WEST VIRGINIA—PM–10

Designated area	Designation		Classification	
	Date	Type	Date	Type
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Hancock and Brooke Counties (part): The City of Weirton	12/27/2004	Attainment.		
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[FR Doc. 04–23945 Filed 10–26–04; 8:45 am]

BILLING CODE 6560–50–P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[OPP–2004–0243; FRL–7371–6]

L-Glutamic Acid and Gamma Aminobutyric Acid: Order Denying Objections to Issuance of Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final Order.

SUMMARY: By this order, EPA denies the objections filed by the Truth In Labeling Campaign (TLC) and additional citizens to a final rule issued June 21, 2001. That rule exempts from the requirement of a tolerance under section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA) use of L-glutamic acid (LGA) and gamma aminobutyric acid (GABA) on all food commodities when applied/used in accordance with good agricultural practices. EPA is denying the objections because the Agency has evaluated these products and believes them to meet the statutory requirement of reasonable certainty of no harm.

DATES: This order is effective October 27, 2004.

FOR FURTHER INFORMATION CONTACT: Carol E. Frazer, Biopesticides and Pollution Prevention Division (7511C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460; telephone number: (703) 308–8810; fax number: (703) 308–7026; e-mail address: frazer.carol@epa.gov.

ADDRESSES: EPA has established a docket for this action under Docket identification number OPP–2004–0243. All documents in the docket are listed in the EDOCKET index at *http://www.epa.gov/edocket.* Although listed in the index, some information is not publicly available, i.e., CBI or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, is not placed on the Internet and will be publicly available only in hard copy form. Publicly available docket materials are available either electronically in EDOCKET or in hard copy at the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1801 S. Bell St., Arlington, VA, Monday through Friday, excluding legal holidays. The Docket telephone number is (703) 305–5805.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does This Action Apply to Me?

This action is directed to the public in general. However, this action is of particular interest to TLC, the major objector to the use of LGA as a pesticide product and to Lucinda Larson, the only objector who specifically added GABA to her objection as well as LGA. Several other objectors expressed an objection to the **Federal Register** notice exempting the two chemicals from the requirement of a tolerance, without specifying either one. This action is also of interest to Emerald BioAgriculture Corporation, the manufacturer of AuxiGro™, the only pesticide product that uses LGA and GABA as active ingredients, as well as users of AuxiGro™ products. Since various different entities may be interested in this action, the Agency has not attempted to describe all the specific entities that may be affected by this action. If you have any questions regarding the applicability of this action to a particular entity, consult the person listed in the **FOR FURTHER INFORMATION CONTACT** section.

B. How Can I Access Electronic Copies of this Document and Other Related Information?

In addition to using EDOCKET (*http://www.epa.gov/edocket/*), you may access this **Federal Register** document electronically through the EPA Internet under the ''**Federal Register**'' listings at *http://www.epa.gov/fedrgstr/.* A frequently updated electronic version of 40 CFR part 180 is available at E-CFR Beta Site Two at *http://www.gpoaccess.gov/ecfr/.*

II. Background and Statutory Findings

A. What Action Is the Agency Taking?

From June 28, 2001 through January 14, 2002, TLC and others filed a series of objections to EPA's issuance of an exemption from the requirement of a tolerance under section 408 of the FFDCA for use of LGA and GABA on all food commodities when applied/used in accordance with good agricultural practices. EPA is denying the objections because it has reviewed all available data on these pesticides and maintains its conclusion that the uses of these pesticides are safe. None of the objectors filed a hearing request.

B. What Is the Agency's Authority for Taking This Action?

Section 408 of the FFDCA authorizes the establishment by regulation of maximum permissible levels of pesticides in foods. Such regulations are commonly referred to as ''tolerances.'' Without such a tolerance or an exemption from the requirement of a tolerance, a food containing a pesticide residue is ''adulterated'' under section 402 of the FFDCA and may not be legally moved in interstate commerce. 21 U.S.C. 331, 342. Monitoring and enforcement of pesticide tolerances are carried out by the U.S. Food and Drug Administration (FDA) and the U.S. Department of Agriculture (USDA).

Section 408(b)(2)(A)(i) of the FFDCA allows EPA to establish a tolerance only if EPA determines that the tolerance is ''safe.'' Section 408(b)(2)(A)(ii) defines ''safe'' to mean that ''there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information.'' This includes dietary exposure through food and drinking water and exposure other than dietary that occurs in non-occupational settings. In making safety determinations, EPA is required to consider, among other things, ''available information concerning the cumulative effects of the pesticide chemical residue and other substances that have a

common mechanism of toxicity.'' 21 U.S.C. 346a(b)(2)(D)(v). Section 408(b)(2)(C) requires EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance and to ''ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue. . . .'' 21 U.S.C. 346a(b)(2)(C). For pesticides that pose a threshold effect, EPA is directed to apply ''an additional tenfold margin of safety . . . to take into account potential pre- and post-natal toxicity and completeness of the data with respect to exposure and toxicity to infants and children.'' [hereinafter referred to as ''the children's safety factor''] Id. This provision additionally specifies that EPA ''may use a different margin of safety for the pesticide chemical residue only if, on the basis of reliable data, such margin will be safe for infants and children.'' Id. The procedure for establishing tolerance regulations is generally initiated by pesticide manufacturers through the filing with EPA of a petition requesting the establishment of a tolerance. See 21 U.S.C. 346a(d). EPA is required to publish notice of this petition as well as a summary of the petition prepared by the petitioner. Id. 346a(d)(3). After evaluation of the petition, EPA may issue a final tolerance regulation, a proposed tolerance regulation, or an order denying the petition. Id. 346a(d)(4). Once a final tolerance regulation is issued, any person may, within 60 days, file written objections to any aspect of this regulation and may also request a hearing on issues of fact raised by the objections. Id. 346a(g).

EPA regulations specify that if a hearing is requested, the objections must include a statement of the factual issues on which a hearing is requested, the requestor's contentions on such issues, and a summary of any evidence relied upon by the requestor. 40 CFR 178.27. A request for a hearing will be granted if the Administrator determines that the material submitted shows the following: There is genuine and substantial issue of fact; there is a reasonable possibility that available evidence identified by the requestor would, if established, resolve one or more of such issues in favor of the requestor, taking into account uncontested claims or facts to the contrary; and resolution of the factual issues in the manner sought by the requestor would be adequate to justify the action requested. 40 CFR 178.32. EPA's regulations specify that if no hearing is requested, or a requested hearing is denied, EPA will publish in the **Federal Register** its determination on each objection submitted. 40 CFR 178.37(a).

III. Regulatory and Procedural History

LGA and GABA are pesticides produced by Emerald BioAgriculture (formerly Auxein) Corporation. They are currently registered under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. 136 et seq., for use on all food commodities (40 CFR 180.1187 and 180.1188) and exemptions for the requirement of tolerances covering all uses have been established under the FFDCA.

In 1987, EPA approved use of LGA as a plant nutrient inert for seed treatment [40 CFR 180.1001(d)].

In August 1997, EPA published a notice of the first application for a new pesticide product containing both of these active ingredients (62 FR 42782, August 8, 1997) (FRL–5735–1). This notice announced receipt of an application to register a pesticide product, AuxiGro WP (EPA File Symbol 70810–R) containing new active ingredients GABA: gamma aminobutyric acid at 29.2% and glutamic acid at 36.5%, not included in any previously registered product pursuant to the provisions of section 3(c)(4) of the FIFRA, as amended. This product was a plant growth enhancer for use to increase yields and the quality of crop plants and early ripening in certain vegetables. EPA received no comments or objections to this application.

In September 1997, in response to a petition submitted by Auxein Corporation, EPA issued temporary tolerances for glutamic acid (62 FR 46882, September 5, 1997) (FRL–5741–3) and GABA (62 FR 46885, September 5, 1997) (FRL–5741–4) on crops including: snap beans, peanuts, cotton, potatoes, tomatoes, lettuce, green peppers, spinach, broccoli, cauliflower and cabbage to enhance crop yields. These tolerances were scheduled to expire on October 1, 1999. Again, EPA received no comments or objections to the exemptions from the requirement for a tolerance.

Later that same year, EPA published a proposed permanent exemption from the requirement of a tolerance to cover use of both active ingredients (62 FR 56168, October 29, 1997)(FRL–5751–3). Depending on the crop, the first application of AuxiGro was made at first bloom, first bud, at the 4 to 6 leaf stage, or other prescribed growth stage. A subsequent application, for a maximum of two applications, could be made 1 to 3 weeks later. The rate range is 0.10 – 0.75 pounds of formulated product/acre per treatment, not to exceed a maximum of 1.5 lb/A per growing season. This equated to the application of 0.55 lb/A glutamic acid and 0.4 lb/A of GABA applied at the maximum use rate. EPA received no comments or objections to this proposal. EPA finalized this rule the following year (63 FR 679, January 7, 1998)(FRL–5764–4).

On August 20, 1998, after the close of the objection period, Jack Samuels of the Truth in Labeling Campaign (TLC) wrote to EPA objecting to the approval of monosodium glutamate as a pesticide (Ref. 1). EPA responded to the letter on October 13, 1998 after Mr. Samuels' objections were reviewed (Ref. 2).

In September 1998, EPA made a technical amendment to the nomenclature language of the tolerance exemption to change ''glutamic acid' to ''LGA'' (63 FR 51302, September 25, 1998)(FRL–6029–1).

In 2000, Auxein petitioned EPA to modify 40 CFR 180.1187 and 40 CFR 180.1188 by deleting the wording ''when used as a plant growth enhancer'' from the tolerance exemption then in place and, as a result broaden the scope of the tolerance exemption, and to correct the language of the tolerance exemption then in place by changing the term ''raw agricultural commodities'' to ''food commodities'' (65 FR 76241–76244, Dec. 06, 2000). EPA received no comments on the petition.

Auxein submitted efficacy studies to support the broadened use patterns and EPA evaluated the data and determined that the new claims were supported by the data. As a result, in June 2001, EPA finalized the changes proposed by Auxein by modifying 40 CFR 180.1187 and 180.1188 accordingly (66 FR 33195, June 21, 2001)(FRL–6785–6).

On June 28, 2001, Dr. Adrienne Samuels of TLC submitted an Objection to the Exemption from the Requirement of a Tolerance and the group was joined individually by several of their members who also submitted objections.

IV. Response to Objections

A. Summary of Objections Received

There were 57 objectors to the revised tolerance exemption for LGA and GABA. All objections addressed the perception that an exemption for LGA was equivalent to treating crops with ''monosodium glutamate'' or ''processed free glutamic acid'' or ''processed free glutamic acid (MSG)'' or to ''what the Agency calls LGA.'' None of the objections specifically address ''LGA'' or provided scientific evidence or information linking dietary

consumption of LGA to adverse reactions. Similarly, none of the objections specifically cited consumption of GABA as the cause of adverse reactions or provided scientific evidence or information linking connection of dietary consumption of GABA to adverse reactions.

Rather, many objections reported the individual's reactions or someone else's reactions to dietary intake of MSG, and/or to processed free glutamic acid (MSG). These included, with frequency of reaction cited, headache/migraine (12), nausea (5), abdominal cramps (5), allergy (5), shortness of breath (4), and accelerated pulse rate (3). Other symptoms mentioned once or twice included numbness, lethargy, stiffness, distorted vision, coughing, insomnia, and facial twitching. Eight objections noted individuals felt that ingestion of ''small'' or ''tiny'' amounts of MSG elicited some reaction.

B. Agency Response to Summary Objections

As to the general objections on LGA, there is no evidence, and objectors provide no support for a claim, that dietary consumption of LGA causes adverse human health effects. This is the case regardless of whether the dietary consumption is of raw or processed food containing LGA or whether the LGA is produced environmentally by natural events or in the laboratory. In fact, because LGA is a defined chemical structure and a constituent of protein, there is significant exposure to LGA via the diet unrelated to the pesticide use and it is also synthesized endogenously (Ref. 3). Objectors provide no scientific evidence or information to distinguish natural LGA from what objectors refer to as ''processed'' LGA. This is because there is no difference in chemical structure, for example, between LGA found in nature or the human body and LGA produced for pesticide purposes. Where the chemical structure of two chemicals is the same in all contexts, there is no scientific basis to distinguish between the chemicals.

With respect to the symptoms cited by objectors, these symptoms are representative of the ''acute, temporary, and self-limited reactions'' to oral ingestion of MSG, as delineated by an Expert Panel to the Food and Drug Administration (FDA) evaluating the safety of use of MSG (Ref. 3). There has been a long history of inquiry into the safety of MSG as a flavor enhancer in foods. The Expert Panel to FDA concluded that ''...[b]ased on scientifically verifiable evidence, there is a subgroup of presumably healthy individuals within the population that responds generally within one hour of exposure with manifestations of the MSG Symptom Complex to an oral bolus of [greater than or equal to] 3 grams in the absence of food.'' However, the Expert Panel also concluded (emphasis theirs) that ''...no evidence exists to support a role of ingested glutamate in the etiology or exacerbation of...any...long-term or chronic illness.'' Moreover, there is no evidence that dietary consumption of LGA elicits, or has elicited, the ''MSG Symptom Complex'' of reactions. None of the objections identify foods containing LGA as the cause of the reactions cited.

C. Specific Objections and Agency Responses

1. *First objection*. TLC states that LGA naturally bound in protein or freed from protein via the natural human digestion process causes no adverse reactions (i.e., is safe). On the other hand, they state that foreign, unnatural substances are produced from protein containing glutamic acid stereoisomers (i.e., L-glutamic and D-glutamic acid) during natural fermentation, food preparation, and processing. Specifically mentioned are the production of D-glutamic acid and pyroglutamic acid when LGA is freed from protein via (microbial) fermentation, ''high heat (but not acid) hydrolysis,'' ''enzymolysis/autolysis,'' and ''secretion.'' In addition, they state carcinogenic propanols are produced from acid hydrolysis, and carcinogenic heterocyclic amines may be produced from heat but not acid. They state that LGA freed from protein via these mechanisms, and containing the above contaminants causes ''adverse reactions.'' They call these mixtures of chemicals ''processed free glutamic acid'' or ''processed free glutamic acid (MSG).'' No data were presented on the oral or dietary toxicity of any of the contaminants, nor on the doses required to produce toxicity, if any, to humans. Neither did they provide any evidence that the components of ''processed free glutamic acid'' can or do elicit reactions associated with ''MSG Symptom Complex,'' at any level of dietary exposure. Further, TLC states ''...we have never stated these so called contaminants are the cause of adverse reactions.''(Ref. 4)

EPA response. To the extent that objectors are concerned with contaminants that might be found in a pesticide product, EPA notes that its review of data/information submitted on the manufacturing process and on the chemical analyses of the technical grade of the active ingredient revealed none of the above mentioned contaminants. Thus, there is no scientific basis to support objectors' statements regarding the presence of the above mentioned contaminants and, to the extent that objectors' health-based statements are premised on the presence of these contaminants, there is no scientific basis to support objectors' statements. Had the contaminants been present in a pesticide product, a separate tolerance or exemption would typically be necessary to cover residues of such chemicals in or on food.

In addition, as noted above, an apparent primary basis for objections by TLC (both at the EPA and FDA) appears to be derived from their belief that the LGA which is derived from a (or any) manufacturing process is somehow (and in an unspecified manner) different than if it were freed from protein via a mechanism of human digestion, and is somehow different from LGA that humans and other higher organisms synthesize in their bodies, and is somehow different from the LGA that is found in unadulterated, unprocessed, unfermented food. Further, according to TLC, the LGA in lower forms of life (like bacteria) is in some unspecified manner, not equivalent to the LGA found in higher organisms. Again, as noted above, there is no scientific basis to support such an argument. The chemical structure of LGA is the same regardless of the organism in which it is found or regardless of how it is freed from protein. To claim that people may react adversely to the same chemical structure solely on the basis of how it is produced is not a sound scientific proposition.

Specifically, and as an example, when a hydrogen ion becomes disassociated from LGA, the compound is called L-glutamate. When a sodium ion becomes associated with L-glutamate the compound is called monosodium glutamate (MSG). When a potassium or ammonium ion becomes associated with L-glutamate the compounds are called respectively, monopotassium and monoammonium glutamate. When the monosodium, or monopotassium, or monoammonium salts of L-glutamate are dissolved in water the sodium, or potassium, or ammonium ions become disassociated from the glutamate molecule. Thus, ''...[G]lutamate entities from glutamic acid and glutamate entities from the three [ammonium, potassium, and sodium] salts are indistinguishable and, once added to food or water and eaten, glutamate from any source, whether naturally present in food or manufactured by bacteria, is metabolized in the same manner'' (Ref. 5). Likewise, upon release to the

environment (as in a pesticide product, for instance) glutamate entities from LGA or from the three salts would be metabolized in the same manner by organisms in the environment.

2. *Second objection*. In granting the tolerance exemption, the EPA has ''...violated Section 408(c)(2)(A)(i), Section 408(c)(2)(ii), Section (408)(c)(2)(b), and Section 408(b)(2)(D) of the Federal Food, Drug, and Cosmetic Act (FFDCA).''

EPA response. EPA does not agree with TLC that use of LGA or GABA as permitted by the registration and tolerance exemptions violates the specified sections of FFDCA in granting the tolerance exemption for LGA. TLC states that LGA bound in protein and freed via human digestion causes no ''adverse reactions.'' Since the chemical entity LGA is the same regardless of the source of protein or how it is freed from protein, it is the same as the ''truly natural glutamic acid'' referred to by TLC, and thus also would cause no adverse reactions. Further, none of the objectors registered any adverse reactions from dietary consumption of the chemical entity LGA as is normally found in foods. Finally, there is no evidence thus far submitted or thus far available to the Agency that dietary consumption of LGA has caused or will cause adverse effects in the U.S. population, and its subgroups. If such data/information became available, the Agency would then reassess its position with respect to the tolerance exemption for LGA (and also for GABA).

In establishing the tolerance exemption for LGA, the Agency has considered the validity, completeness, and reliability of the extensive scientific data base on LGA, including in its monosodium form (MSG), and concluded that based on that data there is reasonable certainty of no harm resulting from all anticipated dietary exposures to LGA. The Agency considered information on the dietary consumption patterns of humans, as well as the sensitivities of major identifiable subgroups of consumers, including infants and children.

In addition, the strength and weakness of the existing data base, which includes the reports and conclusions of authors cited by TLC, previously has been reviewed and summarized in detail by the 1995 Expert Panel (Ref. 3). The Agency agrees with the conclusions of the subsequently issued summary report of Dr. Donald S. Stevenson (Ref. 6) that there is no scientific basis to support any argument that LGA, or glutamate, or MSG, plays any role in allergenicity including urticaria or anaphylaxis. ''It is illogical to propose that the human immune systems would form antibodies against our own amino acids....All amino acids are too small to be an antigen (allergen)'' (Ref. 6). EPA also agrees with the subsequent report conclusion of Dr. David G. Hattan (Ref. 7) that based on the scientific data ''...we do not concur with the Expert Panel that asthma is a predisposing medical condition associated with the ingestion of MSG.'' Finally, EPA agrees with the conclusions of the subsequently issued summary report of Dr. Roland N. Auer (Ref. 8) that ''[n]o causal relationship has been established between...diseases and oral MSG [or glutamate] ingestion in humans...'' There also is no evidence that ''...retinal diseases are caused, related to or accelerated by MSG [glutamate].''

3. *Third objection*. ''The processed free glutamic acid (referred to in the 1998 Final Rule as LGA) that was granted an exemption from the requirement of a tolerance, is a neurotoxic endocrine disruptor that causes brain lesions [and] endocrine disorders'' which are manifested as growth disorders, learning/behavior/memory deficits, MSG-associated responses, schizophrenia, multiple sclerosis (MS), Parkinson's disease, amyotrophic lateral sclerosis (ALS), etc.

EPA response. The Agency does not agree with the objection that LGA is a neurotoxic endocrine disruptor, and when consumed in the diet will lead to the stated disorders and associated diseases, and to the MSG symptom complex of reactions. As concluded by the Expert Panel to FDA, ''...no evidence exists to support a role of ingested glutamate in the etiology or exacerbation of...any...long-term or chronic illnesses...'' including diseases such as Alzheimer's disease, Huntington's chorea, and amyotrophic lateral sclerosis (Ref. 3).

The Agency is aware of the studies in which LGA, when delivered at high doses to laboratory animals (mice, rats, infant primates) by appropriate route (injection, high-volume force feeding) induces neuronal death-associated lesions at the hypothalamus (and, in rodents, the medulla oblongata). The Agency also is aware of concerns presented by some (Ref. 9) that such findings, if extrapolatable to dietary intake of LGA by humans could have health implications. Such speculations, however, are not supported since there is no scientific evidence to indicate that LGA or MSG as consumed in foods disrupts the neuroendocrine axis. No such glutamate-induced lesions of the hypothalamus or medulla oblongata ever have been seen or described in humans upon autopsy of millions of people - including children - over the years. (Ref. 8). ''Claims that orally ingested MSG [or glutamate] causes or contributes to Alzheimer's disease, Parkinsonism, Huntington's Chorea, amyotrophic lateral sclerosis, obesity, early or late puberty, stunting of growth, or infertility must be viewed with extreme skepticism until some evidence is provided.'' (Ref. 8).

4. *Other specific objection issues raised by TLC.*—a. TLC knows of ''...no white, practically free-flowing crystalline powder that is ubiquitous in nature.''

Agency response. When organic materials, like amino acids,are purified from nature they take on the physical and chemical characteristics of the purified molecule. Upon release of this purified material to the environment, as a pesticide active ingredient for example, it will dissolve in water and will be indistinguishable from the LGA already in the environment.

b. TLC states that EPA ''...falsely asserted that processed free glutamic acid has a long history of food uses''.

Agency response. EPA never has used the term ''processed free glutamic acid.'' This term is used by TLC, and is not used by members of the scientific community. The terms ''LGA'' and ''monosodium glutamate'' define the chemical structures of specific organic molecules and are recognized terms.

c. TLC cites three publications by J. W. Olney to support their conclusion that ''...there is growing recognition that the reactive component of monosodium glutamate is processed free glutamic acid...that causes adverse reactions...regardless of the names of the ingredients that contain it or the uses to which it is put.''

Agency response. The scientific research results of J. W. Olney (e.g., Ref. 10) showing neuronal lesions in certain laboratory animals have been considered by EPA in its finding of safety from dietary exposure in humans to LGA. EPA believes Olney's research conclusions are based on effects due to the recognized molecules ''monosodium glutamate'' or ''LGA'' regardless of the source (e.g., natural or manufactured) and when delivered in highly purified form and at extreme dose levels.

d. TLC cites a report by Martinez (Ref. 11) and concludes that the author ''...found a relationship between glutamate levels in the CSF [cerebrospinal fluid] of the central nervous system, not glutamate levels in the plasma, that were related to migraine headache.''

Agency response. Martinez (Ref. 11) found that glutamic acid levels in CSF

[obtained by lumbar puncture during migraine attack] were lower than in CSF of a ''stress'' control population (e.g., pre-operative surgery patients, acute stroke sufferers, cancer patient, multiple sclerosis sufferers). He also found that glutamic acid levels in plasma of migraine sufferers during attack were lower than in plasma of the ''stress'' control population. No conclusions on relationships between oral consumption of MSG and migraine can be drawn from the results, since the study was not designed to, or intended to, test such a relationship. The study results are best discussed with regard to possible physiological responses (e.g., glutamate release) to brain events (e.g., cortical blood flow, hypoxic ischemia) that occur during migraine.

e. TLC states ''(i)ngestion of processed free glutamic acid causes adverse reactions in susceptible individuals - reactions known to occur as side effects of neurotropic drugs such as valium.''

Agency response. The benzodiazepiene drug Valium (diazepam) is used to treat anxiety disorders, for skeletal muscle relaxation, and as a preoperative anesthetic. It interacts with part of the GABA receptor, in the presence of GABA to enhance GABA-induced changes in membrane potential, thereby augmenting inhibitory effects by stimulating various GABA-ergic pathways. Primary side effects are drowsiness and loss of balance. Thus Valium acts in concert with the neuroinhibitory physiological role of GABA, in apposition to the neuroexcitatory physiological role of L-glutamate.

f. EPA omitted data from the literature on toxic and endocrine-disrupting properties of processed free glutamic acid and its ability to cause adverse effects in humans.

Agency response. TLC did not cite any studies done in humans that show adverse endocrine, neurological, learning, or locomotor effects from exposure to LGA, MSG, or to what TLC refers to as ''processed free glutamic acid.'' EPA believes it has considered all of the scientific literature.

g. TLC states that certain human studies done with placebos induced reactions in control groups and thereby obscured the results of such studies when the control population was compared to the treated group. TLC cites a study by Strong (Ref. 12) who concluded that placebo materials (e.g., capsules) in some earlier human studies may give headaches to ''dietary migraine sufferers.''

Agency response. Strong (Ref. 12) summarized results from six earlier published double-blind studies conducted to test patient sensitivity to tyramine and beta-phenylethylamine. His analysis of the results showed 18% of patients reported headaches from placebos which were concealed in gelatin capsules. In the current study by Strong (Ref. 12), the author was the sole subject in the study. The double-blind component of the study apparently was done with water containing 1 milligram/milliliter (mg/ml) tyramine or with some unspecified amount of unspecified placebo in 20 ml of water. Gelatin capsules were not used. The author suffered headache after consuming 5 of 6 of the tyramine samples, but not from placebo samples. The author self-reported headache from consuming 400 mg of MSG in 15 grams (g) of cottage cheese, from 118 mg partially hydrolyzed vegetable protein in 15 g of ricotta cheese, and 123 g gelatin capsule in potato chips. This part of the study apparently was not double-blinded. The Agency believes the results from an extensive study done by Geha et al. (Ref. 13) represent the best available data in a multicenter, multiphase, double-blind, placebo-controlled study with MSG using 130 self-reporting responders to MSG in the initial phase of the study. A citrus-based placebo beverage was used. The results suggested that ''...large doses of MSG given without food may elicit more symptoms than a placebo in individuals who believe they react adversely to MSG. However, neither persistent nor serious effects from MSG ingestion are observed, and the responses were not consistent upon retesting.''

h. TLC states ''[t]here is no evidence that surface residue from processed free glutamic acid will be gone prior to harvesting crops...and the applicant failed to note there would be residue in and on food crops.'' ''To be effective as a plant growth enhancer...processed free glutamic acid would have to be taken up by the plants.'' Also, all food crops ''[c]ould potentially be treated with processed free glutamic acid.''

Agency response. The tolerance exemption for LGA is supported by a lack of dietary toxicity. Therefore, it is appropriate for the EPA to not require residue data for the pesticidal use of LGA.

i. TLC states they have demonstrated that the glutamic acid in monosodium glutamate or other processed foods is not chemically identical to the LGA found in unadulterated/unprocessed/unfermented food. The glutamate industry has ''failed to distinguish between free glutamic and processed free glutamic acid...and only processed free glutamic acid causes adverse reactions in MSG-sensitive people who ingest amounts that exceed their tolerance levels.''

Agency response. TLC has not demonstrated that the chemical entity LGA is somehow different when it is manufactured. The chemical structure of LGA is the same no matter how it is produced, or from the source from which it is derived.

j. ''...EPA had the audacity to state in 1988 that '[t]he Agency has no information to suggest that glutamic acid will adversely affect the immune or endocrine systems'...and in 2001...EPA had the gall to ignore the subject of endocrine disruptors entirely.''

Agency response. There is no evidence that dietary consumption of LGA or monosodium glutamate causes adverse effects to the immune or endocrine systems of humans including infants and children.

k. TLC states that ''...monosodium glutamate and LGA are given hazard ratings of HR3 (most toxic) indicating an LD_{50} below 400 milligrams/kilogram (mg/kg)...in the sixth edition of 'Dangerous Properties of Industrial Materials.'''

Agency response. The oral LD_{50} values for LGA are reported by the Registry of Toxic Effects of Chemical Substances (RTECS) as >30 g/kg in the rat and 2.3 g/kg in the rabbit. The oral LD_{50} values for MSG are reported at 16.6 g/kg in the rat and 11.4 g/kg in the mouse. These values are consistent with the least toxic category for pesticides, and would not require any precautionary statements for human hazard on the pesticide label. More relevant, is the long history of human dietary exposure to the naturally occurring amino acid, LGA, with no adverse effects - including lethality - ever being attributed, linked, or even expected from such exposures.

l. TLC believes that EPA waived a requirement for a metabolism study with LGA because MSG has GRAS status.

Agency response. A laboratory animal metabolism study (i.e., OPPTS Harmonized Guideline No. 870.7485) is not an EPA requirement for registration of biochemical pesticides (LGA and GABA are classified as biochemical pesticides). Thus, there is no need to waive a requirement for a metabolism study. Yet, the EPA could require such a study for biochemical pesticides if considered warranted. However, such a study in laboratory animals is not warranted because there is extensive knowledge on dietary exposure to, and subsequent metabolism of, LGA in humans without findings of toxicity. Likewise, the GRAS status of MSG

supports, and is consistent with, the Agency's finding for a tolerance exemption for LGA.

m. TLC cites a multigeneration reproduction study (Ref. 14) where mice were fed MSG to support their contention that ''...failure to find differences in growth or adverse reactions of control and experimental groups may very well have been, in part, to the fact that control groups were receiving neurotoxic substances in their basal diets.'' The cited potential component of the basal diet was ''yeast food'' which TLC states ''...invariably contained either protease (which creates processed free glutamic acid during manufacture) or L-cysteine which produces neurotoxic effects...more extensive than the effects of processed free glutamic acid.''

Agency response. In the above cited study, about 800 mice through the F0 to F3 generations were fed basal diet containing 1% MSG, and an additional 800 mice were fed basal diet containing 4% MSG. There were about 1800 mice in the control group, fed basal diet only. There were no observed adverse effects in animals from the control or treated groups. All parameters measured in the control and treated groups were within expected ranges for the mouse. No brain lesions or any other pathological changes were noted. Fertility index, gestation index, viability index, and lactation index were all high, in the MSG-treated animal and control groups. The hypothesis of TLC that neurotoxic components in the basal diet adversely affected the control group animals, and thus masked effects in the dosed group animals when the groups were compared is not supportable when no adverse effects were seen in any group, and all parameters were within expected ranges typical of the normal healthy mouse.

n. TLC states certain animal feeding studies submitted to the Agency were flawed because while they ''...accounted for the amount of food consumed by experimental and control groups [they] did not account for the amount of processed free glutamic acid consumed as opposed to being left on the table.'' ''Every animal owner knows that animals are quite adept at ferreting out and rejecting (not eating) pills or other goodies hidden in their food.''

Agency response. In dietary studies with rodents, test materials are uniformly blended with, and thus uniformly distributed in the food. Therefore, rejection of the diet due to aversion to the test material mixed in the food would be readily determined by a measured decrease in food consumption. Food consumption was accounted for in experimental and control groups in the studies cited, and was comparable among the groups.

o. TLC states that the results from acute toxicity studies done with laboratory animals do not ''...mimic the real life situation wherein animals could be sprayed or otherwise come in contact with Auxigro.

Agency response. The acute toxicity battery of studies were done at doses sufficiently high to allow placement of the test material in the least toxic category for pesticides. Considering the acute inhalation toxicity study as an example, rats were exposed in a chamber to 2.58 mg/L for 4 hours. The only effects observed were piloerection, decreased activity, and red crust around the nose. These minor effects resolved by day 4 after exposure. Also, a very high dose of Auxigro (i.e., 5 g/kg) only caused slight and reversible redness to the animals' skin, and the minor eye irritation effects observed also were reversible. It can be concluded that if animals were sprayed with Auxigro during pesticide application and use, they would not be adversely affected.

p. Agency summary response to objections by TLC on the tolerance exemption for LGA. TLC has not provided any scientific documentation that dietary consumption of LGA has caused harm, or will cause harm to humans, including to infants and children. They have not provided any evidence that LGA is allergenic, or when consumed by humans, adversely affects the endocrine system or the central and peripheral nervous system. They have provided no evidence that LGA is carcinogenic. They have not provided any scientific documentation that an oral bolus of MSG causes any adverse effects in humans beyond those typically associated with the MSG Symptom Complex. Even then, the pesticidal use of LGA represents an exposure scenario quite different than the food additive use of MSG as a flavor enhancer. Use of LGA as a pesticide is unlikely to contribute any significant addition of free glutamic acid already in the human diet, and even if use of LGA as a pesticide did significantly increase free glutamic acid in the diet there are no toxic endpoints that have been identified from dietary consumption of LGA. TLC has maintained that LGA is somehow different than the form found in nature when it is produced by microorganisms, or when it is released from protein by other than human digestive proteolytic enzymes. TLC calls this different material ''processed free glutamic acid'' and maintain that this is the material which causes numerous adverse effects. It mentions certain contaminants that may arise from certain processes that are used, or have been used, in deriving commercially available sources of LGA, but never states that it believes these contaminants are causing adverse effects, or provide any data on dose-response studies to support adverse effects from these materials. In fact, it has ''...never stated these so called contaminants are the cause of adverse reactions.'' Nevertheless, the tolerance exemption set forth under 40 CFR 180.1187 is for LGA, and is not for any other chemical.

D. Summary of Objections by Lucinda Larsen

One objector, Lucinda Larsen, objected to the tolerance exemption for LGA and GABA on the ground that it would allow use of unrestricted amounts of ''potent neurotoxins'' which would interfere with ''...almost all bodily functions.'' If supplemented in the diet, millions of consumers would suffer death or injury from ingestion of the slightest amount of ''processed free glutamic acid'' or ''manufactured free glutamic acid.'' ''The glutamic acid found in nature is bound not freed and [is un]able to interfere with bodily functions.'' The objector believes the EPA has not considered and ''...collect[ed] updated pertinent data from unbiased sources.''

Agency response. The Agency has considered the strength and weakness of the existing scientific data base (e.g., see above) and has concluded that the tolerance exemptions for LGA and for GABA pose no unreasonable risk to human health. Free LGA is found in nature, in human bodies, and in the foods humans eat and it is the same glutamic acid as manufactured from microbial fermentation or by release from proteins. Likewise, free GABA, derived via enzymatic activity (i.e., decarboxylation reaction) from LGA, also is found in humans, plants, and microorganisms. LGA is the most important excitatory neurotransmitter in the central nervous system (CNS). GABA on the other hand is not an excitatory neurotransmitter, but rather is an important inhibitory neurotransmitter.

V. Order Responding to Objections

The exemptions for the requirement of a tolerance for LGA and GABA on all food commodities to which TLC and other objectors filed objections are in force and will remain so.

As detailed in Dr. Andersen's October 13, 1998 response to Mr. Jack Samuels and TLC's first objection to the exemption for LGA in August 1998, EPA

scientists critically appraised all the data at that time and came to the conclusion that Mr. Samuels' objection was unwarranted (Ref. 2). However, EPA wishes to make sure all possible areas of disagreement are covered and has reviewed the latest information submitted by the objectors and believes nothing substantive has been added to the body of data known on these chemicals, and no change in the previous exemption is necessary.

VI. Regulatory Assessment Requirements

As indicated previously, this action announces the Agency's final decision regarding an objection filed under section 408 of FFDCA. As such, this action is an adjudication and not a rule. The regulatory assessment requirements imposed on rulemakings do not, therefore, apply to this action.

VII. Congressional Review Act

The Congressional Review Act, 5 U.S.C. 801 et seq., as added by the Small Business Regulatory Enforcement Fairness Act of 1996, does not apply because this action is not a rule for purposes of 5 U.S.C. 804(3).

VIII. References

1. Letter from Jack L. Samuels to Sue Smith, The White House, Aug. 20, 1998.

2. Letter from J. Andersen to J. Samuels, Oct. 13, 1998.

3. Raiten, D.J. et al., Analysis of Adverse Reactions to Monosodium Glutamate (MSG), American Institute of Nutrition, MD, 1995.

4. e-Mail from J. Samuels to J. Andersen, 7/28/98.

5. Kuznesof, P.M., Expert Report, undated.

6. Stevenson, D.S. Expert Report, undated.

7. Hattan, D.G. Expert Report, undated.

8. Auer, R.N., Expert Report, undated.

9. Olney, J. W. Excitotoxins in Foods. Neurotoxicology 15(3) 535–544, 1994.

10. Olney, J.W., et al., Cytotoxic effects of acidic and sulphur containing amino acids on the infant mouse central nervous system. Exp. Brain Res. 14:61–76, 1971.

11. Martinez, F., et al. Neuroexcitatory amino acid levels in plasma and cerebrospinal fluid during migraine attacks. Cephalalgia. 13:89–93, 1993.

12. Strong, F.C., Why do some dietary migraine patients claim they get headaches from placebos? Clin. Experimental Allergy. 30:739–743, 2000.

13. Geha R. S. et al., Multicenter, double-blind, placebo-controlled, multiple challenge evaluation of reported reactions to monosodium glutamate. J. Allergy Clin. Immunol. 106:973–980, 2000.

14. Anantharaman, K., *In utero* and dietary administration of monosodium L-glutamate to mice: reproductive performance and development in a multigeneration study. *In* ''Glutamic Acid: Advances in Biochemistry.'' L. J. Filer, et al., eds. Raven Press, N.Y., 1979.

List of Subjects in 40 CFR Part 180

Environmental protection, Administrative procedure, pesticides and pests.

Dated: October 18, 2004.

James Jones,

Director, Office of Pesticide Programs.

[FR Doc. 04–24041 Filed 10–26–04; 8:45 am]

BILLING CODE 6560–50–S

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[OPP–2004–0331; FRL–7683–5]

Deltamethrin; Pesticide Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes a tolerance for combined residues of deltamethrin, isomers trans-deltamethrin and α-R-deltamethrin in or on almond hulls; apples, wet pomace; artichoke, globe; barley, bran; cattle, fat; cattle, meat; cattle, meat byproducts; corn, field, forage; corn, field, refined oil; corn, field, stover; corn, pop, stover; corn, sweet, forage; corn, sweet, kernel + cob with husks removed; corn, sweet, stover; egg; fruit, pome, group 11; goat, fat; goat, meat; goat, meat byproducts; grain, aspirated fractions; grain, cereal, group 15, except sweet corn; hog, fat; horse, fat; horse, meat; horse, meat byproducts; lychee (import tolerance); milk, fat (reflecting 0.02 ppm in whole milk); nut, tree, group 14; onion, dry bulb; onion, green; poultry, fat; poultry, meat; poultry, meat byproducts; radish tops; rapeseed; rice, hulls; rye, bran; sheep, fat; sheep, meat; sheep, meat byproducts; sorghum, grain forage; sorghum, grain stover; soybean, seed; soybean, hulls; starfruit (import tolerance); sunflower seeds; vegetable, cucurbit, group 9; vegetable, fruiting, group 8; vegetable, root, except sugar beet, subgroup IB; vegetable, tuberous and corm, subgroup; IC; wheat, bran. Bayer Crop Science LP, formerly Aventis CropScience, requested these tolerances under the Federal Food, Drug, and Cosmetic Act (FFDCA), as amended by the Food Quality Protection Act of 1996 (FQPA).

DATES: This regulation is effective October 27, 2004. Objections and requests for hearings must be received on or before December 27, 2004.

ADDRESSES: To submit a written objection or hearing request follow the detailed instructions as provided in Unit VI. of the **SUPPLEMENTARY INFORMATION**. EPA has established a docket for this action under Docket identification (ID) number OPP –2004–0331. All documents in the docket are listed in the EDOCKET index at *http://www.epa.gov/edocket.* Although listed in the index, some information is not publicly available, i.e., CBI or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, is not placed on the Internet and will be publicly available only in hard copy form. Publicly available docket materials are available either electronically in EDOCKET or in hard copy at the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1801 S. Bell St., Arlington, VA. This docket facility is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The docket telephone number is (703) 305–5805.

FOR FURTHER INFORMATION CONTACT: George LaRocca, Registration Division (7505C), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW.,Washington, DC 20460–0001; telephone number: (703) 305–6100; e-mail address: *larocca.george@epa.gov*.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. Potentially affected entities may include, but are not limited to:

- Crop production (NAICS 111), e.g., agricultural workers; greenhouse, nursery, and floriculture workers; farmers.
- Animal production (NAICS 112), e.g., cattle ranchers and farmers, dairy cattle farmers, livestock farmers.
- Food manufacturing (NAICS 311), e.g., agricultural workers; farmers; greenhouse, nursery, and floriculture workers; ranchers; pesticide applicators.
- Pesticide manufacturing (NAICS 32532), e.g., agricultural workers;