ Relevant portions of the Food Chemicals Codex, 2d ed., and the recently published 3d ed. are reproduced in app. B.

3/ Relevant portions of The United States Pharmacopeia - The National Formulary, official from July 1, 1980, are reproduced in app. B.

replaced by a hydroxy group and the acid neutralized with calcium hydroxide to form the calcium salt. The hydroxy analog, therefore, is not an amino acid, and does not have the same chemical structure as methionine.

A number of animal species, especially poultry and swine, utilize the calcium salt of the hydroxy analog of methionine as effectively as DL-methionine when the hydroxy analog salt is added to their feed ration. That is, the calcium salt of the hydroxy analog of methionine and animal-feed-grade DL-methionine are equivalent and directly competitive products in the animal-feed market.

The calcium salt of the hydroxy analog of methionine is not metabolized by humans, is not included in the Food Chemicals Codex, and is not approved by FDA for use in human nutrition. The calcium salt of the hydroxy analog of methionine is not, therefore, competitive with synthetic L-methionine.

Production Processes

Most processes for the production of synthetic methionine start with acrolein and methyl mercaptan. Acrolein is obtained by the oxidation of propylene, and methyl mercaptan is obtained by reacting methyl alcohol with hydrogen sulfide. Acrolein and methyl mercaptan go through several chemical reactions to produce methionine, and these reactions also utilize chemicals such as hydrogen cyanide, ammonia, and sulfuric acid. All of the chemicals used to produce methionine by synthesis are readily available industrial organic and inorganic chemicals. In addition to the process steps that involve chemical reactions, there are a number of separation, recovery, and purification steps. The reaction product of the methionine chemical synthesis process is DL-methionine or, in a variation of the process, the calcium salt of the DL-methionine hydroxy analog.

The DL-methionine must be further processed in order to produce synthetic L-methionine. A number of physical and chemical methods have been used to separate optical isomers. The principal method used to isolate L-methionine from DL-methionine is through enzymatic decomposition of various chemical derivatives of DL-methionine such as esters, carbamates, and acrylates. A selected enzyme decomposes only the L-methionine derivative, and the D-methionine derivative remains unchanged. The resulting L-methionine is then isolated through routine chemical or physical procedures. The remaining D-methionine derivative is racemized (converted to DL-methionine) chemically or enzymatically and recycled.

The isolation of L-methionine from DL-methionine adds substantially to its cost, and this is the major reason that L-methionine is too costly for use in the animal-feed business at this time.

U.S. Tariff Treatment

Imports of synthetic L-methionine are classified under item 425.0420 of the Tariff Schedules of the United States Annotated (TSUSA). Item 425.0420, methionine, is a statistical annotation under item 425.04, amino acids. The

column 1 rate of duty for item 425.04, and for all annotations thereunder, is 5.6 percent ad valorem. The least developed developing country (LDDC) rate of duty is 4.2 percent ad valorem, and the column 2 rate of duty is 25 percent ad valorem.

The column 1 rate of duty is the most-favored-nation (MFN) rate, and is applicable to imported products from all countries except those Communist countries and areas enumerated in general headnote 3(f) of the TSUS. However, such rate does not apply to products of developing countries which are granted preferential tariff treatment under the Generalized System of Preferences (GSP) or under the LDDC rate of duty column.

Imports of synthetic methionine from Japan are subject to "dumping duties" as a result of an affirmative determination by the Commission in investigation No. AA1921-115 and a finding of dumping by the Department of the Treasury on July 3, 1973. In 1973, the average LTFV margin was * * * percent; the range of LTFV margins was from * * * to * * * percent. Currently, the LTFV margins for synthetic methionine from Japan are under review by the U.S. Department of Commerce. Results from the current review are not available.

The U.S. Industry

In 1973, there were no domestic producers of methionine, as such. Two firms, E. I. du Pont de Nemours & Co., Inc., and Monsanto Co. produced the calcium salt of the hydroxy analog of DL-methionine, DL-2-hydroxy-4-(methylthiobutyrate)Ca. The hydroxy analog is a more advanced product in the sense that additional manufacturing steps and chemical reactions are required in its production. The manufacturing process is, however, cost competitive with the process which yields animal-feed-grade DL-methionine, and the products compete in precisely the same market. In 1977, E. I. du Pont de Nemours & Co., Inc., doubled its domestic capacity to produce the hydroxy analog.

In 1978, Degussa Corp., a U.S. subsidiary of a West German firm, began producing animal-feed-grade DL-methionine in the United States. * * *.

Currently, E. I. du Pont de Nemours & Co., Inc., and the Monsanto Co. produce the calcium salt of the hydroxy analog of DL-methionine in the United States. Monsanto is building a new plant that, when completed, will be the world's largest plant for producing a methionine-related chemical. Plant capacity will be 100 million pounds per year. 1/ * * *.

* * * * * * *

Currently, there are no domestic producers of synthetic L-methionine, nor were there any domestic producers of synthetic L-methionine in 1973. In addition, there are no known domestic producers of natural L-methionine, which would compete with imported synthetic L-methionine.

1/ Chemical Marketing Reporter, Apr. 20, 1981.

Injury or Threat of Injury or Prevention of Establishment of a U.S. Industry by Reason of Imports of Synthetic L-Methionine from Japan

All domestic producers of DL-methionine, or the calcium salt of the hydroxy analog of methionine, were contacted by the Commission and asked the following questions:

(1) If they are now producing, or if they had ever produced, synthetic L-methionine in the United States.

(2) If they intend to produce synthetic L-methionine in the United States.

(3) If they had considered producing synthetic L-methionine in the United States and decided not to for reasons related to the importation of synthetic L-methionine from Japan.

(4) If synthetic L-methionine competes in the same markets with any of their domestically produced products.

Each of the firms responded no to each of the above questions.

The U.S. Markets

There are basically two U.S. markets for methionine. The largest market, by far, is the market for methionine as an additive to animal feeds. The other market is as an additive in therapeutic nutrients for humans. These markets utilize different grades or different forms of methionine, and because of the factors discussed below, there is little or no fungibility of products between the two markets.

The animal-feed market

The principal U.S. market for methionine and the calcium salt of its hydroxy analog is the animal-feed market. The calcium salt of the hydroxy analog of DL-methionine and/or animal-feed-grade DL-methionine are routinely added to poultry and swine feeds. Although the hydroxy analog of methionine is not an amino acid, studies have shown that there is little difference in the efficacy of methionine and its hydroxy analog when these are added to soy-protein animal feeds. In addition, studies have shown that both D-methionine and L-methionine are metabolized by a number of animal species. 1/ 2/ The calcium salt of the hydroxy analog of methionine is directly competitive with

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1/ David H. Baker, and Katherine P. Boebel, "Utilization of the D- and L-Isomers of Methionine and Methionine Hydroxy Analog as Determined by Chick Bioassay," The Journal of Nutrition, vol. 110, May 1980.

2/ Ei Soon Cho, et al., "D-Methionine Utilization in Young Miniature Pigs, Adult Rabbits, and Adult Dogs," Journal of Parenteral and Enteral Nutrition, vol. 4, No. 6, November-December 1980.

animal-feed-grade DL-methionine. When the two products are put on a 100-percent-methionine basis (i.e., 1 pound of DL-methionine is equivalent to 1.2 pounds of the hydroxy analog, calcium salt), then animal-feed-grade DL-methionine and the calcium salt of the hydroxy analog are competitively priced. Since DL-methionine is completely metabolized by poultry, swine, and many other animals, there is no efficacy advantage in the animal-feed market for L-methionine. Because L-methionine is a more advanced and much more expensive product than DL-methionine and offers no nutritional advantage to most animals, L-methionine is not utilized in animal feeds. 1/

According to the U.S. Department of Agriculture, about 4.5 billion chickens and turkeys were produced in 1980 compared with about 3.5 billion in 1973. Hog production was about 64.5 million in 1980 compared with 60.6 million in 1973. Animal-feed-grade DL-methionine or the calcium salt of the hydroxy analog of methionine is routinely added to feed for these animals, so the market for these products is large and growing. Approximately 86 million pounds of feed-grade DL-methionine, and/or the calcium salt of the hydroxy analog of methionine, valued at roughly $97 million, were consumed in the animal feed industry in 1979 (table 1, app. C).

The therapeutic nutrient market

The market for synthetic L-methionine is quite different from that served by domestically produced methionine. In contrast to animal nutrition, L-methionine is not routinely added to the diets of normal healthy humans, but is added to products that are usually consumed under special circumstances and under medical advice or supervision. The U.S. purchasers of synthetic L-methionine are, for the most part, those firms that produce crystalline amino acid solutions for intravenous feeding and those firms that use synthetic L-methionine as an additive to certain soy-based complete nutritional formulations, mostly infant formula diets. In addition, some nutritional preparations used as supplements in specific nutritional deficiencies also contain synthetic L-methionine. Producers of intravenous amino acid solutions often purchase blends or mixtures of 10 to 15 different amino acids rather than L-methionine alone.

Relatively few U.S. firms account for most of the U.S. purchases of synthetic L-methionine. Questionnaires were sent to 5 firms that purchased * * * percent of the quantity of synthetic L-methionine sold by importers during 1980. Details of the purchases by these firms for the period January 1, 1978, through March 31, 1981, are presented in table 2. All of these purchasers stated that for their purposes, there is no other product that can be substituted for L-methionine.

A few years ago, some of the U.S. producers of therapeutic nutrient products used DL-methionine in their products because, at that time, some

1/ The average unit value of sales of animal-feed-grade DL-Methionine and the calcium salt of the hydroxy analog of methionine was $1.14 per pound in 1979; the average unit value of L-methionine sales was $15.10 per pound in 1979.

experts in nutrition believed (based upon animal studies) that both D-methionine and L-methionine were metabolized by humans. Since DL-methionine (which is 50 percent D-methionine and 50 percent L-methionine) is much less costly than the isolated L-methionine, there is an economic incentive to use DL-methionine. FDA regulations, however, prohibit the use of DL-methionine in infant foods, the largest market for therapeutic nutrients.

According to nutritional experts in industry, the FDA, and universities, it is now well established that D-methionine is "poorly utilized" by humans. 1/ 2/ If DL-methionine is fed to humans, either intravenously or internally (through the gastrointestinal system), large amounts of D-methionine are excreted in the urine. The L-methionine is, for all practical purposes, completely metabolized by humans. Thus, L-methionine has become the preferred form of methionine for use in therapeutic nutritional products. Most, if not all, of the producers of therapeutic nutrients containing added methionine now use only synthetic L-methionine.

In comparison with the animal-feed market, the market for synthetic L-methionine is very small. In 1980, for example, sales of L-methionine totaled 77,731 pounds, valued at about $1.2 million (table 3). In terms of quantity, L-methionine sales are about 0.1 percent of the quantity of methionine consumed in animal feeds. In terms of value, the L-methionine market is about 1 percent of the size of the animal-feed methionine market.

Other markets for methionine

The other markets for methionine are not as well defined as the animal feed and therapeutic nutrient markets. Small quantities of DL-methionine are used in some dietary supplement and vitamin and mineral preparations. Small quantities are also used in the fermentation process that produces certain cephalosporin antibiotics. In addition, some DL-methionine is used in drug and pharmaceutical products.

Like many chemicals, methionine is therapeutic when properly used, but can be toxic if consumed at excessive levels. 3/

U.S. Imports

In 1980, there were four importers of synthetic L-methionine. These importers, Ajinomoto U.S.A, Inc.; * * *; Kyowa Hakko U.S.A., Inc., and

1/ Kenneth J. Printen, et al., "Utilization of D-Methionine During Total Parenteral Nutrition in Postsurgical Patients," The American Journal of Clinical Nutrition, vol. 32, June 1979, pp. 1,200-1,205.

2/ Lewis D. Stegink, et al., "D-Methionine Utilization in Adult Monkeys Fed Diets Containing DL-Methionine," The Journal of Nutrition, vol. 110, No. 6, June 1980.

3/ Norlin J. Benevenga, "Toxicities of Methionine and Other Amino Acids," Agricultural and Food Chemistry, vol. 22, No. 1, January-February 1974, pp. 2-9.

Tanabe U.S.A, Inc., accounted for all of the known imports of synthetic L-methionine in 1980. The quantity and foreign value of imports of synthetic L-methionine, by firms, are presented in table 4. Inventories of imported L-methionine, by firms, are presented in table 5 for the period December 31, 1977, through March 31, 1981. Data on all imports of all methionine under TSUSA item 425.0420 are presented in table 6.

The principal importers of synthetic L-methionine are U.S. subsidiaries of Japanese firms, Ajinomoto Co., Inc., Tokyo, Japan; Tanabe Seiyaku Co., Ltd., Osaka, Japan; and Kyowa Hakko Kogyo Co., Ltd., Tokyo, Japan. The only other significant importer of synthetic L-methionine is * * *; all of its imports are from West Germany.

Table 6 presents data on imports of all methionine under TSUSA item 425.0420. Most of the imports of methionine during the period January 1, 1976, through March 31, 1981, were animal-feed-grade DL-methionine. In 1980, 99 percent of total imports of methionine (on the basis of quantity) were of animal-feed-grade DL-methionine from France. The average unit value of imports of animal feed grade DL-methionine from France was $1.18 per pound in 1980 (table 6) compared with the average unit value of $12.29 (table 4) per pound for imported synthetic L-methionine in 1980. In 1980, imports of synthetic L-methionine accounted for about 0.2 percent of the total quantity of all methionine imports and about 2.2 percent of total value of all methionine imports (table 1).

Table 6 shows a drop in imports of methionine from Japan from 6.4 million pounds in 1978 to 68,000 pounds in 1979. Also, this table shows a drop in imports of methionine from West Germany and the Netherlands from 2.3 million pounds collectively in 1977 to 9,000 pounds collectively in 1979. These decreases were, most probably, a result of the startup in mid-1978 of Degussa's U.S. plant that produces animal-feed-grade DL-methionine. It also appears that Degussa's U.S. production of methionine may have displaced most imports of animal-feed-grade DL-methionine from Japan. Degussa's plant had little or no effect on imports from France, however, and imports of animal-feed-grade DL-methionine from France increased 38 percent, from 16.2 million pounds in 1978 to 22.4 million pounds in 1979.

The Petitioner and Other Interested Parties

The petitioner, Kyowa Hakko U.S.A., Inc. (Hakko), is an importer of synthetic L-methionine from Japan. The synthetic L-methionine imported by this firm is manufactured by its parent firm, Kyowa Hakko Kogyo, Tokyo, Japan.

In its petition, Hakko states that synthetic L-methionine is not used in the animal-feed market and is not price competitive with the types of methionine used in the animal-feed market. Also, Hakko states that the application of a dumping duty, since 1973, to imports of synthetic methionine from Japan has not resulted in production of synthetic L-methionine in the United States.

Upon institution of investigation No. 751-TA-4 on May 28, 1981, the Commission allowed until June 19, 1981, for any person with an interest in the

investigation to file written submissions. A submission was filed with the Commission on behalf of Tanabe Seiyaku Co., Ltd., and Tanabe U.S.A., Inc., in support of the Hakko petition. Tanabe stated that synthetic L-methionine is not like any form of synthetic methionine produced in the United States and that no domestic industry has produced synthetic L-methionine in the years since the finding of dumping in 1973. In addition, Tanabe feels that any modification or revocation of the antidumping order with respect to synthetic L-methionine should be made retroactive to July 3, 1973.

A submission was filed with the Commission on behalf of Ajinomoto U.S.A., Inc., in support of the Hakko petition. Ajinomoto states that synthetic L-methionine is used for human consumption, and not used in the animal-feed market, and that synthetic L-methionine is not competitive with any product produced in the United States. In addition, Ajinomoto asks that the antidumping order be modified or revoked with respect to other forms of methionine, in addition to synthetic L-methionine.

No submissions were received by the Commission in opposition to modifying or revoking the antidumping order with respect to synthetic L-methionine from Japan.

APPENDIX A

THE COMMISSION'S NOTICES

UNITED STATES INTERNATIONAL TRADE COMMISSION
Washington, D.C. 20436

Investigation No. 751-TA-4

Synthetic L-Methionine from Japan

NOTICE OF INSTITUTION OF SECTION 751(b) REVIEW INVESTIGATION 1/

AGENCY: United States International Trade Commission.

ACTION: Institution of Section 751(b) review investigation concerning affirmative determination in Investigation No. AA1921-115, Synthetic Methionine from Japan.

SUMMARY: Notice is hereby given that the U.S. International Trade Commission has initiated an investigation pursuant to section 751(b) of the Tariff Act of 1930, 19 U.S.C. § 1675(b) (Supp. III 1979), to review its determination in investigation No. AA1921-115. The purpose of the investigation is to determine whether an industry in the United States would be materially injured, would be threatened with material injury, or the establishment of an industry in the United States would be materially retarded, if the antidumping order regarding synthetic methionine from Japan were to be modified or revoked with respect to synthetic l-methionine provided for in item 425.04 of the Tariff Schedules of the United States.

SUPPLEMENTARY INFORMATION: On May 14, 1973, the Commission determined that an industry in the United States was injured within the meaning of the Antidumping Act, 1921, by reason of imports of synthetic methionine from Japan determined by the Secretary of Treasury to be sold or likely to be sold at less than fair value (hereinafter "LTFV").

1/ Federal Register, 46 F.R. 30216, June 5, 1981.

On July 3, 1973, the Department of the Treasury issued a finding of dumping, 7 Cust. B. 630 (1973); T.D. 73-188, and published notice thereof in the Federal Register, 38 F.R. 18382.

On December 15, 1980, the Commission received a request to review its affirmative determination in investigation No. AA1921-115. The request was filed under section 751(b) of the Tariff Act of 1930 by Kyowa Hakko USA, Inc., an importer of synthetic l-methionine from Japan.

The Commission requested comments from the public regarding the proposed institution of a review investigation in a notice published in the Federal Register on April 15, 1981 (46 F.R. 22087). No comments adverse to institution were received. Accordingly, on the basis of the Kyowa Hakko petition and information obtained by the Commission staff, the Commission on May 28, 1981, voted to institute investigation No. 751-TA-4. The Commission determined that the petition showed that following changed circumstances sufficient to warrant review: (1) the likelihood that there is no industry in the United States which produces synthetic l-methionine, and (2) the likelihood that synthetic l-methionine from Japan is not like any form of syntnetic methionine produced in the United States.

The investigation will be conducted in accordance with section 207.45(b) of the Commission's Rules of Practice and Procedure (46 F.R. 18023) (March 23, 1981). The purpose of this investigation is to determine whether an industry in the United States would be materially injured, would be threatened with material injury, or the establishment of an industry in the United States would be materially retarded if the present antidumping order were to be modified or revoked to exclude synthetic l-methionine. Modification or revocation of the dumping finding as to synthetic l-methionine would not affect the Commission's affirmative determination as to other forms

of synthetic methionine from Japan.

Dates: Pursuant to section 207.45(b) of the Commission's Rules of Practice and Procedure (46 F.R. 18023 (March 23, 1981)), the 120 day period for completion of this investigation began on May 28, 1981, the date of institution.

Public Hearing. Any person with an interest in this investigation may request in writing that the Commission hold a public hearing in connection with this investigation. Any such request must be received by the Commission within 14 days of the date of publication of this notice of investigation in the Federal Register.

Written Submissions.--Any person may submit to the Commission on or before June 19, 1981, written statements of information pertinent to the subject matter of the investigation. A signed original and nineteen true copies of such statements must be submitted in accordance with section 201.8 of the Commission's Rules of Practice and Procedure, 19 CFR § 201.8 (1980).

Any business information which a submitter desires the Commission to treat as confidential shall be submitted separately and each sheet must be clearly marked at the top "Confidential business data." Confidential submissions must conform with the requirements of section 201.6 of the Rules of Practice and Procedure, 19 CFR 201.6. All written submissions, except confidential business data, will be available for public inspection.

FOR FURTHER INFORMATION CONTACT: John MacHatton, supervisory investigator, Office of Investigations, U.S. International Trade Commission, (202) 523-0439; Warren H. Maruyama, Office of the General Counsel, U.S. International Trade Commission, (202) 523-0143.

By Order of the Commission.

Kenneth R. Mason
Secretary

Issued: June 3, 1981

UNITED STATES INTERNATIONAL TRADE COMMISSION
Washington, D.C. 20436

Synthetic L-Methionine From Japan

NOTICE OF COMMISSION REQUEST FOR COMMENTS CONCERNING INSTITUTION OF SECTION 751(b) REVIEW INVESTIGATION 1/

AGENCY: United States International Trade Commission.

ACTION: Request for comments regarding institution of Section 751(b) review investigation concerning affirmative determination in Investigation No. AA1921-115, Synthetic Methionine from Japan.

SUMMARY: The Commission invites comments from the public on whether changed circumstances exist which warrant the institution of an investigation pursuant to section 751(b) of the Tariff Act of 1930, Pub. L. No. 96-39, § 101, 93 Stat. 175-76 (to be codified at 19 U.S.C. 1675(b)), to review the Commission's affirmative determination in investigation No. AA1921-115 to synthetic l-methionine from Japan. The purpose of the proposed section 751(b) review investigation, if instituted, would be to determine whether an industry in the United States would be materially injured, would be threatened with material injury, or the establishment of an industry would be materially retarded, by imports of synthetic l-methionine if the antidumping order regarding synthetic methionine from Japan is modified or revoked with respect to synthetic l-methionine provided for in item 425.04 of the Tariff Schedules of the United States.

SUPPLEMENTARY INFORMATION: On May 14, 1973, the Commission determined that an industry in the United States was injured within the meaning of the

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1/ Federal Register, 46 F.R. 22087, Apr. 15, 1981.

Antidumping Act, 1921, by reason of imports of synthetic methionine from Japan determined by the Secretary of Treasury to be sold or likely to be sold at less than fair value (hereinafter "LTFV").

On July 3, 1973, the Department of the Treasury issued a finding of dumping, 7 Cust. B. 630 (1973), T.D. 73-188, and on July 10, 1973 published notice of the dumping finding in the Federal Register, 38 F.R. 18382.

On December 15, 1980, the Commission received a request to review its affirmative determination in investigation No. AA1921-115. The request was filed pursuant to section 751(b) of the Tariff Act of 1930 by Kyowa Hakko USA, Inc., an importer of synthetic l-methionine from Japan.

Written Comments Requested

Pursuant to section 207.45(b)(2) of the Commission's Rules of Practice and Procedure (46 F.R. 18023)(March 23, 1981), the Commission requests comments on whether the following alleged changed circumstances are sufficient to warrant institution of a review investigation: (1) the likelihood that there is no industry in the United States which produces synthetic l-methionine, and (2) the likelihood that synthetic l-methionine from Japan is not like any form of synthetic methionine produced in the United States.

The purpose of the proposed investigation would be to determine whether an industry in the United States would be materially injured, would be threatened with material injury, or the establishment of an industry would be materially retarded if the antidumping order is modified or revoked with regard to synthetic l-methionine. Revocation or modification of the dumping finding as to synthetic l-methionine would not affect the Commission's

affirmative determination as to other forms of synthetic methionine from Japan.

The Kyowa Hakko Request

Copies of the Kyowa Hakko request and any other public documents in this matter are available to the public during official working hours (8:45 a.m. to 5:15 p.m.) in the Office of the Secretary, U.S. International Trade Commission, 701 E Street NW., Washington, D.C. 20436; telephone 202-523-0161.

Additional Information

Under section 201.8 of the Commission's Rules of Practice and Procedure (19 CFR §201.8), the signed original and 19 true copies of all written submissions must be filed with the Secretary to the Commission, 701 E Street, NW., Washington, D.C. 20436; telephone 202-523-0161. All comments must be filed no later than 30 days after publication of this notice in the Federal Register. Any person desiring to submit a document (or portion thereof) to the Commission in confidence must request business confidential treatment under section 201.6 of the Commission's Rules of Practice and Procedure, (19 CFR §201.6). Such requests should be directed to the Secretary to the Commission and must include a full statement of the reasons why the Commission should grant such treatment. Each sheet must be clearly marked at the top "Confidential Business Data." The Commission will either accept the submission in confidence or return it. All nonconfidential written submissions will be available for public inspection in the Office of the Secretary.

FOR FURTHER INFORMATION CONTACT: John MacHatton, supervisory investigator, Office of Investigations, U.S. International Trade Commission, (202) 523-0439; Warren H. Maruyama, Office of General Counsel, U.S. International Trade Commission, (202) 523-0143.

By Order of the Commission.

Kenneth R. Mason
Secretary

Issued: April 10, 1981

APPENDIX B

EXCERPTS OF REGULATIONS AND STANDARDS

code of federal regulations

21

Food and Drugs

PARTS 170 TO 199

Revised as of April 1, 1980

CONTAINING
A CODIFICATION OF DOCUMENTS
OF GENERAL APPLICABILITY
AND FUTURE EFFECT

AS OF APRIL 1, 1980

With Ancillaries

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as a Special Edition of
the Federal Register

§ 172.320 Amino acids.

The food additive amino acids may be safely used as nutrients added to foods in accordance with the following conditions:

(a) The food additive consists of one or more of the following individual amino acids in the free, hydrated or anhydrous form or as the hydrochloride, sodium or potassium salts:

L-Alanine
L-Arginine
L-Asparagine
L-Aspartic acid
L-Cysteine
L-Cystine
L-Glutamic acid
L-Glutamine
Aminoacetic acid (glycine)
L-Histidine
L-Isoleucine
L-Leucine
L-Lysine
DL-Methionine (not for infant foods)
L-Methionine
L-Phenylalanine
L-Proline
L-Serine
L-Threonine
L-Tryptophan
L-Tyrosine
L-Valine

(b) The food additive meets the following specifications:

(1) As found in "Food Chemicals Codex," National Academy of Sciences-National Research Council (NAS-NRC), 2nd Edition (1972)[2] for the following:

L-Alanine
L-Arginine
L-Arginine Monohydrochloride
L-Cysteine Monohydrochloride
L-Cystine
Aminoacetic acid (glycine)
L-Leucine
DL-Methionine
L-Methionine
L-Tryptophan
L-Phenylalanine
L-Proline
L-Serine
L-Threonine
Glutamic Acid Hydrochloride
L-Isoleucine
L-Lysine Monohydrochloride
Monopotassium L-glutamate
L-Tyrosine
L-Valine

(2) As found in "Specifications and Criteria for Biochemical Compounds," NAS-NRC Publication, 3rd Edition (1972)[2] for the following:

L-Asparagine
L-Aspartic acid
L-Glutamine
L-Histidine

(c) The additive(s) is used or intended for use to significantly improve the biological quality of the total protein in a food containing naturally occurring primarily-intact protein that is considered a significant dietary protein source, provided that:

(1) A reasonable daily adult intake of the finished food furnishes at least 6.5 grams of naturally occurring primarily intact protein (based upon 10 percent of the daily allowance for the "reference" adult male recommended by the National Academy of Sciences in "Recommended Dietary Allowances," NAS Publication No. 1694, 7th Edition (1968)).[2]

(2) The additive(s) results in a protein efficiency ratio (PER) of protein in the finished ready-to-eat food equivalent to casein as determined by the method specified in paragraph (d) of this section.

(3) Each amino acid (or combination of the minimum number necessary to achieve a statistically significant increase) added results in a statistically significant increase in the PER as determined by the method described in paragraph (d) of this section. The

[2]Copies may be obtained from: The National Academy of Sciences, 2101 Constitution Ave. NW., Washington, D.C. 20037.

minimum amount of the amino acid(s) to achieve the desired effect must be used and the increase in PER over the primarily-intact naturally occurring protein in the food must be substantiated as a statistically significant difference with at least a probability (P) value of less than 0.05.

(4) The amount of the additive added for nutritive purposes plus the amount naturally present in free and combined (as protein) form does not exceed the following levels of amino acids expressed as percent by weight of the total protein of the finished food:

	Percent by weight of total protein (expressed as free amino acid)
L-Alanine	6.1
L-Arginine	6.6
L-Aspartic acid (including L-asparagine)	7.0
L-Cystine (including L-cysteine)	2.3
L-Glutamic acid (including L-glutamine)	12.4
Aminoacetic acid (glycine)	3.5
L-Histidine	2.4
L-Isoleucine	6.6
L-Leucine	8.8
L-Lysine	6.4
L- and DL-Methionine	3.1
L-Phenylalanine	5.8
L-Proline	4.2
L-Serine	8.4
L-Threonine	5.0
L-Tryptophan	1.6
L-Tyrosine	4.3
L-Valine	7.4

(d) Compliance with the limitations concerning PER under paragraph (c) of this section shall be determined by the method described in sections 39.166–39.170, "Official Methods of Analysis of the Association of Official Analytical Chemists," 11th Edition (1970).[3] Each manufacturer or person employing the additive(s) under the provisions of this section shall keep and maintain throughout the period of his use of the additive(s) and for a minimum of 3 years thereafter, records of the tests required by this paragraph and other records required to assure effectiveness and compliance with this regulation and shall make such records available upon request at all reasonable hours by any officer or employee of the Food and Drug Administration, or any other officer or employee acting on behalf of the Secretary of Health, Education, and Welfare and shall permit such officer or employee to conduct such inventories of raw and finished materials on hand as he deems necessary and otherwise to check the correctness of such records.

(e) To assure safe use of the additive, the label and labeling of the additive and any premix thereof shall bear, in addition to the other information required by the act, the following:

(1) The name of the amino acid(s) contained therein including the specific optical and chemical form.

(2) The amounts of each amino acid contained in any mixture.

(3) Adequate directions for use to provide a finished food meeting the limitations prescribed by paragraph (c) of this section.

(f) The food additive amino acids added as nutrients to special dietary foods that are intended for use solely under medical supervision to meet nutritional requirements in specific medical conditions and comply with the requirements of Part 105 of this chapter are exempt from the limitations in paragraphs (c) and (d) of this section and may be used in such foods at levels not to exceed good manufacturing practices.

[42 FR 14491, Mar. 15, 1977; 42 FR 56728, Oct. 28, 1977]

[3]Copies may be obtained from: Association of Official Analytical Chemists, P.O. Box 540, Benjamin Franklin Station, Washington, D.C. 20044.

FOOD CHEMICALS CODEX

SECOND EDITION

Prepared by the
Committee on Specifications,
Food Chemicals Codex,
of the
Committee on Food Protection
National Research Council

National Academy of Sciences
Washington, D. C.
1972

NOTICE

The study reported herein was undertaken under the aegis of the National Research Council with the approval of its Governing Board. Such approval indicated that the Board considered the problem of national significance and that the resources of NRC were particularly suitable to the conduct of the project.

The members of the committee were selected for their individual scholarly competence and judgment with due consideration for the balance and breadth of disciplines. Responsibility for all aspects of this report rests with the study committee, to whom sincere appreciation is expressed.

Although the reports of committees are not submitted for approval to the Academy membership or to the Council, each is reviewed according to procedures established and monitored by the Academy's Report Review Committee. The report is distributed only after satisfactory completion of this review process.

Acknowledgment. This study was supported in part by U. S. Food and Drug Administration Research Grant No. FD 00213, administered by the Department of Health, Education, and Welfare, U. S. Public Health Service.

Compliance with Federal Statutes. The fact that an article appears in this Food Chemicals Codex does not exempt it from compliance with requirements of Acts of Congress or with regulations and rulings issued by agencies of the United States Government under authority of these Acts.

Revisions of the federal requirements that affect the Codex standards will be included in Codex Supplements as promptly as practicable.

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DL-METHIONINE

DL-2-Amino-4-(methylthio)butyric Acid

$$\underset{\displaystyle\quad\quad\quad\quad\quad\quad NH_2}{CH_3SCH_2CH_2CHCOOH}$$

$C_5H_{11}NO_2S$ Mol. wt. 149.21

DESCRIPTION

White, crystalline platelets or powder having a characteristic odor. One gram dissolves in about 30 ml. of water. It is soluble in dilute acids and in solutions of alkali hydroxides. It is very slightly soluble in alcohol, and practically insoluble in ether. It is optically inactive. The pH of a 1 in 100 solution is between 5.6 and 6.1.

IDENTIFICATION

A. Add 25 mg. of a previously dried sample to 1 ml. of a saturated solution of anhydrous cupric sulfate in sulfuric acid. A yellow color appears.

B. To 10 ml. of a 1 in 1000 solution add successively, shaking after each addition, 1 ml. of a 1 in 5 solution of sodium hydroxide, 1 ml. of a 1 in 100 glycine solution, and 0.3 ml. of a freshly prepared 1 in 10 solution of sodium nitroferricyanide. Keep the mixture at about 40° for 10 minutes, cool in an ice bath for 2 minutes, then add 2 ml. of 20 percent hydrochloric acid and shake the mixture. A reddish-purple color appears.

C. To 1 ml. of a 1 in 30 solution add 1 ml. of ninhydrin T.S. and 100 mg. of sodium acetate, and heat to boiling. An intense violet-blue color is formed (distinction from hydroxy analog).

SPECIFICATIONS

Assay. Not less than 99.0 percent of $C_5H_{11}NO_2S$, calculated on the dried basis.

Limits of Impurities

Arsenic (as As). Not more than 3 parts per million (0.0003 percent).

Heavy metals (as Pb). Not more than 20 parts per million (0.002 percent).

Lead. Not more than 10 parts per million (0.001 percent).

Loss on drying. Not more than 0.5 percent.

Residue on ignition. Not more than 0.1 percent.

TESTS

Assay. Transfer about 300 mg., accurately weighed, into a glass-stoppered flask. Add 100 ml. of water, 5 grams of dibasic potassium phosphate, 2 grams of monobasic potassium phosphate, and 2 grams of potassium iodide, and mix well to dissolve. Add exactly 50 ml. of 0.1 *N* iodine, stopper the flask, mix well, allow to stand for 30 minutes, and then titrate the excess iodine with 0.1 *N* sodium thiosulfate. Perform a blank determination (see page 2) and make any necessary correction. Each ml. of 0.1 *N* iodine is equivalent to 7.461 mg. of $C_5H_{11}NO_2S$.

Arsenic. A *Sample Solution* prepared as directed for organic compounds meets the requirements of the *Arsenic Test*, page 865.

Heavy metals. Prepare and test a 1-gram sample as directed in *Method II* under the *Heavy Metals Test*, page 920, using 20 mcg. of lead ion (Pb) in the control (*Solution A*).

Lead. A *Sample Solution* prepared as directed for organic compounds meets the requirements of the *Lead Limit Test*, page 929, using 10 mcg. of lead ion (Pb) in the control.

Loss on drying, page 931. Dry at 105° for 2 hours.

Residue on ignition, page 945. Ignite 1 gram as directed in the general method.

Packaging and storage. Store in well-closed, light-resistant containers.

Functional use in foods. Nutrient; dietary supplement.

L-METHIONINE

L-2-Amino-4-(methylthio)butyric Acid

$$CH_3SCH_2CH_2CH(NH_2)COOH$$

$C_5H_{11}NO_2S$ Mol. wt. 149.21

DESCRIPTION

Colorless or white lustrous plates, or a white crystalline powder. It has a slight, characteristic odor. It is soluble in water, in alkali solutions, and in dilute mineral acids. It is slightly soluble in alcohol and practically insoluble in ether.

IDENTIFICATION

L-Methionine responds to *Identification Tests A, B* and *C* under DL-*Methionine*, page 504.

SPECIFICATIONS

Assay. Not less than 99.0 percent of $C_5H_{11}NO_2S$, calculated on the dried basis.

Specific rotation. $[\alpha]_D^{25°}$: Between −6.8° and −8.2°; $[\alpha]_D^{20°}$: between +21.0° and +25.0°.

Limits of Impurities

Arsenic (as As). Not more than 3 parts per million (0.0003 percent).

Heavy metals (as Pb). Not more than 20 parts per million (0.002 percent).

Lead. Not more than 10 parts per million (0.001 percent).

Loss on drying. Not more than 0.5 percent.

Residue on ignition. Not more than 0.1 percent.

TESTS

Assay. Transfer about 300 mg., accurately weighed, into a glass-stoppered flask. Add 100 ml. of water, 5 grams of dibasic potassium phosphate, 2 grams of monobasic potassium phosphate, and 2 grams of potassium iodide, and mix well to dissolve. Add exactly 50 ml. of 0.1 *N* iodine, stopper the flask, mix well, allow to stand for 30 minutes, and then titrate the excess iodine with 0.1 *N* sodium thiosulfate. Perform a blank determination (see page 2) and make any necessary correction. Each ml. of 0.1 *N* iodine is equivalent to 7.461 mg. of $C_5H_{11}NO_2S$.

Specific rotation, page 939. $[\alpha]_D^{25°}$: Determine in a solution containing 4 grams in sufficient water to make 100 ml.; $[\alpha]_D^{20°}$: determine in a solution containing 2 grams in sufficient 6 *N* hydrochloric acid to make 100 ml.

Arsenic. A *Sample Solution* prepared as directed for organic compounds meets the requirements of the *Arsenic Test*, page 865.

Heavy metals. Prepare and test a 1-gram sample as directed in *Method II* under the *Heavy Metals Test*, page 920, using 20 mcg. of lead ion (Pb) in the control (*Solution A*).

Lead. A *Sample Solution* prepared as directed for organic compounds meets the requirements of the *Lead Limit Test*, page 929, using 10 mcg. of lead ion (Pb) in the control.

Loss on drying, page 931. Dry at 105° for 2 hours.

Residue on ignition, page 945. Ignite 1 gram as directed in the general method.

Packaging and storage. Store in well-closed, light-resistant containers.

Functional use in foods. Nutrient; dietary supplement.

THIRD EDITION

FOOD CHEMICALS CODEX

COMMITTEE ON CODEX SPECIFICATIONS

Food and Nutrition Board
Division of Biological Sciences
Assembly of Life Sciences
National Research Council

NATIONAL ACADEMY PRESS
Washington, D.C. 1981

1282

NOTICE The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the Councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the Committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

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FOOD AND NUTRITION BOARD The Food and Nutrition Board was established in 1940. It is a part of the Division of Biological Sciences within the Assembly of Life Sciences of the National Research Council.

The Board serves as an advisory body in the field of food and nutrition. It promotes needed research and helps interpret nutritional science in the interests of public welfare. The Board acts in response to requests from public agencies and, at times, on its own initiative.

The Board is active in areas of dietary guidelines, nutrition and health, food safety, food chemicals specifications, food resources, and international nutrition programs. It has established, among other important guides, recommended dietary allowances, principles and procedures for the evaluation of the safety of foods, specifications of identity and purity for food chemicals, guidelines for nutrient fortification of foods, and recommendations for maternal and infant nutrition. The Food and Nutrition Board draws upon the knowledge and expertise available from the combined resources of academia, government, and industry.

Financial support for the work of the Board is primarily provided by government contracts and grants. In addition, uncommitted support is provided by private foundations and industrial organizations.

Through members of its liaison panels, technical input in aspects of nutrition, food safety, food technology, and food processing is provided.

This study was supported by U.S. Food and Drug Administration Contract No. 223-78-2053 (formerly Grant No. FD 00213).

COMPLIANCE WITH FEDERAL STATUTES The fact that an article appears in this *Food Chemicals Codex* does not exempt it from compliance with requirements of acts of Congress, with regulations and rulings issued by agencies of the United States Government under authority of these acts, or with requirements and regulations of governments in other countries that have adopted the *Food Chemicals Codex*. Revisions of the federal requirements that affect the Codex specifications will be included in Codex supplements as promptly as practicable.

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LEGAL STATUS

The first edition of the *Food Chemicals Codex* was given quasi-legal recognition by means of a letter of endorsement from the Commissioner of Food and Drugs, which was reprinted in the book. At that time (April 1966), the Commissioner stated that "the FDA will regard the specifications in the Food Chemicals Codex as defining an 'appropriate food grade' within the meaning of Sec. 121.101(b)(3) [now §182.1(b)(3)] and Sec. 121.1000(a)(2) [now §172.5(a)(2)] of the food additive regulations," although such endorsement could not be construed to exempt substances from compliance with requirements of acts of Congress or with regulations and rulings issued by the Food and Drug Administration (FDA) under authority of such acts.

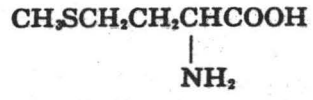
Later, the *Food Chemicals Codex* was officially recognized by FDA when the definitions and procedural and interpretive regulations under §170.30, relating to eligibility of substances for classification as *generally recognized as safe* (GRAS), were revised and published in the *Federal Register* of June 25, 1971 (36 FR 12093).

Food Chemicals Codex specifications have also been adopted, under certain conditions, by the National Health and Medical Research Council of Australia; the Health Protection Branch of the Department of National Health and Welfare of Canada; the Ministries of Agriculture, Fisheries, and Food of Great Britain; and the Department of Health (Food and Nutrition Branch) of New Zealand. In addition, the *Food Chemicals Codex* has served as the source of many specifications developed by

the Joint FAO/WHO Expert Committee on Food Additives, and by the International Union of Pure and Applied Chemistry.

DL-Methionine

DL-2-Amino-4-(methylthio)butyric Acid



$C_5H_{11}NO_2S$ Mol wt 149.21

DESCRIPTION

White, crystalline platelets or powder having a characteristic odor. One g dissolves in about 30 ml of water. It is soluble in dilute acids and in solutions of alkali hydroxides. It is very slightly soluble in alcohol, and practically insoluble in ether. It is optically inactive. The pH of a 1 in 100 solution is between 5.6 and 6.1.

REQUIREMENTS

Identification

A. Add 25 mg of a previously dried sample to 1 ml of a saturated solution of anhydrous cupric sulfate in sulfuric acid. A yellow color appears.

B. To 10 ml of a 1 in 1000 solution add successively, shaking after each addition, 1 ml of a 1 in 5 solution of sodium hydroxide, 1 ml of a 1 in 100 glycine solution, and 0.3 ml of a freshly prepared 1 in 10 solution of sodium nitroferricyanide. Keep the mixture at about 40° for 10 min, cool in an ice bath for 2 min, then add 2 ml of 20% hydrochloric acid and shake the mixture. A red or orange red color appears.

C. To 1 ml of a 1 in 30 solution add 1 ml of ninhydrin TS and 100 mg of sodium acetate, and heat to boiling. An intense violet blue color is formed (distinction from hydroxy analog).

Assay Not less than 99.0% of $C_5H_{11}NO_2S$, calculated on the dried basis.

Arsenic (as As) Not more than 3 ppm.

Heavy Metals (as Pb) Not more than 0.002%.

Lead Not more than 10 ppm.

Loss on Drying Not more than 0.5%.

Residue on Ignition Not more than 0.1%.

TESTS

Assay Transfer about 300 mg, accurately weighed, into a glass-stoppered flask. Add 100 ml of water, 5 g of dibasic potassium phosphate, 2 g of monobasic potassium phosphate, and 2 g of potassium iodide, and mix well to dissolve. Add exactly 50 ml of 0.1 *N* iodine, stopper the flask, mix well, allow to stand for 30 min, and then titrate the excess iodine with 0.1 *N* sodium thiosulfate. Perform a blank determination (see page 2), and make any necessary correction. Each ml of 0.1 *N* iodine is equivalent to 7.461 mg of $C_5H_{11}NO_2S$.

Arsenic A *Sample Solution* prepared as directed for organic compounds meets the requirements of the *Arsenic Test*, page 464.

Heavy Metals Prepare and test a 1-g sample as directed in *Method II* under the *Heavy Metals Test*, page 513, using 20 µg of lead ion (Pb) in the control (*Solution A*).

Lead A *Sample Solution* prepared as directed for organic compounds meets the requirements of the *Lead Limit Test*, page 518, using 10 µg of lead ion (Pb) in the control.

Loss on Drying, page 518 Dry at 105° for 2 h.

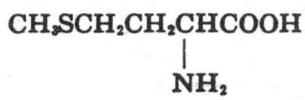
Residue on Ignition, page 533 Ignite 1 g as directed in the general method.

Packaging and Storage Store in well-closed, light-resistant containers.

Functional Use in Foods Nutrient; dietary supplement.

L-Methionine

L-2-Amino-4-(methylthio)butyric Acid



$C_5H_{11}NO_2S$ Mol wt 149.21

DESCRIPTION

Colorless or white lustrous plates, or a white crystalline powder. It has a slight, characteristic odor. It is soluble in water, in alkali solutions, and in dilute mineral acids. It is slightly soluble in alcohol and practically insoluble in ether.

REQUIREMENTS

Identification

L-Methionine responds to *Identification Tests A, B,* and *C* under DL-*Methionine*, page 193.

Assay Not less than 99.0% of $C_5H_{11}NO_2S$, calculated on the dried basis.
Arsenic (as As) Not more than 3 ppm.
Heavy Metals (as Pb) Not more than 0.002%.
Lead Not more than 10 ppm.
Loss on Drying Not more than 0.5%.
Residue on Ignition Not more than 0.1%.
Specific Rotation $[\alpha]_D^{25°}$: Between $-6.8°$ and $-8.2°$; $[\alpha]_D^{20°}$: between $+21.0°$ and $+25.0°$.

TESTS

Assay Transfer about 300 mg, accurately weighed, into a glass-stoppered flask. Add 100 ml of water, 5 g of dibasic potassium phosphate, 2 g of monobasic potassium phosphate, and 2 g of potassium iodide, and mix well to dissolve. Add exactly 50 ml of 0.1 *N* iodine, stopper the flask, mix well, allow to stand for 30 min, and then titrate the excess iodine with 0.1 *N* sodium thiosulfate. Perform a blank determination (see page 2) and make any necessary correction. Each ml of 0.1 *N* iodine is equivalent to 7.461 mg of $C_5H_{11}NO_2S$.
Arsenic A *Sample Solution* prepared as directed for organic compounds meets the requirements of the *Arsenic Test*, page 464.
Heavy Metals Prepare and test a 1-g sample as directed in *Method II* under the *Heavy Metals Test*, page 513, using 20 µg of lead ion (Pb) in the control (*Solution A*).
Lead A *Sample Solution* prepared as directed for organic compounds meets the requirements of the *Lead Limit Test*, page 518, using 10 µg of lead ion (Pb) in the control.
Loss on Drying, page 518 Dry at 105° for 2 h.
Residue on Ignition, page 533 Ignite 1 g as directed in the general method.
Specific Rotation, page 530 $[\alpha]_D^{25°}$: Determine in a solution containing 4 g in sufficient water to make 100 ml; $[\alpha]_D^{20°}$: determine in a solution containing 2 g in sufficient 6 *N* hydrochloric acid to make 100 ml.

Packaging and Storage Store in well-closed, light-resistant containers.
Functional Use in Foods Nutrient; dietary supplement.

U. S. PHARMACOPEIAL CONVENTION, INC.
12601 TWINBROOK PARKWAY, ROCKVILLE, MD. 20852
(301) 881-0666

81 JUL 16 A10:14

July 14, 1981

Kenneth R. Mason
Secretary
United States International Trade
Commission
Washington, D.C. 20436

Dear Mr. Mason:

This replies to your letter of July 9, in which you requested permission to reproduce an excerpt on "methionine" from The United States Pharmacopeia, Twentieth Revision, and The National Formulary, Fifteenth Edition, and their Second Supplement, in an appendix to the Commission's report on investigation No. 751-TA-4 involving methionine from Japan.

The title, Methionine, has been subject to a very rare Pharmacopeial action: the drug substance and dosage forms formerly described by that title have been retitled, Racemethionine, and the title, Methionine, is now applied to a different (although very closely related) drug substance. Enclosed are photocopies of pages 20, 104 and 105 of the Second Supplement which effected that change as of May 1, 1981.

Please note also that these pages contain many cross references to other parts of the book.

This approval is granted, therefore, subject to including in your report the following statement:

> "The use of portions of the text of USP XX-NF XV is by permission of the USP Convention. The Convention is not responsible for any inaccuracy of quotation or for any false or misleading implication that may arise from separation of excerpts from the original text or by obsolescence resulting from publication of a supplement or later edition."

Sincerely,

William M. Heller

William M. Heller

WMH:sam

Enc.

SECOND SUPPLEMENT

A composite supplement comprising the Second Supplement to USP XX and to NF XV

Introduction

Changes and additions listed herein constitute revisions in USP XX and in NF XV effective May 1, 1981, except where otherwise noted.

This Supplement is cumulative; as is indicated on the inside front cover, it includes the content of the First Supplement and its Addendum *a*, and the First Interim Revision Announcement pertaining to USP XX and to NF XV. Accordingly, this cumulative Supplement supersedes the First Supplement and its Addendum *a* and the First Interim Revision Announcement.

This combined USP and NF Supplement is arranged in the order in which the items appear in the USP XX–NF XV main volume.

The format and general editorial style employed in the Supplement serve not only for printing convenience but also for accommodation to computer storage and retrieval processes.

Explanation of Symbols—

Document	*Official Date*	*Symbols*
First Supplement to USP XX and to NF XV	July 1, 1980	■ and ■1
Addendum *a* to the above	July 1, 1980	▲ and ▲1a
First Interim Revision Announcement	July 1, 1980	● and ●1
Second Supplement	May 1, 1981	■ and ■2

Superscript symbol denotes the start of a change; *subscript* symbol with numeral or numeral and letter denotes the end of a change.

Where the superscript and subscript symbols appear together with no intervening text, it means that a word or words have simply been deleted.

The figure(s) following a subscript symbol also denote the official date of the change; thus, the numeral "1" refers to the *First* Supplement, and by inference denotes the official date July 1, 1980.

Addenda to USP–NF Supplements are not cumulative, although the annual Supplements themselves will be cumulative.

Official Title Changes—NOTE—In all instances where "*Monograph title change* (*see Note in Introduction*)" is specified, it is to be understood that the official title given after that specification is to be substituted for the former title in the appropriate places throughout the monograph concerned.

In succeeding Supplements, the notice of each official title change will continue to appear in the original alphabetic position; however, any further revisions of the monograph concerned will be shown under the new, currently official title in its respective alphabetic position.

Preface to USP XX

In the section, *Format and Style* (page xxiv) -

Change to read:

Percentage and ppm - Simply as a matter of preference in style, statements of test limits in the monographs are in terms of percentage, for values exceeding ▲10 parts▲1a per million.

USP XX and NF XV are published by the U.S. Pharmacopeial Convention, Inc., 12601 Twinbrook Pkwy., Rockville, MD 20852. The USP XX–NF XV main volume is distributed for USPC by the Mack Publishing Co., Easton, PA 18042.

All correspondence and suggestions for revisions with respect to either USP or NF should be addressed to: Drug Standards Division, USP–NF, 12601 Twinbrook Pkwy., Rockville, MD 20852.

Methionine

A–38

Monograph title change (see Note in Introduction):

[1]Racemethionine[2]1

Methionine Capsules

Monograph title change (see Note in Introduction):

[1]Racemethionine Capsules[2]1

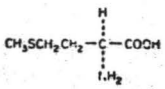
Methionine Tablets

Monograph title change (see Note in Introduction):

[1]Racemethionine Tablets[2]1

Add the following:

[1]Methionine



$C_5H_{11}NO_2S$ 149.21
L-Methionine.
L-Methionine [*63-68-3*].

» Methionine contains not less than 98.5 percent and not more than 101.5 percent of $C_5H_{11}NO_2S$, as L-methionine, calculated on the dried basis.

Packaging and storage—Preserve in well-closed containers.

Reference standard—*USP Methionine Reference Standard*—Dry at 105° for 3 hours before using.

Identification—The infrared absorption spectrum of a potassium bromide dispersion of it, previously dried, exhibits maxima only at the same wavelengths as that of a similar preparation of USP Methionine RS.

Specific rotation ⟨781⟩: between +21.9° and +24.1°, calculated on the dried basis, determined in a solution in 6 *N* hydrochloric acid containing 200 mg in each 10 ml.

pH ⟨791⟩: between 5.6 and 6.1 in a solution (1 in 100).

Loss on drying ⟨731⟩—Dry it at 105° for 3 hours: it loses not more than 0.3% of its weight.

Residue on ignition ⟨281⟩: not more than 0.4%.

Chloride ⟨221⟩—A 0.73-g portion shows no more chloride than corresponds to 0.50 ml of 0.020 *N* hydrochloric acid (0.05%).

Sulfate ⟨221⟩—A 0.33-g portion shows no more sulfate than corresponds to 0.10 ml of 0.020 *N* sulfuric acid (0.03%).

Arsenic ⟨211⟩: 1.5 ppm.

Iron ⟨241⟩: 0.003%.

Heavy metals, *Method I* ⟨231⟩: 0.0015%.

Assay—Transfer about 140 mg of Methionine, accurately weighed, to a 125-ml flask, dissolve in a mixture of 3 ml of formic acid and 50 ml of glacial acetic acid, add 2 drops of crystal violet TS, and titrate with 0.1 *N* perchloric acid VS to a green end-point. Perform

a blank determination, and make any necessary correction. Each ml of 0.1 *N* perchloric acid is equivalent to 14.93 mg of $C_5H_{11}NO_2S$.[2]1

The United States Pharmacopeia

TWENTIETH REVISION

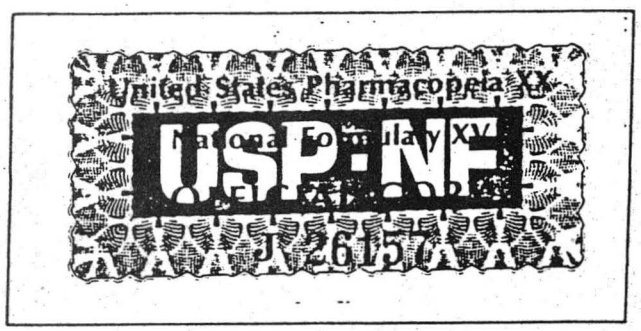
Official from July 1, 1980

The National Formulary

FIFTEENTH EDITION

Official from July 1, 1980

United States Pharmacopeial Convention, Inc.
12601 Twinbrook Parkway, Rockville, Md. 20852



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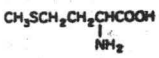
Methionine



$C_5H_{11}NO_2S$ 149.21
Methionine, DL-.
DL-2-Amino-4-(methylthio)butyric acid [*59-51-8*].

» Methionine contains not less than 99.0 percent and not more than 100.5 percent of $C_5H_{11}NO_2S$, calculated on the dried basis.

Packaging and storage—Preserve in well-closed, light-resistant containers.

Identification—

A: Add 25 mg to 1 ml of a saturated solution of anhydrous cupric sulfate in sulfuric acid: a yellow color appears.

B: To 10 ml of a solution (1 in 1000) add in succession, shaking after each addition, 1 ml of sodium hydroxide solution (1 in 5), 1 ml of aminoacetic acid solution (1 in 100), and 0.3 ml of freshly prepared sodium nitroferricyanide solution (1 in 10). Keep the mixture at about 40° for 10 minutes, cool in an ice bath for 2 minutes, then add 2 ml of 2 *N* hydrochloric acid, and shake the mixture: a red or orange-red color appears.

C: To 1 ml of a solution (1 in 30) add 1 ml of triketohydrindene hydrate TS and 100 mg of sodium acetate, and heat to boiling: an intense violet-blue color is formed (*distinction from hydroxyl analog*).

pH ⟨791⟩: between 5.6 and 6.1, in a solution (1 in 100).

Clarity and color of solution—Dissolve 450 mg in 15 ml of water: the solution is clear and colorless.

Loss on drying ⟨731⟩—Dry it at 105° for 4 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩: not more than 0.1%.

Chloride ⟨221⟩—A 750-mg portion shows no more chloride than corresponds to 0.20 ml of 0.020 *N* hydrochloric acid (0.020%).

Sulfate ⟨221⟩—A 750-mg portion shows no more sulfate than corresponds to 0.40 ml of 0.020 *N* sulfuric acid (0.050%).

Selenium ⟨291⟩: 0.003%.

Heavy metals, *Method II* ⟨231⟩: 0.002%.

Iron ⟨241⟩—Dissolve 1 g in 45 ml of water, and add 2 ml of hydrochloric acid: the limit is 0.001%.

Assay—Transfer about 300 mg of Methionine, accurately weighed, to a glass-stoppered flask. Add 100 ml of water, 5 g of dibasic potassium phosphate, 2 g of monobasic potassium phosphate, and 2 g of potassium iodide, and mix to dissolve. Add 50.0 ml of 0.1 *N* iodine VS, insert the stopper in the flask, mix, and allow to stand for 30 minutes. Titrate the excess iodine with 0.1 *N* sodium thiosulfate VS, adding 3 ml of starch TS as the end-point is approached. Perform a blank determination (see *Residual Titrations* ⟨541⟩). Each ml of 0.1 *N* iodine is equivalent to 7.461 mg of $C_5H_{11}NO_2S$.

Methionine Capsules

» Methionine Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_5H_{11}NO_2S$.

Packaging and storage—Preserve in well-closed, light-resistant containers.

Identification—Macerate the contents of a number of Capsules, equivalent to about 100 mg of methionine, in 100 ml of water, and filter the solution. The solution responds to *Identification test B* under *Methionine*.

Weight variation ⟨931⟩: meet the requirements for *Capsules*.

Assay—Transfer, as completely as possible, the contents of not less than 20 Methionine Capsules to a 1000-ml volumetric flask. Wash the emptied capsules with cold water, and transfer the washings to the flask. Add water to volume, and mix. Filter, if necessary, through a dry filter into a dry flask, discarding the first 20 ml of the filtrate. Transfer an accurately measured volume of the subsequent filtrate, equivalent to about 300 mg of methionine, to a glass-stoppered flask, and proceed as directed in the *Assay* under *Methionine*, beginning with "Add 100 ml of water."

Methionine Tablets

» Methionine Tablets contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of $C_5H_{11}NO_2S$.

Packaging and storage—Preserve in well-closed, light-resistant containers.

Identification—A filtered solution of Tablets, representing a concentration of approximately 1 in 1000 of methionine, responds to *Identification test B* under *Methionine*.

Disintegration ⟨701⟩: 30 minutes, simulated gastric fluid TS being used as the test medium.

Weight variation ⟨931⟩: meet the requirements for *Tablets*.

Assay—Weigh and finely powder not less than 20 Methionine Tablets. Weigh accurately a portion of the powder, equivalent to about 600 mg of methionine, and transfer completely to a 100-ml volumetric flask. Add about 75 ml of water, and allow to stand for 30 minutes with occasional swirling. Dilute with water to volume, and mix. Filter, if necessary, through a dry filter into a dry flask, discarding the first 20 ml of the filtrate. Transfer an accurately measured volume of the subsequent filtrate, equivalent to about 300 mg of methionine, to a glass-stoppered flask, and proceed as directed in the *Assay* under *Methionine*, beginning with "Add 100 ml of water."

APPENDIX C

STATISTICAL TABLES

Table 1.--Synthetic L-methionine and all other forms of methionine 1/: U.S. production, imports, exports, and apparent U.S. consumption, 1978-80

(Quantity in thousands of pounds; value in thousands of dollars; unit value per pound)

Item	U.S. production	U.S. imports					U.S. exports 2/	Apparent consumption 2/	Ratio (percent) of imports to consumption 2/	
		From Japan	From West Germany	From France	From other sources	Total			Japan	Total
	Quantity									
1978:										
Synthetic L-methionine--	0	***	***	***	***	***	0	***	***	100.0
All other forms of methionine	55,006	***	***	***	***	***	4,500	***	***	***
Total	55,006	6,372	421	16,205	2,498	25,496	4,500	76,000	8.4	33.5
1979:										
Synthetic L-methionine--	0	***	***	***	***	***	0	***	***	100.0
All other forms of methionine	70,689	***	***	***	***	***	7,200	***	***	***
Total	70,689	*** 68	9	22,420	5	22,502	7,200	86,000	.1	26.2
1980:										
Synthetic L-methionine--	0	***	***	***	***	49	0	49	***	100.0
All other forms of methionine	4/ ***	***	***	***	***	22,106	9,900	4/ ***	***	4/ ***
Total	4/ ***	85	67	21,895	108	22,155	9,900	4/ ***	.1	4/ ***
	Value									
1978:										
Synthetic L-methionine--	-	***	***	***	***	***	-	***	***	100.0
All other forms of methionine	66,805	***	***	***	***	***	4,600	***	***	***
Total	66,805	7,658	627	17,923	2,764	28,972	4,600	91,200	8.4	31.8
1979:										
Synthetic L-methionine--	-	***	***	***	***	***	-	***	***	100.0
All other forms of methionine	80,689	***	***	***	***	***	7,200	***	***	***
Total	80,689	***1,000	101	22,808	7	23,916	7,200	97,400	1.0	24.6
1980:										
Synthetic L-methionine--	-	***	***	***	***	603	-	603	***	100.0
All other forms of methionine	4/ ***	***	***	***	***	26,538	11,900	4/ ***	***	4/ ***
Total	4/ ***	707	359	25,935	140	27,141	11,900	4/ ***	0.6	4/ ***

See footnotes at end of table.

Table 1.—Synthetic L-methionine and all other forms of methionine 1/: U.S. production, imports, exports, and apparent U.S. consumption, 1978-80--Continued

(Quantity in thousands of pounds; value in thousands of dollars; unit value per pound)

Item	U.S. production	U.S. imports					U.S. exports 2/	Apparent consumption 2/	Ratio (percent) of imports to consumption 2/	
		From Japan	From West Germany	From France	From other sources	Total			Japan	Total
	Unit value 5/									
1978:										
Synthetic L-methionine	-	***	***	***	***	***	-	***	-	-
All other forms of methionine	$1.21	***	***	***	***	***	$1.02	***	-	-
Average	1.21	1.20	1.49	1.11	1.11	1.14	1.02	1.20	-	-
1979:										
Synthetic L-methionine	-	***	***	***	***	***	-	***	-	-
All other forms of methionine	1.14	***	***	***	***	***	1.00	***	-	-
Average	1.14	***14.71	11.22	1.02	1.40	1.06	1.00	1.13	-	-
1980:										
Synthetic L-methionine	-	***	***	***	***	12.31	-	12.31	-	-
All other forms of methionine	4/ ***	***	***	***	***	1.20	1.20	4/ ***	-	-
Average	4/ ***	8.31	5.36	1.18	1.30	1.23	1.20	4/ ***	-	-

1/ In this table, data on the calcium salt of the hydroxy analog of methionine are included within the data for all other forms of methionine. The hydroxy analog is not believed to be produced outside of the United States, so import data are for methionine only.

2/ Estimated and rounded. Estimates based, in part, upon official statistics of the U.S. Department of Commerce.

3/ * * *.

4/ Preliminary. For Commission use only.

5/ Calculated from rounded figures.

Source: Production data compiled from official statistics of the U.S. International Trade Commission, except as noted. Import data compiled from statistics of the U.S. Department of Commerce and from data submitted in response to questionnaires of the U.S. International Trade Commission.

Table 2.—Synthetic L-methionine: Purchases for consumption, by firms, 1978-80, January-March 1980, and January-March 1981

Firm	1978	1979	1980	January-March	
				1980	1981
	Quantity (pounds)				
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
Total	***	***	***	***	***
	Value (dollars) 2/				
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
Total	***	***	***	***	***
	Unit value 3/				
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
Average	***	***	***	***	***

1/ * * *.
2/ Net delivered cost.
3/ Calculated from rounded figures.

Source: Compiled from data submitted in response to questionnaires of the U.S. International Trade Commission.

Table 3.--Synthetic L-methionine: Sales of U.S. imports, by firms, 1978-80, January-March 1980, and January-March 1981

Firm	1978	1979	1980	January-March 1980	January-March 1981
	Quantity (pounds)				
Ajinomoto U.S.A., Inc	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
Kyowa Hakko U.S.A., Inc	***	***	***	***	***
Tanabe U.S.A., Inc	***	***	***	***	***
Total	40,479	62,880	77,731	***	22,641
	Value (dollars)				
Ajinomoto U.S.A., Inc	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
Kyowa Hakko U.S.A., Inc	***	***	***	***	***
Tanabe U.S.A., Inc	***	***	***	***	***
Total	575,796	949,435	1,151,699	***	334,803
	Unit value 2/				
Ajinomoto U.S.A., Inc	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
Kyowa Hakko U.S.A., Inc	***	***	***	***	***
Tanabe U.S.A., Inc	***	***	***	***	***
Average	14.22	15.10	14.82	***	14.79

1/ * * *.

2/ Calculated from rounded figures.

Source: Compiled from data submitted in response to questionnaires of the U.S. International Trade Commission.

Table 4.--Synthetic L-methionine: U.S. imports, by firms, 1978-80, January-March 1980, and January-March 1981

Firm	1978	1979	1980	January-March 1980	January-March 1981
	Quantity (pounds)				
Ajinomoto U.S.A., Inc	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
Kyowa Hakko U.S.A. Inc	***	***	***	***	***
Tanabe U.S.A., Inc	***	***	***	***	***
Total	***	***	49,106	***	***
	Value (dollars) 2/				
Ajinomoto U.S.A., Inc	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
Kyowa Hakko U.S.A., Inc	***	***	***	***	***
Tanabe U.S.A., Inc	***	***	***	***	***
Total	***	***	603,306	***	***
	Unit value 2/3/				
Ajinomoto U.S.A., Inc	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
***	***	***	***	***	***
Kyowa Hakko U.S.A., Inc	***	***	***	***	***
Tanabe U.S.A., Inc	***	***	***	***	***
Average	***	***	12.29	***	***

1/ * * *.

2/ At the foreign port of exportation. Includes all costs incurred in bringing the merchandise to the foreign port of exportation but does not include ocean transportation, brokerage fees, marine insurance or other costs incurred in bringing the merchandise to the U.S. port of importation.

3/ Calculated from rounded figures.

Source: Compiled from data submitted in response to questionnaires of the U.S. International Trade Commission.

Table 5.--Synthetic L-methionine: U.S. importers' inventories, by firms, Dec. 31, 1977-80, Mar. 31, 1980, and Mar. 31, 1981

(In pounds)

Firm	Dec. 31--				Mar. 31--	
	1977	1978	1979	1980	1980	1981
Ajinomoto U.S.A., Inc-----	***	***	***	***	***	***
***	***	***	***	***	***	***
***	***	***	***	***	***	***
***	***	***	***	***	***	***
Kyowa Hakko U.S.A., Inc---	***	***	***	***	***	***
Tanabe U.S.A., Inc--------	***	***	***	***	***	***
Total----------	5,941	***	***	32,515	***	***

1/ * * *.

Source: Compiled from data submitted in reponse to questionnaires of the U.S. International Trade Commission.

Table 6.--Methionine: U.S. imports for consumption, by principal sources, 1976-80, January-March 1980, and January-March 1981

Source	1976	1977	1978	1979	1980	January-March-- 1980	1981
	Quantity (1,000 pounds)						
France	15,764	13,546	16,205	22,420	21,895	6,490	6,811
Japan	9,313	6,915	6,372	68	85	14	44
FR Germ	2,918	2,067	421	9	67	1	60
Nethlds	160	240	119	0	80	0	0
China P	0	0	0	0	26	4	4
Norway	0	0	0	0	1/	0	0
Canada	197	120	10	5	0	0	0
U King	0	1/	1	0	0	0	1
All other	7,461	7,775	2,368	0	0	0	0
Total	35,813	30,663	25,496	22,502	22,155	6,510	6,919
	Value (1,000 dollars)						
France	13,513	14,121	17,923	22,808	25,935	7,145	8,668
Japan	8,440	7,563	7,658	1,000	707	177	97
FR Germ	2,435	2,247	627	101	359	15	139
Nethlds	108	234	151	-	96	-	-
China P	-	-	-	-	43	7	8
Norway	-	-	-	-	1/	-	-
Canada	185	137	6	7	-	-	-
U King	-	1/	3	1/	-	-	2
All other	6,053	7,847	2,604	-	-	-	-
Total	30,734	32,150	28,972	23,916	27,141	7,343	8,914
	Unit value (per pound)						
France	$0.86	$1.04	$1.11	$1.02	$1.18	$1.10	$1.27
Japan	0.91	1.09	1.20	14.65	8.27	12.36	2.22
FR Germ	0.83	1.09	1.49	11.47	5.35	12.92	2.32
Nethlds	0.67	0.97	1.27	-	1.20	-	-
China P	-	-	-	-	1.62	1.48	1.74
Norway	-	-	-	-	0.89	-	-
Canada	0.94	1.14	0.65	1.36	-	-	-
U King	-	169.50	4.35	-	-	-	3.36
All other	0.81	1.01	1.10	-	-	-	-
Average	0.86	1.05	1.14	1.06	1.23	1.13	1.29

1/ Less than 500.

Source: Compiled from official statistics of the U.S. Department of Commerce.

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