MEDICAL AND POPULAR PRESS COVERAGE OF TRYPTOPHAN NUTRITIONAL SUPPLEMENTS, 1970 to PRESENT

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Mass Media

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Brian,
Your work is outstanding!
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TRYPTOPHAN AS AN ADJUNCT REMEDY

Introduction and Background

In 1948, a particular culture of *Bacillus subtilis* which leaked tryptophan (TRP) and other amino acids into its growth medium was documented in the scientific literature. Within a decade, this method for producing tryptophan (TRP) replaced the protein-based extraction methods is use and soon became the most cost-effective production method. During the 1960s, bacterial fermentation methods for food production were perfected (i.e. factory-based yogurt production), enabling the massive production of TRP-pharmaceutical products (tablets, capsules, etc.) to begin. By the end of the 1970s, TRP was typically produced using Bacillus cultures grown in large chambers, and both the Bacillus and its growth medium were extracted for their various end-products applicable to pharmaceutical and food industry (Jaffe 1994). .

During the late 1960s, Tryptophan (TRP) also became increasingly popular due to a number of medical studies published about its use as an adjunct remedy to treat depression. Prior to this time, the cost of producing TRP prevented it from becoming a popular as an over-the-counter (OTC) product. As the popularity of taking TRP as a depression remedy and sleep aid grew during the 1970s, more attempts were made to produce TRP both as an OTC product and a prescribed adjunct remedy. About the same time, the FDA made several attempts to regulate the OTC industry, sponsoring bills which prohibited the sales of vitamins and minerals if the daily dose in each capsule/tablet exceeded 150% of their recommended daily allowance (Pollner 1992).

As the use of OTC TRP grew in popularity, several discoveries were made about its biochemical and pharmacological effects. A number of medical journal articles recommended its use not only as an adjunct to regular anti-depressants, but also as a remedy for various neurological diseases linked to serotonin and melatonin pathways in the brain. In short time this led to popularization of its use as an OTC remedy for treating tension and stress-related disorders, specific psychiatric conditions like schizophrenia and manic-depression, and neurochemically-defineable diseases like Parkinsonism, tardive dyskinesia and epilepsy.

As the number of potential uses for TRP increased and became popular, TRP was recommended and/or prescribed not only by M.D.s and Psychiatrists, but also by allied health practitioners such as nurses, licensed dieticians and counselors. This had minimal impact on the growth of psychiatry and biomedicine uses for TRP at first, but increased public interest in the value of the use of nutritional supplements as part of a regular regime. In turn, professional concerns began to surface regarding the right for patients (consumers) to decide upon and purchase their own Over-the-counter (OTC) nutritional supplements for use as 'medicines.' This resulted in a number of questions posed by physicians in the professional literature, the most poignant being 'would patients ultimately come to rely upon their own opinions or the opinions of non-physicians and allied health professionals to define or "improve" their prescribed regimens?' and 'would these be used in addition to or as substitutes for regular prescriptions defined by medical doctors?'

In 1973, the FDA decided to take legal actions against OTC remedies due to this growing concern. By then, the growing popularity of the use of TRP as a psychiatric medicine and the related mass marketing techniques led the FDA to restrict OTC sales of TRP and other amino acid products. As a result, these substances were removed from the "Generally Regarded as Safe" (GRAS) list and several production/distribution generic drug companies were brought to court for promoting them as OTC products.

In 1976, a new GRAS was filed, with TRP once again included in the safe category. The FDA claimed this change to be due to a "filing" or "typescript" error. This "error" however gave Congress and the general public the opportunity to react to the proposed restrictions. As a result, fearing a loss or reduction of consumer choice, Congress passed the Rogers-Proxmire Amendments limiting FDA involvement in regulating OTC nutritional supplements (Pollner 1992).

Early Tryptophan Use

From 1970 to the early 1990s, the marketing of TRP for a variety of nervous and neuromuscular system disorders increased. As a result, the numbers and types of articles published in the professional medical journals about these uses also increased (Figures 1 and 2). The recommendations for TRP use made by regular physicians helped to maintain the professional support needed to keep this market active. For the most part, MDs supported TRP use primarily as an adjunct remedy to be prescribed by psychiatrists, not as an OTC supplement (Table 1).

FIGURE 1

NUMBER OF DIFFERENT USES FOR TRP PUBLISHED PER YEAR (SOURCE: INDEX MEDICUS)

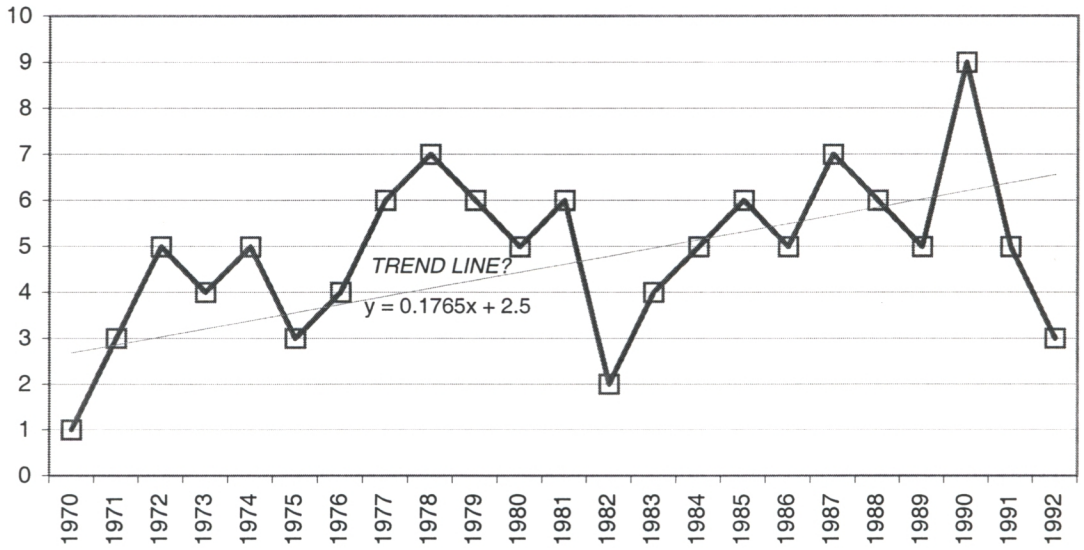
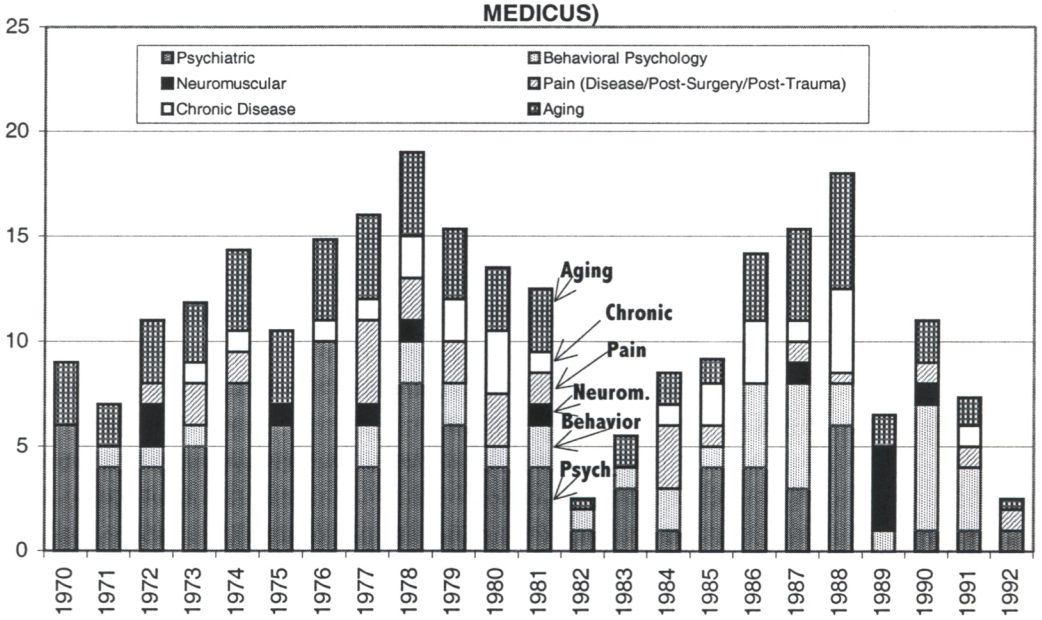


FIGURE 2

TRP USE FOR FIVE MAJOR CATEGORIES OF DISEASE TYPE (INDEX MEDICUS)



Classification Type	**Description of equation** *(Sum N; N = # articles)*
Psychiatric	Depression, affective disorders, mania, bipolarism, schizophrenia
Behavioral Psychology	Total inclusion for: bulimia, insomnia, alcoholism, attention deficit. Partial inclusion for: depression, affective disorders.
Neuromuscular	Parkinsonism, myoclonus, migraine, Tardive Dyskinesia, Rett syndrome
Pain	Includes disease-related, post-surgical, and post-trauma pains, headaches; partial arthritis and anti-inflammatory uses.
Chronic Disease	Epilepsy, rheumatoid arthritis, cancer
Aging	Total inclusion of Alzheimers. Partial conclusion of: Arthritis, insomnia, depression, insomnia, dermal problems, renal problems, hypertension

Table 1. Tryptophan Uses According to Psychiatric and Medical Literature
(Note: for Figure 1 equation, "partial" values were assigned $N_{articles}/2$),)

During the same time TRP was being promoted by physicians for use as an adjunct remedy, TRP was being marketed as an OTC nutritional supplement to treat insomnia, bipolarism or manic depression, dementia, and alcoholism, schizophrenia, myoclonus, migraine headaches, Parkinsonism, tardive dyskinesia, epilepsy, and even cancer. Publicized by a number of popular magazines (Figure 3, Table 2), the most popular uses for TRP related to conditions considered psychological or psychiatric in nature (esp. insomnia, manic disorders, schizophrenic and depression) and/or age-related (esp. depression, insomnia, Parkinsonism, hypertension, hypercholesterolemia).

FIGURE 3

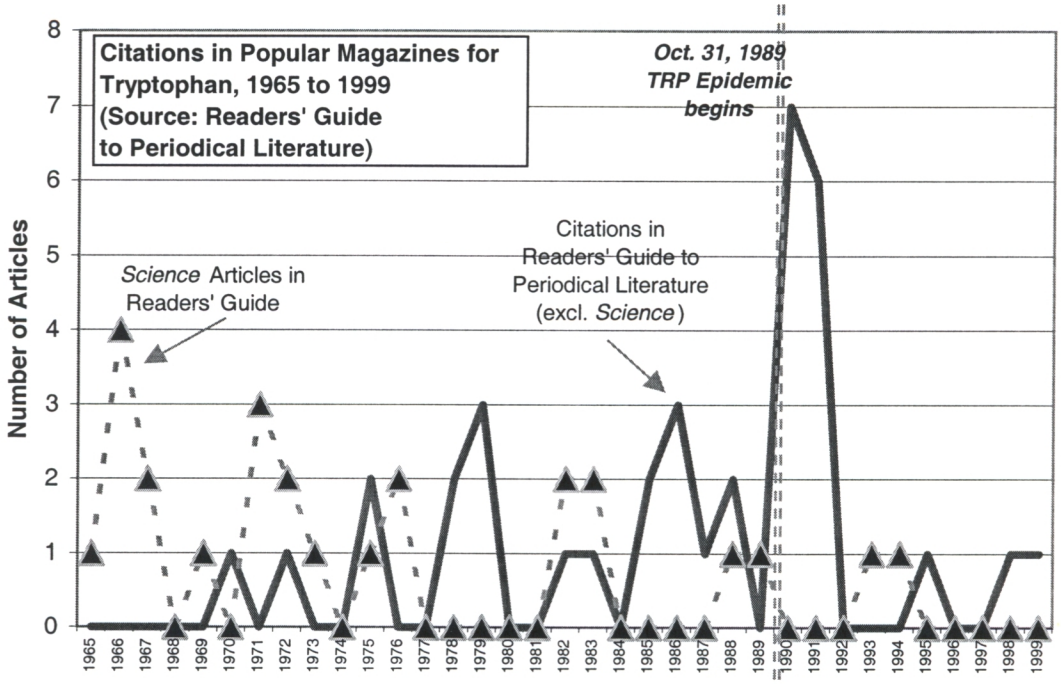


TABLE 2

A Review of TRP uses noted in *The Readers' Guide to Periodical Literature*

Journal	# Articles	Issues
Prevention	7	Insomnia, Pain, Obesity, Cholesterol, Blood Pressure; General
Psychology Today	4	Insomnia, Pain, Aggression
Newsweek	1	Insomnia
Madamoiselle	1	Insomnia
Health	1	Infant Sleep
Saturday Evening Post	1	Depression
Total	***15***	

By the late 1980s, this popularization of TRP on behalf of the popular press promoted its use not only as an adjunct chemical taken with psychiatric prescription drugs, but also as a possible OTC substitute for certain prescription medicines. To the medical world, TRP remained primarily a form of adjunct therapy promoted by psychiatrists, family physicians, counselors, nurses and clinical psychologists. Due to the failure of the FDA to successful regulate its distribution between 1973 and 1976, no further actions were taken to regulate TRP distribution as an OTC remedy. TRP soon became an OTC nutritional supplement dispensed primarily as a self-prescribed remedy.

Tryptophan as a Bioengineered Product

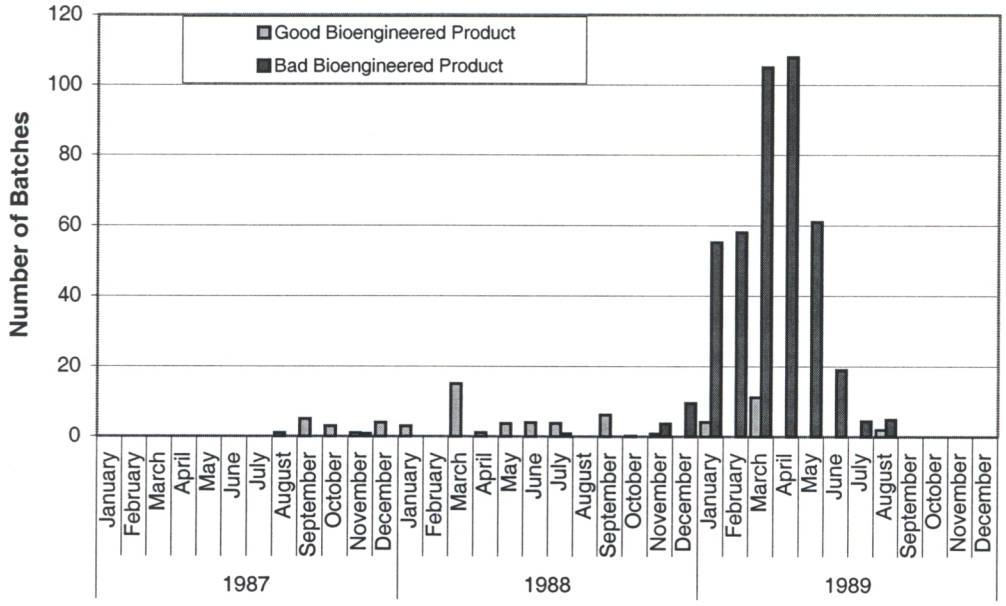
In 1988, a new method of producing TRP was tested by the Japanese company Showa Denko K.K.. Using *Bacillus amyloliquefaciens*, genetic modifications were made to speed up TRP production. Since earlier use of bacterial cultures to produce food substances produced few if any adverse outcomes, the end product of this new method of production was classified as equivalent to previous *Bacillus*-produced TRP products, and therefore considered safe for dispersal as an OTC nutritional supplement. More importantly, no additional monitoring was required for this new method of production (Pollner 1992, Fagan 1997).

In just two months time, this newly bioengineered product went from the factory in Japan to the local grocery stores in the United States. Over the next two months, it reached the consumers' households and began to be used (ca. June and July 1989).

Months after the onset of the first cases of EMS induced by this supplement in July 1989, researchers analyzed the remaining products stored by Showa Denko at its facility in Japan. This study published only in the medical journals in July 1990 suggested that either the bacterial cultures or a post-production process resulted in an end-product which was not effectively filtered out as early as November 1987 and July 1988 (Slutsker, Hoesley, Miller et al., 1990). The bulk of this contamination occurred some time between April and May of 1989, when a new strain of *Bacillus amyloliquifaciens*, subsequently referred to as "Strain V," began to dominate the batch culture and was ultimately linked temporally, not causally, to the contamination (Figure 4).

FIGURE 4

Contaminated Bacillus Cell Cultures, based on TRP sample analysis



According to nutritional science writer Jaffe (1994), changes were made in the Carbon-based filter used to remove products left over from the fermentation process. Company records showed the amount of activated carbon in this filter to be reduced (a claim Showa Denko's attorney claims should have had no effect since prior in situ testing showed no changes in contamination took place following the filter change). A more recently published theory for the development of TRP cases states that some sort of tryptophan by-product of aniline nature was formed (aniline dyes are a known class of toxins with similar symptomatology) (ibid). In the words of a publicly-accepted "genetic engineering expert," John B. Fagan (1997), a combination of FDA, Center for Disease Control and Prevention (CDC) and bioengineering company guidelines and protocols were to blame due to lack of sufficient review of this manufacturing process by the FDA:

> Showa Denko was allowed to sell the tryptophan produced in genetically engineered bacteria without safety testing because they and other companies had been selling tryptophan produced in non-genetically engineered bacteria for years without ill effects. It was considered that the method of production (whether via natural or genetically engineered bacteria) was immaterial and that, since tryptophan had already been shown to be safe, the new material needed no testing. In effect they considered it substantially equivalent to the tryptophan that had been sold for many years (November 1997).

The result of the distribution and use of this TRP throughout the United States was the development of the first TRP-related eosinophilia myalgia syndrome (EMS) cases by late summer 1989 (previous cases had been linked to aniline dyes and "toxic oil" contained in the seeds of many mustard family plants, i.e. rapeseed). In spite of

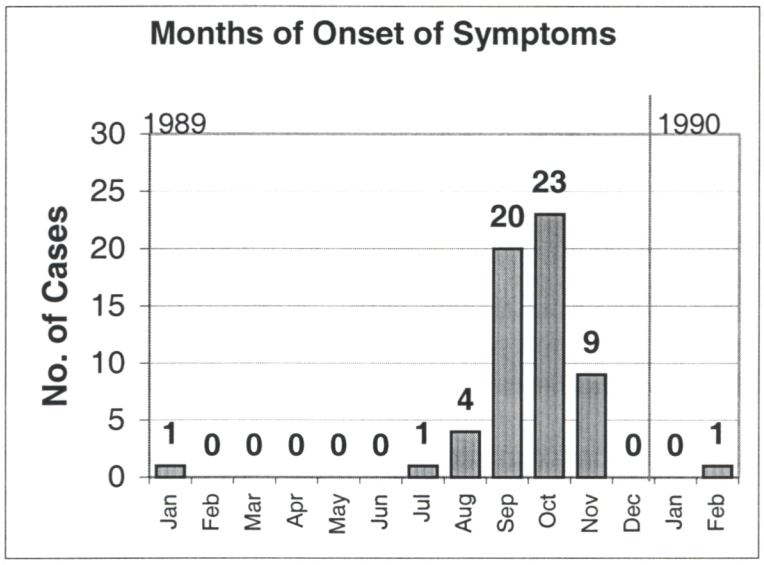
extensive reviews of this issue, no cause for the EMS could be defined by either CDC or FDA. A major reason for this lack of final decision is the lack of evidence. Following a visit of Showa Denko by CDC in May 1990, "unprofessional company behaviors" became suspect when records detailing the bioengineering and production process couldn't be located. Further along in this query, the CDC learned that the original bacterial culture and batch extracts felt to be responsible for this poisoning were destroyed by the company "for safety reasons" (Abelson 1991; Fagan 1997).

The First EMS Cases

The first official reports of EMS-related deaths were reported by a State Epidemiologist in New Mexico to CDC on October 31, 1989 as part of a monthly disease report (Center for Disease Control 1990). That same month, Oregon EMS cases reached their peak, along with cases reported in several other states (Slutsker, Hoesley, Miller et al 1990) (Figure 5). The states most impacted by TRP-related EMS based on prevalence rates were New Mexico (26.6 cases per million people), Oregon (21.6), South Carolina (15.2), and Minnesota (14.5), each representing foci from which the epidemic spread to other regions. New York (8.5) and California (9.5) represent other possible foci for the two coastal regions due to their international shipping ports (in contrast with Minnesota, which is located at the northern Mississippi River/Great Lakes region, the Mississippi Delta/River ports of Louisiana had the lowest prevalence in the United States) (Swygert, Maes, Sewell et al. 1990).

FIGURE 5.

Oregon Cases of Tryptophan Poisoning, Jan 1989 to Feb 1990



This sudden change in EMS incidence nationally led to an immediate response from CDC from October 31st to mid-November. Following an initial review, confirmation of a possible link of EMS to TRP products was established by the end of the first week of November, leading to the announcement of a recall of TRP-products on November 17, 1989 (Center for Disease Control 1989a, 1989b, 1989c, 1990).

The first cases of TRP-related poisoning in Oregon surfaced as early as July 1989, with one possible early case suspected for January 1989. According to the review published by Slutsker, Hoesley, Miller et al (1990), the extremely early case documented in this case study was due to either: 1) exaggeration of another disease, 2) direct relationship to one of the earliest contaminated batches of TRP products, or, more likely, 3) a condition similar to EMS but not directly linked to the TRP-poisoning experience.

From September to November 1989, EMS incidence maintained its prevalence peak. The initial recall of OTC TRP in November (officially underway in December), and a considerable amount of media coverage on this issue, led to a reduction in the number of new cases being reported to CDC. By January 1st, about 1000 cases had been reported, an amount which increased about 100 cases per month into the summer of 1990. Confirmation required history of TRP use and three clinical characteristics: 1) myalgia or muscle pain, 2) eosinophilia depicted by CBC, and 3) a scleroderma-like skin condition (Swygert, Maes, Sewell et al. 1990). Later symptoms discovered as part of this syndrome included lung problems and rheumatic-like arthritis. In Oregon, 8 new deaths could be linked to TRP after the November 1989 and March 1990 recalls.

MEDIA COVERAGE

Professional Journals

Biomedicine. In very short time, the moderate amount of support tryptophan received was greatly reduced, being outnumbered by the professional criticisms which erupted in the professional medical journals in just a few weeks (Figure 6). These reactions came in the form of case studies of people who presented with the new illness, reviews of unique symptomatology attached to particular cases, examples of clinical and laboratory findings used to define given cases, as well as numerous criticisms about the use of OTC supplements in general and recollections of past events of similar tragedies involving other popular adjunct remedies.

FIGURE 6

Number of Monthly Articles on TRP published in Medical Journals
(Source: Index Medicus, Oct. 1988 to Dec. 1991 inclusive)

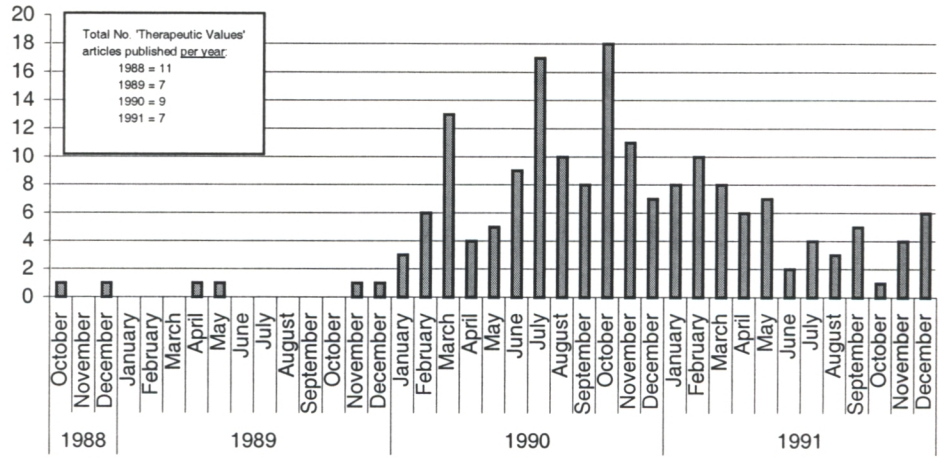
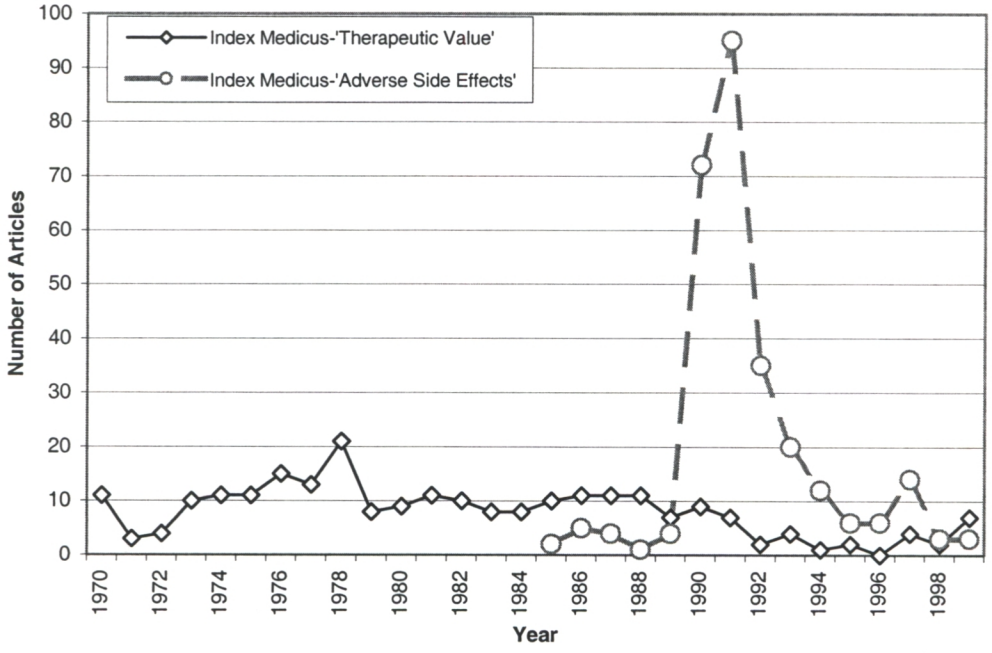


FIGURE 7

Professional Journal Articles Published before and after the 1989 TRP Recall
(based on *Index Medicus* entries, 1970 to 1999)



During the next two years, as the number of professional MD articles about the TRP issue reduced greatly in number, professional medical opinions reached their peak in 1991 and by 1993 were uncommon (Figure 7). In turn, these same issues came to dominate the more popular magazines. These public opinions which were expressed by the magazines were derived primarily from public hearings, investigative news stories, letters to the editor published by regular newspapers, legal news reports and occupational newsletters, and medico-legal publications. Together these changes in preferred media tools suggest other agendas in the works for each of the groups involved. A review of the content of these articles reveals a considerable amount of hostility being expressed by groups representing the various sides of this now political issue. Important concerns discussed (and disputed) relate to possible changes in OTC supplement availability and use, and any of the related regulatory policies in the works. It is also important to note that this change in media focus diverted the public attention from other more relevant issues and discoveries being made in the upcoming months.

A number of these important biomedical outcomes for this epidemic, published in the literature but never released to the public or openly shared with the general public even in health newsletters published by large universities, include:

- discovery of a possible contaminant—DiTRP--in Dec. 1990 (Anonymous 1990).
- The development of animal models in the first months of 1990—Lewis Rat--to test the hypotheses about the cause (Crofford, Rader, Dalakas 1990).
- a May 1990 CDC visitation to Showa Denko suggesting poor management as the most likely the cause for contamination, i.e. loss (destruction) of valuable bioengineering and production notes, inadequate company record keeping, and total destruction of the organism responsible for the toxin ()
- the conclusion that this was linked to bioengineering problems and not TRP in pure form.

It is interesting to note that the underlying goal to support TRP use as a medicine on behalf of MDs continued in spite of these problems. Psychiatric journals, for example, refused to stop publishing articles on TRP following its two recalls in November 1989 and March 1990. As a result, several articles about the neurochemical and physiological activity of TRP and its potential clinical use continued to appear each year until 1996. In 1993, when TRP was re-introduced to the market as a prescription substance regulated by the FDA, the medical journal articles once again began to detail its potential therapeutic value in increasing frequency.

Allied Health Professions. Journals published by the allied health professions represent as an important link between the MD biomedical profession and the general public. In general, allied health professionals like Emergency Medical Technicians, Emergency Department staff, Nurses, Physician's Assistants, and various Laboratory technicians read this medical literature along with the popular literature and professional medical literature. (Although MDs read these articles as well, they were less supporting of these "alternatives.") The Cumulative Index for Nursing and Allied Health Literature (CINAHL) bibliography provides insight into how the OTC/TRP tragedy was taken by a profession which at the time offered considerable support for the use of OTCs and dietary supplements by patients.

Prior to the tryptophan-recall, popular uses for it noted in CINAHL included insomnia and pain relief (Table 3). Most likely, these professional health care providers not only supported the uses of TRP by psychiatrists, but also cited their own 'professional

expertise' and education as reasons for their support. One example of this is the role played by nurses also licensed as Dieticians. Articles published in their trade magazines suggest they provided some of the strongest support for the use of dietary practices and nutritional supplements to control medical problems throughout the years prior to the recall (Cerrato 1988; Engle 1997). The most vocal trade magazine for nurses was Nurse's Drug Alert, which provided information about TRP both before and after the epidemic. News for the Nursing Legal Consultant published the most focused coverage on legal issues regarding OTC and/or TRP-related dietary recommendations. Not too surprisingly, a number of alternative/complementary health care articles were included in this portion of the CINAHL bibliography, most of which remained pro-active regarding dietary therapy and OTC supplement use even after the recall of TRP (Anderson 1998; Anonymous 2000; Meyers 2000).

Immediately following the recall, a chiropractor's perspective on the issue--"Nutrition. What we haven't been told about L-tryptophan" (Goldberg 1990) appeared in CINAHL. Other articles were less pointed about the politics of this event. This compares with later CINAHL articles which gave various responses to several well-defined TRP-related issues. Such articles include "The Power of Pasta" (Cerrato 1997), "Nutrition supplements: science vs hype"(Armsey Jr., Green 1997), and "The ban on "nature's sleeping pill"" (Anonymous 1994).

TABLE 3 TRP Articles in Cumulative Index to Nursing and Allied Health Literature
(relative to Nov 1989, date of the CDC announcement and recall)

Journal	*(Number of Articles)* Before	After	Topics
Newsweek	1	0	insomnia remedy
Psychology Today	1	0	insomnia remedy
Physical Therapist	1	0	Relief of Burning Pain
Nurses' Drug Alert	5	2	Pain, Co-medication with anti-depressants, Carbohydrate-fatigue, neurotoxicity; recall, the manufacturer
RN	0	1	TRP and pasta
Physician Assistant	0	1	the legacy of its use
News for the Legal Nurse Consultant	0	2	Legal issues
Hospital Practitioner	0	1	Erythromyalgia Syndrome
California Berkeley Wellness Letter	0	1	Issues
Harvard Medical School Health Letter	0	1	"Natural Disaster"
Chiropractic Journal	0	1	OTC and "the truth" about TRP
Journal of the American Dietetic Association	0	2	Toxicity Issue
American Journal of Clinical Nutrition	0	3	TRP and the serotonin path; exercise and recovery; CNS
Journal of Laboratory and Clinical Medicine	0	1	Lung/respiration activity
Alternative Medicine Review	0	1	5-hydroxy-TRP
Journal of Musculoskeletal Pain	0	1	Therapeutic efficacy--IL-5 interference; recovery
Office Nurse	0	1	TRP in pasta
Alternative Health and the Conscious Individual	0	2	purchasing TRP; TRP for memory
Canadian Journal of Applied Physiology	0	1	Exercise and TRP
Alternative Medicine	0	1	5-hydroxy-TRP
Emergency Medicine	0	1	the legacy of its use
Archives of Physical Medicine and Rehabilitation	0	1	EMS recovery

Public Reaction

The initial public reaction to the TRP recall was mixed and at times became quite polarized. The most common question concerning the masses was 'Is this recall another example of governmental (or FDA) "over-regulation?' For this reason, most of the public reaction to the TRP recall was highly critical and came in two forms. Magazine articles provide insight into this issue as a national experience. Newspaper response tells us about local concerns regarding this issue.

Popular Health Magazine Coverage. In March 1989, TRP was recommended in a very brief Science News article for use by young alcoholics under 20 years of age who suffer drinking problems along with clinical depression, suicide tendencies, and imprisonment (Bower 1989). A month later, (just prior to the production of bad TRP by Showa Denko KK) a writer for the magazine Runner's World asked "Is L-Tryptophan a magic bullet?" (Higdon 1989).

Following the publication of the TRP deaths in November 1989, several months passed before much was published in the popular magazines. In March 1990, People magazine interviewed Dr. Gerald Gleich, the immunologist who discovered the link between the EMS and L-tryptophan (Breu 1990). In April, Consumers' Research Magazine described this issue as the "risk of dietary supplement use" (Hunter 1990). Yet, another month later, an author for Woman's Day magazine gave her opinion succinctly: "The Tryptophan Tragedy. Throw it Out" (Houck 1990).

By summer (almost one year after the initial epidemic), the popular press medical magazines began informing the people about the final outcome and implications of this

tragedy. A review published by FDA Consumer (FDA 1990, June) focused on the growing need for regulations felt by medical professionals. At the time of publication, the TRP recall was expanded to include parenteral hospital formulas; so it is important to note that what not emphasized in this story was the fact that not all of TRP was recalled, just products linked to the bioengineering firm Showa Denko K.K. In spite of a subsiding epidemic (which at the time was becoming clear to CDC staff, due to the results of their inspection of the factory in Japan the month before), HHS Secretary Louis W. Sullivan, M.D. felt it proper to state "We are confronted with a major public health problem."

Very few additional deaths followed the summer of 1990. The manufacturing cause for this problem (bioengineered organisms which were genetically altered) wouldn't become part of the popular/professional science press until two months later (i.e. JAMA, NEJM, Science and Nature journals: Slutsker and Hoesly 1990, Belongia 1990; Gershon 1990, Roberts 1990; Raphals 1990). Another two months would pass before a possible toxin was discovered, news of which remained only in the scientific and professional medical journals (Science--Roberts 1990, JAMA--Anonymous 1990).

As news of the suspected chemical cause made its way to certain people, several political responses ensued. Harvard Health Letter (Vol. 15 Issue 12, p8, 1/2p, Oct90) continued to cite this as being a problem related to contamination, inferring some manufacturing related cause related to just the OTC products industry. Jeremy Rifkin's response (then head of Foundation on Economic Trends) used this news to further his

argument against the use of bioengineered compounds (Science--Raphals 1990), a concern equally expressed a few months later by editors of Nature (Editor 1991).

In June 1991 (now 1.5 years past the EMS peak) FDA Consumer once again tried to clarify its impressions about the history of this epidemic and the important issues attached to this series of events. FDA Consumer defined the problem as primarily of bioengineering origin and not so much an OTC product-related problem (Segal 1991). This led the Segal to state his own conclusion thusly: "it appears that the problem is not with the amino acid itself, but rather with the product becoming contaminated as a result of a change in the firm's manufacturing process." It is important to note however that the FDA still had its underlying political agenda attached to the recall. This was not verbalized in most of these writings. This agenda (regulation of TRP production and dispensing) wouldn't become popular news or produce results for another year.

Meanwhile, in January 1992, Vegetarian Times replied to a letter asking whatever happened to TRP? (Moll 1992). That same month, Better Nutrition for Today's Living asked its readers if they felt it was time to get TRP back on the shelves (Murray 1992). (A year later, the same question would be posed to a columnist in The Oregonian). Still, the best demonstration of how popular magazines covered the tryptophan is how this issues appeared in the various popular health journals (Figure 8). Popular magazines remained true to their original purpose and cause, i.e. typical nutritional/exercise magazines like Nutrition Forum, Men's Health, Shape, Self, Body Bulletin, and Joe Weider's Muscle and Fitness supported OTC marketing. Most of the more middle-road

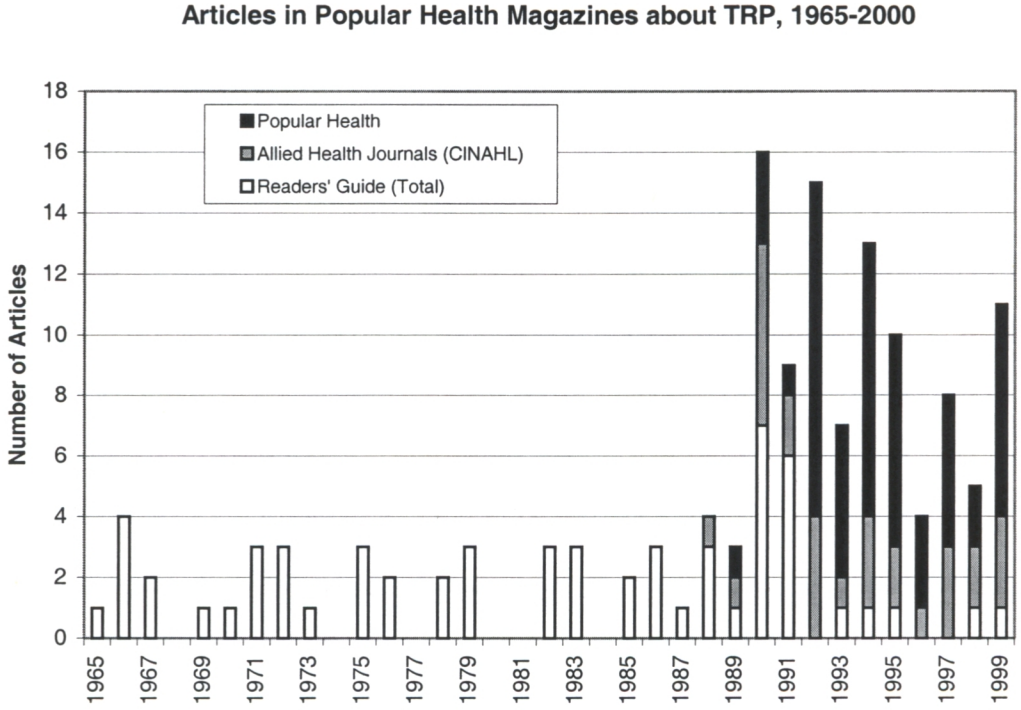
magazines and newsletters like Health Weekly, American Health, National Health, Cortlandt Forum ceased publishing supporting articles.

Women's Day, as noted earlier, took the conservative approach to this issue ("Throw it Out"), promoting claims that improving the amount of TRP-containing foods in your diet was fine, but using OTC supplements was not (interestingly, at least this value was held by the writers of their articles, but not necessarily their advertisers). Other magazines for women simply stopped making public statements (Women's Health Weekly, Herizons, Mothering, Parenting).

The most conservative magazines and newsletters turned out to be Environmental Nutrition, Berkeley Letter, Harvard Health Letter, Health Letter on the CDC, and especially FDA Consumer. Each of these was more supporting of regulation and controlled (i.e. prescribed) use. Other professional journals ended up being marginally supportive. They often not only promoted use of OTCs, even the TRP substitute 5HTP, but also demonstrated some underlying anti-regulation or "anti-Big Business" goals with their writing (i.e. Journal of Nutrition, Journal of Nutritional Medicine, American Journal of Psychology, International Review of Psychology).

Statistically, the amounts of popular magazine coverage on TRP and the related regulatory policies which came about had increased greatly by the mid-1990s. The statistics for this (Figure 8), in part demonstrate the increase. However, it is important to note that one of the bibliographic sources (EBSCO Master File Premier—used to search "Popular Health" magazine articles) had recently developed, and so it's listings may in part derived from that point in time forward (ca. mid-1990s to present).

Figure 8.



Business Magazine Coverage. Support for the production of TRP through bioengineering never ceased in spite of the public controversy and attitudes expressed by major groups acting against the large corporation-sponsored bioengineering and agritech industries. Since the first production of TRP through cell membrane leakage in 1948, large industries have provided much of the support for TRP and other amino acid production industries. As a result, little changes have occurred in these industries in spite of the public reaction to the TRP issue and its connection to the bioengineering controversy.

Tryptophan Press Coverage, 1970 to Present

During the initial years of developing this business in the United States for TRP production (ca. 1993, the end of the TRP recall), the FDA finalized its decisions about how to regulate TRP production and deliver it to the marketplace. The earlier Japanese company had by then suffered significantly from American legal actions taken against in, resulting in tens of millions of dollars in payments generated by these lawsuits. Since no civil laws existed in Japan for such legal actions to be based upon, American law was allowed to take precedence, resulting in the large financial rewards. This subsequently led Japan to develop its own legal policy for future international legal claims (O'Brien 1996, Shichi 1996).

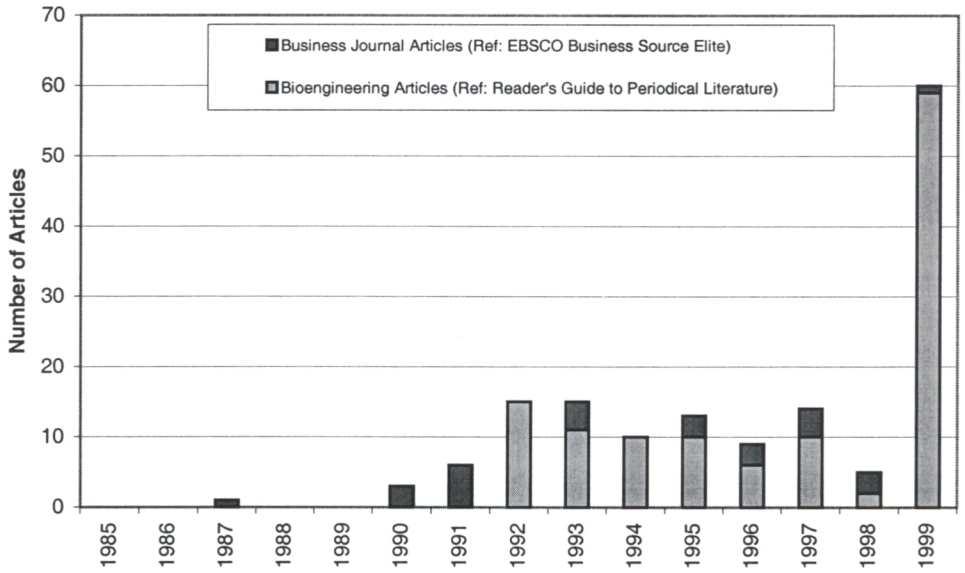
As the FDA began the transition of returning TRP to the marketplace, it gave the rights to produce TRP back to bioengineering firms attached to the Japanese industries (ca. 1993-4). The production facility was then set up in the United States, allowing for more effective filtering and safety monitoring methods to be employed. In several years, a number of other American-borne agritech companies began claiming their stakes in this rapidly growing "nutriceutical" market. Suddenly, the goal of this market shifted from producing not just OTC supplements, and more into producing nutritional chemicals used by large-scale livestock industries.

This changed the focus of the TRP market from a consumer health to the amino acid chemical industry. The results of these changes are best portrayed by the related trade and business journals. For this reason, the increase in articles on bioengineering noted by Reader's Guide to Periodical Literature roughly correlates with the number of

articles on these business ventures appearing in the popular business journals (data drawn from EBSCO's 'Business Source Elite' popular/trade magazine database) (Figure 9).

Figure 9.

General Bioengineering and Business Journal Articles, 1985-1999



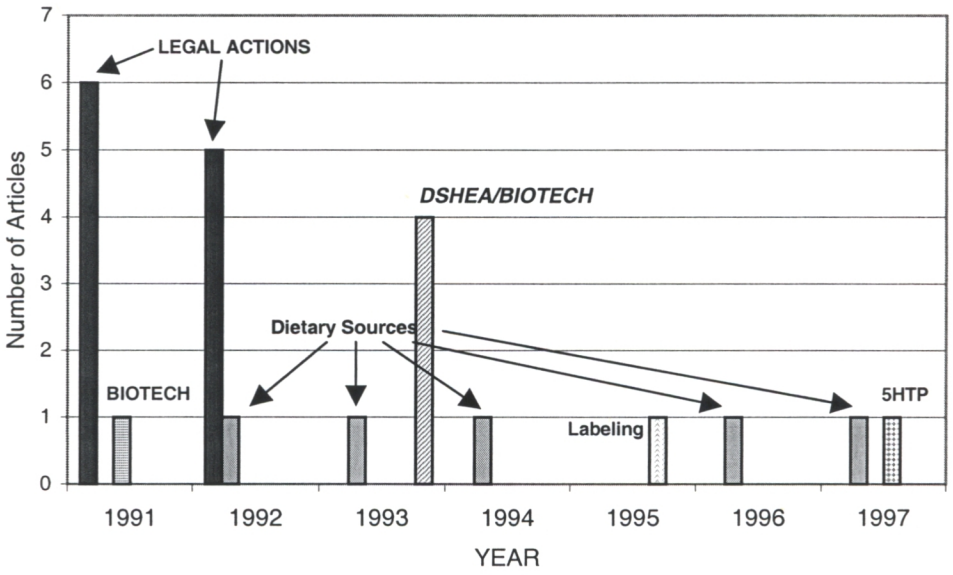
Examples of responses of the business community to the TRP recall and recovery begin with an article published in Forbes which laid blame on the FDA for not regulating the OTC industry or bioengineering enough to have prevented this epidemic (Abelson 1991). Abelson even went so far as to remind readers of the FDA's inability to "crack down" on OTC that have "unproven health claims" on their labels. He ends his article stating: "Could 31 deaths have been prevented? Maybe not. But much could have been done to reduce the likelihood of their happening"(ibid).

Later reactions to this issue were unemotional. Business as a whole supported the recall and the return of its producers to the American markets. This is best demonstrated by the numerous brief news items published in such chemical trade journals as Chemical Marketing Reporter (Anonymous 1994, Lerner 1997, Anonymous 1997) and Chemical Week (Walsh 1997). Food Technology took on the issue pertaining to legalization of bioengineered food products, a product central to its cause and the existence of the trade magazine since the 1960s (IFT Expert Report on Biotechnology and Foods, 2000a, b, c).

Local Newspaper Coverage

For the most part, newspaper coverage related to TRP represents primarily local issues. Reviewing TRP and/or EMS as an Oregon issue published in The Oregonian, we find that twenty-two articles were published between 1991-1999 dealing with Tryptophan either as a major topic or in passing (articles published in 1989 and 1990 were not reviewed for this study due to lack of index). These articles begin with coverage of the legal issue, using three local Oregon cases as examples, upon which they based much of this investigative reporting (Figure 10).

Figure 10. Oregonian Coverage of TRP Issues, 1991 to 1997



Using the characteristics of these articles defined by Bennett (1997, p. 17), the articles published by The Oregonian about tryptophan can be grouped as follows. The major gist of the article may be: a) question of blame—FDA or bioengineering? b) a cover-up of the cause by the Japanese producer, c) several local human interest stories regarding Oregon and Washington victims, and a series of articles about the use of natural (food) sources for tryptophan instead of the Over-the-counter remedy, d) the legal conflict which ensued and its related arbitration, e) the development of yet another Over-The-Counter (OTC) remedy (5HTP) purportedly of similar toxicity, and g) the moderately high incidence of cases in Oregon and Washington. The last two characteristics which Bennett listed, examples of visual impact and links to sex/crime, were not immediately found. However, an article about a high profile individual that was

published in a business journal is worthy to note, involving a popular New York ice hockey athlete (Otis 1991).

Lawsuits. Most of the early Oregonian articles on this issue detailed the story and events of three local people who were part of a local class action lawsuit filed against Showa Denko KK (January--Anonymous 1991, April and June--O'Neill 1991a, 1991b). On January 31, 1992, a story from the "wire reports" was published announcing a "secret settlement" made between a quadriplegic victim (whose illness was a result of the substance?) and the manufacturer of the supplement. The estimate of total victims in this article was 6000 (up 1000 from the year before) (Anonymous 1992).

On July 31, 1992, the news was about a local woman in Vancouver who initiated a suit against the manufacturer for her prolonged "physical and mental pain, diminished earning capacity, past and future loss of wages, and physical handicap" (as described by McCarthy). By then, eighty-eight lawsuits were filed by Oregon and Washington residents regarding this claim. A year earlier, the first three to complete legal arbitration were awarded a total of 2.2 million dollars. A number of these suits would be dismissed, and the remaining ones settled by the end of the year.

Revived Public Interest. The next series of articles about TRP in the Oregonian begin with several passing statements made by readers writing to popular columnists and editors. Like the readers inquiring into Vegetarian Times a year earlier, one Oregonian wrote Graedon and Graedon's "People's Pharmacy" column, Food Day Section, and wanted to know "What happened to tryptophan? . . . Will they ever bring Tryptophan back?" (Graedon and Graedon 1993, January 26th). Graedon and Graedon's reply simply

stated: 1) tryptophan was produced by a company that utilized a "new manufacturing technique" which ended up contaminating the end product, and 2) due to this tryptophan was permanently removed from OTC market "until its safety and efficacy can be proven . . . probably no drug company will want to underwrite the expense of such research."

The second flurry of writings about this issue came late in 1993. Two letters to the editor were published in response to The Oregonian Editor's column "Try a Dose of Truth" (Editor 1993, September 7th). The responses were entitled "New Regulations a Hindrance to Consumers" (Bettenberg 1993, September 18th) and "FDA Oversteps Authority" (Bell 1993, October 3rd). Both of these letters criticized the Dietary Supplement Health and Education Act under consideration by the Senate, in which the TRP case was used as the primary reason for the public needed such legislation to be passed.

Between the publication of these two letters, a lengthier reaction to similar news was published in The Oregonian in the "In my Opinion" section on September 21st entitled "FDA's L-Tryptophan Dangers Hogwash," by naturopathic physician Noel Patterson. Patterson criticized FDA attempts to regulate OTC products, arguing that the main reason for the TRP controversy was a bioengineering problem not an OTC production technique (Peterson 1993). No subsequent items discussing TRP along with the DHSEA controversy could be found in The Oregonian.

The TRP food source issue was a recurring theme in the Oregonian (and TV news). In 1992, 1994, 1996, and 1997, this use of tryptophan was mentioned in passing. First, it was promoted as a nutrient found in milk that helps you get to sleep, followed by

two articles referring to Thanksgiving (Turkey has been considered a source for this amino acid, a claim disputed by some who in turn provided evidence for another cause) (Anonymous 1992; Gallo 1994; Pratt 1996; Davis 1997).

Summary. This coverage of TRP as a food-related chemical, not dietary supplement, by The Oregonian demonstrates the transition away from the OTC-TRP recall issue and related DSHEA issue into more semi-conservative social attitudes about food and health in general. This implies that in the "official" newspaper setting, the history of TRP and DSHEA represent "the past" and these topics as pertinent news items considered "dead."

Recent Tryptophan Issues

In recent years, both magazine and newspaper coverage have been more complacent about TRP-related issues. Professional magazines continue to research the use and efficacy of this amino acid clinically. Popular and business magazines maintain a readership devoted to their political agendas.

For the most part, the TRP market has been replaced by the Melatonin and 5HTP OTC product markets. One salesperson I spoke with about this (who was in charge of ordering the products for a local natural foods store), stated her major concern was the higher prices that have resulted from this "charade." Tryptophan sells for five to six times the original price, and by prescription only, whereas its substitute 5HTP has considerably higher costs than the original TRP costs of the late 1980s (taking the assumptions about inflation into this reasoning as well).

Magazines. Several TRP-EMS related issues have reappeared briefly in magazines in recent years. Psychology Today has called it a "natural form of Prozac" (Firshein 1998). One professional business journal termed it a memory-aid for businessmen (Worswick 1998). Other popular and trade magazines have promoted it for use in treating dementia (Hikal and Hikal 1998), depression (Davis 1997, 1998), obesity (Pine 1997), insomnia (Tolin 1997), and PMS (Firshein 1996).

Like the OTC sales of the TRP-derivative 5HTP which led to an attempt to withdraw this substance from the market (RMD 1995, Morgenthaler 1997, Grady 1998, Anonymous 1998); this failed due to the inability of the scientist to prove his claim that a similar toxin also appeared in these new products.

Other public reactions to this issue are as numerous as they are diverse. A strong attempt was made to question the efficacy of the animal models developed for discerning the cause for the TRP cases (a common argument for conspiracy theorists) (Jaffe 1994). Manders (1995) published a strong article in Social Policy against the regulation and policy issues which erupted due to this recall, emphasizing the less expensive alternatives which once existed for highly popular anti-depressants like Prozac and several newly manufactured TRP-related derivatives. Joe Weider's Muscle & Fitness magazine has remains a strong supporter of OTC industry issues and deregulation in general. In 1996, the Mothers for Natural Law (MFNL) used the TRP-EMS argument to launch "The American Campaign to Ban Genetically Engineered Foods" (Salomon 1997). In 1999, attempts were still being made by the Mayo Foundation to claim the OTC supplements

are the cause for the illnesses for much the same reason as its earlier studies and published proofs about TRP suggested (Anonymous 1999).

Newspapers. Newspapers tend to be in tune with the popular magazine and business journal reports noted earlier. Recent New York Times coverage published in the Science Section details the use of TRP for bulimia treatment (Anonymous 1999). The Washington Post published a TRP related article on serotonin and depression (Proulx 1997), and another about the adulteration or contamination of the second generation of TRP-OTC products--5HTP (Okie 1998). The majority of Oregonian articles which mention TRP will most like remain focused on just diet, food chemistry, Thanksgiving, and the potential values of nutrients (not nutriceuticals necessarily) as personal health care supplements.

Who's To Blame?

On June 30th, New York Times journalist Marian Burros discussed the issues of regulating bioengineering production methods for foods and nutritional supplements. Burros cited FDA Commissioner David A. Kessler as the expert, who stated his opinion about regulating such businesses: "This is not a voluntary system. For a second expert, Burros quoted Michael Hansen, a Research Associate for the Consumer's Union, who said "Everything is left up to the discretion of the companies. The company is on the honor system" (Burros 1992).

Since then, the TRP market has pretty much become a large scale industry supported by large agrichemical/pharmaceutical firms, highly regulated by the FDA and

the policies and guidelines published by the various bioengineering/biomedical/ pharmacal professional groups. These actions have resulted in the successful writing and passage of the Dietary Supplement and Health Education Act and the development of standards upon which later legal actions may be taken should the safety concerning an OTC product become questioned. Assigning blame for the EMS cases is no longer the primary focus of many of these activities. As a result, the exact cause for this tragedy remains unclear and TRP and its 5HTP analog remain closely monitored therapeutic compounds. In the end, the 1989 to 1990 TRP epidemic has been blamed on such things as:

- a governmental agency political move (spawned by the 1970s OTC TRP problems)
- the lack of adequate FDA regulation and monitoring (Abelson 1991)
- company mismanagement of the production line (Jaffe 1994—aniline dye contaminant)
- FDA/CDC distrust in the consumer's ability to make an educated decision
- too much public trust in OTC remedies
- corporate conspiracy generated by biotechnology/pharmaceutical companies
- too much trust in bioengineering firms and their genetic manipulation processes
- a high degree of distrust regulators felt towards manufacturers of OTC products due to lack of regulation

The Tryptophan tragedy has effectively changed the health care system-related regulatory procedures for over the counter nutritional supplement markets. Due to the kinds of manufacturing processes involved with these industries, the actions of consumers have some impact on these fields. These impacts appear minimal at the national level, and more effective at a very specific or local level. The role of media in

these actions is threefold. Media works at the professional and business level to keep the industries motivated and active when it comes to need for change. It also works at the local level to send out warnings whenever needed, and hopefully arrest tragic outcomes from happening due to whatever causes exist for these tragedies. Finally, the impact of media during and after the tryptophan epidemic demonstrates the ability for single media events to spur on further media events and subsequent social and political action. The benefits of these effects are not only to the consumer, but also to the producer and government it appears. At least when it comes to public health-related issues.