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**OHIO STATE BOARD OF PHARMACY**77 S. High Street, 17th Floor; Columbus, Ohio 43266-0320  
614/466-4143 (FAX: 614/752-4836)**CONTROLLED SUBSTANCE ACT****DRUG ABUSE/MISUSE REPORT**

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**EPHEDRINE**

One of the important responsibilities of the Board is the administration and enforcement of Ohio's Controlled Substance Act. This act provides the Board with the authority and responsibility for adopting rules for the administration and enforcement of Revised Code Chapter 3719. and prescribing the manner of keeping and the form and content of records to be kept by persons authorized to manufacture, distribute, dispense, conduct research in, prescribe, administer, or otherwise deal with controlled substances. The act provides that the rules shall be designed to:

1. facilitate surveillance of traffic in drugs, to prevent the improper acquisition or use of controlled substances or their diversion into illicit channels;
2. aid the state board of pharmacy and state, local, and federal law enforcement officers in enforcing the laws of Ohio and the federal government dealing with drug abuse and control of drug traffic.

The Board also has the authority to add, transfer, or remove a compound, mixture, preparation, or substance from the schedules. The Board may also classify any non-narcotic substance that may be sold over-the-counter without a prescription, pursuant to the federal Food, Drug and Cosmetic Act, as a prescription drug should a pattern of abuse develop.

Ephedrine is a drug which may result in serious adverse side effects and harm due to misuse or abuse. Ephedrine is a potent central nervous system stimulant and is capable of producing the following adverse effects: nervousness, dizziness, tremors, alterations in blood pressure or heart rate, headache, gastrointestinal distress, chest pain, myocardial infarctions, stroke, seizures, psychosis, and death.

Ephedrine and the isomer - pseudoephedrine - was mentioned as the drug involved in more than 75 deaths in Calendar Year 1993 and approximately 3,000 emergency room visits in Calendar Year 1992. The data used in the following tables was obtained from the annual reports of the National Institute on Drug Abuse's Drug Abuse Warning Network.

<b><u>MEDICAL EXAMINERS</u></b>						
<b>(DRUG ABUSE RELATED DEATHS REPORTED)</b>						
	1988	1989	1990	1991	1992	1993
	# MENTIONS	# MENTIONS	# MENTIONS	# MENTIONS	# MENTIONS	# MENTIONS
	<u>(RANK)</u>	<u>(RANK)</u>	<u>(RANK)</u>	<u>(RANK)</u>	<u>(RANK)</u>	<u>(RANK)</u>
EPHEDRINE	19 (49)	21 (48)	18 (59)	18 (60)	30 (47)	36 (49)
PSEUDO- EPHEDRINE	*	11 (64)	16 (61)	24 (53)	27 (49)	39 (47)

*\*Figures Not Available.*

<b>EMERGENCY ROOMS</b>					
(DRUG ABUSE RELATED EPISODES)					
	1988	1989	1990	1991	1992
	# MENTIONS	# MENTIONS	# MENTIONS	# MENTIONS	# MENTIONS
	(RANK)	(RANK)	(RANK)	(RANK)	(RANK)
EPHEDRINE	57 (139)	66 (127)	907 (75)	955 (69)	902 (69)
PSEUDO-EPHEDRINE	405 (54)	404 (53)	2133 (49)	2123 (49)	1994 (48)

**Abuse And Misuse Of OTC Ephedrine Products**

In July of 1993, the Ohio Board received a report from a concerned citizen regarding the sale and abuse of over-the-counter products containing ephedrine by “kids” and “adult drug abusers” between the ages of eight years and twenty-eight years. The products - Effedrine and Minithins - were being sold in quantities of 100 to these “kids and adult drug abusers” by convenience stores in Mansfield Ohio - a city of approximately 70,000 citizens.

The concerned citizen reported further that several young adults had to be admitted to Richland Memorial Hospital to “get off of it”, that they were going through withdrawal, that some were violent, and some had not eaten for several weeks. The person also reported that some of the kids had suffered convulsions from abusing the drugs, that the drugs are referred to as white crosses, and are being sold on the streets.

In March of 1994, the Board received correspondence from Deborah Pryce, Member of Congress from the 15th District of Ohio, regarding the death of Carl Richardson, a seventeen-year-old athlete, due to the ingestion of a lethal amount of ephedrine. The letter was accompanied by a copy of a letter U.S. Representative Pryce received from the Madison County Prevention Assistance Coalition Team (PACT); a press release; the autopsy report; and a letter from the Franklin County Coroner’s office stating the cause of death.

Copies of U.S. Representative Deborah Pryce’s correspondence and accompanying documents were forwarded to the nine members of the Board of Pharmacy on March 25, 1994. On April 14, 1994, the Board of Pharmacy considered the abuse of ephedrine as an agenda item and decided to take the “necessary steps to require, pursuant to the provisions of division (J) of Ohio Revised Code Section 3719.44, a prescription for over-the-counter drug products that contain ephedrine and are being abused”.

On Friday, May 13, 1994, the Board of Pharmacy received a FAX from the State Information Branch of the Food and Drug Administration regarding a Texas Department of Health Press Release issued on May 12, 1994 and bearing the following heading:

**“Health Commissioner Bans Formula One, Restricts Ephedrine Sales”**

The following portions of the press release demonstrate the widespread nature and danger of over-the-counter products containing ephedrine if they are abused or misused.

*Dr. David R. Smith, Texas Commissioner of Health, today prohibited the sale of ephedrine in this state to persons younger than 18. Ephedrine is an ingredient of popular drugs sold as diet supplements or "pep pills." In the same order, the commissioner banned from the market one of the best known ephedrine-containing products, Nature's Nutrition Formula One, commonly called Formula One.*

*Dr. Smith's actions result from a Texas Department of Health (TDH) investigation into numerous reports of illness and at least one death linked to the possible use of ephedrine-containing products. In an Austin press conference, Dr. Smith said, "although our investigation is not yet finished, we have found that the unrestricted sale and use of ephedrine and related chemicals pose an immediate and serious threat to human life and health."*

....

*The TDH investigation into both over-the-counter and health food distributor sources of ephedrine-containing products followed reports of illness in adolescents and teenagers as well as adults who have taken the drugs either to lose weight or to experience a "speed-like high," according to Dr. Smith.*

*Separate incidents of alleged overdoses requiring medical treatment have occurred in Austin, Longview, Amarillo and other cities. At least one death, that of an Austin woman in April, may also have been associated with the use of ephedrine.*

*The specific action against sales of Formula One, and an accompanying order that its Dallas manufacturer, Alliance USA, recall the product from the market, are based on a Texas Attorney General's agreement with TDH that Formula One is not properly labeled.*

*Although the Formula One ingredients label lists Ma Huang, a Chinese herbal source of ephedrine, and kola nuts, which contain caffeine, it fails to list ephedrine and caffeine as ingredients. The label further fails to include a required consumer warning about those stimulants.*

On May 24, 1994, the Board of Pharmacy received correspondence and material from the father and mother of a seventeen-year-old athlete who died from an overdose of ephedrine. Their son, Carl, was the young man involved in the Madison County Prevention Assistance Coalition Team press release which accompanied the letter from Deborah Pryce, a member of the U.S. House of Representatives.

Contact by our office in May 1994 with the New Mexico Board of Pharmacy regarding ephedrine abuse in their state confirmed the fact that ephedrine-containing products were being sold to young adults (15 years old). Testimony was received during a public rules hearing conducted by the New Mexico Board of Pharmacy on March 16 and 17, 1992 that over-the-counter ephedrine-containing products were being consumed in toxic amounts by 15-year-old girls.

An LPN working in an emergency room at the Roosevelt General Hospital in Portales, New Mexico on December 5, 1991 related how he had treated three 15-year-old girls who had consumed 24 to 33 tablets of ephedrine-containing over-the-counter drugs for "kicks". Written testimony was also received by the New Mexico Board of Pharmacy from a hospital pharmacist and emergency room physician working at the Artesia General Hospital in Artesia, New Mexico regarding two instances where a young child and adult female had been presented to the emergency room for treatment of an ephedrine overdose. Both had ingested an over-the-counter product with the name of "Go Power".

The first letter was written by an MD whose practice is located in Albuquerque and specializes in treating allergies. The physician stated in his letter that "giving ephedrine during a severe asthmatic attack could lead to severe increase in cardiac rate, leading to an abnormal rhythm and possibly to death. This is much more likely to occur during an asthmatic attack when the oxygenation level is decreased. In essence, Ephedrine offers nothing over the newer medications, and indeed may be dangerous." ....

The New Mexico Board of Pharmacy classified over-the-counter products containing more than 0.5% ephedrine as a prescription-only drug product. Discussions in late 1994 with representatives of the New Mexico Board of Pharmacy indicated that they were experiencing problems with products that were exempted by their rule when it was adopted. The rule exempted products containing ephedrine that also contained "one or more additional active medicinal ingredients which are not classified as sympathomimetics".

Near the end of May 1994, the Ohio Board of Pharmacy office was contacted by the Legislative Aide for Senator Merle Grace Kearns - Philip H. Serghini - and Nicci Crocker, an intern. The parents of the young man who had died of an overdose of ephedrine were constituents of Senator Kearns. Mr. Serghini suggested that the problem could be addressed legislatively through Sub. H.B. 391, legislation that included an emergency clause and that was presently pending before the Health and Human Services committee of the Senate. Discussions as to how the problem might be successfully addressed were held with Senator Kearns's legislative aide and the intern.

A decision to place ephedrine in Schedule V of the Controlled Substance Act was made and an amendment drafted by the Legislative Service Commission. This approach would not ban the sale of products containing ephedrine nor require that they be dispensed pursuant to a prescription issued by a practitioner. The proposed amendment restricted the sale of the products to pharmacies and by pharmacists. Classifying ephedrine as a Schedule V controlled substance provided sufficient controls to prohibit its sale and promotion in Ohio except for legitimate medical purposes.

By placing ephedrine-containing drug products in Schedule V, they can be purchased for legitimate medical purposes without a prescription by persons who are 18 years or older. Each sale has to be made by a pharmacist, the most knowledgeable health professional regarding drugs and their abuse.

A written record of each sale of these products is made by the pharmacist and the record includes the name and address of the purchaser, the date of purchase, product purchased, and quantity purchased. The records are maintained by the pharmacy for two years and are open for inspection and review by drug law enforcement officers and Pharmacy Board agents.

The sale by a pharmacist also provides the opportunity for the pharmacist to question the purchaser and perform prospective drug utilization review as it relates to other medications (OTC and prescription) that the purchaser consumes. The pharmacist can also at the time of purchase counsel the patient as to the proper use of the drug product and the possible adverse reactions that can occur.

On June 28, 1994, the Board office was contacted by Senator Kearns' office and asked to meet with the Senator and Kevin J. Kraushaar, Asst. General Counsel and Director of State Governmental Relations for the Nonprescription Drug Manufacturers Association. The meeting was held in Senator Kearns' office. Also attending the meeting was Anthony C. Novello, who was registered with the Joint Committee on Agency Rule Review as a legislative agent for the Sandoz Pharmaceuticals Corporation. The purpose of the meeting was to discuss a possible amendment requested by Mr. Kraushaar.

Agreement was reached during the meeting that an amendment would be prepared by the Legislative Service Commission to provide the Board of Pharmacy with the authority to except products containing ephedrine from Schedule V of the Controlled Substance Act that have not been associated with abuse.

The amendment placing ephedrine in Schedule V of Ohio's Controlled Substance Schedules and providing the Board of Pharmacy with the ability to except products from Schedule V was approved by the Senate Health and Human Services Committee on Tuesday, June 28, 1994. The amended bill was voted on by the Senate later that day, passed, and sent to the House of Representatives for concurrence. The House considered the Sub. H.B. 391 later that afternoon and concurred with the Senate amendments. The legislation was signed by Governor Voinovich on July 21, 1994 and ephedrine was placed into Schedule V of the Controlled Substance Act on that date.

Emergency rules were adopted by the Board effective August 15, 1994 and compliance bulletins mailed to all wholesalers and terminal distributors of dangerous drugs licensed with the Board of Pharmacy. Bulletins were also sent to manufacturers of over-the-counter products that contained ephedrine or who manufactured ephedrine.

The definition of ephedrine was drafted using the following description of Ephedrine in the Eleventh Edition of The Merck Index:

Ephedrine is  $\alpha$ -[(Methylamino)ethyl]benzene-methanol;  $\alpha$ -[1-(methylamino) ethyl]benzyl alcohol; 2-methylamino-1-phenyl-1-propanol; 1-phenyl-1-hydroxy-2-methylaminopropane; 1-phenyl-2-methylaminopropanol;  $\alpha$ -hydroxy- $\beta$ -methylaminopropylbenzene; a product which occurs in the Chinese herb Ma Huang (*Ephedra vulgaris*, *Ephedra sinica* Stapf, *Ephedra equisetina* Bunge, *Gnetaceae*) and in several other *Ephedra* spp. Isomeric forms include *d*- and *l*-ephedrine as well as *d*- and *l*-pseudoephedrine with *l*-ephedrine and *d*-pseudoephedrine as the naturally occurring isomers.

The rules adopted by the Board require that over-the-counter products containing a Schedule V controlled substance may not be sold to anyone who is younger than eighteen years of age and that the Schedule V controlled substance product may only be sold at retail for a legitimate medical need and that the purchaser furnishes information to the pharmacist which establishes the legitimate medical need for the controlled substance.

On August 23, 1994, the Board approved adopting an emergency rule to exempt two products containing ephedrine and all products containing the isomer of ephedrine known as pseudoephedrine from Schedule V of the controlled substance schedules. The rule was submitted to the Governor and an Executive Order approving the emergency rule and making it effective immediately was signed on August 24, 1994.

Rules adopted to date to implement the provisions of Sub. H.B. 391 were effective on November 25, 1994; December 15, 1994, March 13, 1995 (Criteria to be considered in denying a petition for exception or removing a drug product exception), and Exceptions (amended 1/10/96).

Petitions for excepting the following products were received by the Board following the placement of ephedrine in Schedule V by the Legislature: "DynaFed Asthma Relief"; "Diet Pep"; "Ultra Diet Pep"; "Turbo Charge"; "Extra Strength Guarana"; "Hydrosal Hemorrhoidal Ointment"; "all products containing Ma Huang"; "Theodrine Tablets"; "Bronkaid Dual Action Caplets"; "Breathe Easy Herb Tea"; Theophylline, Ephedrine HCl and Phenobarbital Tablets, USP"; "Primatene Tablets"; and "Primatene Dual Formula Action Tablets". Action by the Board on these petitions was delayed until rules could be promulgated establishing the criteria for denying a petition and until the Board received a formal Attorney General's opinion regarding whether or not the Board must except individual products from Schedule V of the Controlled Substance Act pursuant to a Chapter 119. rule.

Following receipt of the official Attorney General's Opinion issued November 29, 1994 stating that the Board must except particular products by adopting rules naming the particular products and adoption of Administrative Code Rule 4729-12-10 on March 13, 1995 setting the criteria for denying a petition to except a product from Schedule V of Ohio's Controlled Substance Act, the Board considered the petitions at their meeting of April 27, 1995. The decisions rendered by the Board regarding the petitions were as follows:

<b><u>Product</u></b>	<b><u>Action of the Board</u></b>
“Dynafed Asthma Relief”	exception denied
“Diet Pep”	exception denied
“Ultra Diet Pep”	exception denied
“Turbo Charge”	exception denied
“Extra Strength Guarana”	exception denied
“Hydrosal Hemorrhoidal Ointment”	exception approved
“all products containing Ma Huang”	exception denied
“Theodrine Tablets”	exception denied
“Bronkaid Dual Action Caplets”	exception approved
“Breathe Easy Herb Tea”	exception denied
“Theophylline, Ephedrine HCl and Phenobarbital Tablets, USP”	exception denied
“Primatene Tablets”	exception approved
“Primatene Dual Formula Action Tablets”	exception approved

The petitions requesting that “Dynafed Asthma Relief”; “Diet Pep”; “Ultra Diet Pep”; “Turbo Charge”; “Extra Strength Guarana”; and “Breathe Easy Herb Tea” be excepted from Schedule V of the Controlled Substance Act were denied for the following reasons:

1. The products were not distributed, advertised, and promoted in a manner which reduces the likelihood of inappropriate use and/or abuse.
2. The labeling and the name of the product did not reduce the likelihood of inappropriate use and/or abuse; and
3. The products have a significant potential for inappropriate use and/or abuse.

The petition submitted by the National Nutritional Food Association (NNFA) requesting that “all products containing Ma Huang” was denied for the following reasons:

1. Ohio Attorney General Opinion (94-083) advised the Board that they may only except particular drug products containing Ephedrine by the name of the particular product; and
2. There is a lack of standardization of labeling of products containing Ma Huang. This lack of standardization in the labeling and naming of products containing Ma Huang does not reduce the likelihood of their inappropriate use and/or abuse.

The petitions requesting that “Theodrine Tablets” and Theophylline, Ephedrine HCl and Phenobarbital Tablets, USP” be excepted were denied due to the fact that they both contain the controlled substance - phenobarbital. Division (K) of Ohio Revised Code section 3719.44 specifically states that the Board “may except any other drug product containing ephedrine from being included as a schedule V controlled substance if it determines that the product does not contain any other controlled substance.” Since these products contain a controlled substance, the Board does not have the legal authority to except them from Schedule V.

Products whose petitions were approved were included in Proposed Amended Rule 4729-12-09 by the Board during their meeting of September 18-22, 1995. The proposed rule was filed with the appropriate state agencies on October 20, 1995 and a public notice of a 119. hearing published in the Cleveland Plain Dealer on October 25, 1995. The public hearing was held on Tuesday, November 28, 1995 at 1:00 p.m. in Room 1914, Vern Riffe Center for Government and the Arts, 77 S. High Street, Columbus, Ohio. The proposed amended rule was published as follows for public comment during that hearing:

4729-12-09 Exceptions.

Pursuant to division (K) of section 3719.44 of the Revised Code, each of the following products containing ephedrine, its salts, its isomers, or the salts of its isomers is declared to be exempt from classification as a schedule V controlled substance:

- (A) All products that contain the isomer known as pseudoephedrine or its salts, but do not also contain any of the isomer known as ephedrine or its salts.
- (B) BRONKOID DUAL ACTION CAPLETS.
- (C) HYDROSAL HEMORRHOIDAL OINTMENT.
- (D) PRIMATENE DUAL FORMULA ACTION TABLETS.
- (E) PRIMATENE TABLETS.

Following the public hearing and consideration of additional information submitted by Traditional Medicinals, the Board moved to amend the proposed rule by adding "Breathe Easy Herb Tea" to the list of excepted products and refile the proposed amended rule with the Joint Committee on Agency Rule Review (JCARR). The following proposed amended rule was refiled with JCARR on November 29, 1995 as follows:

4729-12-09 Exceptions.

Pursuant to division (K) of section 3719.44 of the Revised Code, each of the following products containing ephedrine, its salts, its isomers, or the salts of its isomers is declared to be exempt from classification as a schedule V controlled substance:

- (A) All products that contain the isomer known as pseudoephedrine or its salts, but do not also contain any of the isomer known as ephedrine or its salts.
- (B) "BREATHE EASY®" HERB TEA.
- (C) "BRONKOID® DUAL ACTION" CAPLETS.
- (D) "HYDROSAL®" HEMORRHOIDAL OINTMENT.
- (E) "PRIMATENE® DUAL ACTION FORMULA" TABLETS.
- (F) "PRIMATENE®" TABLETS.

The proposed amended rules were considered by the Joint Committee on Agency Rule Review during their meeting on December 12, 1995 and their jurisdiction ended December 28, 1995. Accordingly, the proposed refiled rule was filed by Board staff on December 29, 1995 with the required state agencies with an **effective date of January 10, 1996.**



**National Institute of Drug Abuse - Drug Abuse Warning Network Data**

As the state agency responsible for the enforcement of all of the laws governing the legal distribution of drugs in the state, the Ohio Board receives copies of the Annual Drug Abuse Warning Network publications. Review of the annual data for the years 1988 through 1993 documents the fact that ephedrine and its isomer, pseudoephedrine, have been implicated by medical examiners in the deaths of 259 individuals. Emergency room data for the years 1988 through 1992 indicates that ephedrine and its isomer, pseudoephedrine, have been involved in 14,825 drug abuse related episodes.

The DAWN data is derived from a consistently reporting, nonrandom sample of 431 participating emergency rooms in 21 metropolitan areas, and 78 medical examiner facilities located primarily in 26 metropolitan areas.

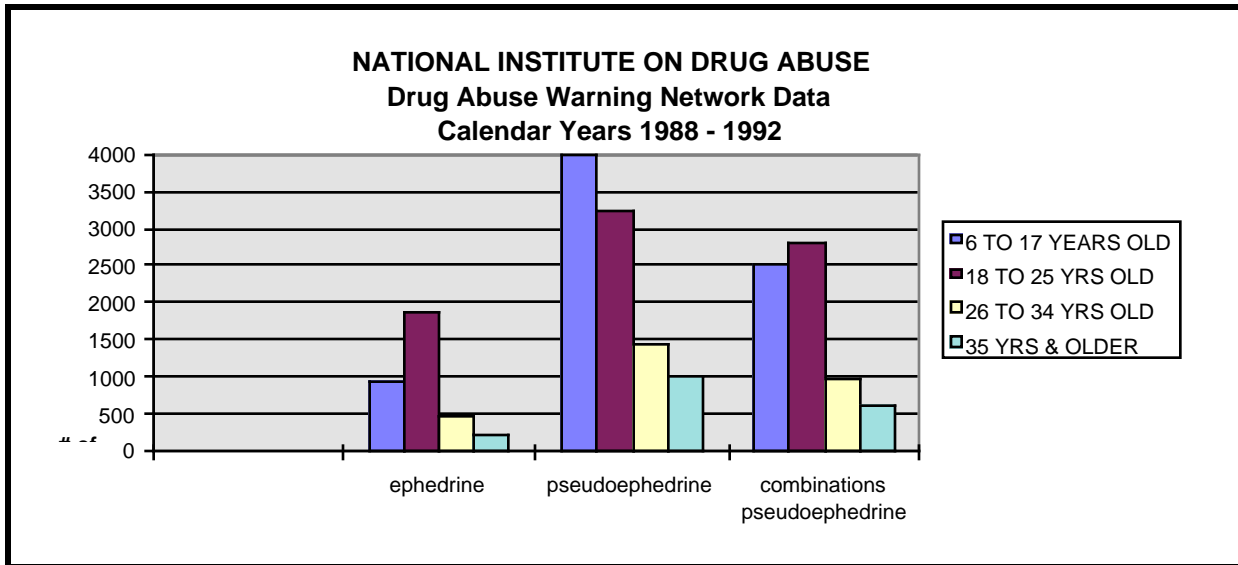
The disturbing aspect of the emergency room data is the fact that it does not include rural areas and includes large metropolitan areas in only 17 states and the District of Columbia. The data also does not take into account changes occurring in the delivery of health care in the United States and the fact that many patients are being encouraged to visit urgent care centers or contact a primary care physician before seeking treatment in an emergency room.

Two deaths are known to have occurred to date in Ohio due to toxic levels of ephedrine - a 17-year-old male athlete from Plain City, Ohio in January 1994 and a 29-year-old male from Hillsboro, Ohio in November 1994. Neither of these deaths are included in the NIDA DAWN data since the only Ohio coroner's office included on the national NIDA panel is in Cuyahoga County. The autopsies in both of these Ohio cases were conducted by the Franklin County Coroner's office.

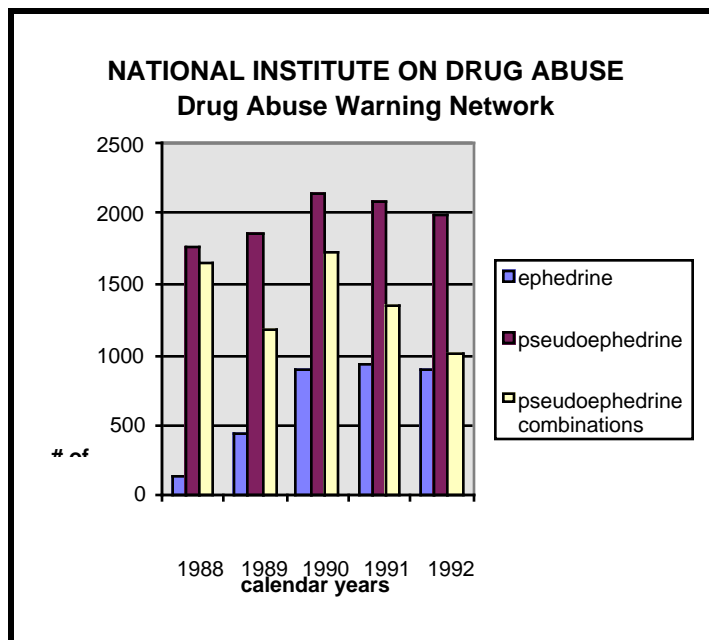
A dramatic increase in drug abuse related episodes in emergency rooms due to ephedrine and its isomer occurred in 1990. Seven hundred eighty-two (782) episodes were reported in 1989 and 4,915 in 1990 - a 529% increase. Unfortunately, there is no indication in the DAWN reports as to why this significant increase occurred. Did the increase reflect a change in reporting or did an actual increase in incidents occur during the year? If the increase is real, was it due to the introduction and the aggressive promotion of products like "Effedrine", "MiniThins" and "Pep Thins" by mail order firms in magazines or convenience stores near schools?

NIDA, in its 1991 Annual DAWN report, published Table 2.06c, Drugs Mentioned Most Frequently By Emergency Rooms in 1991 According To Age of Patient. Pseudoephedrine, an isomer of ephedrine, was ranked number twelve in the number of mentions in patients 6 to 17 years old (903). Unfortunately, the data published by NIDA in its annual report did not include combination products for this age group. This table also does not appear in previous annual DAWN reports. Accordingly, the Board requested this information from NIDA for the calendar years 1988 - 1992.

The following graph was generated from data provided by the National Institute on Drug Abuse. The data was obtained through the Drug Abuse Warning Network and a special report generated by NIDA at the request of the Board of Pharmacy for age-related data for ephedrine and pseudoephedrine containing products. The data indicates the number of Emergency Room visits where these drugs were mentioned by the different age groups over a five-year period.



The following graph provides data obtained from the Drug Abuse Warning Network regarding the number of emergency room episodes reported for ephedrine, pseudoephedrine, and pseudoephedrine combination products. The data is reported for each of the calendar years 1988 through 1992.



### **Products Containing Ephedrine**

One of the most frustrating problems is a lack of data on over-the-counter drug products that contain ephedrine or its isomer - pseudoephedrine. The Ohio Board of Pharmacy maintains a database of prescription drugs and over-the-counter drug products that contain controlled substances. An initial review of the Board's database following discussions regarding the abuse of the ephedrine and its isomer, pseudoephedrine, revealed only approximately 174 over-the-counter products that would be affected by placing ephedrine and its isomers in Schedule V of Ohio's Controlled Substance Act. Data from LADDIS, the Board of Pharmacy's Licensure and Dangerous Drug Information System, indicated that only 109 prescription products contained ephedrine or its isomer, pseudoephedrine.

It is now obvious, however, that there may be 500 or more over-the-counter products in the marketplace that contain ephedrine and/or its isomer, pseudoephedrine. A considerable number of over-the-counter products containing ephedrine are being marketed with labels indicating the ephedrine ingredient as Ma Huang, Ephedra, or the American Desert Herb. Few, if any, of the ephedrine products which are being promoted through the mail in muscle magazines or sold in convenience stores have an NDC number. The majority of the labels also do not indicate the amount of ephedrine that each dosage unit contains. If the labels do indicate the amount of ephedrine in each dosage unit, there is no assurance that the information is correct.

The federal Drug Enforcement Administration published the following information in a report dated February 23, 1995 regarding the labeling of Ma Huang products with misleading and false information:

*A large number of products containing Ephedra are sold in health food stores (Table 4) as diet aids or as energy boosters. Non-technical sources of information promote Ephedra as a "natural" agent for weight reduction, stimulation, and asthma/congestion relief. Ephedra extracts, which are as much as 700 % more concentrated in ephedrine than Ephedra powder, are still advertised and distributed as an herbal product and under the current Dietary Supplement Health and Education Reform Act (DSHEA) both are considered foods. However, there is speculation that some of these natural products are spiked with synthetic ephedrine. Ms. Michelle Reynolds, President-elect of the North American Alliance for Traditional Chinese Medicine and President of Pharma-Botanixx has alerted the FDA by means of a letter to the Chief of FDA-FDA Docket Management that "in our clinical research we repeatedly found products masquerading as natural food supplements that "extended" or "spiked" the naturally occurring active ingredients of ephedrine and pseudo-ephedrine found in the Chinese herb known commonly as Ma Huang." Such products may be fraudulent under the current status of the DSHEA.*

### **Manner Of Distribution, Advertising, And Promotion Of OTC Products Containing Ephedrine**

The death of Carl Richardson and subsequent scheduling of ephedrine as a Schedule V controlled substance has made drug law enforcement officials aware of the fact that a considerable number of over-the-counter products that allegedly contain ephedrine in the form of Ma Huang are being advertised and promoted in publications appealing to young women and male athletes. Many of these products are being sold through the mail and through individual community based distributorships in an exciting new marketing concept referred to as "NETWORK MARKETING".

The advertisements appearing in body building magazines offer ephedrine-containing products with claims that they are "*legal drugs*" which:

- ◆ increase endurance by over 200% during workouts
- ◆ increase concentration
- ◆ increase strength from day one
- ◆ triple training intensity.

The same advertisement in the June 1993 issue of MUSCLEMAG even states that the drug product sold as "EPH + 25" is available for only a limited time and that the purchaser should "order now before the FDA takes the product off the market".

Promotional material used by many distributors promote the herbal products containing ephedrine as "foods" and "dietary supplements". Promotional material for these products use the following marketing phrases:

Promotional phrases used to sell Ma Huang products for weight control and pep:

- ◆ *Lose Weight Now With "ENER-DIET"; Controls Your Appetite and Keeps You Feeling Full of Pep*
- ◆ *"SLIM CARE" - The All Natural Weight Loss System*
- ◆ *LOSE WEIGHT WITHOUT DIETING!!! PATENTED FAT BURNER*
- ◆ *"Nature's POWER TRIM" - LOSE WEIGHT WITHOUT DIETING!!!*

Promotional phrases used to sell Ma Huang products as stimulants:

- ◆ *"NATROL HIGH" - Stay Alert & Feel Alive with This Powerful Picker Upper*
- ◆ *"HERBAL DYNAMITE"- When you need it NATURES ULTRA BOOST is an explosion of pure herbal dynamite. Nature's Ultra Boost combines impressive doses of the 2 strongest natural energizers available. Ephedra and Guarana. One tablet is all it takes to "pep up".*

- ◆ *“THERMOJETICS” Herbal Tablets Green - To lose Weight and feel Great and for better results. a. Thermos twice a day b. \* . . .*
- ◆ *“THERMOJETICS” - Helps curb appetite, increases energy, aids metabolism*
- ◆ *“EXCEL - The Human Energy Company” - Herbs for active men and woman - Ultra High Performance - An herbal dietary supplement*
- ◆ *“UP YOUR GAS” - FAST ACTING ENERGY! - All Natural Energy Tablets. - Here’s the most outrageous pill of its kind on the market. Once you try it, you’ll know why we call it UP YOUR GAS. This zany new power-packing formula is guaranteed to make your day. Sure, most people will laugh when they hear the name. But once they try it, the laughing stops. So the next time you feel yourself running out of gas, reach for UP YOUR GAS.*

The June 1995 edition of “FLEX - THE VOICE OF CHAMPIONS”, a body building publication carried advertisements for at least eight products containing ephedrine. Seven of the advertisements stated that the active ingredient was Ma Huang. The following is a list of the ephedrine-containing products that were advertised in this issue of the publication:

<b>BODY BUILDING PRODUCTS</b>		
<u>Name Of Product</u>	<u>Listed Ingredient</u>	<u>Manufacturer/Distributor</u>
“Dymetadrine 25”	none listed	Nutrition Discounters, Inc.
“Dymetadrine”	none listed	Muscle Express
“Ephedrine”	none listed	Hops Inc.
“Ephedrine HCl”	ephedrine HCl 25mg	National Supplement Warehouse
“Diet Fuel”	Ma Huang	TwinLab, Inc.
“Ripped Fuel Thermogenic Protein Drink	Ma Huang	TwinLab, Inc.
“Ripped Fuel Caps”	Ma Huang	TwinLab, Inc.
“Ripped Fuel Tea”	Ma Huang	TwinLab, Inc.
“Ripped Fast”	Ma Huang	Universal
“Quick Fix”	Ma Huang	Universal
“Cut Up”	Ma Huang	Sports One, Inc.

This publication also carried two articles which discussed ephedrine - the first article was titled “Supplements That Don’t Suck - These are not only cool but effective”. The article then listed “Ma Huang” on “THE ALL PRO LIST” of cool and effective supplements. Many other products are advertised that may contain Ma Huang. The ads for these products have not been included in the information above since they did not mention ephedrine or Ma Huang in the ad or show it as an ingredient on the label of products appearing in the advertisement.

The marketing strategy to encourage athletes to purchase over-the-counter ephedrine-containing products involves claims that they will help clients lose "weight and inches". The advertisements claim that the Ephedra will stimulate "Thermogenesis" in your body and that "Thermogenesis" is "the process of metabolizing brown fats". These products are marketed under the following names: "Thermogenic Enhancer"; "ThermaLoss"; and "Thermo T".

On July 19, 1994, the Board received a State Action Information Letter (94-7) from the Director of Federal-State Relations for the federal Food and Drug Administration - Heinz Wilms. The first news item reported that the state of Florida classified all ephedrine products as prescription drugs as of May 29, 1994. The news item also reported that the President of the Florida Council Against Health Fraud gave a presentation at the annual State Dietetic Association Conference titled "Sports Nutrition - Getting Ripped UP, Not OFF ... Nutrition, Athletes, and Health Fraud". The presenter stated that she had researched advertising of ephedrine-containing products in muscle magazines and concluded that **more ephedrine is sold to sports enthusiasts than any other group, including asthmatics.**

### **Labeling**

Many of the over-the-counter ephedrine-containing products are being aggressively marketed to persons likely to use such products for purposes different from those approved by the federal Food and Drug Administration. The labeling of these products comply with the federal laws and regulations but the brand name, colors, associated graphics, and size of print of pertinent information suggest uses different than those for which they have been approved. The brand name "MiniThins" hardly suggests that the product is to be used for treating wheezing and shortness of breath due to asthma.

One of the over-the-counter ephedrine-containing products sold by the same firm that sells "Mini-Thins" - BDI Pharmaceuticals, a division of Body Dynamics, Inc., bears the brand name "U.S.A. Ephedrine". The label contains a prominent American flag.

Another interesting over-the-counter product containing ephedrine is sold as a Hyper-Thermogenic Fruit Punch under the product name of "RIPPED FORCE". The instructions on the label of this product read as follows:

*DIRECTIONS: Begin drinking RIPPED FORCE 20 minutes before your workout and continue to sip during the workout. Finish drinking 15 minutes before training is completed.*

This product is being sold in gyms for use by body builders when working out. The label indicates under a panel titled "Technical Facts" that the eight ounces of fluid contains 340 mg ephedrine derived from 6% Ma Huang Extract and 1000 mg of caffeine derived from 10% Kola Nut Extract.

On June 7, 1995, the Board of Pharmacy received a 15 g. packet of "Thermogen Herbal Tea" from a sixteen-year-old high school student from Northwestern Ohio. The packet was given to the student by another student to "pep him up". The product is distributed by Life Services Network and was allegedly purchased from a local health food store by another sixteen-year-old student. The label carries the false and misleading statement on the front of the packet:

*This delightful natural Ma Huang herbal tea is a delicious appetite satisfying drink. Chinese use of Ma Huang as a natural food goes back 5000 years.*

The correct information is that under the name of Ma Huang, species of Ephedra have been used as a "medicine" in China for thousands of years. There is nothing to suggest in peer reviewed scientific literature and/or references that this herb has ever been used as a "natural food" in China.

### **Patient Counseling - Over-The-Counter Drugs**

The following excerpts taken from the article appearing in the Oregonian on May 17, 1994 titled "FDA's Prescription May Be Dangerous":

*Most Americans assume that drugs available without a prescription can be used safely without any problem. But the words "safe and effective" are relative terms and in FDA jargon mean the public shouldn't be harmed if they consume the product for the purposes and under the conditions stated on the label and package insert.*

*The FDA apparently believes that consumers read and understand all labeling which certainly isn't the case. In the first place, at least 20 percent of the consuming public are functionally illiterate and couldn't read the instructions and warnings on their best day.*

*Warnings and labeling are also presented in the abstract without emphasis such as "Do not consume alcohol while using this drug." Such a flat and unemotional statement doesn't make the impact it should on the 50 percent of our population who consume beer, wine or other alcoholic beverages.*

*People taking this product need professional advice as it interacts with at least 20 other drugs ....*

*While the creative minds on Madison Avenue develop marketing strategies that will generate increased sales for these [OTC] medications, the government also has a responsibility to make sure the public gets advice from the drug information experts, the pharmacists and physicians who can specifically counsel consumers on their medication use.*

### **Drug Utilization Review And Over-The-Counter Drugs**

Of all the health professions, pharmacy is the only one that is presently using computers to create common databases of drug therapy information for patients and using computers in performing drug utilization review.

While access to these common databases is presently restricted to pharmacies having a common ownership, several of these databases are wide area networks and permit patients to obtain their prescription drugs in any state where the commonly-owned pharmacies are located. Efforts are also presently underway to establish national networks between pharmacies that are owned by many different corporations and individuals.

Unlike other health care professionals, pharmacists have a minimum of five years of education on the actions and indications of drugs, adverse drug reactions, and drug interactions. The community pharmacist is also the most accessible of all the health professionals interfacing directly with patients. This accessibility and face-to-face contact with the patient has also provided pharmacists with the ability to earn the trust of patients.

Pharmacists are also capable of determining the likelihood that a drug product is being misused or abused. The ability and responsibility to make this decision was established by the United States Congress in 1970. The federal Controlled Substance Act imposes a criminal liability on pharmacists when dispensing a prescription for a controlled substance or selling a Schedule V over-the-counter controlled substance for purposes other than legitimate medical use.

Ephedrine is the only drug listed in United States Pharmacopoeia Drug Information (USPDI) tables of adverse reactions for sympathomimetic amines that can be purchased over-the-counter without any restrictions. This drug, however, has one of the highest profiles regarding reported problems in these tables. The only drug that has a higher profile is epinephrine - a drug which is not available in solid oral dosage form.

### **Ma Huang**

Ma Huang (a.k.a. ephedra) is a natural product and is the botanical source of the drug ephedrine. The action of Ma Huang is due to the presence of ephedrine and pseudoephedrine. Ephedrine, obtained from either the natural source (Ma Huang) or manufactured synthetically, has the same pharmacological effects and potential to cause harm. Many products containing Ma Huang do not disclose the fact that they contain the drug ephedrine nor the amount of ephedrine in each dose. Many of these products also do not disclose the possible side effects of ephedrine and the danger of taking ephedrine with other medications or in certain disease conditions.

Many products containing ephedrine are sold under names which indicates that the products provide the consumer with additional energy and pep when their action is actually due to the stimulant action of ephedrine on the central nervous system as well as the cardiovascular system. The labeling of these products often indicate that they are natural dietary supplements.

The federal Food and Drug Administration published an article titled "**Adverse Events with Ephedra and Other Botanical Dietary Supplements**" in the September 1994 Medical Bulletin. The FDA article stated that they have been receiving increasing numbers of adverse events associated with the use of products which include Ma Huang and are marketed as dietary supplements for weight loss, energy, and ergogenic (performance enhancing) and body-building purposes. The article further states that the "*reported reactions vary from the milder adverse effects known to be associated with sympathomimetic stimulants (e.g., nervousness, dizziness, tremors, alterations in blood pressure or heart rate, headache, gastrointestinal distress) to chest pain, myocardial infarction, hepatitis, stroke, seizures, psychosis, and death. These adverse reactions have been reported both in young, otherwise healthy individuals and persons with confounding or complicating conditions such as hypertension. In addition, a stimulant "overdose" syndrome has been reported in children and teenagers who have used these products.*"

The Ohio Board of Dietetics notified the Board of Pharmacy on November 9, 1994 that they supported the reclassification of ephedrine-containing products as Schedule V controlled substances and the emergency rules adopted in August, 1994. The Dietetic Board's support was based on the fact that they had received a number of complaints on weight loss programs using various ephedrine-containing products. The Dietetics Board provided copies of advertisements which implied that ephedrine-containing products enhanced thermogenesis, increased metabolism, and accelerated fat burning with and without caffeine, diet, and exercise.

The Dietetic Board notified the Board of Pharmacy that they were not aware of reports in nutrition literature citing the effectiveness of ephedrine-containing products for weight loss. Adverse reactions reported in complaints and/or interviews with consumers by the Dietetics Board included constipation, abdominal cramping, insomnia, rapid heart beat, anxiety, and elevated blood pressure.

The following are some of the products known to contain ephedrine in either the natural or synthetic form: "Up Your Gas", "Formula One", "Super Diet Pills", "Thermo-Chi", "Green Dragon", "Mini-Thins", "Excel", and "High Energy". "Thermogenic" teas and fruit punches containing Ma Huang are also being marketed in the United States. A "Hyper-thermogenic" fruit punch is being sold to weight lifters in gyms throughout the United States under the name of "RIPPED FORCE".

The January 30, 1995 issue of "The Tan Sheet", a publication of F-D-C Reports, Inc. carried an article on pages 16, 17, and 18 titled "**GNC NAMED IN MA HUANG CLASS ACTION LAWSUIT REQUESTING PRODUCT RECALL**". The article went on to explain that a class action complaint had been filed on January 26, 1995 in the U.S. District Court in Southern Florida on behalf of 30-year-old Charles Nanney of Dade County, Florida. The suit claimed that Mr. Nanney "*suffered a stroke and cerebrovascular disease in 1994 after consuming GNC's Ma Huang*". The lawsuit requested the following actions by the federal court:

1. A permanent injunction requiring General Nutrition Corporation and the supplier of the Ma Huang product, to recall the product and reimburse all persons who purchased the product.

2. A permanent injunction to prevent the sale of "GNC's Ma Huang" until such time as the product is certified to be safe and to require the defendants to establish a fund for medical testing and monitoring of the plaintiff and those similarly situated for conditions caused by exposure to and ingestion of the product.

On April 19, 1995, the Board of Pharmacy received a faxed letter from Varro E. Tyler, Ph.D., Sc.D. in response to a request that he evaluate a document submitted to the Board by a distributor of products containing Ma Huang. The document was titled "**Safety of Chinese Ephedra (Ma Huang)**". Dr. Tyler is a recognized authority on plant drugs (herbs) and their uses and is the author of the text titled "**The Honest Herbal**". The following comments are taken from Dr. Tyler's response to the Board following his evaluation of the document:

*The paper itself makes a number of claims that either are outright erroneous or are worded in such a way that they will be misunderstood by the reader. For example, the statement, "The active ingredients in ephedra are less toxic than the actives in tomatoes and potatoes," is terribly misleading to the nonscientific reader. Apparently, the authors are referring to the glycoalkaloids that are found in certain members of the Solanaceae, but only under specific conditions--e.g., when potato tubers have begun to green and sprout. There is no question that, under normal conditions, ephedra is far more toxic than either tomatoes or potatoes on a weight basis; I personally believe it is reprehensible to make a statement such as the authors have included.*

*To continue, they state, "The chemical similarity of ephedrine does not correlate with the illicit [sic] drug abuse of amphetamines.:" As the authors previously note, ephedrine is almost identical chemically to amphetamine and is now being abused in much the same way that amphetamine was, so why does not the abuse of ephedrine correlate with the abuse of amphetamines? In my opinion and the opinion of other experts in the field, it certainly does correlate.*

*A statement such as, "Obviously, more like chicken soup (also used for bronchial conditions) than amphetamines," is just total nonsense. Anyone who believes that ephedra is more closely related to chicken soup than to chemically similar amphetamines just is unaware of the nature of the constituents and the physiological activities of those constituents that are contained in ephedra.*

*Earlier in the article, the authors indicate their unawareness of any damage done to individuals who have consumed ephedra. That may have been the case when the authors wrote the article in 1993; however, such data is now accumulating because the Food and Drug Administration has decided to collect it, and that administration notes in a recent article [Pharmacy Today, vol. 1, number 8, p. 3, April 15, 1995] during the last year having received more than 100 reports of injuries and adverse reactions related to a single product containing ma huang (ephedra) and*

*caffeine. They note, "Reported reactions range from serious, life-threatening conditions such as irregular heartbeat, heart attack, stroke, seizures, hepatitis, and psychosis to relatively minor and temporary conditions such as dizziness, headache, and gastrointestinal distress. Several deaths have been associated with the product." Obviously, the lack of information or the author's unawareness of it in 1993 has now been replaced in 1995 by substantial statistics indicating that ephedra products containing caffeine should not be consumed, and presumably the same would apply to persons who consume ephedra products and drink caffeinated beverages.*

*Continuing with additional misstatements in the McCausland and Hennen paper, the authors write, "Recently it has been shown that ephedra can cause weight loss." There is no substantial scientific information to support this statement. Ephedra, or its contained ephedrine, is not an anorectic agent. Consequently, in addition to the hazard imposed by the unsupervised use of ephedra, there is an element of fraud involved because the product does not have the claimed activity.*

*In summarizing the paper in question, I believe it is fair to say that it is typical of what I have termed "advocacy literature." It is a diatribe that is directed primarily toward consumers in an effort to urge them to purchase a product or products, rather than presenting a balanced account of the benefits and side effects of a very potent herbal product. I believe that a paragraph in the monograph on ephedra in my book, *The Honest Herbal*, 3rd edition, page 120, more adequately summarizes the situation:*

*"Unfortunately, ephedra and its contained ephedrine also increased both systolic and diastolic blood pressure. They also increased heart rate and may cause palpitations as well as nervousness, headache, insomnia, and dizziness. Although the herb may be a very useful one in the treatment of various asthmatic and congestive conditions, the side effects indicated render its indiscriminate use highly inadvisable, particularly in persons suffering from heart conditions, hypertension, diabetes, or thyroid disease."*

*When I wrote that paragraph, the misuse or abuse of ephedra was at a very low level, and the [sic] I saw no need to restrict the availability of the herb to public. However, the misuse or abuse of the product has increased so rapidly in the last couple of years that I now believe that products containing ephedra should be sold only by professionals who are competent to provide adequate advise to the intended consumer. The products should also be standardized to note the concentration of ephedrine in the recommended dose. Few products meet this criterion. Therefore, it seems to me to be perfectly logical for the State Board of Pharmacy in Ohio to designate ma huang (ephedra) as Schedule 5 Controlled Substance that may be sold only under the supervision of a pharmacist for legitimate medical purposes.*

*McCausland and Hennen note, "Chinese ephedra has 5000 years of recorded use in China (without a warning label and without any reports of death)." If we assume that there was a mechanism for reporting adverse drug effects in the early years in China - an assumption that is probably not valid - this may be the case; however, it is necessary to remind readers of their article that ephedra in China was principally a prescribed drug, not a self-selected one. It was utilized in prescriptions written by physicians and by patients under the care of physicians or other health-care practitioners. Obviously, additional care is needed in this country to prevent both the therapeutic and economic abuse of an herb that can be a very useful drug, if properly employed, and one that can cause serious health problems to the consumer, if it is not properly utilized.*

On May 8, 1995, the Board received a faxed Press Release from the Texas Department of Health titled "*State Wins Settlement of Federal Lawsuit Against Alliance USA*". Alliance USA is the company that sold "Nature's Nutrition Formula One" that was banned by the Texas Department of Health on May 12, 1994. The news release stated further that "*This agreement signals that at least one ephedrine-containing product has been successfully challenged for inappropriate marketing and formulation. TDH has continuing concerns about the safety of all ephedrine-containing products which are sold for uses other than as bronchodilators for asthma sufferers or for decongestion. Our investigation into reports of injuries and some deaths associated with ephedrine use or abuse will continue. And the Texas Board of Health has proposed tightening the rules governing over-the-counter sales of any ephedrine products in this state.*"

The Spring 1995 *Pulse Check* report issued by the United States Office of National Drug Control Policy reported the appearance of ephedrine use in the Dover/Philadelphia area. The publication stated that "While this is the first mention of ephedrine in the Mid-Atlantic area, previous *Pulse Check* reports from Texas and Florida mentioned the appearance of ephedrine in their drug markets." *Pulse Check* is an information gathering tool used by the President's Office of National Drug Control Policy to provide a current subjective look at drug use and availability across the country. The publication summarizes information gathered through the use of quarterly phone conversations with drug-use experts throughout the country. Sources are ethnographers and epidemiologists working in the drug field, drug treatment providers, and law enforcement officials.

The April 1995 Executive Summary issued by the Office of National Drug Control Policy reported in the Chapter titled "The Current Drug Situation" the following:

*Emerging Drug Use Trends: In Florida and Texas, teenagers and college students are reported to be using ephedrine, a chemical precursor of an amphetamine and a component of over-the-counter cold medications. It is often taken as a substitute for amphetamines, and its use could presage an increase in amphetamine use.*

The May 1995 issue of Environmental NUTRITION (Vol. 18 No. 5) included the following information in an article titled "Respect grows for Botanicals, But can you trust the herbs you buy?":

*Just how beneficial are botanicals? Are they safe? Should there be government regulation of plant preparations? EN quizzed some experts who attended a recent conference on botanicals, cosponsored by the Food and Drug Administration and the National Institutes of Health Office of Alternative Medicine.*

***A Blurry Distinction.*** *Make no mistake about it, botanicals, also known as "phyto-medicines," are big business: 1994 sales are estimated at \$1.5 billion, according to the American Herbal Products Association, an industry trade group. A trend toward self-help and preventive medicine has increased the use of botanicals as complements to or substitutes for conventional drug therapy, though they are still regulated as dietary supplements, not drugs, by the FDA.*

*Manufacturers who claim their preparations prevent, alleviate or cure any specific disease, however, automatically become subject to drug regulations, and must pass muster with the FDA, as do all drugs, by submitting research proving safety and effectiveness. Dietary supplements, on the other hand, do not have to prove either. The status of botanicals as dietary supplements, then, leaves the door open for product variability and possible fraud.*

The federal Food and Drug Administration published a notice of proposed rulemaking in the Thursday, July 27, 1995 Federal Register (Vol. 60, No. 144; Pg. 38643). The proposed rule would amend the final monograph for over-the-counter (OTC) bronchodilator drug products to remove the ingredients ephedrine, ephedrine hydrochloride, ephedrine sulfate, and ractephedrine hydrochloride and to classify these ingredients as not generally recognized as safe and effective for OTC use. The notice further stated that this action was being taken by FDA for the following reasons:

- A request from the U.S. Department of Justice, Drug Enforcement Administration (DEA) to restrict OTC availability of ephedrine because of its illicit use as the primary precursor utilized in the synthesis of the controlled substances methamphetamine and methcathinone.
- New information that shows that the misuse and abuse of OTC ephedrine drug products has the potential for causing harm.
- Comments made by FDA's Pulmonary-Allergy Drugs Advisory Committee and the Nonprescription Drugs Advisory Committee on November 14, 1994.

Written comments regarding the FDA proposed rulemaking were to be submitted by September 25, 1995. Comments were submitted by the Board to FDA (Docket No. 95N-0205) with the following summary:

**SUMMARY**

*The Ohio Board of Pharmacy, at its August 1995 Board meeting discussed the proposed rule removing all products containing ephedrine from the over-the-counter market. **The Ohio Board of Pharmacy agrees with FDA's conclusion that the best resolution for the misuse/abuse problem with this drug is for ephedrine, singly or in combination products, not to be available OTC in either its synthetic or natural form.***

*The Board is convinced that the increasing misuse and abuse of all over-the-counter products containing ephedrine can only be solved by removing ephedrine from the over-the-counter market. The widespread and aggressive marketing of products containing ephedrine as a safe and effective stimulant and/or dietary supplement for weight loss for consumption by consumers, especially young people who may suffer injury or death, will continue unless ephedrine is removed from the over-the-counter marketplace.*

In response to a statement that GNC was not aware of any class action suit (see page 13) regarding Ma Huang products, the Board contacted the offices of Robles & Gonzales in Miami, Florida. Discussions with an attorney in the office determined that the lawsuit is ongoing. A copy of the Amended Class Action Complaint and Demand for Jury Trial was received by the Board office on October 2, 1995. The defendants in the Amended Complaint and Demand for Jury Trial are the General Nutrition Corporation and Ultimate Nutrition Products, Inc.

The "General Allegations" portion of the amended complaint reads as follows:

**GENERAL ALLEGATIONS**

18. *At all times material hereto, Defendants were in the business of selling, designing, manufacturing, or distributing, inter alia, nutritional supplements for sale to the general public.*
19. *Sometime prior to November 10, 1994, Defendants designed, manufactured, distributed or sold a product known as "MA HUANG" to the general public or for the purpose of sale to the general public. Defendants knew that the product would be used without inspection for defects.*

20. *In July of 1994, Plaintiff purchased "MA HUANG" from Defendant, GENERAL NUTRITION CORPORATION. Class members similarly situated also purchased or otherwise obtained the product directly from retailers. When purchased and used by Plaintiff and class members the product was, at all times, in its original carton, firmly sealed, and in the same condition that it was in when Defendants manufactured, sold, or delivered it.*
21. *Plaintiff and all Class members similarly situated, used and ingested the product as a nutritional supplement in accordance with the Defendants' directions. Defendants had knowledge of this use of the product and intended to be so used.*
22. *The product contains the dangerous substances ephedrine or ephedra alkaloids.*

The law firm has moved for class certification and is awaiting a decision on this issue by the United States District Court for the Southern District of Florida (CASE NO. 95-0161-CIV-KEHOE).

On September 27, 1995, the federal Food and Drug Administration announced that members of the Food Advisory Committee and other outside experts would meet October 11-12, 1995 to consider the safety of food products, such as dietary supplements and herbal teas, that contain ephedrine alkaloids. The note to correspondents stated the following:

*Over the past few years FDA has received widespread reports of injuries that may be associated with food products with ingredients such as Ma Huang and Chinese ephedra that contain ephedrine, pseudoephedrine, norpseudoephedrine from Ephedra sinica and other related species. The committee will hear FDA and outside presentations on the significance and extent of serious adverse events related to these products. The events include chest pain, myocardial infarction, hepatitis, stroke, seizures, psychosis and death. ....*

On October 11, 1995, the federal Food and Drug Administration announced that the Food Advisory Committee would meet on November 17, 1995 to discuss recommendations on foods, such as some teas and dietary supplements, that contain ephedrine alkaloid. The meeting was to be held at the Holiday Inn, 2460 Eisenhower Ave., Alexandria, VA. The Board of Pharmacy has been informed, however, that the meeting was not held as scheduled and that it is to be rescheduled in the future. More details are available from Catherine DeRoeover of FDA's Center for Food Safety and Applied Nutrition, (202) 205-4251.

On October 12, 1995, the Associated Press reported the following:

*Washington (AP) - The Food and Drug Administration says Americans who take dietary supplements that contain the stimulant ephedrine may put themselves at risk for heart attacks, seizures and other severe problems.*

*Ephedrine by itself is a powerful stimulant and the primary ingredient in certain illegal drugs. But dietary supplements such as the Chinese herb ma huang naturally contain ephedrine also, and are sold with little federal oversight. Proponents claim these supplements boost energy and help weight loss.*

*Prompted by growing concern that these products contain enough ephedrine to cause serious and sometimes fatal heart and nervous system side effects, the FDA is considering more stringently regulating the supplements.*

*More than 330 Americans have suffered side effects from ephedrine-containing products, including 12 deaths, says an FDA report presented Wednesday to the agency's scientific advisers.*

*The Advisory committee on Wednesday began reviewing research into about 100 ephedrine-containing supplements, to help the FDA decide how far to go in regulating them.*

On October 31, 1995, a reporter with the Detroit News called to obtain information about ephedrine and Ma Huang. The reporter stated that he was writing a story regarding "soda drinks" that contained Ma Huang and were being marketed to young kids in the Detroit area. The reporter stated that the name of the products and labels were appealing to young kids. He stated that there were several drinks being sold as "The Drink", "The Black Drink" and "Fuk Ola". The Board was not aware of these products at this time and had not seen any of the products in Ohio.

Nicholas T. Reuter, Consumer Protection Office of the federal Food and Drug Administration, reported at the Annual Meeting of the National Association of State Controlled Substance Authorities in Albuquerque, New Mexico (November 1-4, 1995) the following:

- ◆ *The issue of dietary supplements is one which has been of increasing concern to FDA over the past several years.*
- ◆ *New laws passed by Congress however, limit FDA to their jurisdiction, and basically exclude such product from the definition of food additives. The new laws however require labeling to list the types and quantities of ingredients along with a statement of nutritional support.*
- ◆ *The burden is now on FDA to prove that a product is not safe.*
- ◆ *Currently, over half of all adverse reactions are the result of ephedrine products. On Nov. 14 -17 an advisory group will meet on this subject.*

The November 6, 1995 issue of Newsweek included an article titled "Highs and Lows of Herbal Ecstasy". The author of the article, Susan Miller, reported that "a 16 year old from Atlanta noticed teenagers flocking to a booth which advertised Herbal Ecstasy. The sixteen-year-old related to the reporter the following: "The vendor told us these little blue pills were a safe, all-natural energy source with no side effects and that we needed to take a lot." The vendor recommended that Valerie [a sixteen-year-old who doesn't smoke or drink] and who weighs around 110 pounds, take 10 pills and her friend, 50 pounds heavier, 15. Within 30 minutes, Valerie's heart started pounding wildly and she fainted three times. Her friend became violently ill. Both were rushed to the hospital and had their stomachs pumped. "They told us we almost died," says Valerie. The article further reports that "Herbal Ecstasy--its name purposefully misspelled- is advertised on TV and in magazines like High Times as a safe organic alternative to illicit street drugs. Sold in record stores, nightclubs, and head shops for about \$10 for a package of five, the pills are particularly popular among teenagers and clubgoers looking for a "legal high".

The November 1995 issue of Consumer Reports in its "Memo to Members" on page 693 carried the following description for the report titled "Herbal Roulette":

*"Herbal Roulette" (page 698) exposes a recent change in Federal law that gives companies free rein to sell "dietary supplements" and herbal remedies that could be helpful - or poisonous - with only the mildest of Federal safety and labeling requirements. In this nearly unregulated market, where sellers can push their mysterious potions pretty much at will, buyers must indeed beware.*

On December 30, 1995, two newspapers in northeastern Ohio carried stories about a 26-year-old resident of Massillon, Ohio who suffered a paralyzing stroke after having consumed 11 "diet pills" containing Ma Huang for a period of three and one-half days. The doctor treating the patient was quoted as follows: "There's nothing to this point that would explain why she had a stroke except the herbal medicine,". The articles appeared in Canton, Ohio's newspaper - "The Repository", and Massillon, Ohio's newspaper - "The Independent".

### **RESULTS OF OHIO BOARD OF PHARMACY INQUIRIES REGARDING DEATHS IN OHIO INVOLVING EPHEDRINE/PSEUDOEPHEDRINE**

A total of eighty-seven letters were sent to county coroners in the state of Ohio on September 1, 1995 for information regarding any autopsies where ephedrine or pseudoephedrine were determined to be a factor in the death of the individual. The letter requested information regarding deaths during the time period of January 1, 1993 through the current date, in which the drug(s) ephedrine, pseudoephedrine, or Ma Huang was a factor.

Fifty replies were received by January 6, 1996. Nine deaths were reported by five counties as a result of the survey and are listed in the following table with the results of the toxicology screens that were performed. Lethal levels of ephedrine were reported in three of the cases as the cause of death.

Madison and Union counties reported the same death. Pickaway County, reported a death as a consequence of "cardiac arrhythmia due to massive lethal intoxication with ephedrine" on 10/14/91. Henry County reported that they reviewed their records for calendar year 1995 and that there were no deaths due to ephedrine, pseudoephedrine, or Ma Huang.

Geauga County reported on October 10, 1995 that a review of their records for the period January 1, 1993 to the present reflected the presence of ephedrine in the urine of one individual and that it was **not** a factor in the cause of death (Gunshot wound of head, with perforations of skull and brain).

Mahoning County reported that they have no way of easily obtaining the information requested but that current staff members did not remember any cases related to ephedrine, pseudoephedrine, or Ma Huang. The deputy coroner who replied to the request for information, however, suggested contacting the National Association of Medical Examiners for similar reports and included copies of two issues of "N.A.M.E. NEWS". These newsletters are published by the National Association of Medical Examiners and included information regarding the deaths of infants mentioning ephedrine (33) and pseudoephedrine (15).

The Mahoning County deputy coroner also related that he had seen "several pediatric deaths where ephedrine, pseudoephedrine, or phenylpropanolamine were present, some at "elevated levels", but due to a lack of overall data, it was not always easy or simple to tell the significance of the levels."

Summit County reported that they had "neither the computer facilities nor the personnel to comply with" the request for information.

An additional death due to toxic levels of ephedrine has also been documented by the Board. Neither the county where the death occurred (Fayette) nor the county conducting the autopsy (Franklin) have responded to the survey as of October 23, 1995.

The counties that have not responded as of February 1, 1996 are as follows:

Ashtabula	Coshocton	Harrison	Lucas	Sandusky
Butler	Erie	Holmes	Mercer	Seneca
Carroll	Fayette	Jefferson	Ottawa	Shelby
Champaign	Franklin	Knox	Perry	Tuscarawas
Clark	Gallia	Lake	Pike	Van Wert
Clinton	Greene	Logan	Preble	Wyandot
Columbiana	Hardin			

\* Survey returned by U.S. Postal Service as unable to forward

<u>County</u>	<u>Decedent</u>	<u>Drug</u>	<u>Blood</u> <i>mcg/ml</i>	<u>Urine</u> <i>mcg/ml</i>
Adams	35 yr old white male (06/17/94) cause of death: environmentally-induced hyperthermia	pseudoephedrine	0.37	> 5.0
Fayette	29 yr old male (11/10/94) <b>cause of death: ephedrine poisoning</b>	ephedrine	2.75	NR
Madison/ Union	17 yr old white male (01/07/94) <b>cause of death: toxic levels of ephedrine</b>	ephedrine	4.4	large
Montgomery	38 yr old white male (05/22/93) cause of death: multiple drug intoxication	ephedrine	1.15	13.5
		pseudoephedrine	0.28	8.2
	18 yr old white female (10/26/93) cause of death: suicide (shotgun wound of chest)	ephedrine	>25.0	NR
	23 wks old white male (02/02/94)	ephedrine	NR	3.9
		pseudoephedrine	2.95	109.0
		phenylpropanolamine	0.57	24.2
	cause of death: severe dehydration as consequence of viral illness			
	43 yr old white female (03/02/94) cause of death: hypertensive cardiovascular disease	pseudoephedrine	0.28	36.4
20 yr old white female (06/05/94) cause of death: accident - motor vehicle	ephedrine	1.02	NR	
31 yr old white male (04/25/95) cause of death: accident - motor vehicle	ephedrine	1.00	27.8	
	phenylpropanolamine	0.56	18.2	
Pickaway	39 yr old white male (10/14/91) <b>cause of death: ephedrine intoxication</b>	ephedrine	6.44	positive

*[NR - Not reported]*

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NOTE -- THE BOARD CONTINUES TO RECEIVE INFORMATION REGARDING THIS ISSUE ON A DAILY BASIS AND WILL INCLUDE PERTINENT INFORMATION IN THIS DOCUMENT AS IT IS RECEIVED.

DATE OF THIS REPORT: 03/13/96.