Petition to the FDA Revoke GRAS Status of Monosodium Glutamate

Presented by John Erb

to the United States Food and Drug Agency

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Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5603 Fishers Lane, rm 1061
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Citizen Petition

I, John Erb, the undersigned, submit this petition under Section 409 of the Federal Food, Drug, and Cosmetic Act to request the Commissioner of Food and Drugs to revoke the GRAS standing of the food additive Monosodium Glutamate.

Request of change to Section 182.1 under Title 21 of the Food and Drug Act where the existing wording reads:

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    (a) It is impracticable to list all substances that are generally
recognized as safe for their intended use. However, by way of
illustration, the Commissioner regards such common food ingredients as
salt, pepper, vinegar, baking powder, and monosodium glutamate as safe
for their intended use.
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Be changed to

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    (a) It is impracticable to list all substances that are generally
recognized as safe for their intended use. However, by way of
illustration, the Commissioner regards such common food ingredients as
salt, pepper, vinegar, and baking powder, as safe for their intended use.
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removing the word Monosodium Glutamate from this paragraph and thereby revoking its place on the GRAS list.

Furthermore it is requested that

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182.1045  Glutamic acid.
182.1047  Glutamic acid hydrochloride.
182.1500  Monoammonium glutamate.
182.1516  Monopotassium glutamate
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as GRAS additives also be revoked.

It is further requested that artificial food additives such as Hydrolyzed Vegetable Protein, Autolyzed Yeast Extract, and other additives in which Glutamate is a primary component have their GRAS status revoked.

I further ask the Commissioner for a copy of the research showing the benefits of adding Glutamate containing ingredients to the food supply.

Statement of Grounds

Monosodium Glutamate is an amino acid that affects on almost every major system and organ in the body. Glutamate receptors trigger many different responses and can be over stimulated to cause cell death and other systemic problems. For thirty years, scientists and researchers have used MSG in their experiments to purposely create obese and pre-diabetic test subjects, trigger epileptic seizures, create ischemic strokes, and destroy cell tissues in vivo and in vitro. The amount of studies that use MSG to cause negative effects in test subjects numbers over one thousand, published in a variety of medical and scientific journals in over a dozen different countries.

Monosodium Glutamate added to the diet has been shown to increase the test subjects desire to eat more food faster and more frequently.

There is mounting evidence that not only the rise in human obesity and diabetes is linked to the ingestion of Monosodium Glutamate, but the increase in Autism as well.

In light of the overwhelming evidence showing the detrimental effects of the food additive Monosodium Glutamate, it is requested that the Commissioner of the FDA remove Monosodium Glutamate (and ingredients that contain MSG) from the list of GRAS additives

Human Exposure

Orally:

Monosodium Glutamate is found in unlimited amounts in a wide variety of packaged foods. The list of foods it can be found in is listed in Appendix A. MSG is also added in unlimited amounts in restaurant and industrial food such as hospitals, retirement homes and cafeterias. Because food processors and manufacturers do not have to list the amount of MSG on their packaging, we have no way of knowing what a normal person or child would ingest in a days period. According to industry research 0.6% MSG added to food is optimal for making people eat progressively more and faster (Bellisle F, Monneuse MO, 1991). If this is the case, as much as .6% of a person's daily diet could be made up of MSG. In a daily intake of 2kgs of laced food the adult or child would receive a 12 gram dose of Monosodium Glutamate. A 12 gram dosage of MSG is lethal to a one kg rat. *JECFA Toxicology Study, FAO Nutrition Meetings Report Series, 1974, No. 53*

Subcutaneously:

Though previous JECFA reports have disallowed MSG in foods for infants or those under one year of age, many infants and children receive doses of MSG in a variety of vaccinations. See Appendix C.

Air Transmission:

MSG is now being sprayed on crops and can become airborne. Though the Codex Alimentarius specifically disallows MSG's addition to fresh fruits and vegetables *(GFSA Annex to Table 3)* Auxigro, with 30% MSG content, has been approved by some countries to be sprayed on crops of fresh fruits and vegetables. Airborne effects of MSG sprays have not been studied by the JECFA.

Biological Aspects

Monosodium Glutamate is an amino acid readily utilized by glutamate receptors throughout the mammalian body. These glutamate receptors are present in the central nervous system as the major mediators of excitatory neurotransmission and excitotoxicity. Neural injury associated with trauma, stroke, epilepsy, and many neurodegenerative diseases such as Alzheimer's, Huntington's and Parkinson's diseases and amyotrophic lateral sclerosis may be mediated by excessive activation of the glutamate receptors. Neurotoxicity associated with excitatory amino acids encountered in food, such as monosodium glutamate, has also been linked to glutamate receptors. Glutamate receptors are found in the rat and monkey heart, the conducting system, nerve terminals and cardiac ganglia. They are also present in the kidney, liver, lung, spleen and testis. Therefore, food safety assessment should consider these tissues as potential target sites.

Potential target sites in peripheral tissues for excitatory neurotransmission and excitotoxicity.
Gill SS, Mueller RW, McGuire PF, Pulido OM.
Bureau of Chemical Safety, Health Protection Branch, Health Canada, Ottawa.
Toxicol Pathol. 2000 Mar-Apr;28(2):277-84

Short-term toxicity of Monosodium Glutamate

MSG Used to Trigger Epileptic Seizures

Epileptic convulsions were triggered in rats using small single doses of Monosodium Glutamate.

"Convulsive activity in 3, 10, 60 and 180-day old Sprague-Dawley rats was studied following the i.p. administration of 4 mg g-1 of commercial MSG. The latency period increased with the age of the animals while the duration of the convulsive period was longer in younger animals and shorter in 60-day old rats. Convulsions were predominantly tonic in 3 and 10-day old rats, tonic-clonic in 60-day old rats, and predominantly clonic in 180-day old animals. **The severity of the convulsions and death incidence increased progressively with age.**

Monosodium-L-glutamate-induced convulsions--I. Differences in seizure pattern and duration of effect as a function of age in rats.
Arauz-Contreras J, Feria-Velasco A.
Gen Pharmacol. 1984;15(5):391-5.

"Adult rats (60 days old) were injected intraperitoneally with 5 mg/g monosodium L-glutamate (MSG). During the convulsive period (1 h after injection), uptake and release of [3H]norepinephrine (3H-NE) and [14C]dopamine (14C-DA) were measured. Data suggest that catecholaminergic **neurotransmission may play an important role in the etiopathology of convulsions in the experimental model using MSG.**"

Monosodium L-glutamate-induced convulsions: changes in uptake and release of catecholamines in cerebral cortex and caudate nucleus of adult rats.
Beas-Zarate C, Schliebs R, Morales-Villagran A, Feria-Velasco A.
Epilepsy Res. 1989 Jul-Aug;4(1):20-7.

MSG Used to Trigger CNS and Brain Damage

Single doses of MSG have been used to cause CNS and brain damage in rodents and chicks.

"**Monosodium glutamate (MSG) was used to create a lesion in the CNS of the infant** rat. Subcutaneous injections of MSG in four day old rat pups caused a high degree of cell necrosis in the arcuate nucleus of the hypothalamus"

Reaction of the hypothalamic ventricular lining following systemic administration of MSG.
Rascher K, Mestres P.
Scan Electron Microsc. 1980;(3):457-64.

"**Administration of doses of glutamate (Glu) leads to selective neurodegeneration** in discrete brain regions near circumventriclular organs of the early postnatal mouse. The arcuate nucleus-median eminence complex (ARC-ME) appears to be the most Glu-sensitive of these brain regions, perhaps because of the intimate relationships between its neurons and specialized astroglial tanycytes. A dose of 0.2 mg MSG/g BW s.c. causes clear but discrete injury to specific subependymal neurons of undetermined phenotype near the base of the third ventricle. Slightly higher doses of MSG evoke damage of additional neurons confined to the ventral region of the ARC traversed by tanycytes."

Exogenous glutamate enhances glutamate receptor subunit expression during selective neuronal injury in the ventral arcuate nucleus of postnatal mice.

Hu L, Fernstrom JD, Goldsmith PC.
Neuroendocrinology. 1998 Aug;68(2):77-88

"Various dosages of monosodium glutamate (M.S.G.) were injected to 5 day old male chicks. Body weights, food intake, rate of obesity, semen production, some endocrine criteria and brain pathology were studied til 235 days post injection. **All M.S.G. treated birds showed brain damage** in the rotundus nuclei, and in the area located dorsolaterally to the ventromedial hypothalamic nuclei (V.M.H.). In some of the M.S.G. treated birds, additional brain regions were damaged, i.e. V.M.H., mammillary nuclei, dorsomedial anterior nuclei, ovoid nuclei, subrotundus nuclei, archistriatum and lateral forebrain bundles."

The relation between monosodium glutamate inducing brain damage, and body weight, food intake, semen production and endocrine criteria in the fowl.
Robinzon B, Snapir N, Perek M.
Poult Sci. 1975 Jan;54(1):234-41.

MSG Used to Damage Eye Cells in Vivo and in Vitro

Single doses of MSG have been used to trigger damage to various structures of the eye.

"**Monosodium L-glutamate is known to cause intracellular swelling, necrosis, and disappearance of most inner retinal neurons, with concomitant thinning of inner retinal layers within hours** after subcutaneous injection into neonatal rodents. A similar process can be observed in adult rat retina after intravitreal glutamate injection. To better describe and compare this process with that reported after systemic application, adult Sprague-Dawley rat eyes were intravitreally injected with 1 mumol monosodium L-glutamate and the retinas studied by LM and EM over a 2-month period. Results demonstrated that adult rat retina experienced severe degenerative changes which progressed in two stages: an initial stage of massive intracellular swelling and a second stage of necrosis and cell loss."

Histologic changes in the inner retina of albino rats following intravitreal injection of monosodium L-glutamate.
Sisk DR, Kuwabara T.
Graefes Arch Clin Exp Ophthalmol. 1985;223(5):250-8.

"**Monosodium glutamate added to 12-day chick embryo retinas in culture causes severe morphologic damage** to the retina as judged by light microscopic examination. Damage is evident after a few hours with concentrations as low as 0.3 mM. Glutamyltransferase induction is also appreciably inhibited by the amino acid. General protein synthesis and RNA synthesis appear to be less affected."

Effects of monosodium glutamate on chick embryo retina in culture.
Reif-Lehrer L, Bergenthal J, Hanninen L.
Invest Ophthalmol. 1975 Feb;14(2):114-24.

MSG Used to Create Obese Test Subjects

In studies of new diet and diabetes drugs and treatments, a test subject must be used that will exhibit the characteristics of obesity and hyperinsulinemea. For scientists to create replicable results the factor that triggers obesity in the experimental test group must be 100% replicable. For guaranteed results researchers regularly use injections of MSG subcutaneously on test subjects on the day of birth or shortly thereafter.

> "Monosodium glutamate (MSG) was administered by various methods to mice and rats of various ages and the incidence of obesity was later measured. Newborn mice were injected subcutaneously with 3 mg MSG/g body-weight at 1, 2, 3, 6, 7, and 8 d of age; 16% died before weaning. Of the survivors, 90% or more became markedly obese. The proposed schedule of **injections in the newborn was almost 100% reliable in inducing a high extent of adiposity**. "
>
> **The induction of obesity in rodents by means of monosodium glutamate.**
> Bunyan J, Murrell EA, Shah PP.
> Br J Nutr. 1976 Jan;35(1):25-39.

This replicable finding has been given the names 'monosodium glutamate obese rat' or 'MSG treated rat'.

Here are a few of the hundreds of studies that have used the rodent scientifically categorized as the MSG Treated Rat, a term synonymous with obesity, lethargy and hyperinsulinaemia:

Effect of adrenalectomy on the activity of small intestine enzymes in monosodium glutamate obese rats.
Mozes S, Sefcikov Z, Lenhardt L, Racek L. Physiol Res. 2004;53(4):415-22.

Effect of fasting and refeeding on duodenal alkaline phosphatase activity in monosodium glutamate obese rats.
Racek L, Lenhardt L, Mozes S. Physiol Res. 2001;50(4):365-72.

Decreased lipolysis and enhanced glycerol and glucose utilization by adipose tissue prior to development of obesity in monosodium glutamate (MSG) treated-rats.
Dolnikoff M, Martin-Hidalgo A, Machado UF, Lima FB, Herrera E. Int J Obes Relat Metab Disord. 2001 Mar;25(3):426-33

Effects of chronic administration of sibutramine on body weight, food intake and motor activity in neonatally monosodium glutamate-treated obese female rats: relationship of antiobesity effect with monoamines.
Nakagawa T, Ukai K, Ohyama T, Gomita Y, Okamura H.
Exp Anim. 2000 Oct;49(4):239-49.

Effects of monosodium glutamate-induced obesity in spontaneously hypertensive rats vs. Wistar Kyoto rats: serum leptin and blood flow to brown adipose tissue.
Iwase M, Ichikawa K, Tashiro K, Iino K, Shinohara N, Ibayashi S, Yoshinari M, Fujishima M.
Hypertens Res. 2000 Sep;23(5):503-10.

Obesity induced by neonatal monosodium glutamate treatment in spontaneously hypertensive rats: an animal model of multiple risk factors.
Iwase M, Yamamoto M, Iino K, Ichikawa K, Shinohara N, Yoshinari M, Fujishima M.
Hypertens Res. 1998 Mar;21(1):1-6.

The Ways in Which MSG Triggers Obesity In Test Subjects:

MSG increases the appetite.

MSG added to food of sheep has resulted in an increase in appetite:

Sheep with oesophageal fistulas were used in sham-feeding experiments to assess how sham intakes were affected by additions of monosodium glutamate (MSG) to the various straw diets. MSG at 5-40 g/kg fine and coarse ground straw increased sham intakes by 146% (P = 0.04) and 164% (P = 0.01) respectively. These findings indicated that **the intakes of poor-quality diets can be increased by improving their palatability with MSG.**

Factors affecting the voluntary intake of food by sheep. The effect of monosodium glutamate on the palatability of straw diets by sham-fed and normal animals.
Colucci PE, Grovum WL.
Br J Nutr. 1993 Jan;69(1):37-47.

MSG alters rat's ability to regulate food intake:

Caloric regulation and the development of obesity were examined in rats which had received parenteral injections of monosodium glutamate (MSG) as neonates. Rats were injected with either 2 mg/g or 4 mg/g MSG on alternate days for the first 20 days of life. In adulthood, the ability to regulate caloric intake was tested by allowing animals access to diets of varying caloric densities. While control animals maintained relatively constant caloric intakes across dietary conditions, MSG-treated animals demonstrated an inability to respond to caloric challenges. **Treated animals decreased caloric intake on a diluted diet and consumed more calories** than controls when presented with a calorically dense diet."

Juvenile-onset obesity and deficits in caloric regulation in MSG-treated rats.
Kanarek RB, Meyers J, Meade RG, Mayer J.
Pharmacol Biochem Behav. 1979 May;10(5):717-21

A connection can be found in human test subjects: Two findings with MSG and human appetite are discovered:

1. When a human subject eats a meal with MSG, they become hungry again, sooner.
2. Humans will eat more food laced with MSG than control food without it.

"Subjects consumed soup preloads of a fixed size containing different concentrations of monosodium L-glutamate (MSG). Effects on appetite following these preloads, and when no soup was consumed, were assessed in 3 studies.The most important finding concerning MSG showed that motivation to eat recovered more rapidly following a lunchtime meal in which MSG-supplemented soup was served."

Umami and appetite: effects of monosodium glutamate on hunger and food intake in human subjects.
Rogers PJ, Blundell JE.
Physiol Behav. 1990 Dec;48(6):801-4.

"MSG's effects on the palatability of two experimental foods were investigated in 36 healthy young men and women. MSG improved palatability ratings, with an optimum at 0.6%. Weekly tests of free intake showed that subjects fed the experimental foods with 0.6% MSG added ate progressively more and faster, indicating increasing palatability with repeated exposure. MSG facilitated intake of some but not all target foods, and was associated with positive (increased calcium and magnesium intake) or adverse (increased fat intake) nutritional effects. It is concluded that MSG can act as a palatability enhancer in the context of the French diet. It can facilitate long-term intake in both young and elderly persons **but it should be utilized cautiously so as to improve nutrition.**

Monosodium glutamate as a palatability enhancer in the European diet.
Bellisle F, Monneuse MO, Chabert M, Larue-Achagiotis C, Lanteaume MT, Louis-Sylvestre J.
Physiol Behav. 1991 May;49(5):869-73.

MSG increases the secretion of Insulin.

MSG has been shown in rats to over stimulate the pancreas resulting in hyperinsulinemia. The excess insulin in the blood increases the conversion of glucose into adipose tissue.

"Early postnatal administration of monosodium glutamate (MSG) to rats induces obesity, hyperinsulinemia and hyperglycemia in adulthood, thus suggesting the presence of insulin resistance. We therefore investigated the effects of insulin on glucose transport and lipogenesis in adipocytes as well as insulin binding to specific receptors in the liver, skeletal muscle and fat tissues. **An increase of plasma insulin was found in 3-month-old rats treated with MSG during the postnatal period"**

Late effects of postnatal administration of monosodium glutamate on insulin action in adult rats.
Macho L, Fickova M, Jezova, Zorad S.
Physiol Res. 2000;49 Suppl 1:S79-85.

Even just adding MSG to the mouth of a rat can trigger an increase in insulin release:

"**When the oral cavity was infused by MSG solution, a transient increase in blood insulin level was recognized at 3 min after this oral stimulation**. These observations support the conclusion that taste stimulation of MSG induces cephalic-phase insulin secretion."

Cephalic-phase insulin release induced by taste stimulus of monosodium glutamate (umami taste).
Niijima A, Togiyama T, Adachi A.
Physiol Behav. 1990 Dec;48(6):905-8.

A connection can be found in human test subjects:

"To further study glutamate metabolism, we administered 150 mg/kg body wt of monosodium glutamate (MSG) and placebo to seven male subjects who then either rested or exercised. **MSG administration resulted in elevated insulin levels.**"

Glutamate ingestion and its effects at rest and during exercise in humans.
Mourtzakis M, Graham TE.
J Appl Physiol. 2002 Oct;93(4):1251-9.

"Monosodium (L)-glutamate (10 g) was given orally in a double-blind placebo-controlled cross-over study to 18 healthy volunteers, aged 19-28 years, with an oral (75 g) glucose load. CONCLUSIONS: **Oral (L)-glutamate enhances glucose-induced insulin secretion in healthy volunteers in a concentration-dependent manner.**"

Effects of oral monosodium (L)-glutamate on insulin secretion and glucose tolerance in healthy volunteers.
Chevassus H, Renard E, Bertrand G, Mourand I, Puech R,Molinier N, Bockaert J, Petit P, Bringer J.
Br J Clin Pharmacol. 2002 Jun;53(6):641-3.

MSG reduces the excretion of Ketones.

MSG has been shown in rats to reduce Ketone secretion, resulting in an obese rat with a propensity for creating adipose tissue(fat):

"MSG-treated rats showed shorter naso-anal and tail length, and a more marked intraperitoneal fat deposition than control rats. Plasma levels of **total ketone bodies were decreased in the MSG-treated rats as compared to control rats.**"

Decreased ketonaemia in the monosodium glutamate-induced obese rats.
Nakai T, Tamai T, Takai H, Hayashi S, Fujiwara R, Miyabo S.
Life Sci. 1986 Jun 2;38(22):2009-13.

A connection can be found in human test subjects:

"**Production and use of ketone bodies are lower in obese women** than in lean controls."

Ketone body metabolism in lean and obese women.
Vice E, Privette JD, Hickner RC, Barakat HA.
Metabolism. 2005 Nov;54(11):1542-5.

MSG reduces the excretion of Growth Hormone (GH) during adolescence.

MSG has been shown in rats to reduce Growth Hormone secretion, resulting in an obese rat with stunted stature:

Rats were treated with monosodium glutamate (MSG), 4 mg/g on alternate days for the first 10 days of life, to induce lesions of the arcuate nucleus and **destroy the majority of growth hormone-releasing hormone (GHRH) neurones.**

Depletion of hypothalamic growth hormone-releasing hormone by neonatal monosodium glutamate treatment reveals an inhibitory effect of betamethasone on growth hormone secretion in adult rats.
Corder R, Saudan P, Mazlan M, McLean C, Gaillard RC.
Neuroendocrinology. 1990 Jan;51(1):85-92.

A connection can be found in human test subjects:

In obese individuals, ...GH secretion is impaired without an organic pituitary disease and the severity of the secretory defect is proportional to the degree of obesity.

Growth hormone status in morbidly obese subjects and correlation with body composition.
Savastano S, Di Somma C, Belfiore A, Guida B, Orio F Jr, Rota F, Savanelli MC, Cascella T, Mentone A, Angrisani L, Lombardi G, Colao A.
J Endocrinol Invest. 2006 Jun;29(6):536-43.

A recent study compared data from both humans and rats fed MSG prenatally through the mother's diet, and made the following recommendation:

"**Oral administration of MSG to pregnant rats affects birth weight of the offspring,** and reduces GH serum levels are lowered in animals that received MSG during prenatal life via maternal feeding.....The flavouring agent MSG--at concentrations that only slightly surpass those

found in everyday human food, exhibits significant potential for damaging the hypothalamic regulation of appetite, and thereby determines the propensity of world-wide obesity. **We suggest to reconsider the recommended daily allowances of amino acids and nutritional protein, and to abstain from the popular protein-rich diets, and particularly from adding the flavouring agents MSG."**

Obesity, voracity, and short stature: the impact of glutamate on the regulation of appetite.
Hermanussen M, Garcia AP, Sunder M, Voigt M, Salazar V, Tresguerres JA.
Eur J Clin Nutr. 2006 Jan;60(1):25-31.

MSG Triggers Diabetes In Test Subjects:

The food additive Monosodium Glutamate is used to purposely create Diabetic rodents:

"The number of diabetic patients is increasing every year, and new model animals are required to study the diverse aspects of this disease. An experimental obese animal model has reportedly been obtained by injecting monosodium glutamate (MSG) to a mouse. We found that ICR-MSG mice on which the same method was used developed glycosuria. Both female and male mice were observed to be obese but had no polyphagia, and were glycosuric by 29 weeks of age, with males having an especially high rate of incidence (70.0%). Their blood concentrations of glucose, insulin, total cholesterol, and triglycerides were higher than in the control mice at 29 weeks. These high concentrations appeared in younger males more often than in females, and were severe in adult males. Also, the mice at 54 weeks of age showed obvious obesity and increased concentrations of glucose, insulin, and total cholesterol in the blood. The pathological study of ICR-MSG female and male mice at 29 weeks of age showed hypertrophy of the pancreatic islet. This was also observed in most of these mice at 54 weeks. It was recognized as a continuation of the condition of diabetes mellitus. From the above results, **these mice are considered to be useful as new experimental model animals developing a high rate of obese type 2 (non-insulin dependent) diabetes mellitus** without polyphagia."

Type 2 diabetes mellitus in obese mouse model induced by monosodium glutamate.
Nagata M, Suzuki W, Iizuka S, Tabuchi M, Maruyama H, Takeda SAburada M, Miyamoto K.
Exp Anim. 2006 Apr;55(2):109-15.

"**Administration of monosodium glutamate (MSG) to KK mice during the neonatal period resulted in a syndrome of obesity, stunting and hypogonadism.** In some animals the genetic predisposition to diabetes was unmasked with the development of marked hyperglycaemia and or hyperinsulinaemia. Food intake was not increased compared to controls. The elevated plasma glucose and insulin in fed MSG treated mice fell rapidly with food deprivation. Glucose disposal was comparable in MSG treated and control mice after IP glucose, but after oral glucose MSG treated mice showed impaired glucose tolerance. **Insulin secretion was defective in MSG treated mice.**"

Effects of monosodium glutamate administration in the neonatal period on the diabetic syndrome in KK mice.
Cameron DP, Poon TK, Smith GC.
Diabetologia. 1976 Dec;12(6):621-6.

Not all rodent species become obese with MSG ingestion, some just get Diabetes:

Neuronal necrosis in the arcuate and ventromedial hypothalamus regions is easily induced in 1-day-old Chinese hamsters by the administration of monosodium glutamate (MSG). **New-born Chinese hamsters injected with MSG showed no sign of obesity, even when grown up, but apparently developed a diabetic syndrome.**

Diabetic syndrome in the Chinese hamster induced with monosodium glutamate.
Komeda K, Yokote M, Oki Y.
Experientia. 1980 Feb 15;36(2):232-4.

MSG crosses the Placenta endangering the fetus.

MSG has been shown to cross the placental barrier in rats, and new studies suggest that in cases where human mothers who suffer from intrauterine infection are at risk to Glutamate causing excitotoxic perinatal brain injury to the fetus:

"Monosodium-L-glutamate given subcutaneously to pregnant rats caused acute necrosis of the acetylcholinesterase-positive neurons in the area postrema. The same effect has been observed in the area postrema of fetal rats. The process of neuronal cell death and the elimination of debris by microglia cells proved to be similar in pregnant animals and in their fetuses. However, embryonal neurons were more sensitive to glutamate as judged by the rapidity of the process and the dose-response relationship. **These observations raise the possibility of transplacental poisoning in human fetuses after the consumption of glutamate-rich food by the mother**."

Neurotoxicity of monosodium-L-glutamate in pregnant and fetal rats.
Toth L, Karcsu S, Feledi J, Kreutzberg GW.
Acta Neuropathol (Berl). 1987;75(1):16-22.

"**Monosodium glutamate (MSG) was shown to penetrate placental barrier** and distribute almost evenly among embryonic tissues using 3H-Glu as a tracer. When a lower (1.0 mg/g) and a higher (2.5 mg/g) doses of MSG were alternatively injected to Kunming maternal mice in every other days from mating to deliveries, obvious injury occurred in the ability of memory retention and Y-maze discrimination learning of adult filial mice pregnantly treated with higher doses (2.5 mg/g) of MSG. Meanwhile, the neuronal damages were observed in not only arcuate nucleus but also ventromedial nucleus of hypothalamus. Characteristic cytopathological changes induced by MSG showed swollen cytoplasm, dark pyknotic nuclei and loss of neurons.These experimental findings indicated that MSG performed its transplacental neurotoxicity in a dose-dependent manner. The excessive activation of Glu receptors and the overloading of intracellular Ca2+ induced by **MSG ultimately leading to neuronal death may result in the reduction of the capability of learning and memory** in adult filial mice pregnantly treated with MSG."

Transplacental neurotoxic effects of monosodium glutamate on structures and functions of specific brain areas of filial mice
Gao J, Wu J, Zhao XN, Zhang WN, Zhang YY, Zhang ZX.
Sheng Li Xue Bao. 1994 Feb;46(1):44-51.

"Administering GLU to newborn rodents completely destructs arcuate nucleus neurons, and results in permanently elevated plasma leptin levels that fail to adequately counter-regulate food intake. Chronic fetal exposure to elevated levels of GLU may be caused by chronic maternal over-nutrition or by reduced umbilical plasma flow. **We strongly suggest abandoning the flavoring agent monosodium glutamate and reconsidering the recommended daily allowances of protein and amino acids during pregnancy**."

Does the thrifty phenotype result from chronic glutamate intoxication? A hypothesis.
Hermanussen M, Tresguerres JA.
J Perinat Med. 2003;31(6):489-95

Oral administration of MSG in the pregnant mother's diet has been shown to accumulate at twice the maternal level in the brains of fetal mice:

"Monosodium glutamate (MSG) was shown to penetrate placental barrier and to distribute to embryonic tissues using [3H]glutamic acid ([3H]Glu) as a tracer. However, the distribution is not even; **the uptake of MSG in the fetal brain was twice as great as that in the maternal brain** in Kunming mice. Other maternal mice were given per os MSG (2.5 mg/g or 4.0 mg/g body weight) at 17-21 days of pregnancy, and their offspring behaviors studied. The results showed that maternal oral administration of MSG at a late stage of pregnancy decreased the threshold of convulsion in the litters at 10 days of age. Y-maze **discrimination learning was significantly impaired** in the 60-day-old filial mice."

Effects of maternal oral administration of monosodium glutamate at a late stage of pregnancy on developing mouse fetal brain.
Yu T, Zhao Y, Shi W, Ma R, Yu L.
Brain Res. 1997 Feb 7;747(2):195-206.

In human fetal development, Glutamate is a major contributor to growth of the CNS and brain:

"Glutamate receptors have multiple roles in the central nervous system. Recent evidence suggests that the iontropic **glutamate receptors are critical during brain development**, particularly for corticogenesis, neuronal migration, and synaptogenesis. In this study, we examined subunit mRNA expression and binding sites of the NMDA, AMPA, and kainate receptors from gestational weeks 8-20 in human fetal brain. Expression of glutamate receptors was high during several periods in these brains. These results demonstrate that **glutamate receptors are expressed early in human brain development**."

Ontogeny of ionotropic glutamate receptor expression in human fetal brain.
Ritter LM, Unis AS, Meador-Woodruff JH.
Brain Res Dev Brain Res. 2001 Apr 30;127(2):123-33.

Human fetal development has been shown to be jeopardized by high amounts of Glutamate:

"Children undergoing perinatal brain injury often suffer from the dramatic consequences of this misfortune for the rest of their lives. Despite the severe clinical and socio-economic significance, no effective clinical strategies have yet been developed to counteract this condition. This review describes the pathophysiological mechanisms that are implicated in perinatal brain injury. These include the **acute breakdown of neuronal membrane potential followed by the release of excitatory amino acids such as glutamate** and aspartate. Glutamate binds to postsynaptically located glutamate receptors that regulate calcium channels. The resulting calcium influx activates proteases, lipases and endonucleases which in turn destroy the cellular skeleton. Clinical studies have shown that intrauterine infection increases the risk of periventricular white matter damage especially in the immature fetus. This damage may be mediated by cardiovascular effects of endotoxins."

Perinatal brain damage--from pathophysiology to prevention.
Jensen A, Garnier Y, Middelanis J, Berger R.
Eur J Obstet Gynecol Reprod Biol.2003 Sep 22;110 Suppl 1:S70-9.

"We found evidence that the thrifty phenotype may be the consequence of fetal hyperglutamatemia. Maternal glutamate (GLU) reaches the fetal circulation, as part of the materno-fetal glutamine-glutamate exchange. Glutamine is absorbed from the maternal circulation, and deaminated for nitrogen utilization, resulting in a fetal production of GLU. GLU is extracted as it returns to the placenta. **When the umbilical plasma flow is low, GLU may be trapped in the fetal circulation, and reaches neurotoxic levels.**"

Does the thrifty phenotype result from chronic glutamate intoxication? A hypothesis.
Hermanussen M, Tresguerres JA.
J Perinat Med. 2003;31(6):489-95.

MSG's Ocular Toxicity:

MSG given both subcutaneously and orally in diet causes long term destruction of various ocular structures:

"In rodents, **daily injection of neurotoxic monosodium L-glutamate (MSG) during the postnatal period induces retinal lesions, optic nerve degeneration** with an alteration of visual pathway and an absence of the b-wave in the electroretinogram. Animals received daily doses of glutamate during the first ten days after birth according to two protocols. The two treatments similarly destroyed 56% of the overall population of the ganglion cell layer: 30% of displaced amacrine and 89% of ganglion cells."

Neurotoxic effects of neonatal injections of monosodium L-glutamate (L-MSG) on the retinal ganglion cell layer of the golden hamster: anatomical and functional consequences on the circadian system.
Chambille I, Serviere J.
J Comp Neurol. 1993 Dec 1;338(1):67-82.

"Changes in the transparency and size of lenses in rats were investigated following administration of monosodium-L-glutamate (MSG), MSG (5 mg/g b.w.) was injected subcutaneously on the 9th and 10th days after birth.. The incidence of cataract increased with age, reaching more than 75% at 4 months of age. Morgagni's globules were histologically detected in the opacity of the posterior lens cortex. Degenerative changes of the lens epithelium were observed in the mature cataract. The size and weight of the lens were smaller than those of controls. These findings indicate that **administration of MSG could be an etiologic factor in cataract formation** in the developing rat."

Morphological studies on cataract and small lens formation in neonatal rats treated with monosodium-L-glutamate
Kawamura M, Azuma N, Kohsaka S.
Nippon Ganka Gakkai Zasshi. 1989 May;93(5):562-8.

"The purpose of this study was to investigate the effects of glutamate accumulation in vitreous on retinal structure and function, due to a diet high in sodium glutamate. Three different diet groups were created, consisting of rats fed on a regular diet (diet A), a moderate excess of sodium glutamate diet (diet B) and a large excess of sodium glutamate diet (diet C). After 1, 3 and 6 months of the administration of these diets, amino acids concentrations in vitreous were analyzed. Significant accumulation of glutamate in vitreous was observed in rats following addition of sodium glutamate to the diet as compared to levels with a regular diet. In the retinal morphology, thickness of retinal neuronal layers was remarkably thinner in rats fed on sodium glutamate diets than in those on a regular diet. Functionally, ERG responses were reduced in rats fed on a sodium glutamate diets as compared with those on a regular diet. **The present study suggests that a diet with excess sodium glutamate over a period of several years may increase glutamate concentrations in vitreous and may cause retinal cell destruction.**"

A high dietary intake of sodium glutamate as flavoring (ajinomoto) causes gross changes in retinal morphology and function.
Ohguro H, Katsushima H, Maruyama I, Maeda T, Yanagihashi S, Metoki T, Nakazawa M.
Exp Eye Res. 2002 Sep;75(3):307-15.

MSG causes Genotoxicity:

MSG has been shown to be Genotoxic to a variety of organs and tissues in the mammalian body:

Monosodium glutamate (MSG) continues to function as a flavor enhancer in West African and Asian diets. The present study examines the modulatory effects of dietary antioxidant vitamin C (VIT C), vitamin E (VIT E) and quercetin on **MSG-induced oxidative damage in the liver, kidney and brain** of rats. In addition, the effect of these antioxidants on the possible genotoxicity of MSG was investigated in a rat bone marrow micronuclei model. MSG administered intraperitoneally at a dose of 4 mg/g body wt markedly increase malondialdehyde (MDA) formation in the liver, the kidney and brain of rats. The antioxidants tested protected against MSG-induced liver toxicity significantly. VIT E failed to protect against MSG-induced genotoxicity. **The results indicate that dietary antioxidants have protective potential against oxidative stress induced by MSG and, in addition, suggest that active oxygen species may play an important role in its genotoxicity.**

Monosodium glutamate-induced oxidative damage and genotoxicity in the rat: modulatory role of vitamin C, vitamin E and quercetin.
Farombi EO, Onyema OO.
Hum Exp Toxicol. 2006 May;25(5):251-9.

Other Human MSG studies:

MSG connected with adult-onset olivopontocerebellar degeneration:

In patients with recessive, adult-onset olivopontocerebellar degeneration associated with a partial deficiency of glutamate dehydrogenase, the concentration of glutamate in plasma was significantly higher than that in controls. Plasma alpha-ketoglutarate was significantly lower. Oral administration of monosodium glutamate resulted in excessive accumulation of this amino acid in plasma and lack of increase in the ratio of plasma lactate to pyruvate in the glutamate dehydrogenase-deficient patients. Decreased glutamate catabolism may result in **an excess of glutamate in the nervous system and cause neuronal degeneration.**

Abnormal glutamate metabolism in an adult-onset degenerative neurological disorder.
Plaitakis A, Berl S, Yahr MD.
Science. 1982 Apr 9;216(4542):193-6.

MSG connected with amyotrophic lateral sclerosis (ALS) :

Glutamate levels were determined in the fasting plasma of 22 patients with early-stage primary amyotrophic lateral sclerosis (ALS) and compared to those of healthy and diseased controls. There was a significant increase (by approximately 100%, p less than 0.0005) in the plasma glutamate of the ALS patients as compared with the controls. Oral glutamate loading (60 mg of monosodium glutamate per kilogram of body weight, taken orally after overnight fasting) resulted in significantly greater elevations in the plasma glutamate and aspartate levels in the ALS patients than in the controls. Glutamate, a potentially neuroexcitotoxic compound, is thought to be the transmitter of the corticospinal tracts and certain spinal cord interneurons. **A systemic defect in the metabolism of this amino acid may underlie primary ALS.**

Abnormal glutamate metabolism in amyotrophic lateral sclerosis.
Plaitakis A, Caroscio JT.
Ann Neurol. 1987 Nov;22(5):575-9.

MSG and the Alteration of the brain: a model for ADHD/Autism

The Erb Hypothesis:

Attention Deficit Disorder, Attention Deficit Hyper Active Disorder, Asperger's Syndrome and Autism are linked. They strike the same percentage of males vs females and have similar characteristic traits. The Erb hypothesis published in 2003 states that Monosodium Glutamate as a food and vaccine additive triggers unchecked brain cell growth. This results in an overgrowth of certain areas of the brain rendering them damaged or destroyed, while accelerating the development of other areas (hence Savants). The genetics and level of MSG exposure determines what level a child will be: ADD, ADHD, Asperger's or Autism.

Autism (or autistic like behaviors) was only known in a handful cases world wide in 1940. ADHD and Autism did not even exist as a diagnosis. In 1950 MSG was introduced to the food supply and the growth of these syndromes has matched the increase in MSG intake in the western diet. As of 2006 there is reported to be one in every hundred children now being born with Autism in the United States.

One of the main characteristics of Autism is a heavier brain. The theory of Mercury causing Autism does not explain the brain overgrowth. Mercury does not enhance cell tissue growth.

In the first 8 weeks of fetal growth the placental barrier is not yet fully formed. This period is when the brain stem, brain, and eyes begin to form.

12 grams a day of MSG in a mother's blood stream could have an enormous affect on the fetal development. Even after the placental barrier has been formed there is not a single human study to show that MSG does not easily transport into the fetus.

Accelerated and abnormal brain growth in the Autistic:

Autism most commonly appears by 2 to 3 years of life, at which time the brain is already abnormally large. This raises the possibility that brain overgrowth begins much earlier, perhaps before the first clinically noticeable behavioral symptoms. OBJECTIVES: To determine whether pathological brain overgrowth precedes the first clinical signs of autism spectrum disorder (ASD) and whether the rate of overgrowth during the first year is related to neuroanatomical and clinical outcome in early childhood.

Within the ASD group, every child with autistic disorder had a greater increase in HC between birth and 6 to 14 months (mean [SD], 2.19 [0.98]) than infants with pervasive developmental disorder-not otherwise specified (0.58 [0.35]). Only 6% of the individual healthy infants in the longitudinal data showed accelerated HC growth trajectories (>2.0 SDs) from birth to 6 to 14 months; 59% of infants with autistic disorder showed these accelerated growth trajectories. CONCLUSIONS: **The clinical onset of autism appears to be preceded by 2 phases of brain growth abnormality: a reduced head size at birth and a sudden and excessive increase in head size between 1 to 2 months and 6 to 14 months. Abnormally accelerated rate of growth may serve as an early warning signal of risk for autism.**

Evidence of brain overgrowth in the first year of life in autism.
Courchesne E, Carper R, Akshoomoff N.
JAMA. 2003 Jul 16;290(3):393-4.

To establish whether high-functioning children with autism spectrum disorder (ASD) have enlarged brains in later childhood, and if so, whether this enlargement is confined to the gray and/or to the white matter and whether it is global or more prominent in specific brain regions. RESULTS: Patients showed a significant increase of 6% in intracranium, total brain, cerebral gray matter, cerebellum, and of more than 40% in lateral and third ventricles compared to controls. The cortical gray-matter volume was evenly affected in all lobes. After correction for brain volume, ventricular volumes remained significantly larger in patients. CONCLUSIONS: **High-functioning children with ASD showed a global increase in gray-matter,** but not white-matter and cerebellar volume, proportional to the increase in brain volume, and a disproportional increase in ventricular volumes, still present after correction for brain volume.

Increased gray-matter volume in medication-naive high-functioning children with autism spectrum disorder.
Palmen SJ, Hulshoff Pol HE, Kemner C, Schnack HG, Durston S, Lahuis BE, Kahn RS, Van Engeland H.
Psychol Med. 2005 Apr;35(4):561-70.

MSG proven to accelerate the growth of neurons and stimulate proliferation:

"It has been widely accepted that neurogenesis continues throughout life. Neural stem cells can be found in the ventricular zone of the embryonic and in restricted regions of the adult central nervous system, including subventricular and subgranular zones of the hippocampal dentate gyrus. The network of signaling mechanisms determining whether neural stem cells remain in a proliferative state or differentiate is only partly discovered. **Recent advances indicate that glutamate (Glu), the predominant excitatory neurotransmitter in mature neurons, can influence immature neural cell proliferation and differentiation,** as well., Glu can influence proliferation and neuronal commitment as well, and acts as a positive regulator of neurogenesis. Brain injuries like ischemia, epilepsy or stress lead to severe neuronal death and additionally, influence neurogenesis, as well. Glu homeostasis is altered under these pathological circumstances, implying that therapeutic treatments mediating Glu signaling might be useful to increase neuronal replacement after cell loss in the brain."

Glutamate as a modulator of embryonic and adult neurogenesis.
Schlett K.
Curr Top Med Chem. 2006;6(10):949-60.

Appendix A List of Ingredients

Involving MSG

These contain Monosodium Glutamate

Glutamate	**Glutamic acid**	**Gelatin**
Monosodium glutamate	**Calcium caseinate**	**Textured protein**
Monopotassium glutamate	**Sodium caseinate**	**Yeast nutrient**
Yeast extract	**Yeast food**	**Autolyzed yeast**
Hydrolyzed protein (any protein that is hydrolyzed)	**Hydrolyzed corn gluten**	Natrium glutamate (natrium is Latin/German for sodium)

Opposing Research

The petitioner is aware of the following research documents claiming the safety of Monosodium Glutamate in Food.

Report of Joint Executive Committee on Food Additives (JECFA) of the WHO in 1970. This report does not cover any of the health issues raised in the petition.

Report of the Federation of American Societies for Experimental Biology (FASEB) 1995. This Report does not cover any of the health issues raised in this petition.

Conclusions

There are few chemicals that we are exposed to that have as many far reaching physiological affects on living beings as Monosodium Glutamate does. MSG directly causes obesity, diabetes, triggers epilepsy, destroys eye tissues, is genotoxic in many organs and is the probable cause of ADHD and Autism. Considering that MSG's only reported role in food is that of 'flavor enhancer' is that use worth the risk of the myriad of physical ailments associated with it? Does the public really want to be tricked into eating more food and faster by a food additive?

MSG is entering our bodies in record amounts with absolutely no limits. The studies outlined in this report often use a smaller proportional dosage than the average child may ingest daily.

Consider the children of the United States who eat MSG in their school cafeterias, hospitals, restaurants and homes. They deserve foods free of added MSG, a substance so toxic that scientists use it purposely to trigger diabetes, obesity and epileptic convulsions.

I petition the swift deletion of MSG from the GRAS list of the Food Act. Perhaps we will see a reduction in obesity, diabetes, ADHD and Autism once the excess Glutamate threat to our health has been removed.

Certification

I, John Erb, the undersigned certify to the best of my knowledge and belief of myself, that this petition includes all the information and views on which the petition relies, and that it includes representative data and information known to myself which are unfavorable to the petition.

John Edward Erb
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Virginia Beach, VA
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757 287 1868

December 28, 2007

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Division of Dockets Management
Food and Drug Administration
Department of Health and Human Services
5603 Fishers Lane, rm 1061
Rockville MD. 20852

Amendment to Citizen Petition of John Erb on MSG

I, John Erb, the undersigned, ask that the petition I have submitted to the FDA asking for the revocation of the GRAS status of Glutamate be amended with the following:

I ask for a categorical exclusion under 25.30.

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