classification of circulatory systems devices to Glenn Rahmoeller. Submission of data relative to tentative classification findings is also invited. Those desiring to make formal presentations should notify Glenn Rahmoeller by August 10, 1979, and submit a brief statement of the general nature of the evidence or arguments they wish to present, the names and addresses of proposed participants, references to any data to be relied on, and also an indication of the approximate time required to make their comments.

Open committee discussion. The Committee will discuss comments which FDA received in response to proposed cardiovascular device classifications and recommend revisions as may be appropriate.

Closed committee deliberations. The Committee will discuss premarket approval applications. This portion of the meeting will be closed to permit discussion of trade secret data (5 U.S.C. 552b(c)(4)).

Each public advisory committee meeting listed above may have as many as four separable portions: (1) An open public hearings, (2) an open committee discussion, (3) a closed presentation of data, and (4) a closed committee deliberation. Every advisory committee meeting shall have an open public hearing portion. Whether or not it also includes any of the other three portions will depend upon the specific meeting involved. The dates and times reserved for the separate portions of each committee meeting are listed above.

The open public hearing portion of each meeting shall be at least 1 hour long unless public participation does not last that long. It is emphasized, however, that the 1 hour time limit for an open public hearing represents a minimum rather thant a maximum time for public participation, and an open public hearing may last for whatever longer period the committee chairman determines will facilitate the committee's work.

Meetings of advisory committees shall be conducted, insofar as is practical, in accordance with the agenda published in this **Federal Register** notice. Changes in the agenda will be announced at the beginning of the open portion of a meeting.

Any interested person who wishes to be assured of the right to make an oral presentation at the open public hearing portion of a meeting shall inform the contact person listed above, either orally or in writing, prior to the meeting. Any person attending the hearing who does not in advance of the meeting request an opportunity to speak will be allowed to make an oral presentation at the hearing's conclusion, if time permits, at the chairman's discretion.

Persons interested in specific agenda items to be discussed in open session may ascertain from the contact person the approximate time of discussion.

A list of committee members and summary minutes of meetings may be obtained from the Public Records and Documents Center (HFC–18), 5600 Fishers Lane, Rockville, MD 20857, between the hours of 9 a.m. and 4 p.m., Monday through Friday. The FDA regulations relating to public advisory committees may be found in 21 CFR Part 14.

The Commissioner, with the concurrence of the Chief Counsel, has determined for the reasons stated that those portions of the advisory committee meetings so designated in this notice shall be closed. The Federal Advisory Committee Act (FACA), as amended by the Government in the Sunshine Act (Pub. L. 94–409), permits such closed advisory committee meetings in certain circumstances. Those portions of a meeting designated as closed, however, shall be closed for the shortest possible time, consistent with the intent of the cited statutes.

The FACA, as amended, provides that a portion of a meeting may be closed where the matter for discussion involves a trade secret; commercial or financial information that is privileged or confidential; information of a personal nature, disclosure of which would be a clearly unwarranted invasion of personal privacy; investigatory files compiled for law enforcement purposes; information the premature disclosure of which would be likely to significantly frustrate implementation of a proposed agency action; and information in certain other instances not generally relevant to FDA matters.

Examples of portions of FDA advisory committee meetings that ordinarily may be closed, where necessary and in accordance with FACA criteria, include the review, discussion, and evaluation of drafts of regulations or guidelines or similar preexisting internal agency documents, but only if their premature disclosure is likely to significantly frustrate implementation of proposed agency action; review of trade secrets and confidential commercial or financial information submitted to the agency; consideration of matters involving investigatory files compiled for law enforcement purposes; and review of matters, such as personnel records or individual patient records, where disclosure would constitute a clearly unwarranted invasion of personal privacy.

Examples of portions of FDA advisory committee meetings that ordinarily shall not be closed include the review, discussion, and evaluation of general preclinical and clinical test protocols and procedures for a class of durgs or devices; consideration of labeling requirements for a class of marketed drugs or devices; review of data and information on specific investigational or marketed drugs and devices that have previously been made public; presentation of any other data or information that is not exempt from public disclosure pursuant to the FACA, as amended; and, notably deliberative sessions to formulate advice and recommendations to the agency on matters that do not independently justify closing.

Dated: July 12, 1979.

Sherwin Gardner,

Acting Commissioner of Food and Drugs.

[FR Doc. 79–22068 Filed 7–16–79; 8:45 am]

BILLING CODE 4110–03–M

Advisory Committees Meetings

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: This notice announces forthcoming meetings of public advisory committees of the Food and Drug Administration (FDA). This notice also sets forth a summary of the procedures governing committee meetings and methods by which interested persons may participate in open public hearings conducted by the committees and is issued under section 10(a) (1) and (2) of the Federal Advisory Committee Act (Pub. L. 92–463, 86 Stat. 770–776 (5 U.S.C. App. I)), and FDA regulations (21 CFR Part 14) relating to advisory committees. The following advisory committee meetings are announced:

Committee name	Date, time, place	Type of meeting and contact person
1. Miscellaneous External Drug Products Panel.	August 3 and 4, 9 a.m., Conference Rm. B, Parklawn Bldg.; 5600 Fishers Lane, Rockville, MD. (August 3), Holiday Inn, Bethesda, MD. (August 4)..	Open public hearing August 3, 9 a.m. to 10 a.m.; open committee discussion August 3, 10 a.m. to 4:30 p.m.; August 4, 9 a.m. to 4:30 p.m.; John T. McElroy (HFD–510), 5600 Fishers Lane, Rockville, MD 20857, 301–443–1430.

General function of the Committee. The Committee reviews and evaluates available data concerning the safety and effectiveness of nonprescription drug products.

Agenda—Open public hearing. Any interested persons may present data, information, or views, orally or in writing, on issues pending before the Committee. Those who desire to make such a presentation should notify the contact person before July 23, 1979, and submit a brief statement of the general nature of the data, information, or views they wish to present, the names and addresses of proposed participants, and an indication of the approximate time desired for their presentation.

Open committee discussion. The Panel will review data submitted in response to the over-the-counter (OTC) review's call for data for this Panel (see also 21 CFR 330.10(a)(2)). The Panel will be reviewing, voting upon, and modifying the content of summary minutes and categorization of ingredients and claims.

Committee name	Date, time, place	Type of meeting and contact person
2. Panel on Review of Allergenic Extracts	August 9, 10, and 11, 2:30 p.m., Rm. 719, 11400 Rockville Pike, Rockville, MD	Open public hearing August 9, 2:30 p.m. to 3:30 p.m.; open committee discussion August 9, 3:30 p.m. to 5:30 p.m. August 10, 8 a.m. to 5:30 p.m., August 11, 8 a.m. to 12:30 p.m.; Clay Sisk (HFB–5), 8800 Rockville Pike, Bethesda, MD 20014, 301–443–5455.

General function of the Committee. The Committee reviews and evaluates available data on the safety and effectiveness of biological products.

Agenda—Open public hearing. Any interested persons may present data, information, or views, orally or in writing, on issues pending before the Committee.

Open committee discussion. The Committee will review the final sections of the Panel report to include epidermal extracts, pollen extracts, insect extracts, alum precipitated allergenic extracts, plant oleoresins, and recommendations on standardization, manufacturing, and future clinical testing of allergenic extracts.

Committee name	Date, time, place	Type of meeting and contact person
3. Oral Cavity Panel	August 14 and 15, 9 a.m., Conference Rm. M, Parklawn Bldg; 5600 Fishers Lane, Rockville, MD.	Open public hearing August 14, 9 a.m. to 10 a.m.; open committee discussion August 14, 10 a.m. to 4:30 p.m.; open public hearing August 15, 9 a.m. to 10 a.m.; open committee discussion August 15, 10 a.m. to 4:30 p.m.; John T. McElroy (HFD–510), 5600 Fishers Lane, Rockville, MD 20857, 301–443–1430.

General function of the Committee. The Committee reviews and evaluates available data concerning the safety and effectiveness of nonprescription drug products.

Agenda—Open public hearing. Any interested persons may present data, information, or views, orally or in writing, on issues pending before the Committee. Those who desire to make such a presentation should notify the contact person before July 31, 1979, and submit a brief statement of the general nature of the data, information, or views they wish to present, the names and addresses of proposed participants, and an indication of the approximate time desired for their presentation.

Open committee discussion. The Panel will review data submitted in response to the over-the-counter (OTC) review's call for data for this Panel (see also 21 CFR 330.10(a)(2)). The Panel will be reviewing, voting upon, and modifying the content of summary minutes and categorization of ingredients and claims.

Committee name	Date, time, place	Type of meeting and contact person
4. Antimicrobial Panel	August 17 and 18, 9 a.m. Conference Rm. K, Parklawn Bldg., 5600 Fishers Lane, Rockville, MD, (August 17); Holiday Inn, Bethesda, MD, (August 18)..	Open public hearing August 17, 9 a.m. to 10 a.m.; open committee discussion August 17, 10 a.m. to 4:30 p.m.; August 18, 9 a.m. to 4:30 p.m.; Lee Geismar (HFD–510), 5600 Fishers Lane, Rockville, MD 20857, 301–443–6057.

General function of the Committee. The Committee reviews and evaluates available data concerning the safety and effectiveness of nonprescription drug products.

Agenda—Open public hearing. Any interested persons may present data, information, or views, orally or in writing, on issues pending before the Committee. Those who desire to make such a presentation should notify the contact person before August 14, 1979, and submit a brief statement of the general nature of the data, information, or views they wish to present, the names and addresses of proposed participants, and an indication of the approximate time desired for their presentation.

Open committee discussion. The Committee will review data submitted in response to the over-the-counter (OTC) review's call for data for this Panel (see also 21 CFR 330.10(a)(2)). The Panel will be reviewing, voting upon, and modifying the content of summary minutes and categorization of ingredients and claims.

Committee name	Date, time, place	Type of meeting and contact person
5. Ad Hoc Subcommittee of the Drug Abuse Advisory Committee to Study the "Effects of Scheduling".	August 24 and 25, 9 a.m., Conference Rm. O, Parklawn Bldg., 5600 Fishers Lane, Rockville, MD. (August 24), Holiday Inn, Chevy Chase, MD. (August 25)..	Open public hearing August 24, 9 a.m. to 10 a.m.; open committee discussion August 24, 10 a.m. to 4:30 p.m.; August 25, 9 a.m. to 4:30 p.m.; Robert C. Nelson (HFD–120), 5600 Fishers Lane, Rockville, MD 20857, 301–443–3800.

General function of the Committee. The Committee advises on the scientific and medical evaluation of information gathered by the Department of Health, Education, and Welfare and the Department of Justice on the safety, efficacy, and abuse potential of drugs and recommends actions to be taken on the marketing, investigation, and control of such drugs.

Agenda—Open public hearing. Any interested persons may present data, information, or views, orally or in writing, on issues pending before the Committee.

Open committee discussion. The subcommittee will prepare its report to the Drug Abuse Advisory Committee on its study of the "effects of scheduling."

Committee name	Date, time, place	Type of meeting and contact person
6. Peripheral and Central Nervous System Drugs Advisory Committee.	August 27 and 28, 9 a.m., Conference Rm. O, Parklawn Bldg., 5600 Fishers Lane, Rockville, MD..	Open public hearing August 27, 9 a.m. to 10 a.m.; open committee discussion August 27, 10 a.m. to 4:30 p.m.; August 28, 9 a.m. to 4:30 p.m.; Robert C. Nelson (HFD-120), 5600 Fishers Lane, Rockville, MD 20857, 301-443-3800.

General function of the Committee. The Committee reviews and evaluate available data on the safety and effectiveness of marketed and investigational prescription drugs for use in the treatment of neurological disease.

Agenda—Open public hearing. Any interested persons may present data, information, or views, orally or in writing, on issues pending before the Committee.

Open committee discussion. The Committee will discuss safety and effectiveness of papaverine, ethaverine, and similar or related drugs; and evaluate safety and effectiveness of aspirin in transient ischemic attacks.

FDA public advisory committee meeting may have as many as four separable portions: (1) An open public hearing, (2) an open committee discussion, (3) a closed presentation of data, and (4) a closed committee deliberation. Every advisory committee meeting shall have an open public hearing portion. Whether or not it also includes any of the other three portions will depend upon the specific meeting involved. There are no closed portions for the meetings announced in this notice. The dates and times reserved for the open portions of each committee meeting are listed above.

The open public hearing portion of each meeting shall be at least 1 hour long unless public participation does not last that long. It is emphasized, however, that the 1 hour time limit for an open public hearing represents a minimum rather than a maximum time for public participation, and an open public hearing may last for whatever longer period the committee chairman determines will facilitate the committee's work.

Meetings of advisory committees shall be conducted, insofar as is practical, in accordance with the agenda published in this **Federal Register** notice. Changes in the agenda will be announced at the beginning of the open portion of a meeting.

Any interested person who wishes to be assured of the right to make an oral presentation at the open public hearing portion of a meeting shall inform the contact person listed above, either orally or in writing, prior to the meeting. Any person attending the hearing who does not in advance of the meeting request an opportunity to speak will be allowed to make an oral presentation at the hearing's conclusion, if time permits, at the chairman's discretion.

Person's interested in specific agenda items to be discussed in open session may ascertain from the contact persons the approximate time of discussion.

A list of committee members and summary minutes of meetings may be obtained from the Public Records and Documents Center (HFC-18), 5600 Fishers Lane, Rockville, MD 20857, between the hours of 9 a.m. and 4 p.m., Monday through Friday. The FDA regulations relating to public advisory committees may be found in 21 CFR Part 14.

Dated: July 12, 1979.

William F. Randolph,

Acting Associate Commissioner for Regulatory Affairs.

[FR Doc. 79-22069 Filed 7-16-79; 8:45 am]

BILLING CODE 4110-03-M

[Docket No. 78M-0115]

Burton, Parsons & Co.; Premarket Approval of Preflex® and Flex-Care™ Solutions

Correction

In FR Doc. 18306, published at page 34643, on Friday, June 15, 1979, in the third column, in the last paragraph, in the second line, "July 1, 1979" should be corrected to read "July 16, 1979".

BILLING CODE 1505-01-M

[Docket No. 76N-0064]

Drug Products Containing Papaverine of Ethaverine and Similar or Related Drugs; Extension of Time for B. F. Ascher & Co.

Correction

In FR Doc. 79-19583 appearing at page 36479 in the issue for June 22, 1979, make the following correction: On page 36482, in the first column, in the first paragraph, in the 4th line, substitute "August 21, 1979" for "August 13, 1979".

BILLING CODE 1505-01-M

[Docket No. 78P-0078]

Newport Research Corp.; Approval of Variance for Laser-Aimed Firearms

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The agency announces that a variance from the performance standard for laser products has been approved for an alignment laser product identified as a laser-aimed firearm. The product is designed to produce a narrow laser light beam that is aligned parallel to the firearm bore and that projects a visible spot of light that serves as a means for improving aiming speed and accuracy. The product is used only for law enforcement and military purposes.

DATES: The variance becomes effective August 16, 1979, and ends August 17, 1984; written objections and supporting data by August 16, 1979.

ADDRESS: Written objections and supporting data may be sent to the Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Glenn E. Conklin, Bureau of Radiological Health (HFX–460), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301–443–3426.

SUPPLEMENTARY INFORMATION: The Newport Research Corp., 18235 Mount Baldy Circle, Fountain Valley, CA 92708, submitted an application for a variance from certain provisions of the laser products performance standard (21 CFR 1040.10 and 1040.11) for its laser-aimed firearms. The variance is approved under § 1010.4 (21 CFR 1010.4), which authorizes the granting of variances for electronic products for which there are performance standards promulgated under section 358 of the Public Health Service Act, as amended by the Radiation Control for Health and Safety Act of 1968 (the act) (42 U.S.C. 263f).

The laser-aimed firearms manufactured by the Newport Research Corp. are regarded as alignment laser products as defined in § 1040.10(b)(35) (21 CFR 1040.10(b)(35)), subject to the special requirements of § 1040.11(b)(1) and (2) (21 CFR 1040.11(b)(1) and (2)). Section 1040.11(b) requires that alignment laser products comply with all of the applicable requirements of § 1040.10 for Class I, Class II, or Class III products. It also requires that alignment laser products shall not permit human access, as defined in § 1040.10(b)(12), to laser radiation in the wavelength range of greater than 400 nanometers with a radiant power that exceeds 5.0×10^{-3} watts for any emission duration greater than 3.8×10^{-4} seconds; in addition, the accessible emission limits of Class I may not be exceeded for alignment laser products which utilize any other combination of emission duration and wavelength range.

Under the terms of this variance, the Newport Research Corp. laser-aimed firearms will deviate from the requirements of § 1040.10 in that the product will not be provided with the performance features of a remote control connector (§ 1040.10(f)(3)), key control (§ 1040.10(f)(4)), emission indicator, (§ 1040.10(f)(5)(ii)), and beam attenuator (§ 1040.10(f)(6)).

The applicant advises that laser-aimed firearms are revolvers, riot shotguns, assault rifles, and submachine guns with a built-in class IIIb Helium-Neon laser and a self-contained, battery-driven, power supply. The laser built into each weapon projects an intense, collimated beam of red light parallel to the longitudinal axis of the weapon bore. The beam is forward of the weapon muzzle and is directed down range toward the intended target by the operator. The applicant advises further that class IIIb levels of accessible radiation ranging from 2 to 5 milliwatts are necessary for the product to perform its intended function—aiming the weapon. The applicant states that the product can be used in situations where operators of the product will find it difficult to see the reflection of the beam from the target—e.g., targets in brightly lit areas, targets of dark color, and targets at long range—and in situations requiring immediate response.

A normally-off, momentary pressure switch connected to the weapon trigger controls the emission of radiation. The sighting laser is turned on by applying a slight pressure to the trigger. The travel of the trigger required to turn the laser on, thereby causing the emission, is much less than that required to fire the weapon. The sighting laser is turned off, thereby terminating the laser radiation emission, by releasing the pressure on the weapon trigger.

The applicant advises that the Newport Research Corp. laser-aimed firearms will be used on a controlled basis by trained military personnel and law enforcement officers in marksmanship training, routine law enforcement and crime prevention, hostage rescue, and riot control. The applicant asserts that the operator will be trained to use laser radiation for sighting purposes only at appropriate times. Laser radiation, when produced, will be directed at intended human or other targets during tactical operations that represent potential or actual life-or-death situations. Laser radiation will also be produced during tactical training that simulates life-or-death situations and during target practice and weapons familiarization programs. In all cases, production of laser radiation emissions will be carried out under the expert judgment and control of trained military personnel and law enforcement officers.

The applicant has requested a variance from the performance requirements for a remote control connector (§ 1040.10(f)(3)), emission indicator (§ 1040.10(f)(5)(ii)), beam attenuator (§ 1040.10(f)(6)), and key control (§ 1040.10(f)(4)) on the general basis that these performance features are not appropriate for lethal firearms used exclusively in military and law enforcement agency applications. Generally, the applicant states that the four features would be inappropriate for the laser-aimed weapon on the basis that incorporation of these features would require installation of additional structures to contain them on weapons that are specifically designed to be lightweight, compact, and streamlined to facilitate fast handling in emergency situations.

Specifically, the applicant states that a remote control connector on a weapon designed to be personally operated and controlled by military and law enforcement personnel is inappropriate. There is no feasible tactical situation in which a remotely operated safety interlock or the remote operation of the sighting laser would be required, or even desirable. The incorporation of a remote control connector, the applicant states, could be hazardous to the operator in life-or-death situations, because it is subject to malfunction or unintentional misuse. A suitable means of radiation protection is provided as a result of the operator's normal rules of conduct. In accordance with an operator's training, when the weapon is employed in life-or-death situations, the operator will direct the laser radiation emission(s) only at intended targets. At all other times the weapon would be aimed at targets for training applications, holstered, as in the case of handguns, or handled with the finger removed from the trigger (laser-off position), as in the case of long guns (i.e., rifles, shotguns, etc.). In addition, operators are familiarized with the safety rule never to point weapons at humans in nontactical situations. Safety rules and procedures are explicitly reinforced in the user information provided with the laser products.

The applicant states that incorporating a visible or audible emission indicator, with emission delay on the laser-aimed weapon, would be potentially hazardous to an operator's life in tactical situations requiring maximum covertness, and also in emergency situations that require

immediate response. Suitable means of radiation protection are provided by the operator's normal training, experience, and rules of conduct that require the operator to control weapons at all times, and not to point them at unintended targets. Another means of radiation protection is provided by the operator's constant awareness of the functional state of the weapon, due to the normally-off, momentary switch that controls the emission of laser radiation. User information furnished with the product instructs the operator immediately to detach the battery pack (energy source) from the weapon should the switch malfunction to prevent the possibility of further emission of laser radiation.

The applicant states that incorporation of a beam attenuator onto the laser-aimed weapon is inappropirate and may be hazardous to an operator in tactical situations. A protruding beam attenuator could become snagged in an operator's clothing, thereby preventing the operator from responding immediately in an emergency. A beam attenuator is subject to malfunction or to unintentional misues. For example, if the beam attenuator were inadvertently left in the beam-blocking position, or if the beam attenuator malfunctioned in such a way as to delay or prevent the operator from disengaging it to the beam-on position, the operator would be unable to react quickly in life-or-death situations. Similarly, if, as a matter of routine, the operator were required to check the status of the beam attenuator before using the weapon, fast action during tactical procedures would be precluded. The applicant further states that there is no possible tactical procedure in which a beam attenuator would serve a useful function. The beam attenuator is intended to give the operator the ability to block the beam while adjustments are made on the laser product or related equipment, during which access to laser radiation is neither required nor desirable. In many laser products, the laser system must remain on during the adjustment procedures, although in other cases the laser system remains on at the discretion of the operator. In these cases, emission of laser radiation is not required for the product function. However, there may be a good reason for not terminating emission, or it may merely be inconvenient to do so. None of the above situations is likely to occur for the laser-aimed weapon because there are no adjustments that must be made during which it is necessary or desirable to sustain laser radiation emission with a beam attenuator engaged in a beam-blocking or attenuating condition. Therefore, because a beam attenuator could serve no useful function, its incorporation onto a laser-aimed weapon is inappropriate. Suitable means of radiation protection are provided by the operator's normal training and experience, and by rules of military and law enforcement agencies that require an operator to control weapons at all times and not to point the weapons at unintended targets. Additionally, the operator is constantly aware of the operational state of the weapon due to the normally-off momentary trigger switch that controls the ability of the weapon to produce laser radiation emission.

The applicant states that the addition of a key control to the laser-aimed weapon could be hazardous because a protruding key could become snagged in the operator's clothing, and prevent the appropriate response in a tactical situation. Also, a protruding key could be inadvertently displaced from or left in the off position, again, frustrating the appropriate response by an operator in a life-threatening situation. Routine checking of the position of the key before using the weapon in tactical situations would inhibit fast handling of the weapons in emerging situations. Keys and key switches are subject to malfunction, breakage, loss, or theft. All of the above factors would diminish reliability and could prevent usage of the laser-aimed weapon in tactical applications. A suitable means of radiation protection is achieved through the laser normally-off momentary switch connected to the weapon trigger. The operator is aware of the inability of the weapon to produce laser radiation without employment of finger pressure on the switch. Another suitable means of radiation protection is provided by the limited access of persons to the laser product because weapon sales or leasing by the applicant are restricted to governmental military and law enforcement agencies, who, in addition, control the access of persons to the arms supply. Thus, the possibility of access to the laser-aimed weapon by unauthorized, unqualified persons is remote.

The Newport Research Corp. application for variance has been reviewed by the Bureau of Radiological Health. The Director of the Bureau believes that the relatively new, commercial, laser-aimed firearms are alignment laser products, that, at the present time, the laser products standards (21 CFR 1040.10 and 1040.11(b)) do not appropriately address. Therefore, the Director has concluded that the laser-aimed firearm is intended for a special purpose and that incorporation of the features objected to by the applicant would inhibit the product from being employed effectively in emergency, life-or-death tactical situations in which immediate response by the operator is required, and under which conditions of malfunction or misue could be potentially hazardous to operators.

A means of radiation protection is provided by restricting sales of the product to military and law enforcement agencies that would limit access to the product. This action would inhibit use of the product by unauthorized an untrained persons. Thus, the use potential of the product is limited to routine and emergency tactical and training applications. In these applications, the potential for requiring the general public to be exposed to laser radiation emission above Class I levels is extremely remote. Another means for radiation protection is the normally-off, momentary switch that controls the emission of laser radiation. Because finger pressure must be kept on the trigger to sustain emission of laser radiation, the likelihood of the laser system being inadvertently turned on, or left in a condition of continuous operation, is eliminated. In the event of malfunction of the normally-off switch, where termination of laser radiation emission does not ensue immediately upon release of the trigger, the operator is instructed to remove the battery pack to terminate emission. Thus, the Director has also concluded that suitable means of radiation protection are provided.

Therefore, the Director of the Bureau of Radiological Health has approved the requested variance from 21 CFR 1040.10(f)(3, (4), (5)(ii), and (6) for the Newport Research Corporation laser-aimed firearms. The applicant will use suitable means of radiation protection as described in the variance application and below in accordance with § 1010.4(a)(2):

1. The sales and leasing of the laser-aimed firearms by the manufacturer or owner are to be restricted to governmental military and law enforcement agencies. The conditions of restricted sales and leasing are to be fully stated along with the user and purchasing information that is required under 21 CFR 1040.10(h).

2. The laser system incorporated into the laser-aimed firearm is to be nonremovable, 21 CFR 1040.10(c)(2).

3. The laser system is to be turned on only by using a normally-off, momentary switch whose actuation is significantly distinct, but not necessarily physically

separate, from the trigger action of the weapon itself to prevent inadvertent firing of the weapon.

The variance is granted for a period of 5 years. In accordance with § 1010.4(d), the applicant is directed to modify the tag, label, or other certification required by § 1010.2 (21 CFR 1010.2) under this variance to state the following: "This product is in conformity with DHEW performance standards for laser products under 21 CFR Part 1040, except with respect to those characteristics authorized by Variance No. 79001, effective August 16, 1979."

The agency has reviewed the potential environmental impact of this variance and has concluded that the action will not significantly affect the quality of the human environment, and that an environmental impact statement is not required. A copy of the environmental impact assessment report is on file in the office of the hearing Clerk, Food and Drug Administration.

Variance No. 79001 becomes effective August 16, 1979, and ends August 17, 1984, unless written objections and supporting data are filed with the Hearing Clerk (HFA–305) on or before August 16, 1979, requesting that the variance be modified or not granted. If objections and supporting data are submitted, the effective date of the variance will be stayed until the Director, Bureau of Radiological Health, rules on them. Under § 1010.4(c)(3) the applicant will be notified of any stay by certified mail, and a notice of the stay will be published in the **Federal Register**. FDA will rule on the objections within 60 days. The ruling will be published in the **Federal Register** and constitutes final agency action subject to judical review under section 358(d) of the Public Health Service Act, as amended by the Radiation Control for Health and Safety Act of 1968 (42 U.S.C. 263f(d)).

The application for this variance and all related correspondence, except information covered by the confidentiality provisions of section 360A(e) of the act (42 U.S.C. 263i(e)), have been placed on public display in the office of the Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857, and may be seen from 9 a.m. to 4 p.m., Monday through Friday.

Dated: July 9, 1979.

William F. Randolph,

Acting Associate Commissioner for Regulatory Affairs.

[FR Doc. 79–21964 Filed 7–16–79; 8:45 am]

BILLING CODE 4110–03–M

[Docket No. 79N–0190; DESI 5378]

Amphetamines: Drugs for Human use; Drug Efficacy Study Implementation; Amendment or Previous Notice and Opportunity for Hearing

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) announces its decision that the indication for the management of exogenous obesity should be removed from the labeling of drug products containing an amphetamine. An opportunity for hearing is offered in the notice.

DATE: Hearing requests due on or before August 16, 1979.

ADDRESSES: Communications forwarded in response to this notice should be identified with the reference number DESI 5378, directed to the attention of the appropriate office named below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

Supplements (identify with NDA number): Division of Neuropharmacological Drug Products (HFD–120), Rm. 10B–04, Bureau of Drugs.

Original abbreviated new drug applications and supplements thereto and notices of claimed investigational exemption for a new drug (identify as such): Division of Generic Drug Monographs (HFD–530), Bureau of Drugs.

Request for Hearing (identify with Docket number appearing in the heading of this notice): Administrative Proceedings Staff—Hearing Clerk Office (HFA–305), Rm. 4–65.

Requests for the report of the National Academy of Sciences-National Research Council: Public Records and Document Center (HFI–35), Rm. 12A–12.

Requests for opinion of the applicability of this notice to a specific product: Division of Drug Labeling Compliance (HFD–310), Bureau of Drugs.

Other communications regarding this notice: Drug Efficacy Study Implementation Project Manager (HFD–501), Bureau of Drugs.

FOR FURTHER INFORMATION CONTACT: Ronald L. Wilson, Bureau of Drugs (HFD–32), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301–443–3650.

SUPPLEMENTARY INFORMATION:

Definition

For the purpose of this notice, the term "amphetamine," the name ordinarily used to designate the racemic form of the drug, is used to cover several drugs or isomers within a class, and the term "dl-amphetamine" is used when reference to the racemate is intended. Unless otherwise stated in the text, the term "amphetamine" includes dextroamphetamine, dl-amphetamine, methamphetamine (which is used in this notice to cover both the dextro-isomer and the racemate), a mixture of dextroamphetamine and dl-amphetamine, and salts of the drugs. The drug products described below, which are the subject of this notice, contain an amphetamine in either the single-entity or combination form.

1. NDA 5–378; Desoxyn Tablets containing 2.5 milligrams or 5 milligrams methamphetamine hydrochloride per tablet, Desoxyn Gradumet Tablets containing 5, 10, or 15 milligrams methamphetamine hydrochloride per tablet, and Desoxyn Elixir containing 20 milligrams methamphetamine hydrochloride per 30 milliliters; Abbott Laboratories, 14th and Sheridan Rd., North Chicago, IL 60064.

2. NDA 5–540; Methedrine Tablets contining 2 milligrams or 5 milligrams methamphetamine hydrochloride per tablet; formerly marketed by Burroughs Wellcome & Co., 3030 Cornwallis Rd., Research Triangle Park, NC 27709.

3. NDA 5–756; Drinalfa Tablets containing 5 milligrams methamphetamine hydrochloride per tablet; E. R. Squibb & Sons, Inc., P.O. Box 400, Princeton, NJ 08544.

4. NDA 5–969; Racemic Desoxyephedrine Hydrochloride Tablets containing 5 milligrams dl-methamphetamine hydrochloride per tablet; High Chemical Co., 1760 N. Howard St., Philadelphia, PA 19122.

5. NDA 6–003; Miller-Drine Tablets containing 10 milligrams dl-methamphetamine hydrochloride per tablet; Smith, Miller & Patch, Inc., 401 Joyce Kilmer Ave., New Brunswick, NJ 08902.

6. NDA 10–093; Biphetamine "7½" Capsules, Biphetamine "12½" Capsules, and Biphetamine "20" Capsules, containing 3.75 milligrams, 6.25 milligrams, and 10 milligrams each of dextroamphetamine and amphetamine per capsule, respectively, all as cation exchange resin complexes of sulfonated

polystyrene; Pennwalt Prescription Products, 755 Jefferson Rd., Rochester, NY 14623.

7. NDA 11–522; Obetrol Tablets containing 2.5 milligrams or 5 milligrams of amphetamine asparate, amphetamine sulfate, dextroamphetamine saccharate, and dextroamphetamine sulfate, per tablet; Obetrol Pharmaceuticals, Division of Rexar Pharmaceutical Corp., 396 Rockaway Ave., Valley Stream, NY 11581.

8. NDA 12–042; Eskatrol Spansules containing 15 milligrams dextroamphetamine sulfate and 7.5 milligrams prochlorperazine maleate per sustained-release capsule; Smith, Kline & French Laboratories, 1500 Spring Garden St., Philadelphia, PA 19101.

9. NDA 17–071; Benzedrine Sulfate Spansule containing 15 milligrams of amphetamine sulfate per capsule; Smith, Kline & French Laboratories.

10. NDA 17–078; Dexedrine Spansules containing 5, 10, and 15 milligrams of dextroamphetamine sulfate per sustained release capsule; Smith, Kline & French Laboratories.

11. ANDA 83–563; Amphetamine Sulfate Tablets containing 5, 10, 15, or 20 milligrams of amphetamine sulfate per tablet; Delco Chemical Co., 7 MacQuesten Pkwy., North, Mt. Vernon, NY 10550.

12. ANDA 83–564; Delcobese Spansules containing 1.25, 2.5, 3.75, or 5 milligrams of amphetamine adipate, amphetamine sulfate, dexroamphetamine adipate, or dextroamphetamine sulfate per sustained release capsule; Delco Chemical Company.

13. ANDA 83–735; Dexampex Tablets containing 5 milligrams or 10 milligrams of dextroamphetamine sulfate; Lemmon Pharmacal Co., Sellersville, PA 18960.

14. ANDA 83–889; Methamphetamine Hydrochloride Tablets containing 10 milligrams of methamphetamine hydrochloride per tablet; Lemmon Pharmacal Co., P.O. Box 30, Sellersville, PA 18960.

15. ANDA 83–900; Benzedrine Tablets, containing 5 milligrams or 10 milligrams amphetamine sulfate; Smith, Kline & French Laboratories.

16. ANDA 83–902; Dexedrine Elixir containing 5 milligrams per 5 milliliters of dextroamphetamine sulfate; Smith, Kline & French Laboratories.

17. ANDA 83–903; Dextroamphetamine Sulfate Tablets containing 5 milligrams or 10 milligrams of dextroamphetamine sulfate per tablet; Lannett Co., 9000 State Rd., Philadelphia, PA 19136.

18. ANDA 83–930; Dextroamphetamine Sulfate Tablets containing 10 milligrams of dextroamphetamine sulfate per tablet; Halsey Drug Co., Inc., 1827 Pacific St., Brooklyn, NY 11233.

19. ANDA 84–001; Ferndex Tablets containing 5 milligrams dextroamphetamine sulfate, Ferndale Laboratories, Inc., 780 W. Eight Mile Rd., Ferndale, MI 48220.

20. ANDA 84–051; Dextroamphetamine Sulfate Tablets containing 5 milligrams or 10 milligrams of dextroamphetamine sulfate per tablet; Rexar Pharmacal Corp., 396 Rockaway Ave., Valley Stream, NY 11582.

21. ANDA 84–125; Dextroamphetamine Sulfate Tablets containing 5 milligrams dextroamphetamine Sulfate; Purepac Pharmaceutical Co., 200 Elmora Ave., Elizabeth, NJ 07207.

22. ANDA 84–931; Methamphetamine Hydrochloride Tablets containing 5 milligrams or 10 milligrams of methamphetamine hydrochloride per table; Rexar Pharmacal Corp.

23. ANDA 84–935; Dexedrine Tablets containing 5 milligrams of dextroamphetamine sulfate per tablet; Smith Kline & French Laboratories.

24. ANDA 84–986; Daro Tablets containing 5 milligrams of dextroamphetamine sulfate per tablet; Vitarine Co., Inc., 227–15 N. Conduit Ave., Springfield Gardens, NY 11413.

25. ANDA 85–212; Dextroamphetamine Sulfate Tablets containing 5 milligrams of dextroamphetamine sulfate per tablet; Stanrabs, Inc., Box 3108, Portland, OR 97208.

26. ANDA 85–370; Dextroamphetamine Sulfate Tablets containing 5 milligrams of dextroamphetamine sulfate per tablet; Cord Laboratories, 2555 W. Midway Blvd., Broomfield, CO 80020.

27. ANDA 85–371; Dextroamphetamine Sulfate Tablets containing 10 milligrams of dextroamphetamine sulfate per tablet; Cord Laboratories.

28. ANDA 85–892; Dextroamphetamine Sulfate Tablets containing 10 milligrams of dextroamphetamine sulfate per tablet; Vitarine Co.

29. ANDA 86–521; Dextroamphetamine Sulfate Tablets containing 5 milligrams of dextroamphetamine sulfate per tablet; M. M. Mast & Co., 4152 Ruple Rd., Cleveland, OH 44121.

30. Dexamyl Spansule Capsules and Tablets containing dextroamphetamine sulfate and amobarbital; Smith Kline & French Laboratories; products are not the subject of an approved NDA.

It is the responsibility of every drug manufacturer or distributor to review this notice to determine whether it covers any drug product that the person manufactures or distributes. Such person may request an opinion of the applicability of this notice to a specific drug product by writing to the Division of Drug Labeling Compliance (address given above).

Background

In a **Federal Register** notice of February 12, 1973 (38 FR 4249), the Food and Drug Administration revised 21 CFR 130.46 (subsequently recodified as 21 CFR 310.504) to announce its findings that single-entity oral anorectic drug products containing amphetamine or dextroamphetamine are effective as short-term adjuncts in the management of obesity. Amphetamine, dextroamphetamine, methamphetamine hydrochloride, and dl-methamphetamine hydrochloride were the subject of a Drug Efficacy Study (DESI) notice published in the **Federal Register** on July 19, 1974 (39 FR 26459). In that notice amphetamine and dextroamphetamine were evaluated as effective for the treatment of narcolepsy and minimal brain dysfunction in children, and all the drugs were determined to be effective as short-term adjuncts in the management of obesity.

In **Federal Register** notices of March 30, 1973 (38 FR 8290), September 35, 1973 (38 FR 26748), and May 23, 1975 (40 FR 22570), FDA withdrew approval of all combination products containing an amphetamine, except for Eskatrol Spansules (NDA 12–042), on the basis of a lack of substantial evidence of effectiveness and a lack of proof of safety. Hearing requests were submitted by Smith Kline & French in response to the **Federal Register** notice of February 12, 1973 (38 FR 4279) for Eskatrol Spansules and their Dexamyl products (related products which are not the subject of an approved NDA0. The hearing request for Eskatrol Spansules is still under review by FDA, while the hearing request for the Dexamyl products is the subject of a court ruling. *Smithkline Corp.* v. *FDA*, 58i7 F.2d 1107 (D.C. Cir. 1978). With respect to Eskatrol and Dexamyl, the action announced in this notice is in addition to the proceedings presently pending before the agency concerning those drugs.

In another notice of February 12, 1973 (38 FR 4249), the Commissioner of Food and Drugs recognized that the use of amphetamines for long periods of time may lead to drug dependence and abuse. Their potential for abuse is related to their action as a central

nervous system stimulant; they can produce intense psychological dependence and severe social dysfunction. When the drugs were approved for use as an adjunct in the management of obesity, they were approved on a benefit/risk basis which took into consideration their potential for abuse. By limiting the use of these drugs to a short period of time and reducing the opportunity for misuse through regulatory action, the Commissioner concluded that they met the safety requirements of the Federal Food, Drug, and Cosmetic Act and were appropriate, on a benefit/risk basis, for the treatment of obesity for a few weeks as an adjunct to a regimen of weight reduction based on caloric restriction. He stated, however, that persistent abuse of these drugs would necessitate taking further steps to restrict their availability and use.

The policy of the Food and Drug Administration regarding the use of amphetamines in the treatment of obesity, as stated in the February 12, 1973 notice (38 FR 4249), was promulgated as a regulation (21 CFR 310.504; formerly codified as 21 CFR 130.46). The regulation provides the marketing conditions for amphetamines and refers to their efficacy review which found limited effectiveness for the drugs in the treatment of obesity. In light of the conclusions in this notice concerning the marketing conditions for amphetamines, a future **Federal Register** notice will propose revocation of this regulation.,

In a **Federal Register** notice of October 14, 1977 (42 FR 55374), the Commissioner stated that legally manufactured and marketed amphetamines are continuing to be abused at a level that constitutes an apparently significant public health problem. He further stated that recent information made available to FDA has revealed that, in spite of the restrictions imposed over the last 5 years, there is evidence for the following conclusions:

1. Among prescription drugs, the anorectic agents are commonly used for nonmedical purposes.

2. Among the anorectic drugs, amphetamines account for more abuse episodes than other drugs in the class and also have the highest rate of abuse of all drugs in the class.

3. There has been no significant decrease in the rate of abuse of amphetamines over the past 3 years. The major reduction in their abuse appears to have occurred between 1970 and 1973 as a result of regulatory actions taken during that time, and little additional change has occurred since then.

4. A significant amount of the amphetamines used for abuse purposes comes from supplies that are legally manufactured, shipped, or prescribed.

5. There is no new evidence to challenge the previous FDA conclusion that amphetamines have no advantage over the nonamphetamine anorectic drugs as an adjunct in the treatment of obesity.

The October 14, 1977 notice also stated that because of this continuing level of abuse of amphetamines, the Commissioner believes that, consistent with his stated intent in the February 12, 1973 notice, further action under the act may be necessary to protect the public health. To provide an open forum for comments on information provided in the notice on the abuse of legally manufactured amphetamines, the Commissioner announced that a public hearing would be held on December 2, 1977. He specifically requested well-documented comment on the merits of the following possible course of action:

1. Remove the anorectic indication from the labeling of amphetamine drug products.

2. Retain the indication of narcolepsy for dextroamphetamine and dl-amphetamine products, and retain the indication of minimal brain dysfunction for dextroamphetamine, dl-amphetamine and methamphetamine products. (A notice published in the **Federal Register** of October 24, 1978 (43 FR 49573) eliminated the term "minimal brain dysfunction" from physician labeling in order to more accurately describe the behavioral syndromes of this indication.)

3. Require patient labeling which would provide certain information on use and warnings concerning the potential for abuse of these drugs.

On November 22, 1977 (42 FR 59917), the agency announced that the administrative record of the public hearing would remain open for 30 days after the December 2, 1977 hearing to permit sufficient time for all interested persons to submit written data, information, or views on the current patterns of medical use and abuse of amphetamines.

Review of Testimony and Written Submissions

Since the public hearing was held, FDA has carefully reviewed the testimony and written submissions (written submissions will hereafter be referred to in the text as comments). Among those who participated in the public hearing or submitted comments were representatives from the Drug Enforcement Administration, National Institute of Drug Abuse, Canadian Ministry of Health, the academic and scientific community, industry groups, health organizations, and consumer groups. A total of 36 persons gave testimony and 31 persons submitted comments. Of the 55 persons who testified or commented on the removal of the anorectic indication from the labeling of amphetamine products, 30 persons supported the action, while 25 persons opposed it. The 14 persons who testified or commented on retaining the indication of narcolepsy and minimal brain dysfunction presented unanimous support for this action. Of the 14 persons who testified or commented on patient labeling for amphetamine products, 12 supported the action, while 2 opposed it. The most substantial testimony and comments have been identified and are briefly discussed below in alphabetical order according to the last name of the person:

1. *Mr. Peter Bensinger, Administrator of the Drug Enforcement Administration (DEA).*—Mr. Bensinger reported that substantial evidence has been presented for many years to FDA and Congressional committees which shows that amphetamines are frequently used for nonmedical purposes by a sizable segment of the population, that such use can result in severe physical and psychological impairment, and that legally manufactured products provide for and sustain such usage. On the diversion of legally manufactured products, he stated that DEA estimates that reported thefts account for roughly one-tenth of the amphetamines actually diverted, the remaining nine-tenths being diverted primarily through promiscuous script writing physicians, forged prescriptions, illegal sales, and dispensing fat clinics. According to Mr. Bensinger, a principal factor in the higher rate of diversion for amphetamines is their ready availability through dispensing physicians. He reported that one physician in New England was responsible for dispensing 2 percent of the annual methamphetamine quota of the United States, or roughly one million dosage units. He added that despite the expenditure of substantial resources to bring action against this physician, the approved indication for short-term obesity treatment provides this physician and many others with considerable latitude to skirt the law.

2. *Dr. David Brillinger, Professor of Statistics, University of California at Berkeley.*—Dr. Brillinger stated that

neither the October 14, 1977 notice nor the IMS America report presents a complete statistical analysis of the time series data since they did not spell out the assumptions of the fitted statistical models on which their conclusions are based. He stated that the conclusions of the report and the notice appear essentially subjective. He concluded that the assumptions and validity of statistical models, confidence intervals, error analysis, and possible component series should be explored in the prediction of DAWN mentions data.

3. *Dr. James Cooper, Director of the Office of Medical and Professional Affairs at the National Institute on Drug Abuse (NIDA).*—Dr. Cooper stated that NIDA believes that the benefits of amphetamines to the individual and the public in the treatment of obesity are outweighed by the public health risks associated with the use of these substances. The data sources available to NIDA show that incidence and prevalence of non medical use of amphetamines remain high. He reported that, despite the prescribing of alternative non amphetamine anorectics, the strict scheduling of amphetamines, and the exercising of restraint by physicians in prescribing amphetamines, data suggest that the incidence and prevalence of non medical use of amphetamines is actually increasing, particularly among the young. Based on an analysis of these data which was summarized in his testimony, Dr. Cooper stated that NIDA supports removing the indication for obesity from amphetamines, and requiring that package labeling warn consumers of the potential harmful effects of amphetamines from continuous long-term use.

4. *Dr. John S. de Cani, Professor and Chairman, Department of Statistics, University of Pennsylvania.*—Dr. de Cani disagreed with FDA's decision to exclude the DAWN data from consistently reporting crisis centers. He also suggested using the amphetamine quota data instead of prescription data to calculate the denominator for the problem index (abuse rate).

Dr. de Cani stated that for all Schedule II anorectic drugs, the average number of monthly DAWN mentions decreased from 1974 through 1976 for each of the four consistently reporting facility groups (crisis centers, emergency rooms, medical examiners, and all facilities). For example, in Table 1 of his testimony, Dr. de Cani observed that the average number of monthly DAWN mentions decreased 20.7 percent from 1974 to 1975 and 5 percent from 1975 to 1976 for emergency rooms; for medical examiners the decreases were 27.6 percent from 1974 to 1975 and 27.3 percent from 1975 to 1976. Dr. de Cani also stated that for all Schedule II anorectic drugs, the number of average monthly DAWN mentions per 1,000 kilograms of amphetamine quota decreased from 1974 through 1976 for each of the four facility groups.

5. *Dr. John D. Griffith, Chief of the Stimulant Unit of the Addiction Research Center (NIDA).*—Dr. Griffith testified that amphetamine abuse is not a harmless practice, but can produce severe adverse effects and dependency on the drug. He stated that dependency often begins with a therapeutic use of the drug, but the use escalates into a chronic, repetitive pattern. This dependency, according to Dr. Griffith, becomes very serious when the chronic use of amphetamines produces insomnia and anxiety, among other symptoms, which gives the person the predisposition to use or abuse barbiturates, alcohol, and minor tranquilizers. He further stated that dependency on amphetamines is as difficult to treat as narcotic addiction. Dr. Griffith also testified that amphetamines are now known to produce a psychosis of a paranoid type which may result from either chronic or acute exposure to amphetamines. A month's prescription for an amphetamine will, according to Dr. Griffith, produce a psychosis in perhaps 80 percent of the patients if the drug is taken improperly. Furthermore, he stated that there is no valid method for identifying or excluding patients who are sensitive to amphetamines as to dependency or psychosis or both. In conclusion, he stated that patients are not only placed at risk when they use amphetamines, but are given a drug that is not much better than placebo for weight loss.

6. *Dr. Lester Grinspoon, Associate Professor of Psychiatry at Harvard University.*—Dr. Grinspoon supports the removal of the anorectic indication from the labeling of amphetamines. He reported that there appear to be few conditions that justify prescribing amphetamines. He questioned the use of amphetamines for weight reduction under any circumstances. He commented that after the 3–4 week euphoric high, which may cause diminished food intake and consequent weight loss, amphetamines are no longer effective as anorectics unless the user increases the dose, thus initiating a pattern of abuse. He commented that amphetamines are useful to a very select group suffering from certain varieties of narcolepsy and a number of truly hyperkinetic children, but should be prescribed only after their potential dangers are carefully weighed against their possible value.

7. *Dr. John Henderson, Director of the Bureau of Drugs and Health Protection Branch of the Canadian Ministry of Health.*—Dr. Henderson stated that legislation passed in Canada on November 1, 1971, essentially restricted the use of amphetamines to the treatment of narcolepsy, hyperkinetic disorders in children, mental retardation, epilepsy, and Parkinsonism. Any physician who needs to prescribe amphetamines for individual patients for conditions outside the approved list must obtain the authorization of the Bureau of Drugs of the Health Protection Branch. Dr. Henderson pointed out that only 36 such requests have been received for the 12-month period preceding November 1977. As there are 38,000 physicians in Canada, he observed that "Canadian physicians are practicing a high standard of medical care with a very low use of the more hazardous members of the amphetamine class of drugs." After Canada passed the legislation in 1971 that virtually ended the use of amphetamines for treating obesity, the importation of amphetamine drugs (amphetamines are not manufactured in Canada) had dropped from 757 kilograms in 1971 to 0.710 kilograms in 1977.

8. *Mr. David Joranson, Drug Abuse Policy Specialist with the Wisconsin Bureau of Alcohol and Other Drug Abuse and Dr. Karl Marquardt, Executive Secretary of the Pharmacy Examining Board of Wisconsin.*—Dr. Marquardt and Mr. Joranson conducted a study in Wisconsin on the abuse problem of a name brand amphetamine which involved a high volume of sales in some pharmacies. At the request of the Controlled Substances Board and Pharmacy Examining Board, they reviewed data that had been compiled and tabulated through the Automation of Reports of Consummated Orders System (ARCOS) of DEA and identified 465 pharmacies that had purchased 800,000 dosage units of this name brand amphetamine in 1975. Among these 465 pharmacies, 10 were identified as the purchasers of the largest quantity of this amphetamine product during 1975. The study then identified 73 physicians who had issued prescriptions for this amphetamine product which were subsequently dispensed by one or more of the 10 pharmacies during 1975. Of the total prescriptions written for this drug product by the 73 physicians, 82.7 percent were written by 8 physicians. One physician had issued 25 percent of

the total prescriptions written by the 73 physicians. Another physician among the 73 had issued 92 percent of his total prescriptions for this amphetamine product. As this name brand amphetamine is only one amphetamine product in Schedule II, Dr. Marquardt and Mr. Joranson pointed out that the problem could be much larger if other amphetamine abuse by overprescribing physicians is considered. They concluded that the problem probably extends to other States, as Wisconsin is ranked 27th in per capita consumption of amphetamines. Mr. Joranson also reported that the Controlled Substances Board supports the three actions outlined in the October 14, 1977 notice.

9. *Dr. Albert Madansky, Professor of Business Administration, University of Chicago.*—For IMS America's data (Figure 8 of the October 14, 1977 notice), Dr. Madansky proposed two different models to predict trends in DAWN mentions. From his first fitted quadratic model, Dr. Madansky predicted that the estimated minimum of the abuse trend occurred in October 1976. From his second logarithmic transformed model, Dr. Madansky predicted that in each year the number of mentions will decrease by 11 percent. He predicted that by the end of 1979, the level of deseasonalized Schedule II mentions from all consistently reporting facilities will drop to 313 per month.

For FDA's data (Figure 9 of the October 14, 1977 notice), Dr. Madansky stated that the statistically significant decreasing trend was found from January 1974 through December 1976 for the observed data (amphetamines mentions with other drugs). He also saw no significant correlation between the prescription sales and Schedule II DAWN mentions for all consistently reporting facilities. He then concluded that the FDA's abuse rate (DAWN mentions/prescriptions) does not provide reliable information about drug abuse.

10. *Dr. John W. Rupel, member of the Wisconsin Medical Examining Board.*—Dr. Rupel explained that the Wisconsin Medical Examining Board is the State governmental agency that licenses and disciplines physicians and defines acceptable standards of professional practice. After an investigation into the dispensing and prescribing of scheduled stimulant drugs by Wisconsin physicians, the Board found that approximately 2 percent of the State's physicians are responsible for prescribing and dispensing the total amount of scheduled anorectic drugs that reached the public through legal channels in 1975. The Board could find no credible scientific evidence that is statistically valid and reliable to show that any of the scheduled anorectic drugs had more than a trivial advantage, at best, over placebo therapy in either the short- or long-term management of obesity. Dr. Rupel reported the investigation revealed that, of all the scheduled anorectic drugs, amphetamines have the most serious and widespread abuse. The findings of the investigation were summarized by Dr. Rupel as follows:

> A tiny fraction of physicians in our State are prescribing and dispensing large amounts of abusable drugs for a condition for which these drugs offer very little, if any, prospect of benefit. The distribution of an abusable substance with no likelihood of significant gain to the patient is a danger to the health, safety, and welfare of the public, and as such constitutes unprofessional conduct.

After reviewing these findings, the Board promulgated an administrative rule that defines as unprofessional conduct the prescribing of an amphetamine for any purpose other than the treatment of narcolepsy, hyperkinesis, drug-induced brain dysfunction, certain refractory forms of depression, or clinical research under appropriate safeguards. Any Wisconsin physician who violates the rule does so at the risk of having his or her license to practice medicine suspended or revoked. In concluding his presentation, Dr. Rupel stated that the Wisconsin experience with amphetamines and the Board's findings clearly support the evidence set out in the October 14, 1977 notice. He urged the removal of the anoretic indication as it would directly assist the efforts to deal with the amphetamine problem at the State level.

11. *Dr. Philip Tannenbaum, Medical Director and Vice-President for Medical Affairs of Smith, Kline and French Laboratories.*—Dr. Tannenbaum said that FDA's use of the problem index or abuse rate (amphetamine DAWN mentions/amphetamine prescription sales) is debatable. He stated that the data bases used to derive this index would overestimate the numerator and underestimate the denominator. For this reason, the relative contribution of DAWN mentions from legitimately produced amphetamines would be overestimated. He suggested that a revised problem index for legitimately produced amphetamines should be used, i.e., DAWN mentions associated with legitimately produced amphetamines/prescription sales + direct physician dispensing + thefts.

Dr. Tannenbaum also disagreed with FDA's decision to exclude from the analysis the following consistently reporting DAWN mentions: all data from crisis centers, all mentions involving jargon terminology, and all mentions for phenmetrazine. He contended that without the above DAWN mentions, the DAWN data (DAWN amphetamine mentions together with other drugs) used in FDA's Figure 9 of the October 14, 1977 notice only accounted for one-fifth of the data included in Figure 8. He also stated that a 27-percent reduction in total DAWN mentions (amphetamine DAWN mentions with other drugs) was still observed between 1974 (1,655 mentions) and 1976 (1,209 mentions) if the data are used from Figure 9 of the October 14, 1977 notice.

12. *Dr. Kennard Yaffe, Chairman of the Committee on Drugs of the Maryland State Medical Society.*—Dr. Yaffe spoke about the promulgation of amphetamine regulations in the State of Maryland when it became apparent to physicians of Maryland that amphetamines were severely abused and that the benefits from their use were very limited. "The benefits," according to Dr. Yaffe, "were thought to be of value in narcolepsy and the hyperkinetic syndrome of childhood, and the greatest abuse was thought to derive from prescribing by physicians of amphetamines for obesity." He briefly described the regulations as allowing amphetamines, except for methamphetamine, to be prescribed for narcolepsy and hyperkinetic syndrome of children, and requiring the conditions to be well documented in the physician's record. For other used, "the physician must ask permission from the Division of Drug Control, setting forth the problem in such detail as to permit a reasoned judgment to be made." Dr. Yaffe stated that this program has produced a sharp decline in the prescribing of amphetamines in Maryland without any problems in the treatment of obesity. He added that the removal of the anorectic indication would assist in reducing the abuse of amphetamines on the State level.

The transcript of the public hearing and a copy of all comments submitted is on file in the office of the Hearing Clerk at the address given above.

Findings of FDA

The testimonies of Drs. de Cani, Madansky, and Tannenbaum, and the comment of Dr. Brillinger were statistical criticisms of FDA's analysis of data provided to FDA from the DAWN system. After a review of their criticisms, the Director of the Bureau of Drugs finds no new information which refutes the conclusions of the October

14, 1977 notice (p. 55375) as revealed by the DAWN data. His response to these statistical criticisms of FDA's analysis of the DAWN and IMS America prescription data is as follows.

1. Dr. Brillinger's comments are valid regarding the assumptions and validity of statistical models, confidence intervals, error analysis, and possible component analysis. However, because of the limited number of data points available for our analysis (36 points), Dr. Brillinger's comments are somewhat more theoretical than practical. In response to Dr. Brillinger's comments, FDA has calculated the estimated slopes, the 95 percent confidence limits of the slopes, and the squared multiple correlation coefficient for several DAWN trend lines, to verify its statistical model. A statistically significant decreasing trend was found between January 1974 and December 1976 for amphetamine DAWN mentions with other drugs. For amphetamine mentions alone, however, no significant decreasing trend was found from January 1974 through December 1976.

2. The results of FDA's analysis of the DAWN data were quite different from Dr. de Cani's findings. For example, DAWN mentions in conjunction with other drugs for all Schedule II anorectics (including phenmetrazine), demonstrated only a 5-percent decrease from 1975 (90 mentions) to 1976 (85 mentions) for the medical examiners, compared to a 27.3-percent decrease cited by Dr. de Cani. The decrease was 1 percent from 1975 (1,334) to 1976 (1,314) for emergency room mentions, compared to a 5-percent decrease cited by Dr. de Cani. As for DAWN mentions alone for all Schedule II anorectic drugs, only a 0.9-percent decrease from 1975 (683 mentions) to 1976 (677 mentions) was found.

The figures cited in Table 2 of Dr. de Cani's testimony paper are also questionable. Because he also did not calculate the correlations between the DAWN mentions and the annual production quota data, his figures of average monthly DAWN mentions per 1,000 kilograms of amphetamine quota are not likely to be reliable.

3. Dr. Madansky failed to explain how satisfactorily his statistical models fit the observed data. He did not demonstrate that his proposed models were better than the linear models used by IMS and FDA for prediction purposes. His long-term extrapolation of the DAWN data to the end of 1979 by the fitted logarithmic model without explaining the appropriate validation procedures of the fitted model is not convincing.

Dr. Madansky evaluated only part of the data presented in the October 14, 1977 notice, namely the DAWN amphetamine mentions in conjunction with other drugs only; the amphetamine DAWN mentions alone were not analyzed. With regard to the correlation of prescription sales and DAWN mentions, his statement is true that there is no significant correlation between 1974 and 1976 for quarterly data. However FDA's reanalysis of the updated data base on monthly prescription sales and DAWN data from January 1974 through June 1978 does show statistically significant correlations.

4. As to Dr. Tannenbaum's comments on FDA's use of the abuse rate, the numerator of the abuse rate used by FDA does not appear to be overestimated. FDA excluded the jargon and crisis center data when calculating this numerator in order to avoid some of the previous criticisms of the DAWN data. Data were excluded from the DAWN crisis centers because of the invalidity of crisis center contacts, the influence of variable case-finding operations, and double counts. Data reported to DAWN in jargon terminology were also excluded because the reliability of the identification was more uncertain than when the report was made in standard medical terminology. In addition, FDA used the DAWN consistently reporting panel of emergency rooms and medical examiners to eliminate much of the instability of the DAWN system. These panels are composed of the facilities that have reported consistently during the time period studied. Thus, FDA's estimated level of abuse used in calculating the abuse rate is not necessarily overestimated as Dr. Tannenbaum indicated.

Dr. Tannenbaum commented that Figure 9 of the October 14, 1977 notice (FDA's data) shows a 27 percent decline in mentions with other drugs between 1974 and 1976. His calculation was based only on DAWN amphetamine mentions with other drugs. When the DAWN amphetamine mentions were examined alone, there was no apparent change between 1974 (604 mentions) and 1976 (621 mentions).

The Director thus finds no new information in the testimony and comments to refute the evidence of the October 14, 1977 notice on the current abuse of amphetamines. He does, however, find additional information which correlates the abuse of amphetamines with legitimate prescribing of the drugs for the treatment of obesity. He finds the testimony of Drs. Marquardt, Rupel, and Yaffe, and Messrs. Bensinger and Joranson especially revealing as to the substantial abuse of amphetamines by high volume prescribers and dispensers of the drug for the treatment of obesity. In addition, the testimonies of Drs. Henderson, Marquardt, and Yaffe demonstrate that when controls are instituted on prescribing amphetamines for this condition, the prescribing of the drugs decreases very sharply without any deprivation or harm to persons who have problems with obesity. Dr. Henderson's testimony further revealed that after legislation was passed in 1971, the overwhelming majority of the physicians in Canada did not request permission to use amphetamines in the treatment of obesity, which undoubtedly indicates that amphetamines are not an essential drug for this condition. Moreover, this information further corroborates the testimony of Drs. Griffith and Grinspoon, who find amphetamines to have limited effectiveness in weight loss.

As to retaining the indication of dl-amphetamine and dextroamphetamine for narcolepsy, and retaining the indication of dl-amphetamine, dextroamphetamine, and methamphetamine for the treatment of children with a behavioral syndrome, the testimony and comments presented on this issue unanimously supported the retention of these indications because of their medical benefit. With regard to their potential for abuse, the Director believes that with the removal of the anorectic indication from the labeling of amphetamine products, these remaining indications will not provide a source of the drugs for abuse. Because at least 80 percent of the legal medical use of these drugs has been for weight reduction, the recommended production quotas for amphetamines will be sharply decreased after the anorectic indication is removed. As this action will substantially reduce the major supply of legally manufactured and dispensed amphetamines, the abuse rate of the drugs will also be reduced as the major source of their diversion will be eliminated. The Director therefore concludes that the continued use of these drugs for narcolepsy and the treatment of children with behavioral syndromes at this time appears to have more medical benefit than risk for abuse.

The October 14, 1977 notice also invited participants to comment on the merits of requiring patient labeling which would provide warnings against using amphetamines for weight reduction (and against using

methamphetamines to treat narcolepsy). Based upon comments received and other available information, the Director concludes that this issue should be deferred until after the action proposed in this notice is implemented. If at that time he determines that legally manufactured amphetamines continue to be abused at an unacceptable level, he will consider patient labeling for amphetamines as an additional measure to curb their abuse. Patient labeling for amphetamines may also be required when the rules have been promulgated under which patient labeling will be required for prescription products in general.

Recent Information

Since the December 2, 1977 hearing, FDA obtained additional DAWN and National Prescription Audit (NPA) data through June 1978 which permitted an updated analysis. Furthermore, FDA was able to obtain data sets from January 1974 through June 1978 on a monthly basis rather than quarterly, thus providing many more individual data points on which to base the statistical analyses. As stated previously in the document, the original analysis of the 1974 through 1976 data excluded the jargon and crisis center data when calculating the numerator of the abuse rate in order to avoid some of the previous criticisms of the DAWN data. It excluded data from the DAWN crisis centers because of the invalidity of crisis center contacts, the influence of variable case-finding operations, and double counts. It also excluded from the first analysis data reported to DAWN in jargon terminology because the reliability of the identification was more uncertain than when the report was made in standard medical terminology. In addition, FDA used the DAWN consistently reporting panel of emergency rooms and medical examiners to eliminate much of the instability of the DAWN system. These panels are composed of the facilities which have reported consistently during the time period studied.

To respond to some of the criticisms of its original analysis, FDA undertook an updated statistical analysis of monthly DAWN mentions and monthly NPA data for the period January 1974 through June 1978 to address several issues raised in these criticisms at the December 2, 1977 public hearing, namely: (1) to determine whether a correlation exists between the monthly DAWN data and the monthly NPA data, (2) to assess the trend over time for both DAWN mentions and NPA data and to fit these data with an appropriate statistical model, (3) to examine the effects of including or excluding jargon groups for amphetamine DAWN mentions alone and amphetamine DAWN mentions with other drugs, and (4) to evaluate the relationship of DAWN mentions for amphetamines versus DAWN mentions for other anorectic drugs and phenmetrazine when adjusted for their relative prescription sales.

FDA's updated statistical analyses generally show a consistent pattern whether data from the jargon group are included or excluded and whether DAWN mentions for amphetamines are used alone or with other drugs. These analyses demonstrate the following:

1. There are observed and predicted downward trends in amphetamine DAWN mentions and amphetamine prescription sales over this period. (See Figures 1 and 2.)

2. There is a significant positive correlation between reported monthly DAWN mentions and the monthly NPA data. As an example of the pattern of this observed correlation, Figure 3 displays a scatter diagram for DAWN mentions for amphetamines alone (jargon excluded) on which the estimated sample correlation is 0.63 ($P<0.01$).

3. Despite observed and predicted downward trends in both monthly DAWN mentions and NPA prescription sales for the period January 1974 through June 1978, the amphetamines have consistently demonstrated over all months statistically significant increases in DAWN mentions compared with other anorectic drugs above what would be expected when these DAWN mentions are adjusted for their relative prescription sales. The procedures for adjusting DAWN mentions by their prescription sales are reasonable because of the existing significant correlations between these two data sets. Figures 4(a) through 4(d) display these relative increases in DAWN mentions associated with amphetamines for four data sets: (a) amphetamines DAWN mentions alone, jargon group excluded, (b) amphetamines DAWN mentions alone, jargon group included, (c) amphetamines DAWN mentions with other drugs, jargon group excluded, and (d) amphetamines DAWN mentions with other drugs, jargon group included.

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Figure 1

The observed and the predicted number of DAWN Mentions from consistently reporting Emergency Rooms and Medical Examiners (Amphetamine alone, without jargon) January 1974 through June 1978 Monthly

Δ = observed DAWN Mentions
x = predicted DAWN Mentions

Fitted Model

$$\hat{y}_{t+4} = 0.22\hat{y}_t + 0.17\hat{y}_{t+1} + 0.33\hat{y}_{t+2} + 0.24\hat{y}_{t+3}$$

(R^2=37.6%, p<0.01)

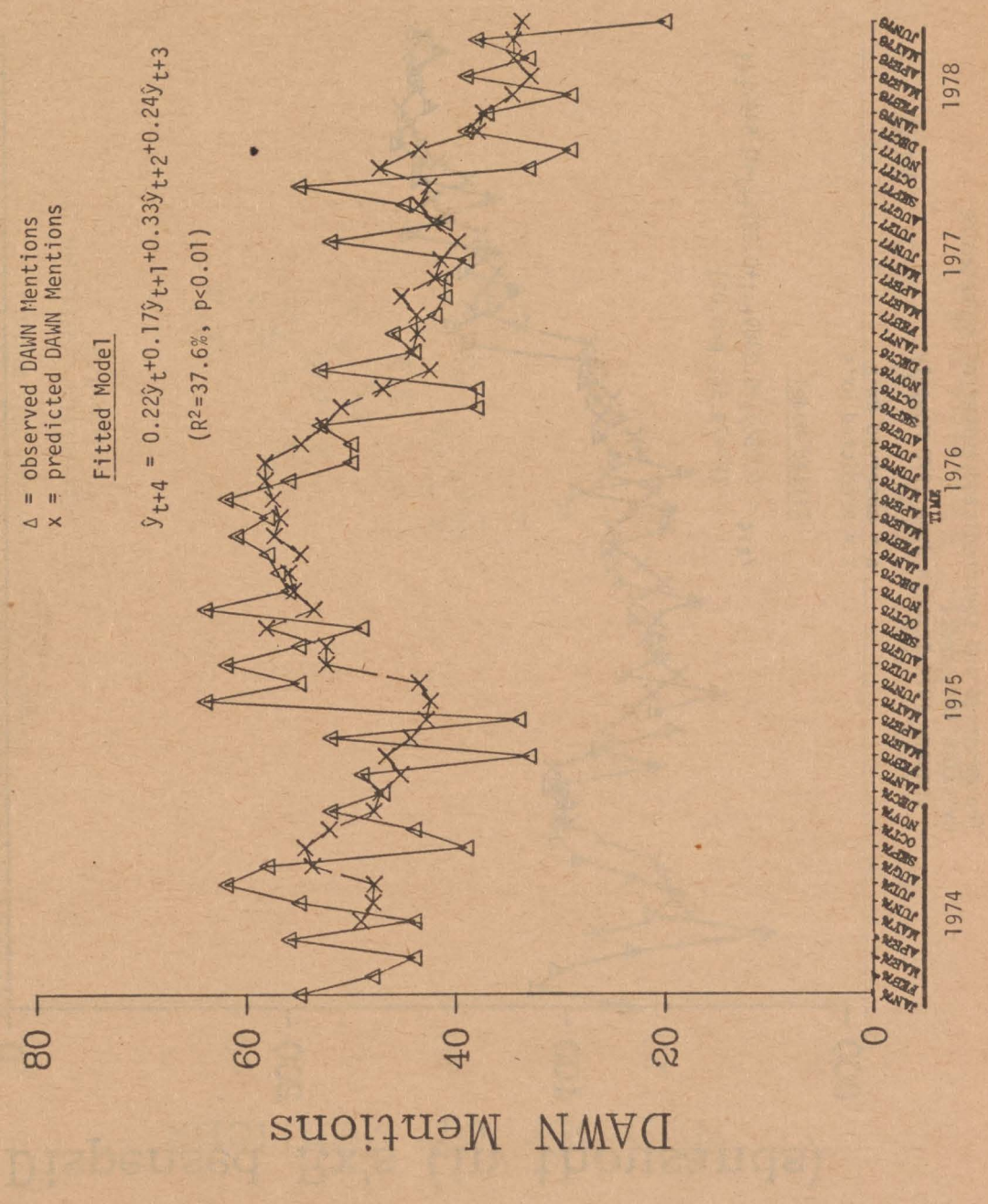


Figure 2

The observed and the predicted number of Amphetamine Rx's (in thousands)
January 1974 through June 1978 Monthly

Δ = observed Rx's
x = predicted Rx's

Fitted Model

$$\hat{y}_{t+4} = 0.086\hat{y}_t + 0.038\hat{y}_{t+1} + 0.32\hat{y}_{t+2} + 0.544\hat{y}_{t+3}$$
$$(R^2 = 74.5\%,\ p < 0.01)$$

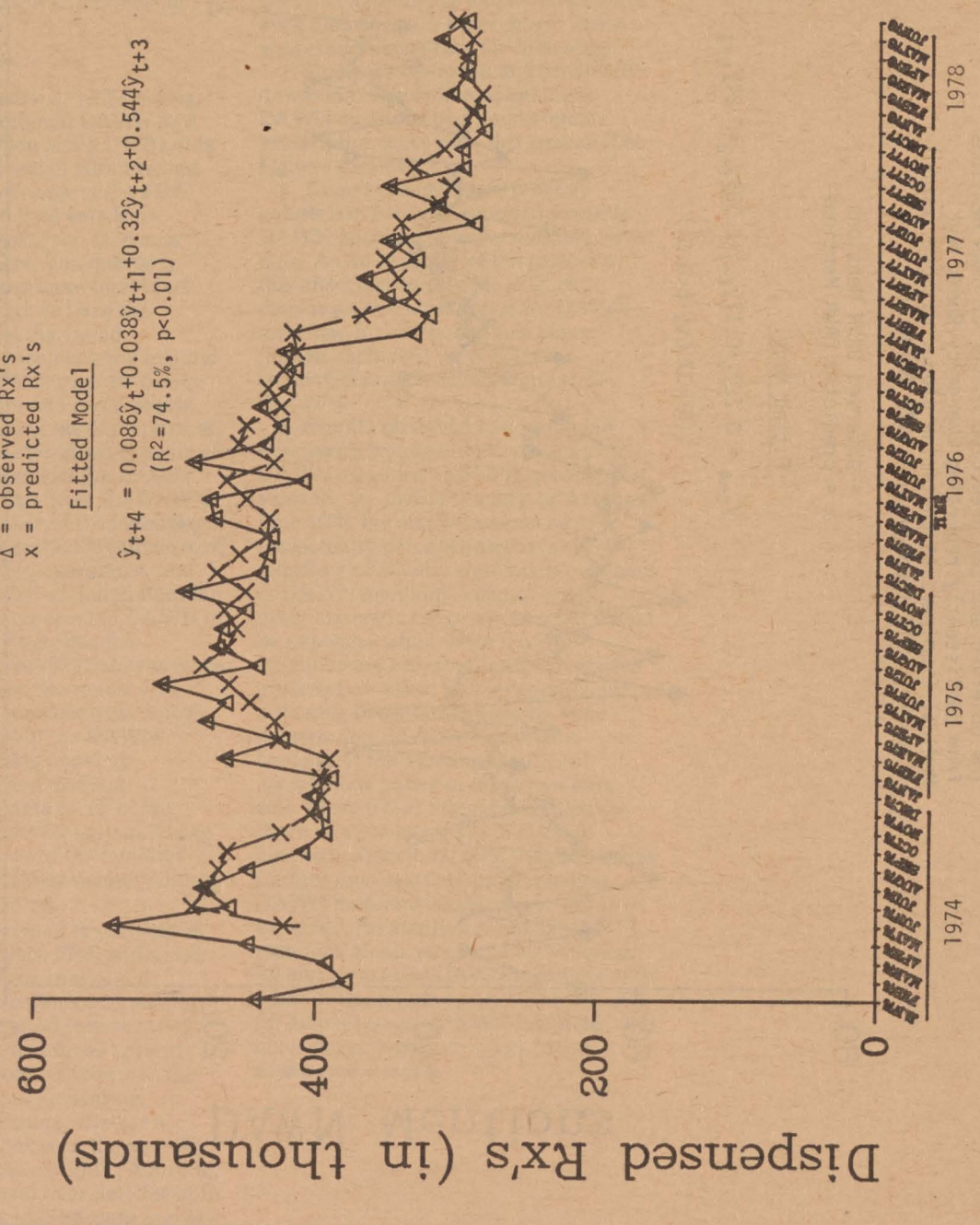


Figure 3

Scatter diagram at time lag 0 (same month) between Amphetamine Rx's (in thousands) and consistently reporting Emergency Rooms and Medical Examiners DAWN Mentions (Amphetamine mentions alone, Jargon excluded)
January 1974 through June 1978 Monthly

Correlation coefficient (r)
= 0.63, p<0.01

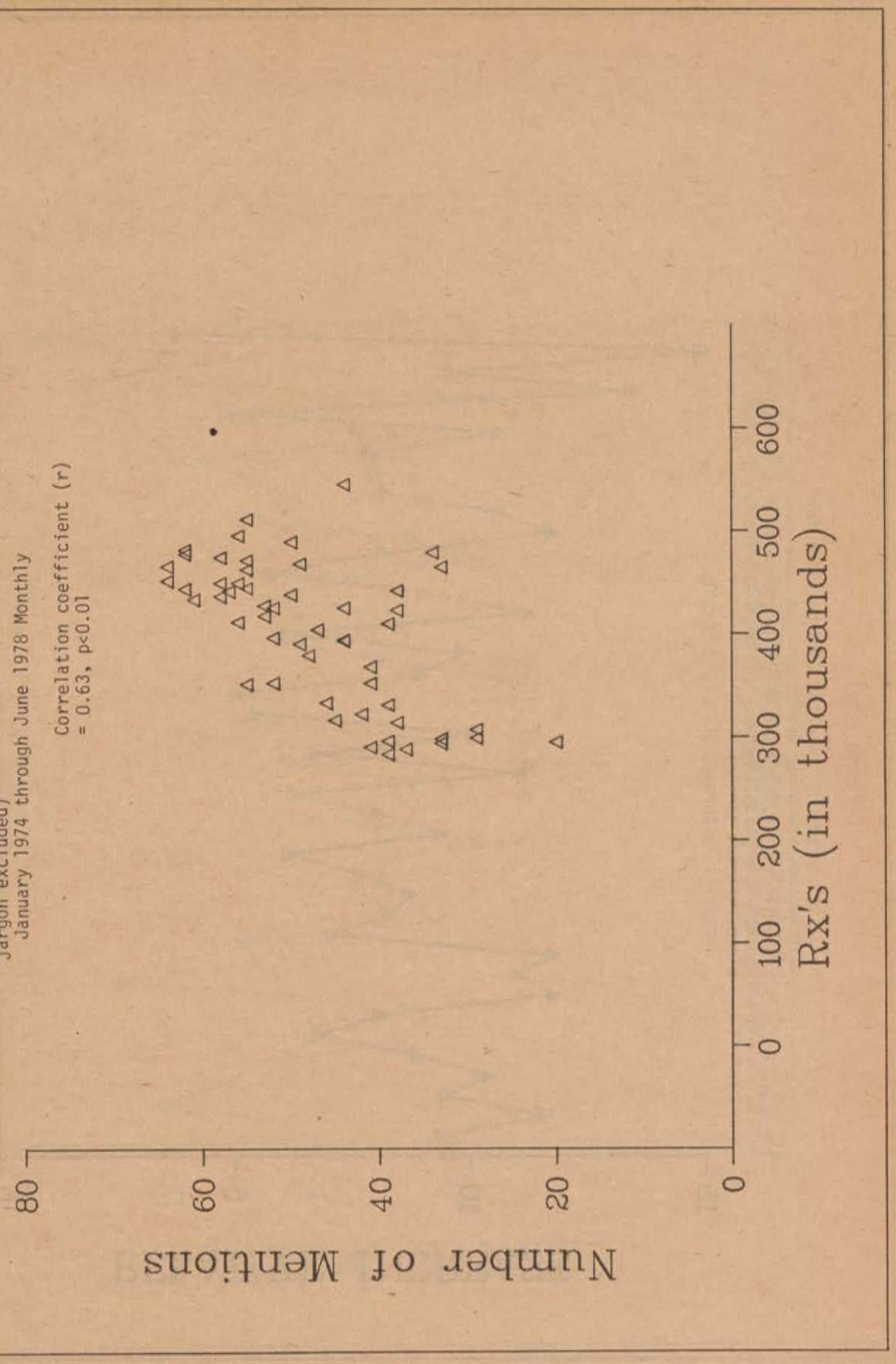


Figure 4(a)

Relative increase of reported DAWN Mentions for Amphetamines vs. other anorectic drugs and phenmetrazine adjusted for relative share of prescription sales (Amphetamines DAWN Mentions alone, without jargon)
January 1975 through June 1978 Monthly

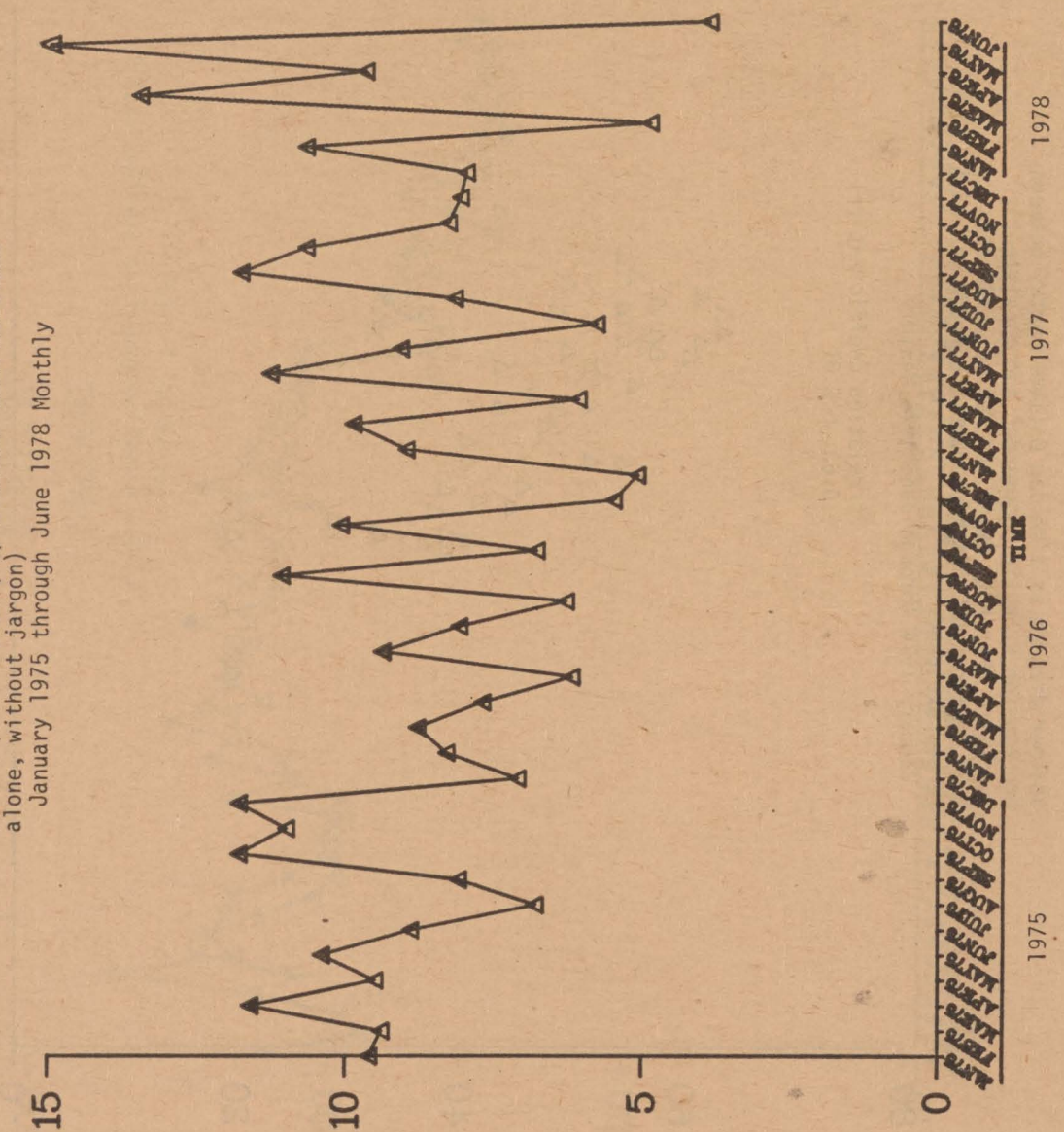


Figure 4(b)

Relative increase of reported DAWN Mentions for Amphetamines vs. other anorectic drugs and phenmetrazine adjusted for relative share of prescription sales (Amphetamines DAWN Mentions alone, with jargon)
January 1975 through June 1978 Monthly

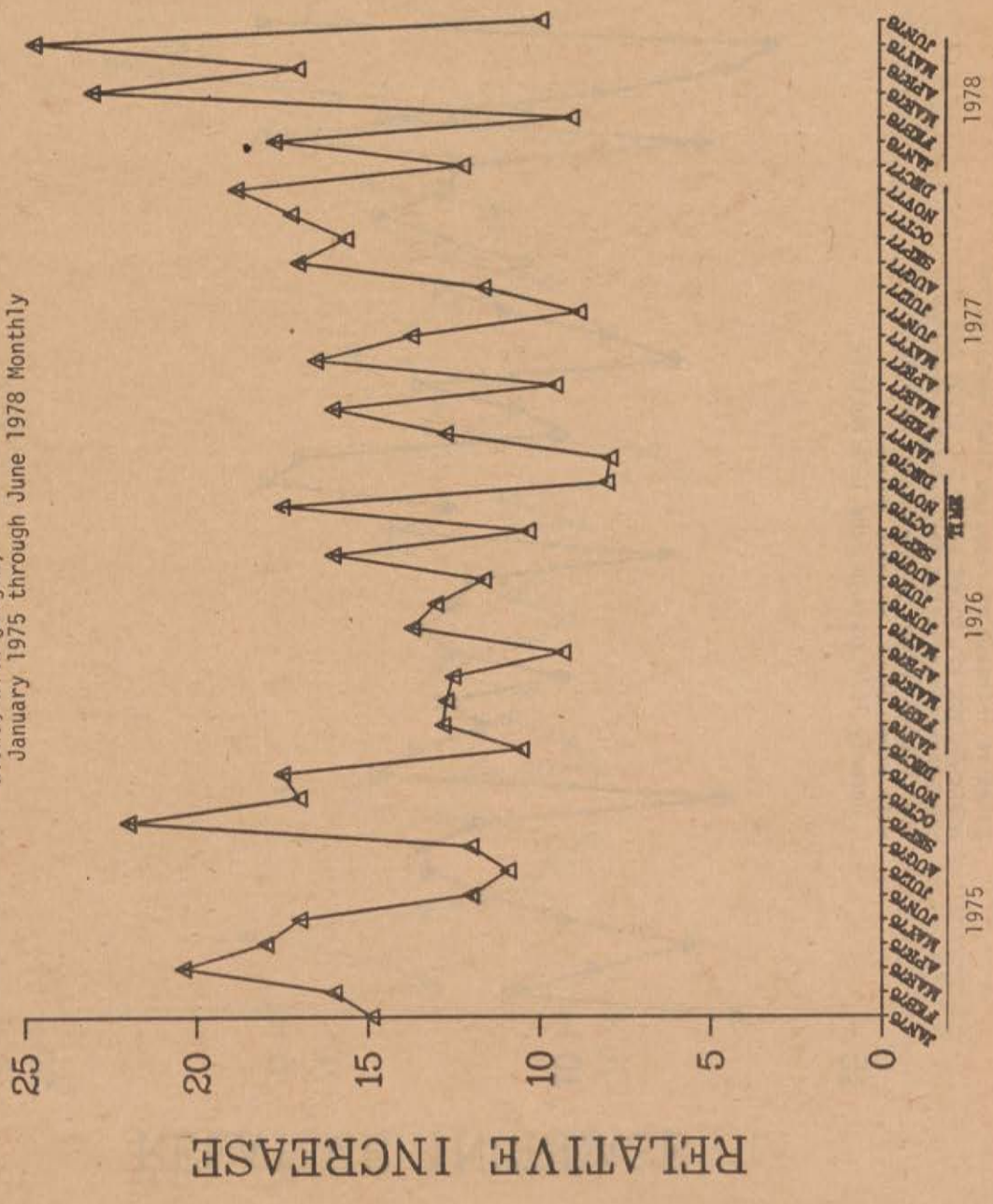


Figure 4(c)

Relative increase of reported DAWN Mentions for Amphetamines vs. other anorectic drugs and phenmetrazine adjusted for relative share of prescription sales (Amphetamines DAWN Mentions with other drugs, without jargon)
January 1975 through June 1978 Monthly

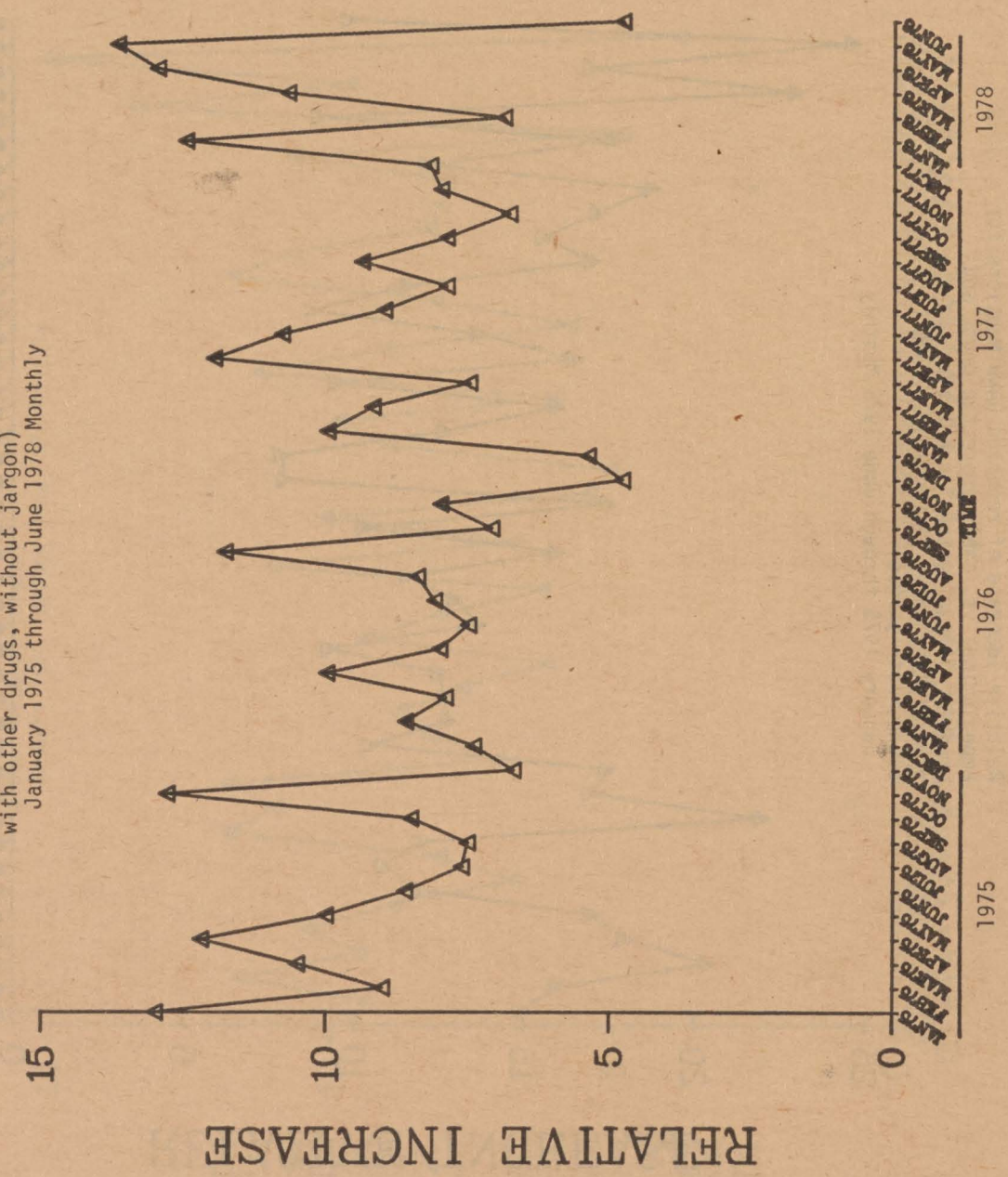
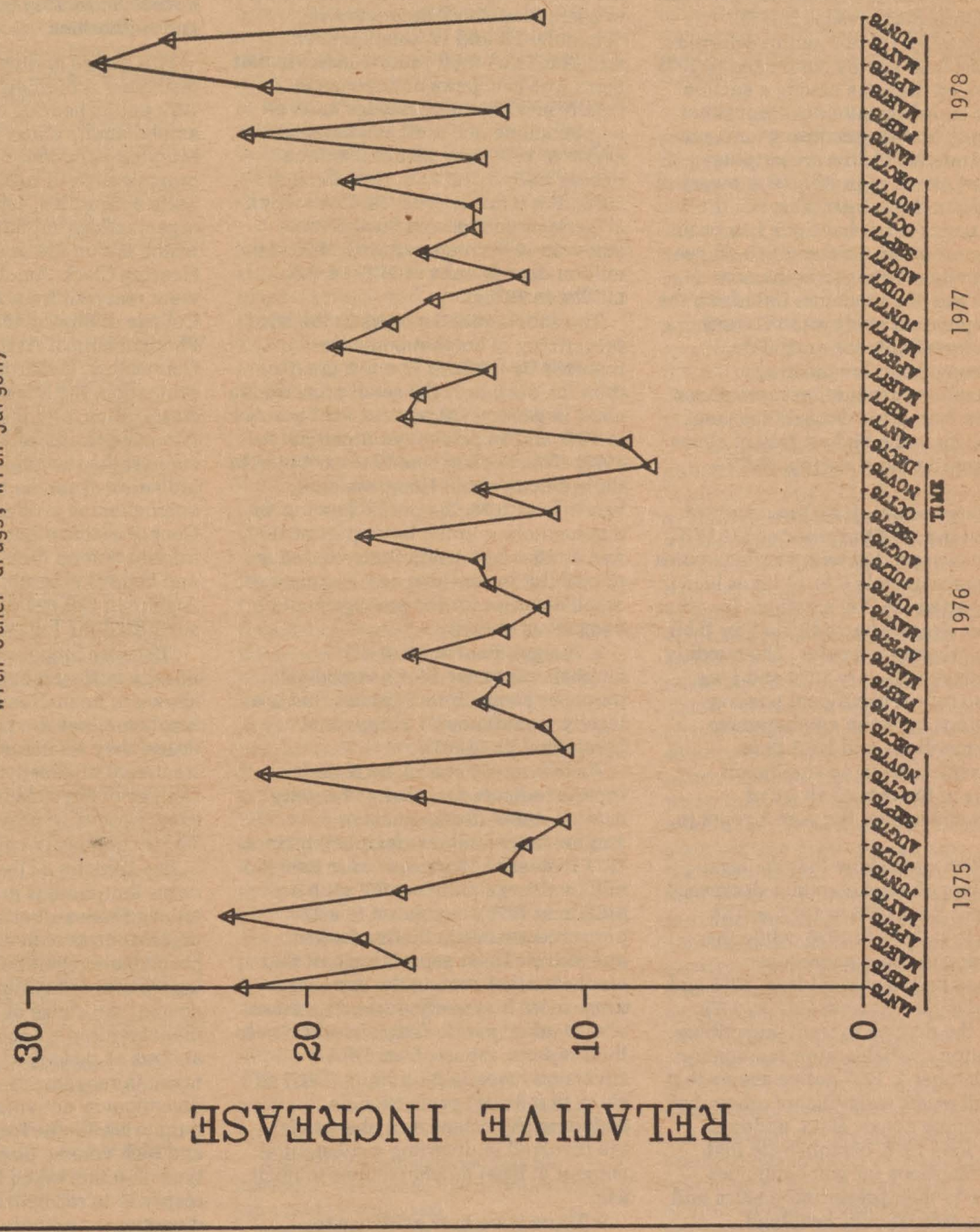


Figure 4(d)

Relative increase of reported DAWN Mentions for Amphetamines vs. other anorectic drugs and phenmetrazine adjusted for relative share of prescription sales (Amphetamines DAWN Mentions with other drugs, with jargon)



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In addition to reanalyzing the DAWN data, FDA has also reviewed information made available since the publication of the October 14, 1977 notice. This information from DEA, NIDA, and the National Clearinghouse for Poison Control Centers demonstrates that there still remains a substantial degree of amphetamine abuse. This recent information is described below as it relates to the conclusions and data described in the October 14, 1977 notice.

1. Among prescription drugs, the anorectic agents are commonly used for non medical purposes (p. 55375).

The October 14, 1977 notice referred to a household survey conducted in 1975 and 1976 on drug use among a sample population in communities throughout the United States. According to recent update from NIDA, the prescription stimulant category is still the category of prescription drugs most abused. The update also shows that there has been an increase in the number of 18–25 year olds who have engaged in the non medical use of stimulants. Data from the rural population study and veterans were not available for an update.

2. Among the anorectic drugs, amphetamines account for more abuse episodes than other drugs in the class and also have the highest rate of abuse of all drugs in the class (pp. 55375–55378).

As stated above, from January 1975 through June 1978 the reported DAWN mentions associated with amphetamines were approximately 8 to 14 times higher than reported DAWN mentions for other anorectic drugs when adjusted for their relative prescription sales. The monthly data between January 1974 and June 1978 also reveal significant positive correlations between amphetamine DAWN mentions and NPA data.

3. There has been no significant decrease in the rate of abuse of amphetamines over the past 3 years (p. 55379).

The NPA data show that the legal prescribing of amphetamines decreased 26 percent from 1976 to 1977 and 14 percent from 1977 to 1978, while the prescribing of other anorectics decreased only 9 percent from 1976 and 1977 and 8 percent from 1977 to 1978. Despite the decline in legal prescribing, information available after publication of the October 4, 1977 notice shows that there still exists a significant amount of amphetamine abuse. Data, updated through June 1978, demonstrate that DAWN mentions for amphetamines correlate to their prescription sales and still have consistently remained proportionately higher than mentions for other anorectics relative to their proportional volume of prescription sales. The conclusion that no significant reduction in the relative occurrence of amphetamine abuse has occurred since January 1974 also continues to be supported by recent data from the National Clearinghouse for Poison Control Centers. These data record the collective experience of the 580 poison centers throughout the United States. For 1977 the data still indicate that Schedule II drug products containing amphetamine continue to be reported more often each year as causing injury to users than do all anorectics in Schedules III and IV combined. In addition, DEA theft reports indicate that there was a 10 percent increase in legally manufactured dosage units of amphetamine and methamphetamine stolen in 1977 over 1976 (5.5 million dosage units in 1977 vs. 5.0 million in 1976). For other anorectics, there was a 27-percent decrease in dosage units stolen in 1977 compared with 1976 (4.0 million dosage units in 1977 vs. 5.5 million in 1976).

The substantial decrease in the legal prescribing of amphetamines as reported by the NPA is much greater than the decline in the retail prescription sales in general (26 percent vs. 3 percent in 1977 and 14 percent vs. 1 percent in 1978). This decline could be attributed to the publicity about Congressional hearings in 1976, the public hearing on amphetamines in the latter part of 1977, and actions by certain States to reduce or prohibit prescribing and dispensing amphetamines for the management of exogenous obesity.

4. A significant amount of amphetamines used for nonmedical purposes comes from supplies that are legally manufactured, shipped, or prescribed (p. 55383).

As previously stated, DEA theft reports indicate that thefts of legally manufactured dosage units of amphetamine and methamphetamine in 1977 increased 10 percent over 1976 (5.5 million dosage units in 1977 vs. 5.0 million in 1976), compared to a 27-percent decrease in thefts of other anorectics. These reports suggest that amphetamines remain the anorectic drugs most frequently desired by those who steal anorectic drugs. In addition to theft reports, reports from DEA's Diversion Investigation Units (DIU) still show that health professionals, including physicians and pharmacists, are involved in diverting a substantial amount of legal amphetamines to illicit use.

5. There is no new evidence to challenge the previous FDA conclusion that amphetamines do not have any advantage over the nonamphetamine anorectic drugs as an adjunct in the treatment of obesity (p. 55384).

No new evidence to refute this conclusion was submitted orally or as comments to the December 2, 1977 public hearing. There is a greater degree of abuse evident for amphetamines than the other anorectics. This is undoubtedly an advantage for the use of nonamphetamine anorectics rather than amphetamines as adjuncts in the treatment of obesity.

Recent Actions by State Organizations and Authorities

This notice earlier described testimony presented at the December 2, 1977 public hearing on the control of amphetamine abuse in the States of Maryland and Wisconsin by the promulgation of regulations. Besides State authorities, several health organizations submitted comments which are on file in the office of the Hearing Clerk. Among them, comments were received from the American College of Physicians, American Pharmaceutical Association, Connecticut Department of Consumer Protection, the Mississippi Medical Association, and the Wisconsin Nurses Association. All of these organizations support the removal of the anorectic indication from the labeling of amphetamine products. The Duval County Medical Society submitted information on their amphetamine abuse and control program, while the American College of Physicians submitted the following statement:

"Because long-term treatment of obesity with amphetamines has been shown to be ineffective and because amphetamines are potentially dangerous drugs, they should not be used in the treatment of obesity. The American College of Physicians supports revocation of approval of amphetamines for use in obesity control."

The Director of the Bureau of Drugs notes that there is an increasing trend among State authorities and organizations of health professionals to promulgate regulations, adopt legislation, or institute programs to combat the abuse of legally manufactured amphetamines. These actions as described below have been taken in response to several types of diversionary activities including burglaries, thefts, forged prescriptions, and high volume dispensers. Often, the type of action taken by the State is in response to recognizing a particular diversionary activity, such as high volume prescribers and dispensers.

With this continuing level of abuse of legally manufactured amphetamines at the State level, these recent actions reflect a grave concern not only of public officials, but also of health professionals including nurses, physicians, and pharmacists. This concern is directly related to the harmful effects of amphetamines upon the individual and society. The Director therefore finds that these actions on the State level demonstrate a long-term, wide spread and growing concern about the abuse of legally manufactured amphetamine products. These actions are described below in chronological order by the date of implementation, including those which were the subject of testimony or comments.

1. The Board of Trustees of the Utah State Medical Association was one of the first organizations of health professionals to take action to combat the abuse of amphetamines. On December 9, 1970, the Board adopted the following resolution:

SINCE, the Utah Society of Internal Medicine has rendered a valuable professional and public service in announcing to the public, by formal resolution, that its member physicians will not prescribe amphetamines or similar drugs in the treatment of obesity because use of such drugs provides no lasting benefit in the treatment of that condition but, instead, frequently results in excessive and harmful use of drugs, and

SINCE, the Utah Society of Internal Medicine has advanced the cause of law enforcement and provided assistance in combating the drug-abuse problem by said resolution in which all pharmacies and law enforcement officials were informed that prescriptions bearing the names of Society members for such drugs should henceforth be considered forgeries, and

SINCE, the Utah State Medical Association concurs with the findings of the Utah Society of Internal Medicine and other medical authorities that the use of amphetamines or similar drugs by drug abusers appears to be related to heroin addiction and to contribute to the drug-connected crime epidemic, and

SINCE, the Utah State Medical Association has the responsibility to encourage its member physicians to forego prescriptions of drugs which have not been demonstrated as beneficial in patient treatment and which are likely to lead to drug abuse and potential addiction, now, therefore, be it

RESOLVED by the Board of Trustees of the Utah State Medical Association that it approves the principle pronounced by the Utah Society of Internal Medicine, and be it further

RESOLVED that Utah State Medical Association physicians be asked to refrain from prescribing amphetamines or similar drugs in the treatment of obesity, and be it further

RESOLVED that the Association send to each of its member physicians a copy of this resolution in such form that any physician may, if he desires, indicate his approval and support of the resolution by affixing his signature thereto and returning the approved resolution to the offices of the Association.

2. Maryland was the first State that acted through legislative action to control the use of amphetamines for the treatment of obesity. In July 1972 the State passed legislation and in August 1973 the State's Board of Medical Examiners promulgated regulations that essentially restricted the use of amphetamines to the treatment of narcolepsy and hyperkinesis. In rare or exceptional cases (i.e. intractable obesity), amphetamines may be used for other purposes. In all such cases, however, the prescribing physician must submit a written justification to the Board. In addition to these restrictions, all prescriptions of amphetamines must contain no more than a 34-day supply.

3. In 1974 the Arizona Board of Medical Examiners enacted a rule which states that the Board found that amphetamines and sympathomimetic drugs have a high potential for abuse. The rule allows the use of amphetamines and sympathomimetic drugs to treat obesity only after all other alternatives have been exhausted, and then for no more than 30 days. It states that any violation of this rule constitutes a danger to the public health and safety, and is considered unprofessional conduct.

4. In late 1976, the Northern Kentucky Pharmacists Association and the Boone County and Campbell-Denton Medical Societies adopted a program to reduce the abuse of legally manufactured amphetamines. Under this voluntary amphetamine control program, physicians agreed to prescribe amphetamines only for narcolepsy, hyperkinesis in children, or neurotic fatigue, and to write the diagnosis or "Phone me if necessary" on the prescription. Only original container amounts are to be specified, and patients are advised to allow the pharmacist 2 to 3 days to order the drug. The program was adopted because people were obtaining amphetamines with prescriptions, either legal or counterfeit, and selling them. Also, there was a large number of burglaries to obtain the drugs.

5. The following resolution was ratified by the Rhode Island Medical Society House of Delegates in May 1977:

WHEREAS amphetamines play no significant therapeutic role in the treatment of intractable obesity, and

WHEREAS amphetamines have a high potential for abuse, and

WHEREAS the drug abuse committee of the Rhode Island Medical Society and the Food and Drug Administration are concerned about the hazards involved in the treatment of intractable obesity by amphetamines, and

WHEREAS the Rhode Island Section of the American College of Obstetrics and Gynecology, and the Rhode Island Chapter of the American Academy of Pedistricians, and the Rhode Island Society of Internal Medicine have taken similar positions

. . . . Therefore be it resolved that the Rhode Island Medical Society be opposed to the use of amphetamines in the treatment of intractable obesity and that this use be limited to specific well recognized medical indications such as narcolepsy, minimal brain dysfunction in children (hyperkinetic behavior disorders) and certain seizure disorders.

6. On July 15, 1977, legislation was passed in New Hampshire on the dispensing of controlled substances. In essence, although a physician may *administer* controlled substances, he or she cannot *dispense* them unless there is a medical emergency. Furthermore, in such an emergency, a Schedule II drug may be dispensed only in 7-day supplies. Although the law is not specifically aimed at amphetamines, the State's experience with high-volume dispensers was an important factor in instituting this law.

7. In response to the December 2, 1977 public hearing, the Duval County Medical Society of Jacksonville, Florida, submitted information on their amphetamine abuse and control program. As described in their submission, physicians and pharmacists in Jacksonville in 1977 instituted a voluntary plan to limit the use of amphetamine, methamphetamine, phenmetrazine, and methaqualone. These substances were removed from pharmacy shelves to eliminate thefts. A 48-hour delay in filling prescriptions allows the pharmacist to verify the prescription and to order from a wholesaler. Prescription sizes are standardized prepackaged amounts so that there are no "leftovers". And finally, the local medical association formally stated to its members that stimulants should not be prescribed for obesity. The immediate result of this effort was an 81-percent reduction in the amount of amphetamines prescribed. The Florida State medical and pharmaceutical associations have endorsed this program and have asked its initiators to expand it State-wide.

8. In May 1977 the Mississippi State Medical Association adopted the following policy on prescribing amphetamines: "Prescribing of amphetamines and other stimulant drugs should be limited to specific, well-

recognized indications. The use of these drugs has no rational basis in the treatment of obesity."

9. The South Carolina Commission on Alcohol and Drug Abuse has convened a task force to investigate the problem of drug abuse in women. Through this task force, which has representatives of the State medical and pharmaceutical associations, the problem of amphetamine abuse was identified. In 1978 the South Carolina Medical Association endorsed the following resolution; it was subsequently endorsed by the South Carolina Pharmaceutical Association:

WHEREAS, the prescribing of amphetamines for weight control has resulted in its abuse in some communities in South Carolina; and

WHEREAS, extended use of this drug in weight control has resulted in what appears to be a medically-sanctioned tolerance and dependency by some patients and has resulted in the added abuse of amphetamines as a street drug; and

WHEREAS, the insomnia and psychomotor agitation resulting from overuse of this drug can lead to the abuse of other drugs, such as sedative-hypnotics, and at times results in acute psychotic episodes: NOW THEREFORE

BE IT RESOLVED that the South Carolina Medical Association go on reocrd as opposing the use of amphetamines for weight control, and, therefore,

BE IT FURTHER RESOLVED, that the South Carolina Medical Association stipulate that prescribing or dispensing these drugs for this purpose is considered unethical and poor medical practice . . . .

A bill based on the Michigan statute regulating amphetamine prescriptions is currently pending before the South Carolina legislature. Although the bill would permit the use of amphetamines to treat obesity, a thorough physical examination and a complete history of the patient would have to be taken, the therapy would be limited to 15 milligrams a day, the maximum prescription size would be 30 days, the maximum duration of therapy would be 90 days, and a diet for weight loss would have to be prescribed along with the amphetamines. In addition, the proposed bill would impose diagnostic conditions that would have to be met prior to prescribing amphetamines for the treatment of hyperactivity and narcolepsy.

10. On August 23, 1978, the Pennsylvania Medical Society adopted a position statement which encourages its members to discontinue the use of amphetamines as an anorexiant because of its deleterious effects. Part of the statement is quoted below which refers to the harm that can be caused by amphetamines even when used on a short-term basis for weight reduction.

Conditions mindful of amphetamines potential for harm assert that in weight reduction the exposure is limited to a relatively short period. Although this may be the intention, it often does not turn out that way. People who have problems controlling their need for constant gratification as indicated by compulsive eating find it hard to put aside a medication that makes them feel good. Many patients consider their attempt to lose weight doomed to failure once they lose this magic potion that protects them from themselves. When the drug is discontinued, a psychologic vacuum is created that must be filled with food. Some patients gain back even more weight then they have lost. So although short-term use of the drug causes a short-term weight loss, it also helps the patient avoid the issue of changing his eating habits. For these reasons we doubt the wisdom of using amphetamines for weight reduction under any circumstances.

11. As described in Dr. Rupel's testimony at the public hearing, the Wisconsin Board of Medical Examiners promulgated final rules on June 1, 1978, that prohibit dispensing and prescribing Schedule II drugs for the treatment of obesity. Amphetamines are permitted only for the treatment of narcolepsy, hyperkinesis, epilepsy, and drug-induced brain dysfunction.

12. The Medical Practice Board of Michigan approved a rule in 1978 which restricted the prescribing of amphetamines. Although amphetamines may still be used to treat obesity, the Michigan rule limits the therapy to a maximum of 15 milligrams a day, a maximum prescription size of 30 days, and a maximum duration of therapy of 90 days. According to the Board, a major factor in adopting the administrative rule was the prescribing of amphetamines for nonmedical purposes, generally occuring under the guise of the treatment of obesity.

13. On January 26, 1979, the Washington State Medical Disciplinary Board adopted rules prohibiting the dispensing or prescribing of any Schedule II stimulant drug for the treatment or control of exogenous obesity. The Board had "recognized that indiscriminate or non-therapeutic prescribing of these drugs was a drug abuse problem in Washington." This action was followed by the enactment of State legislation on May 2, 1979 which made the prescribing of Schedule II stimulant drugs for weight control an illegal act. Violation of this law is a crime punishable by up to two years imprisonment, and fine of up to two thousand dollars. Schedule II stimulants are allowed to be prescribed for the treatment of hyperkinesis, drug-induced brain dysfunction, and certain other indications.

14. On February 14, 1979, the New Jersey State Board of Medical Examiners in the Division of Consumer Affairs of the Department of Law and Public Safety adopted regulations concerning the prescribing, administering, and dispensing of amphetamines and sympathomimetic amines. The rules prohibit the prescribing, ordering, dispensing, administering, selling, or transferring of any amphetamines or sympathomimetic amine drug or compound designated as a Schedule II Controlled Dangerous Substance under New Jersey law, for use in weight management, dieting, or any anorectic purpose, or for the treatment of fatigue. Amphetamines and sympathomimetic amine drugs are permitted for the treatment of narcolepsy, hyperkinesis, and drug-induced brain dysfunction.

Besides the above actions, many states have adopted policies which do not permit reimbursement for prescriptions containing amphetamines for weight loss. A major reason for these policies is the reluctance of the states to use public funds to reimburse prescriptions for a drug whose limited effectiveness in the treatment of obesity is substantially outweighed by its high potential for abuse. Although many states do not allow the drug's reimbursement when prescribed for weight loss, there appears to be no restrictions when amphetamines are used in the treatment of hyperkinesis and narcolepsy.

Benefit Risk Ratio

As Dr. John D. Griffith of NIDA testified at the public hearing, there is a risk associated with the use of amphetamines, directly related to their action as a central nervous system stimulant that can produce toxic reactions, dependency, and social dysfunction. Morever, there is no new evidence that amphetamines have any offsetting advantage over the nonamphetamine anorectic drugs as an adjunct in the treatment of obesity. The anorectic review initiated by FDA in 1972 led to the conclusion that there are no significant differences among the anorectic drugs in their effectiveness in enhancing weight loss over the short term as adjunctive treatment to diet in the management of obesity. Since that time no evidence has been presented to the agency to show that this conclusion was in error. Specifically, no adequate and well-controlled trials are known to the Bureau of Drugs which demonstrate that amphetamines carry an relative

advantage over other anorectic drugs in the management of obesity.

Besides the availability of other anorectic drugs with less risk and equivalent efficacy, the efficacy of amphetamines is limited to a very short period, usually 3 to 4 weeks. Moreover, this exposure often is not limited to 4 weeks according to Dr. Lester Grinspoon of the Harvard Medical School. He testified at the public hearing that "people who have problems controlling there need for constant gratification, as indicated by compulsive eating, find it hard to put aside a medication that makes them feel good [euphoria is a side effect of amphetamines]. What is more, many patients consider their attempts to lose weight doomed to failure once they have lost this magic potion which protects them from themselves. When the drug is discontinued, a psychological vacuum is created which has to be filled with food. On occasion patients have gained back even more weight than they lost, a condition commonly known as rebound phenomenon. So, although short-term use of the drug causes a short-term weight loss, it also helps the patient to avoid the issue of changing his eating habits." In addition, Dr. Grinspoon testified that after the 4-week period amphetamines are no longer effective as anorectics unless the user increases the dose, thus creating a real potential for psychologic dependency and abuse.

From the testimony presented at the public hearing, together with information from the DEA and the NIDA, the Director of the Bureau of Drugs finds that amphetamines are being prescribed and dispensed by certain physicians for weight loss beyond the 4-week period (the physician labeling states a few weeks). Moreover, patients are not only using amphetamines for an extended time for weight loss, but they frequently increase the dosage in an attempt to deal with the diminishing anorexic effect of the drug. The Director therefore finds that the use of amphetamines in the treatment of obesity beyond the conditions of use specified in the physician labeling is exposing patients to the risk of harmful effects through the chronic use of amphetamines. In addition to patients who become involved in a pattern of amphetamine abuse through medical use for the treatment of obesity, other people abuse amphetamines solely for the euphoric and energizing effect.

Besides the damage to society in the form of neglect of family and work, financial irresponsibility, crime, and other antisocial behavior, the Director finds that chronic abuse of amphetamines also produces harmful effects on the health of the user. These harmful effects fall into three major categories: (1) central nervous system effects; (2) habituation, dependence, and addiction; and (3) amphetamine psychosis.

1. *Central Nervous System Effects.* With the development of tolerance to the peripheral adrenergic effects (such as blood pressure response), central nervous system toxic reactions have been reported. These reactions usually involve loss of hypothalmic temperature regulation, with hyperthermia, leading to cardiovascular collapse, convulsions, and death. Convulsions are most often associated with hyperthermia but can also be a complication of high-dose amphetamine use. Status epilepticus, the characteristic seizure pattern, presents a particularly serious threat to the individual. Permanent severe brain damage can result from status epilepticus. Often multiple drug ingestion will potentiate the epileptogenic effect of stimulants, for example, with phencyclidine and lysergic acid. Cerebral vascular complications can be life-threatening and include secondary intracranial hypertension leading to subarachnoid hemorrhage. Stimulant abusers with a history of congenital cerebral aneurysm and arteriovenous malformation are at an added risk of intracerebral hemorrhage. A necrotizing angiitis has been reported in amphetamine abusers. This vascular inflammatory response is especially severe in the cerebral and renal arteries.

2. *Habituation, Dependence, and Addiction.* Scientific literature has shown various degrees of dependence on amphetamines, ranging from mild habituation to strong compulsion and to using the drugs chronically. The more severe cases of dependence show all the characteristics of true addiction. According to Dr. Orina Kalant in "The Amphetamines: Toxicity and Addiction," (Ref. 24) persons who are unable to terminate the continous use of amphetamines have certain features in common. "All of them suffered periodic or chronic states of intoxication, with the usual signs of central nervous system overstimulation and sometimes sympathetic overactivity. Many had anorexia, insomnia, irritability, and erratic behavior. Abuse of other drugs was common, especially barbiturates which were taken to counteract the insomnia. Development of toleance was common, and often marked, and the problems of obtaining the large doses required led in many cases to financial hardship, neglect of family, and antisocial behaviour such as theft and forgery of prescriptions. In addition, physical dependence has been indicated recently by the discovery of certain abnormal electroencephalographic and electro-oculographic patterns during amphetamine withdrawal, which are abolished immediately by restoring the drug" (p. 120). Dr. Lester Grinspoon in "The Speed Culture" states that "the essential 'normality' and general reliability of the initial euphoric effect of amphetamine is what makes the drug so likely to produce dependence" (Ref. 25, p. 173).

3. *Amphetamine Psychosis.* Acute "amphetamine psychosis" is one of the most widely recognized phenomena of psychiatric change associated with amphetamine use. Most often the psychosis is a result of chronic abuse, but even single large doses can produce a toxic hallucinatory paranoid panic state. The amphetamine psychosis was at one time thought to be seen only in "latent" schizophrenics, but this view has been refuted by evidence from many scientific publications. A schizophrenia-like state can be induced in laboratory animals by administration of amphetamine. The most common clinical symptoms of amphetamine psychosis are paranoid delusions and vivid hallucinations of all senses. Occasionally the patient is confused and violently excited. Treatment consists essentially of drug withdrawal, though many patients have received neddless shock and other therapy because of mistaken diagnosis. Unless treatment is directed to the drug abuse rather than to the psychosis, the relapse rate is high.

In most cases of amphetamine psychosis, 1 to 5 years of chronic drug abuse preceded the onset of the psychosis. There is no characteristic mental or emotional picture by which a high risk patient can be identified in advance.

After sub chronic and chronic use and during amphetamine withdrawal, symptoms of depression can be profound. Prolonged sleep and lethargy can lead to severe depression and suicide in some amphetamine users. The psychiatric manifestations of amphetamine abuse are an important cause for hospitalization among adolescents and young adults.

While the hazards from amphetamine abuse are many, little evidence is available to conclude that these risks occur in patients under treatment for narcolepsy or hyperkinesis. Children receiving daily amphetamine for learning disabilities have not shown either growth retardation or a later

tendency to drug abuse. Narcoleptics have been followed for periods of 20 to 30 years on stable daily amphetamine dose schedules. The efficacy of amphetamines in those patients has been supported by well-controlled clinical studies.

References

The following items, as well as statistical analyses of the DAWN data, are on file and available for inspection in the office of the Hearing Clerk, at the address specified at the beginning of this notice.

1. Director, National Institute on Drug Abuse, memorandum to Director, Bureau of Drugs, Food and Drug Administration, March 24, 1977, and attached reports: "Anorectics," 11 pp., and tabulation "Drug Use Among High School Seniors in 1975 and 1976," 2 pp.

2. National Institute on Drug Abuse, "An Investigation of Selected Rural Drug Abuse Programs," DHEW Publication No. (ADM) 77-451, U.S. Government Printing Office, Washington, 1977, 20 pp.

3. Robins, L., "The Relationship of Amphetamine Use to Current Adjustment," unpublished paper, 1977, 13 pp.

4. "National Prescription Audit, Therapeutic Category Report," IMS America, Ambler, PA.

5. Drug Enforcement Administration, U.S. Department of Justice, "Study of Prescription and Drug Abuse Trends of CSA II, III, and IV Amphetamine and Other Anorectic Drugs, January 1, 1974-December 30, 1976," IMS America, Ambler, PA, 1977, 83 pp.

6. Food and Drug Administration data from Poison Control Center reports on anorectics for the years 1972, 1973, 1974, 1975, 4 pp.

7. Administrator, Drug Enforcement Administration, letter to Commissioner of Food and Drugs, December 30, 1976, and attached DEA report, "Amphetamine Diversion," 96 pp.

8. Drug Enforcement Administration, U.S. Department of Justice, "DEA Laboratory Analyses: Schedule II, III, and IV Anorectics," March 16, 1976, 36 pp.

9. Hearings before the Subcommittee on Monopoly of the Select Committee on Small Business, United States Senate, 94th Congress, 2d Session, on Present Status of Competition in the Pharmaceutical industry, U.S. Government Printing Office, Washington, 1977, pp. 14433-15357.

10. Minutes of the Sixth Meeting, Neurologic Drugs Advisory Committee, Food and Drug Administration, Bureau of Drugs, February 3-4, 1977, 24 pp.

11. "National Disease and Therapeutic Index—Drug File," IMS America, Ambler, PA.

12. Drug Enforcement Administration Data on NPA drug list and Project DAWN code numbers, 9 pp.

13. Person, P. H., Jr., "The Drug Abuse Warning Network: A Statistical Perspective," Public Health Reports, 91(5):395-402, 1976.

14. Food and Drug Administration, Notice of Public Hearing, October 14, 1977, Federal Register 42(199) 55374-55386.

15. Administrator, Drug Enforcement Administration, letter to Director, Bureau of Drugs, FDA, July 13, 1978, and 37-page attachment, updating information.

16. Acting Director, National Institute on Drug Abuse, memorandum to Director, Bureau of Drugs, FDA, July 18, 1978, and 11-page attachment, "Update on Amphetamine/Stimulant Data."

17. Acting Director, Division of Poison Control, Bureau of Drugs, memorandum to Director, Bureau of Drugs, FDA, July 24, 1978, and 1-page attachment, "Update on Amphetamine Data."

18. Anthony, J. C., "The Effect of Federal Drug Law on the Incidence of Drug Abuse," *Journal of Health, Politics, Policy, and Law*, Spring 1979.

19. "Basic Neurochemistry," 2d Edition, Edited by Siegel, G. J., R. W. Albers, R. Katzman, and B. W. Agranoff, Little, Brown & Co., Boston, 1976, p. 721-722.

20. "The Pharmacological Basis of Therapeutics," 5th Edition, Edited by Goodman, S., and A. Gilman, MacMillan, New York 1975, p. 496-497.

21. Meyler, L. and A. Herxheimer, "Side Effects of Drugs," Williams and Wilkins, Baltimore, 1968, p. 3-7.

22. "Current Concepts on Amphetamine Abuse," Edited by Ellinwood, E. H., and S. Cohen, N. I. M. H. Rockville, MD, 1972, Chapter 17-19.

23. "Clinical Neurology," Edited by Baker, A. B., and L. H. Baker, Harper and Row, New York, 1976, Vol. 2, Chapter 20, p. 25.

24. "The Amphetamines: Toxicity and Addiction," 2d Edition, Kalant, O. J., University of Toronto Press, Toronto, 1973.

25. Grinspoon, L. and P. Hedblom, "The Speed Culture: Amphetamine Use and Abuse in America," Harvard University Press, Cambridge, 1975.

26. Finney, D. J., "Statistical Logic in the Monitoring of Reactions to Therapeutic Drugs," *Methods of Information in Medicine*, Vol. 10, No. 4, p. 237-245, 1971.

Conclusions

The Director of the Bureau of Drugs concludes that the evidence of continuing misuse and abuse of amphetamines, the severe risk of dependence and harmful effects that they present, and the availability of alternative drugs with less risk create an unfavorable benefit-to-risk ratio in the continued marketing of the drugs for use as an anorectic agent when compared to the limited benefit expected. Therefore the Director proposes to remove the indication for the management of exogenous obesity from the labeling of drug products containing an amphetamine. Accordingly, the July 19, 1974 Federal Register notice is amended to read as follows, insofar as it pertains to single-entity drug products containing amphetamine, dextroamphetamine, methamphetamine hydrochloride, or dl-methamphetamine hydrochloride. A mixture of amphetamine and dextroamphetamine is regarded as a single-entity drug for the purposes of this notice.

Such drugs are regarded as new drugs (21 U.S.C. 321(p)). Supplemental new drug applications are required to revise the labeling in and to update previously approved applications providing for such drugs. An approved new drug application is a requirement for marketing such drug products.

In addition to the products specifically named above, this notice applies to any drug product that is not the subject of an approved new drug application and is identical to a product named above. It may also be applicable, under 21 CFR 310.6, to a similar or related drug product that is not the subject of an approved new drug application. It is the responsibility of every drug manufacturer or distributor to review this notice to determine whether it covers any drug product that the person manufactures or distributes. Such person may request an opinion of the applicability of this notice to a specific drug product by writing to the Division of Drug Labeling Compliance (address given above).

A. *Effectiveness classification.* The Food and Drug Administration has reviewed all available evidence and concludes that single-entity drug products containing amphetamine or dextroamphetamine, or a salt thereof, or methamphetamine hydrochloride, or dl-methamphetamine hydrochloride are:

1. Effective for the indications in the labeling conditions below.

2. Effective but lack evidence of safety for use as a short-term adjunct in the management of obesity.

(For purposes of this notice a mixture of amphetamine and dextroamphetamine is regarded as a single-entity drug product):

B. *Conditions for approval and marketing.* The Food and Drug Administration is prepared to approve abbreviated new drug applications and supplements to previously approved new drug applications under the conditions described herein:

1. *Form of drug.* The drug is in capsule, tablet, or liquid form suitable for oral administration. It may be in controlled-release form.

2. *Labeling conditions.* a. The label bears the statement, "Caution: Federal law prohibits dispensing without prescription."

b. The drug is labeled to comply with all requirements of the act and regulations, and the labeling bears adequate information for safe and effective use of the drug. The Indications are as follows:

dl-amphetamine, dextroamphetamine, and methamphetamine are indicated as an integral part of a total treatment program which may include other remedial measures (psychological, educational, social) for a stablizing effect in children with a behavioral syndrome characterized by the following group of developmentally inappropriate symptoms: moderate to severe distractability, short attention span, hyperactivity, emotional lability, and impulsivity. The diagnosis of the syndrome should not be made with finality when these symptoms are only of comparatively recent origin. Nonlocalizing (soft) neurological signs, learning disability, and abnormal EEG may or may not be present, and a diagnosis of central nervous system dysfunction may or may not be indicated.

dl-Amphetamine and dextroamphetamine are also effective in the treatment of narcolepsy.

3. *Marketing status.* a. Marketing of such drug products that are now the subject of an approved or effective new drug application may be continued provided that, on or before September 17, 1979 the holder of the application has submitted (i) a supplement for revised labeling as needed to be in accord with the labeling conditions described in this notice, and complete container labeling if current container labeling has not been submitted, and (ii) a supplement to provide updating information with respect to items 6 (components), 7 (composition), and 8 (methods, facilities, and controls) of new drug application form FD–356H (21 CFR 314.1(c)) to the extent required in abbreviated applications (21 CFR 314.1(f)).

b. For any person who does not hold an approved or effective new drug application, the submission of an abbreviated new drug application (21 CFR 314.1(f)) must be obtained before marketing such products. For preparations claiming controlled release, such supplements should contain studies comparing blood levels occurring with the controlled-release form with blood levels occurring with single units of the conventional form given multiple times. For example, when comparing a 30-milligram controlled-release form normally given every 12 hours with a 10-milligram conventional form normally given every 4 hours, the comparison should involve one unit of the controlled-release form given once and one unit of the 10-milligram form given every 4 hours for three doses. Protocols for these studies are required to be submitted under a Notice of Claimed Investigational Exemption for a New Drug (IND). Marketing before approval of a new drug application will subject such products, and those persons who caused the products to be marketed, to regulatory action.

OPPORTUNITY FOR HEARING

Therefore, notice is given to the holders of the new drug applications and to all other interested persons that the Director of the Bureau of Drugs proposes to issue an order under section 505(e) of Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(e)), withdrawing approval of all new drug applications and all amendments and supplements thereto providing for the indication as described in this announcement for the management of exogenous obesity, on the ground that new information has shown the drugs to be a risk to the patient, as well as to society, when offered for use for this indication, and that this information, evaluated together with the information available when the applications were approved, shows that such drugs are not shown to be safe for use under the conditions of use on the basis of which the applications were approved. An order withdrawing approval will not issue with respect to any application(s) supplemented in accord with this notice to delete this indication, except for those combination products which are only approved for this indication.

In addition to the specific ground for the proposed withdrawal of approval stated above, this notice of opportunity for hearing encompasses all issues relating to the legal status of the drug products subject to it, e.g., any contention that a product is not a new drug because it is generally recognized as safe and effective within the meaning of section 201(p) of the act or because it is exempt from part or all of the new drug provisions of the act pursuant to the exemption for products marketed prior to June 25, 1938, contained in section 201(p) of the act, or pursuant to section 107(c) of the Drug Amendments of 1962, or for any other reason.

In accordance with section 505 of the act (21 U.S.C. 355) and the regulations promulgated thereunder (21 CFR parts 310, 314), the applicants and all other persons who manufacture or distribute a drug product that is identical, related, or similar to a drug product named above (21 CFR 310.6) are hereby given an opportunity for a hearing to show why approval of the new drug applications providing for the claim involved should not be withdrawn and an opportunity to raise, for administrative determination, all issues relating to its legal status.

An applicant or any other person subject to this notice who decides to seek a hearing, shall file (1) on or before August 16, 1979, a written notice of appearance and request for hearing, and (2) on or before September 17, 1979, the data, information, and analyses relied upon to justify a hearing, as specified in 21 CFR 314.200. Any other interested person may also submit comments on this proposal to withdraw approval. The procedures and requirements governing this notice of opportunity for hearing, a notice of appearance and request for hearing, a submission of data, information, and analyses to justify a hearing, other comments, and a grant or denial of hearing are contained in 21 CFR 314.200.

The failure of an applicant or any other person subject to this notice pursuant to 21 CFR 310.6 to file timely written appearance and request for hearing as required by 21 CFR 314.200 constitutes and election not to make use of the opportunity for a hearing concerning the action proposed with respect to the drug product and a waiver of any contentions concerning the legal status of the drug product. A request for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing that there is a genuine and substantial issue of fact that requires a hearing. If it conclusively appears from the face of the data, information, and factual analyses in the request for the hearing that there is no genuine and substantial issue of fact that precludes the withdrawal of approval of the application, or when the request for hearing is not made in the required format or with the required analyses, the Commissioner of Food and Drugs will enter summary judgment against the person who requests the hearing, making findings and conclusions, denying a hearing.

All submissions pursuant to this notice of opportunity for hearing must be filed in quintuplicate. Such submissions, except for data and information prohibited from public disclosure under 21 U.S.C. 331(j) or 18 U.S.C. 1905, may be seen in the office of the Hearing Clerk between 9 a.m. and 4 p.m., Monday through Friday.

Federal Food, Drug, and Cosmetic Act sec. 502, 505, 52 Stat. 1050–1053, as amended (21 U.S.C. 352, 355) and under the authority delegated to the Director of the Bureau of Drugs (21 CFR 5.82))

Dated: July 10, 1979.

J. Richard Crout,

Director, Bureau of Drugs.

[FR Doc. 79-21953 Filed 7-16-79; 8:45 am]

BILLING CODE 4110-03-M

[Docket No. 78P-0314]

Lase-Aim-Inc.; Approval of Variance for Laser Target Designator, Model LA-300

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The agency announces that a variance from the performance standard for laser products has been approved for an alignment laser product identified as a Laser Target Designator, Model LA-300, The product is designed to produce a narrow laser light beam that is aligned parallel to a firearm bore and that projects a visible spot of light that serves as a means for improving aiming speed and accuracy. The product is used only for law enforcement and military purposes.

DATES: The variance becomes effective August 16, 1979, and ends August 17, 1984; written objections and supporting data by August 16, 1979.

ADDRESS: Written objections and supporting data to the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Glenn E. Conklin, Bureau of Radiological Health (HFX-460), Food and Drug Administration, Department of Health, Education, and Welfare 5600 Fishers Lane, Rockville, MD 20857, 301-443-3426.

SUPPLEMENTARY INFORMATION: Lase-Aim-Inc., 2905 Granite Creek Rd., Santa Cruz, CA 95066, submitted an application for a variance from certain provisions of the laser products performance standard (21 CFR 1040.10) for its alignment laser product. The variance is approved under § 1010.4 (21 CFR 1010.4), which authorizes the granting of variances for electronic products for which there are performance standards promulgated under section 358 of the Public Health Service Act, as amended by the Radiation Control for Health and Safety Act of 1968 (the act) (42 U.S.C. 263f).

Under the terms of this variance, the Laser Target Designator, Model LA-300, will deviate from the requirements of the standard in that the Class III product will not be provided with the performance features of a remote control connector (§ 1040.10(f)(3)), key control (§ 1040.10(f)(4)), emission indicator (§ 1040.10(f)(5)(ii)), and beam attenuator (§ 1040.10(f)(6)).

Elsewhere in this issue of the **Federal Register**, the Food and Drug Administration (FDA) is issuing a notice of an approved variance, No. 79001, under Docket No. 78P-0078, for a laser-aimed firearm having the same laser product performance features and similar design. The Director of the Bureau of Radiological Health notes that all aspects of the requested variance for the Laser Target Designator, Model LA-300, are identical with those upon which variance No. 79001 was granted. Therefore, the Director has approved the requested variance under the same conditions, as follows:

1. The sales and leasing of the Laser Target Designator by the manufacturer or owner are to be restricted to governmental military and law enforcement agencies. The conditions of restricted sales and leasing are to be fully stated along with the user and purchasing information that is required under 21 CFR 1040.10(h).

2. The laser system incorporated into the Laser Target Designator is to be nonremovable, 21 CFR 1040.10(c)(2).

3. The laser system is to be turned on only by using a normally-off, momentary switch whose actuation is significantly distinct but not necessarily physically separate from the trigger action of the weapon itself to prevent inadvertent firing of the weapon.

In accordance with § 1010.4(d), the applicant is directed to modify the tag, label, or other certification required by § 1010.2 (21 CFR 1010.2), under this variance, to state the following: "This product is in conformity with DHEW performance standards for laser products under 21 CFR Part 1040, except with respect to those characteristics authorized by Variance No. 79003, effective August 16, 1979."

The agency has reviewed the potential environmental impact of this variance and has concluded that the action will not significantly affect the quality of the human environment, and that an environmental impact statement is not required. A copy of the environmental impact assessment report is on file in the office of the Hearing Clerk, FDA.

Variance No. 79003 becomes effective August 16, 1979, and ends August 17, 1984, unless written objections and supporting data are filed with the Hearing Clerk (HFA-305) on or before August 16, 1979, requesting that the variance be modified or not granted. If objections and supporting data are submitted, the effective date of the variance will be stayed until the Director, Bureau of Radiological Health, rules on them under the procedures of § 1010.4(c).

The application for this variance and all related correspondence, including documents displayed under Docket No. 78P-0078 upon which this variance is based, except information covered by the confidentiality provisions of section 360A(e) of the act (42 U.S.C. 263i(e)), have been placed on public display in the office of the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857, and may be seen from 9 a.m. to 4 p.m., Monday through Friday.

Dated: July 9, 1979.

William F. Randolph,

Acting Associate Commissioner for Regulatory Affairs.

[FR Doc. 79-21955 Filed 7-16-79 8:45 am]

BILLING CODE 4110-03-M

Office of Education

Community Education Advisory Council; Meeting

AGENCY: Office of Education, HEW, Community Education Advisory Council.

ACTION: This notice sets forth the schedule and proposed agenda of the forthcoming meeting of the Planning Committee of the Coummunity Education Advisory Council. It also describes the functions of the Council from which this Planning Committee is formed. Notice of these meetings is required under section 10(a)(2) of the Federal Advisory Committee Act, Pub. L. 92-634. This document is intended to notify the general public of their opportunity to attend.

DATES: Meeting: August 2 and 3, 1979.

ADDRESS: Shoreham Americana Hotel, 2500 Calvert Street, N.W., Washington, D.C. 20008.

FOR FURTHER INFORMATION CONTACT: Margaret Beavan, Office of Education, Department of Health, Education, and Welfare, 7th and D Streets, S.W., Regional Office Building Three, Room 5622, Washington, D.C. 20202. Telephone: (202) 245-0691.

SUPPLEMENTARY INFORMATION: The Community Education Advisory Council is authorized under Public Law 93-380. The Council is established to advise the Commissioner of Education on policy matters relating to the interest of community schools.

All sessions of this meeting are open to the public. The meeting will begin each day at 9:00 a.m. and end at 4:30