

recommendations pertaining to activities to be undertaken by the Department to address the problems of rape.

**Agenda:** The entire meeting will be open to the public. The Advisory Committee will provide input to Title VI, Rape Prevention and Control, of the Mental Health Systems Act.

Substantive information may be obtained from the contact person listed above. Ms. Debbie Clawson, Assistant to the Executive Secretary, Rape Prevention and Control Advisory Committee, Room 15-99, 5600 Fishers Lane, Rockville, Maryland 20857, telephone number (301) 443-1910, will furnish upon request summaries of the meeting and rosters of the committee members.

Dated: January 12, 1981.

Elizabeth A. Connolly,  
*Committee Management Officer, Alcohol, Drug Abuse, and Mental Health Administration.*

[FR Doc. 81-1553 Filed 1-15-81; 8:45 am]

BILLING CODE 4110-88-M

#### **Treatment and Rehabilitation Work Group; Meeting**

In accordance with Section 10(a)(2) of the Federal Advisory Committee Act (5 U.S.C. Appendix I), announcement is made of the following national advisory body scheduled to assemble during the month of February 1981.

The Treatment and Rehabilitation Work Group of the Interagency Committee on Federal Activities for Alcohol Abuse and Alcoholism, February 3; 2:00 p.m.—open. Conference Room A, Parklawn Building, 5600 Fishers Lane, Rockville, Maryland 20857. Contact: Mr. David Clough, Room 11-19, Parklawn Building, 5600 Fishers Lane, Rockville, Maryland 20857, (301) 443-2070.

**Purpose:** The Treatment and Rehabilitation Work Group evaluates all Federal efforts in the areas of alcohol abuse and alcoholism treatment and rehabilitation; provides for the communication and exchange of information necessary; and seeks to coordinate and enhance these programs and activities. Any reports or recommendations are submitted to the Interagency Committee on Federal Activities for Alcohol Abuse and Alcoholism.

**Agenda:** Tentative agenda items include updated reports from work group members, a followup report on the Treatment Alternatives to Street Crime (TASC) program, and a report on criminal justice/alcoholism treatment issues.

Substantive program information may be obtained from the contact person listed above. The NIAAA Committee Management Office will furnish summaries of the meeting and a roster of Committee members upon request. Contact Ms. Helen Garrett, Room 16C-21, Parklawn Building, 5600 Fishers Lane, Rockville, Maryland 20857, (301) 443-2860.

Dated: January 12, 1981.

Elizabeth A. Connolly,  
*Committee Management Officer, Alcohol, Drug Abuse, and Mental Health Administration.*

[FR Doc. 81-1554 Filed 1-15-81; 8:45 am]

BILLING CODE 4110-88-M

#### **Centers for Disease Control**

##### **Control Technology Assessment of Chemical Process Batch Unit Operations; Open Meeting; Cancellation**

The notice of a meeting on the Control Technology Assessment of Chemical Process Batch Unit Operations, to be held January 22, 1981, was published in the Federal Register (46 FR 1030) on Monday, January 5, 1981. This open meeting is cancelled until further notice.

Dated: January 12, 1981.

William H. Foege,  
*Director, Centers for Disease Control.*

[FR Doc. 81-1656 Filed 1-15-81; 8:45 am]

BILLING CODE 4110-87-M

#### **Food and Drug Administration**

##### **Consumer Participation; Open Meeting**

**AGENCY:** Food and Drug Administration.  
**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) announces a forthcoming consumer exchange meeting to be chaired by Frederick R. Carlson, District Director, Boston District Office, Boston, MA.

**DATE:** The meeting will be held at 10 a.m., Thursday, January 29, 1981.

**ADDRESS:** The meeting will be held at the Food and Drug Administration Bldg., 2d Floor Conference Room, 585 Commercial St., Boston, MA 02109.

**FOR FURTHER INFORMATION CONTACT:** Yolán L. Harsanyi, Consumer Affairs Officer, Food and Drug Administration, 585 Commercial St., Boston, MA 02109, 617-223-5857.

**SUPPLEMENTARY INFORMATION:** The purpose of this meeting is to encourage dialogue between consumers and FDA officials, to identify and set priorities for current and future health concerns, to enhance relationships between local consumers and FDA's Boston District

Office, and to contribute to the agency's policymaking decisions on vital issues.

Dated: January 12, 1981.

William F. Randolph,  
*Acting Associate Commissioner for Regulatory Affairs.*

[FR Doc. 81-1556 Filed 1-15-81; 8:45 am]

BILLING CODE 4110-03-M

#### **Consumer Participation; Open Meeting**

**AGENCY:** Food and Drug Administration.  
**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) announces a forthcoming consumer exchange meeting to be chaired by Loren Y. Johnson, District Director, Philadelphia District Office, Philadelphia, PA.

**DATE:** The meeting will be held at 9:30 a.m., Wednesday, February 25, 1981.

**ADDRESS:** The meeting will be held at the Federal Bldg., Rm. 3306 (3d Floor), 600 Arch St., Philadelphia, PA 19106.

**FOR FURTHER INFORMATION CONTACT:** Bob Lockett, Consumer Affairs Officer, Food and Drug Administration, U.S. Customhouse, Rm. 900, 2d and Chestnut Sts., Philadelphia, PA 19106, 215-597-0837.

**SUPPLEMENTARY INFORMATION:** The purpose of this meeting is to encourage dialogue between consumers and FDA officials, to identify and set priorities for current and future health concerns, to enhance relationships between local consumers and FDA's Philadelphia District Office, and to contribute to the agency's policymaking decisions on vital issues.

Dated: January 12, 1981.

William F. Randolph,  
*Acting Associate Commissioner for Regulatory Affairs.*

[FR Doc. 81-1557 Filed 1-15-81; 8:45 am]

BILLING CODE 4110-03-M

#### **Ophthalmic Device Section of the Ophthalmic, Ear, Nose, and Throat; and Dental Devices Panel; Meeting**

**AGENCY:** Food and Drug Administration.  
**ACTION:** Notice.

**SUMMARY:** This notice announces a forthcoming meeting of a public advisory committee 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 meeting is announced:

**Ophthalmic Device Section of the Ophthalmic, Ear, Nose, and Throat; and Dental Devices Panel**

**Date, time, and place:** February 5 and 6, 9 a.m., Holiday Inn, 8777 Georgia Ave., Silver Spring, MD.

**Type of meeting and contact person:** Open public hearing, February 5, 9 a.m. to 10 a.m., open committee discussion, February 5, 10 a.m. to 5 p.m.; open public hearing, February 6, 9 a.m. to 10 a.m., open committee discussion, February 6, 10 a.m. to 5 p.m.; Max W. Talbott, Bureau of Medical Devices (HFK-460), Food and Drug Administration, 87557 Georgia Ave., Silver Spring, MD 20910, 301-427-7538.

**General function of the Committee:** The Committee reviews and evaluates available data on the safety and effectiveness of devices currently in use and makes recommendations for their regulation.

**Agenda—Open public hearing:** Interested persons are encouraged to present information pertinent to intraocular lenses and the intraocular lens clinical investigation (February 5) and on contact lenses and contact lens products (February 6). Those desiring to make formal presentations should notify the contact person by January 22, 1981, 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 an indication of the approximate time required to make their comments.

**Open committee discussion.** The Section will conduct reviews of premarket approval applications of intraocular lenses and will discuss other statistical/epidemiological questions pertaining to intraocular lenses (February 5) and will conduct reviews of premarket approval applications for contact lens products (February 6).

**Applications for reimbursement.** Must be received by January 26, 1981.

**Board of Tea Experts**

**Date, time, and place:** February 9, 10 a.m., Rm. 700, 850 Third Ave., Brooklyn, NY.

**Type of meeting and contact person:** Open public hearing, 10 a.m. to 11 a.m., open committee discussion, 11 a.m. to 4:30 p.m.; Robert H. Dick, Food and Drug Administration, 850 Third Ave., Brooklyn, NY, 11232, 212-965-5739.

**General function of the Committee:** The Board advises on establishment of uniform standards of purity, quality, and fitness for consumption of all teas imported into the United States pursuant to 21 U.S.C. 42.

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

**Open committee discussion:** Discussion and selection of tea standards.

**Applications for reimbursement:** Must be received by January 28, 1981.

FDA public advisory committee meetings 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 or 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.

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 requested from the Dockets Management Branch (formerly the Hearing Clerk's office) (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, between 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.

Applications for reimbursement for participation in the meeting listed above should be sent to the Office of Consumer Affairs (HFE-88), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, rather than to the Dockets Management Branch as prescribed in § 10.210 of the regulations

(21 CFR 10.210). If you wish to submit an application or wish more information regarding the reimbursement program, please call 301-443-3170.

FDA has established expedited procedures for review of any application for reimbursement for participation in the meetings announced in this notice. The Office of Consumer Affairs, FDA, will file any application for reimbursement for participation in the meetings announced in this notice in the docket for this notice.

Dated: January 9, 1981.

**William F. Randolph,**  
Acting Associate Commissioner for  
Regulatory Affairs.

[FR Doc. 81-1558 Filed 1-15-81; 8:45 am]

**BILLING CODE 4110-03-M**

[Docket No. 75N-0184; DESI 597, 3265, 10837, and 9489]

**Certain Anticholinergics/  
Antispasmodics in Combination With a  
Sedative, and Single-Entity  
Antispasmodics, in Conventional  
Dosage Form; Drug Efficacy Study  
Implementation; Notice of Opportunity  
for Hearing**

**AGENCY:** Food and Drug Administration.

**ACTION:** Notice.

**SUMMARY:** This notice reclassifies certain anticholinergics or antispasmodics in combination with a sedative, and single-entity antispasmodics in conventional dosage form to lacking substantial evidence of effectiveness, proposes to withdraw approval of the new drug applications, and offers an opportunity for a hearing on the proposal.

**DATES:** Any request for hearing must be submitted on or before February 17, 1981. All data and information relied upon in support of any such request and any other comments must be submitted on or before March 17, 1981.

**ADDRESSES:** Communications in response to this notice should be identified with the Docket No. 75N-0184 and the reference number DESI 597, 3265, 10837, or 9489, as appropriate, and directed to the attention of the appropriate office named below.

Requests for hearing, supporting data, and other comments: Dockets Management Branch (HFA-305), Rm. 4-62, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

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

Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

**FOR FURTHER INFORMATION CONTACT:** Suzanne O'Shea, Bureau of Drugs (HFD-32), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-3650.

**SUPPLEMENTARY INFORMATION:** In notices published in the *Federal Register* of June 22, 1971 (36 FR 11875) (DESI 10837), July 27, 1972 (37 FR 15026) (DESI 597), September 18, 1973 (38 FR 26138) (DESI 9489), and November 11, 1975 (40 FR 52649) (DESI 3265), the Food and Drug Administration (FDA) classified anticholinergic or antispasmodic drugs in combination with a sedative, and antispasmodic drugs alone, as possibly effective for various gastrointestinal diseases. The indications lacking substantial evidence of effectiveness were specifically named in the notices. All other indications were classified as possibly effective. The possibly effective indications are set forth below:

#### DESI 10837

1. Tridihexethyl chloride and meprobamate (NDA 11-043 Milpath-200, Milpath-400, and NDA 10-837 Pathibamate-200 and Pathibamate-400): As adjunctive therapy in peptic ulcer and in the irritable bowel syndrome; functional diarrhea; drug induced diarrhea; ulcerative colitis; urinary bladder spasm; and urethral spasm.

#### DESI 597

1. Mepenzolate bromide and phenobarbital (NDA 10-679 Cantil with Phenobarbital Tablets): Motility disorders of the lower GI tract; acute enterocolitis; mild chronic ulcerative colitis; rectospasm; diverticulitis; post-gastrectomy diarrhea; diarrhea associated with diverticulitis.

2. Oxyphencyclimine hydrochloride and phenobarbital (NDA 13-515 Daricon PB): Peptic ulcers; hiatal hernia; functional bowel syndrome; chronic ulcerative colitis; bladder spasm with or without infection; urethral spasm.

3. Propantheline bromide and phenobarbital (NDA 9-014 Pro-Banthine with Phenobarbital Tablets): peptic ulcer; urinary bladder spasm; functional gastrointestinal disturbances; acute and chronic pancreatitis; ileoanal anastomosis; hyperhidrosis; ureteral spasm; infantile colic; useful ileostomies.

4. Glycopyrrrolate and phenobarbital (NDA 12-950 Robinul PH Tablets and Robinul PH Forte): As adjunctive therapy for gastric and duodenal ulcer; esophagitis; hiatal hernia; spastic and irritable colon; functional bowel distress; splenic flexure syndrome; ileocolitis; diverticulitis; some

neurogenic disturbances; acute enteritis; diarrhea; and intestinal viral infections.

5. Piperidolate hydrochloride and phenobarbital (NDA 8-907 Dactil with Phenobarbital): functional gastric disorders; post-gastrectomy syndrome.

6. Dicyclomine hydrochloride and phenobarbital (NDA 7-409 Bentyt with Phenobarbital): symptomatic control of functional gastrointestinal disorders; chronic irritable bowel; spastic constipation; mucous colitis; spastic colitis; biliary dyskinesia; gastrointestinal spasm secondary to organic disease.

#### DESI 9489

1. Tridihexethyl chloride and phenobarbital (NDA 9-489 Pathilon with Phenobarbital): peptic ulcer; gastric hyperacidity; gastric hypermotility; spastic and irritable colon; functional diarrhea; pylorospasm; gastritis where symptoms are due to hyperacidity.

#### DESI 3265

1. Piperidolate hydrochloride (NDA 8-907 Dactil Tablets): Irritable bowel syndrome and acute enterocolitis.

In a notice published in the *Federal Register* of November 11, 1975 (40 FR 52644) anticholinergic/sedative or antispasmodic/sedative combinations and antispasmodics alone were temporarily exempted from the time limits established for implementing certain phases of the Drug Efficacy Study. In order to qualify for the exemption manufacturers of anticholinergic/sedative combinations were required to undertake studies of the products as adjunctive therapy in the treatment of peptic ulcer, or in the treatment of the irritable bowel syndrome or acute enterocolitis. Manufacturers of antispasmodic/sedative combinations or antispasmodics alone were required to perform studies of their products in treating the irritable bowel syndrome or acute enterocolitis. The notice set forth a timetable for submitting protocols and for starting, reporting on, and completing the studies.

In a notice published in the *Federal Register* of June 20, 1978 (43 FR 26490), FDA extended the deadline for completion of the studies for 1 year. The notice also stated that abbreviated new drug applications for identical products would be conditionally approved if certain conditions were met. Among other things, it was required that the manufacturers of conditionally approved products conduct clinical studies. However, no study would be necessary if another manufacturer was conducting a study of a drug product containing the same ingredients to

which the same efficacy conclusions would apply. The conditionally approved products have the same legal status as products initially covered by the exemption. The notices setting forth the exemption also apply to certain related drugs that are not the subject of an approved new drug application or a conditionally approved abbreviated new drug application.

No data were submitted to support the indications found by FDA to lack substantial evidence of effectiveness. The data submitted to comply with the exemption have been reviewed. Several studies require detailed analysis and will be the subject of a future *Federal Register* notice. The drug products affected by those studies are not listed above. However, many of the studies were seriously incomplete, and did not show that each component of the combination products makes a significant contribution to the effectiveness of the product. Analyses of these studies follow.

1. Studies were completed which investigated the effectiveness of Bentyt with Phenobarbital Tablets (Merrell-National Laboratories), Dactil with Phenobarbital Tablets (Merrell-National Laboratories), and Pro-Banthine with Phenobarbital Tablets (G. D. Searle & Co.) in treating the irritable bowel syndrome. However, none of the studies showed that each of the components makes a significant contribution to the effectiveness of the product. 21 CFR 300.50(a). In most cases, there was a trend toward improvement of the conditions regardless of the treatment. The sponsors acknowledge the lack of a showing of the effectiveness of their products.

2. Pfizer submitted the results of a completed double-blind, placebo controlled study on the effectiveness of Daricon PB Tablets as adjunctive therapy in duodenal ulcer. The patients took antacids concomitantly, after meals and before bed as needed.

The study does not show that each component makes a significant contribution to the effectiveness of Daricon PB. 21 CFR 300.50(a). The patients were evaluated at the final global rating as worse or unchanged, improved, or symptom free. In the patient and investigator rating there is very little difference in the proportions of "improved" and "symptom free" patients. In addition, when the "improved" and "symptom free" groups are combined, there is little difference between any of the treatment groups.

The sponsor claims that patients receiving Daricon PB consumed the least amount of antacids during the study except during the fourth week when

placebo patients consumed the least antacids. Placebo patients consumed less antacids than phenobarbital and plain Daricon patients, except for the fourth week when the placebo patients consumed more than phenobarbital patients. Throughout the study Daricon patients consumed the most antacids.

Pfizer claims that the Daricon PB group had the lowest number of symptoms per patient per week for four of seven symptoms. However, the sponsor also stated that "the small patient population large within-group variation prevented statistical significance."

3. Robins submitted a status report on a double-blind, parallel investigation of Robinul PH in treating functional upper and lower gastrointestinal disorders. Robins claims that the data suggest that Robinul PH is helpful in alleviating symptoms and that the contribution of each component is evident.

The study is not adequate and well-controlled. 21 CFR 314.111(a)(5). The patients receiving Robinul PH had the greatest proportion of liquid or soft stools, and placebo patients had the most variable stools. Thus, it is not clear that the subjects were assigned to test groups in a way that minimizes bias. 21 CFR 314.111(a)(5)(a)(2)(ii). The test and control groups are not comparable because the Robinul PH used in the study contains 1.10 milligrams of glycopyrrolate per tablet, but the control group was given only 1.0 milligram of glycopyrrolate per tablet. In addition, the sponsor does not specify the patients who took concomitant drugs or those who had concomitant diseases, nor is there any explanation of the difference between "evaluable patients" and "patients completing the study." 21 CFR 314.111(a)(5)(ii)(a)(2)(iii).

Robins claims that Robinul PH is superior in normalizing stools after the first week. However, the patient diaries do not evaluate bowel habits. It is not clear, therefore, that adequate steps were taken to minimize bias in measuring responses. 21 CFR 314.111(a)(5)(ii)(a)(3).

In addition, the contribution of each component to the combination has not been demonstrated. 21 CFR 300.50(a). Although Robins claims that Robinul PH is superior in stool normalization, the physicians rating charts indicate that all drugs were equally effective. Robins claims that Robinul PH is effective treatment for night pain. However, Robinul (glycopyrrolate) alone and phenobarbital alone are as effective as Robinul PH in the treatment of night pain after the second week. For day pain, Robinul is as effective as Robinul PH. For duration of pain, there is little

difference Robinul and Robinul PH. All treatments were shown to be equally effective in the global evaluation. The sponsor claims that the study demonstrates the clinical superiority of Robinul PH, but acknowledges that no statistical superiority has been shown.

No study was submitted for Robinul PH Forte.

4. Reed and Carnrick submitted data from a partially completed study of the effectiveness of Sidonna Tablets in treating the irritable bowel syndrome. The sponsor was able to study less than half the intended number of cases, but the specific number is not defined. The study is not adequate and well-controlled, nor do the results of the study demonstrate that each component makes a significant contribution to the combination product. 21 CFR 314.111(a)(5); 300.50(a).

The study's protocol was not submitted for review as required by the November 11, 1975 notice. The dose is not given for any of the test drugs used. Thus, it is not clear that the test drugs were standardized as required by 21 CFR 314.111(a)(5)(ii)(b). Several patients should not have been admitted to the study: those with depression, character disorders, migraines, diverticulosis, and those receiving antidiarrheal drugs, ampicillin, and Bentyl. 21 CFR 314.111(a)(5)(ii)(a)(2)(iii). The sponsor analyzed only the physicians' ratings because this rating was based in part on the patients' daily logs. The patients' daily logs should have been analyzed separately from the physicians' rating in order to minimize bias. 21 CFR 314.111(a)(5)(ii)(a)(3).

The sponsor found no statistical evidence of the superiority of Sidonna. The sponsor found no significant difference among treatment groups in abdominal pain, abdominal distention, and borborygmi. Sidonna and placebo were equally effective in treating mucus in stool. Significant differences exist at 2 weeks, but not at 4 weeks, in alleviation of diarrhea. However, the greatest improvement was in the simethicone and placebo groups and poorest in the Sidonna group. In the global assessment, there were no significant differences among the treatment groups at 2 weeks or 4 weeks. The highest percentage of improved patients occurred in the placebo group. Thus it has not been shown that each component makes a significant contribution to the combination product. 21 CFR 300.50(a).

5. Data submitted for six irritable bowel syndrome studies are seriously incomplete. The data obtained from these studies are inadequate to draw any conclusions on the effectiveness of the product. Merrell-National terminated

a study of Dactil Tablets because only one patient entered the study. Only 19 patients completed the study of Endo Laboratories' Valpin 50 PB tablets. Lederle Laboratories studied only 22 patients in investigating Pathilon with Phenobarbital Tablets. Twenty-three patients completed Merrell-National's study of Cantil with Phenobarbital Tablets. In a joint study of Lederle's Pathibamate 200 and Wallace's Milpath 200, approximately 60 patients were analyzable. In a joint study of Lederle's Pathibamate-400 and Wallace's Milpath-400, 129 patients met protocol requirements and completed the study. The sponsors had planned on studying 500 patients. All sponsors acknowledge that the data submitted are insufficient to draw any conclusions on the effectiveness of their products.

Most of the above sponsors have requested additional time to study additional patients, as did Beecham Laboratories for Daricon PB Tablets, Robins for Robinul PH Tablets, Merrell-National for Bentyl with Phenobarbital, and Reed and Carnrick for Sidonna Tablets. The deadline for completion of studies has already been extended for 1 year. The Director of the Bureau of Drugs believes that adequate time has been allowed to investigate the effectiveness of these products. Therefore, requests for additional time in which to submit data are denied.

6. In addition to the incomplete study on irritable bowel syndrome (above), Merrell-National submitted a statement, "The Rationale for Cantil with PB in Peptic Ulcer." It claims that Cantil is currently effective for peptic ulcer, that the management of peptic ulcer is often complicated by anxiety, and that phenobarbital is an effective anti-anxiety, sedative agent. Therefore, Merrell-National asserts that Cantil with PB should be allowed to remain on the market for the treatment of peptic ulcer. No data were submitted on any studies for the use of Cantil with PB Tablets in peptic ulcer. Substantial evidence of effectiveness must be demonstrated by adequate and well-controlled clinical investigations. 21 U.S.C. 355; 21 CFR 314.111(a)(5). Clearly, this submission does not meet the statutory standard.

7. Roche Laboratories did not submit data from a clinical study in support of Librax. Instead, it submitted data from an ongoing study of the prevalence of emotional factors in association with certain gastrointestinal disorders. To date, 312 patients have been studied. Roche claims that patients with gastrointestinal disorders show higher emotional stress than other types of

patients, or persons with no medical disorders.

Roche also submitted the results of a medical marketing summary undertaken in August and September 1974 in which physicians were asked to indicate their preference concerning the use of anticholinergic/sedative drugs in various diseases. It also submitted the results of pharmacology studies in mice, from which it claims that both the tranquilizer and anticholinergic components are effective in protecting against stress-induced gastric mucosal erosion.

Clearly, none of these submissions fulfill the requirement that substantial evidence of effectiveness be shown by adequate and well-controlled studies. 21 U.S.C. 355; 21 CFR 314.111(a)(5). Moreover, because the study of emotional factors in gastrointestinal disorders is incomplete, the amount of reliance appropriately placed on that study is in question. The Director has already granted one time extension for the study of these drugs. Because adequate time has already been provided, no further extension is warranted.

No person has yet provided data that would support upgrading any of these products to effective. In addition, the Director believes that the time allowed for investigating the effectiveness of these products has been adequate for the design and conduct of acceptable studies. Accordingly, the temporary exemption granted by the November 11, 1975 and June 20, 1978 notices, as they pertain to these drugs, is revoked in a notice appearing elsewhere in this issue of the Federal Register.

#### Notice of Opportunity for Hearing

On the basis of all of the data and information available to him, the Director of the Bureau of Drugs is unaware of any adequate and well-controlled clinical investigation, conducted by experts qualified by scientific training and experience, meeting the requirements of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) and 21 CFR 314.111(a)(5) and, for combination products, 21 CFR 300.50, demonstrating the effectiveness of the drugs.

Therefore, notice is given to the holders of the following new drug applications and conditionally approved abbreviated new drug applications, to manufacturers of the following related products, and to all other interested persons that the Director of the Bureau of Drugs proposes to issue an order under section 505(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(e)), withdrawing approval of the

new drug applications and all amendments and supplements thereto on the ground that new information before him with respect to the drug products, evaluated together with the evidence available to him when the applications were approved, shows there is a lack of substantial evidence that the drug products will have the effect they purport or are represented to have under the conditions of use prescribed, recommended, or suggested in the labeling.

#### DESI 597

1. NDA 7-409; Bently with Phenobarbital Capsules containing dicyclomine hydrochloride 10 milligrams and phenobarbital 15 milligrams; Merrell-National Laboratories, Division of Richardson-Merrell, Inc., 110 E. Amity Rd., Cincinnati, OH 45215.

2. NDA 8-907; Dactil with Phenobarbital tablets containing piperidolate hydrochloride 50 milligrams and phenobarbital 16 milligrams; Merrell-National Laboratories.

3. NDA 12-950; Robinul PH Tablets and Robinul PH Forte containing glycopyrrolate 1 milligram and phenobarbital 16 milligrams, and glycopyrrolate 2 milligrams and phenobarbital 16 milligrams; A. H. Robins Co., 1407 Cummings Dr., Richmond, VA 23220.

4. NDA 10-679; Cantil with Phenobarbital Tablets containing mepenzolate bromide 25 milligrams and phenobarbital 16 milligrams; Merrell-National Laboratories.

5. NDA 13-515; Daricon PB Tablets containing oxyphenycyclimine hydrochloride 5 milligrams and phenobarbital 15 milligrams; Pfizer Laboratories, Division of Pfizer, Inc., 235 E. 42d St., New York, NY 10017.

6. NDA 9-014; Pro-Banthine with Phenobarbital Tablets containing propantheline bromide 15 milligrams and phenobarbital 15 milligrams; G. D. Searle & Co., P.O. Box 5110, Chicago, IL 60680.

#### DESI 3265

1. NDA 8-907; Dactil Tablets containing piperidolate hydrochloride 50 milligrams; Merrell-National Laboratories.

#### DESI 9489

1. NDA 9-489; Pathilon with Phenobarbital Tablets containing tridihexethyl chloride 25 milligrams and phenobarbital 15 milligrams; Lederle Laboratories Division, American Cyanimid Co., Pearl River, NY 10965.

#### DESI 10837

1. NDA 10-837; Pathibamate-200 Tablets and Pathibamate-400 Tablets containing tridihexethyl chloride 25 milligrams and meprobamate 200, and tridihexethyl chloride 25 milligrams and meprobamate 400 milligrams; Lederle Laboratories.

2. NDA 11-043; Milpath-200 Tablets and Milpath-400 Tablets containing tridihexethyl chloride 25 milligrams and meprobamate 200, and tridihexethyl chloride 25 milligrams and meprobamate 400 milligrams; Wallace Laboratories, Division of Carter-Wallace, Inc., Half-Acre Rd., Cranberry, NJ 08512.

The following products, not reviewed by NAS/NRC, were subject to the exemption notices of November 11, 1975, and June 20, 1978: 1. NDA 12-750; Librax Capsules containing clidinium bromide 2.5 milligrams and chlordiazepoxide 5 milligrams; Roche Laboratories, Division of Hoffman-LaRoche, Inc., Nutley, NJ 07110.

2. NDA 13-430; Valpin 50 PB Tablets and Valpin PB Tablets containing anisotropine methylbromide 50 milligrams and phenobarbital 15 milligrams, and anisotropine methylbromide 15 milligrams and phenobarbital 15 milligrams; Endo Laboratories, 1000 Stewart Ave., Garden City, NY 11530.

3. ANDA 86-281; Meprobamate with Tridihexethyl Chloride Tablets containing 200 milligrams meprobamate and 25 milligrams tridihexethyl chloride; Chelsea Laboratories, Inc., 428 Doughty Blvd., Inwood, NY 11696.

4. ANDA 86-526; Meprobamate with Tridihexethyl Chloride Tablets containing 400 milligrams meprobamate and 25 milligrams tridihexethyl chloride; Chelsea Laboratories, Inc.

5. ANDA 86-791; T.C.M. 200 Tablets containing 200 milligrams meprobamate and 25 milligrams tridihexethyl chloride; Zenith Laboratories, Inc., 140 Legrand Ave., Northvale, NJ 07647.

6. ANDA 86-792; T.C.M. 400 Tablets containing 400 milligrams meprobamate and 25 milligrams tridihexethyl chloride; Zenith Laboratories, Inc.

The following products are not the subject of an approved new drug application. The NDA number listed is for identification purposes and is the NDA number of the manufacturer's original product to which the product listed below is related.

1. NDA 9-014; Probitol Tablets containing propantheline bromide 7.5 milligrams, and phenobarbital 15 milligrams; G. D. Searle & Co.

2. Ref. No. 90-006 (No NDA); Sidonna Tablets containing simethicone 25 milligrams, butabarbital sodium 16

milligrams, hyoscyamine sulfate 0.1037 milligram, scopolamine hydrobromide 0.0065 milligram and atropine sulfate 0.0194 milligram; Reed and Carnrick, 30 Boright Ave., Kenilworth, NJ 07033.

In addition to the holders of the new drug applications specifically named above, this notice of opportunity for hearing applies to all persons who manufacture or distribute a drug product not the subject of an approved new drug application, that is listed above or that is identical, related, or similar to a drug product named above, as defined in 21 CFR 310.6. It is the responsibility of every drug manufacturer or distributor to review this notice of opportunity for hearing to determine whether it covers any drug products that the person manufactures or distributes. An opinion of the applicability of this notice to a specific drug product may be obtained by writing to the Division of Drug Labeling Compliance (address given above).

In addition to the grounds 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 (including identical, related, or similar drug products as defined in 21 CFR 310.6) 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 under the exemption for products marketed before June 25, 1938, contained in section 201(p) of the act, or under 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 subject to this notice under 21 CFR 310.6 are hereby given an opportunity for a hearing to show why approval of the new drug application(s) should not be withdrawn and an opportunity to raise, for administrative determination, all issues relating to the legal status of a drug product named above and of all identical, related or similar drug products.

An applicant or any other person subject to this notice under 21 CFR 310.6 who decides to seek a hearing, shall file (1) on or before February 17, 1981, a written notice of appearance and request for hearing, and (2) on or before March 17, 1981, the data, information, and analyses relied on to justify a hearing, as specified in 21 CFR 314.200. Any other interested person may also submit comments on this notice. 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 persons subject to this notice under 21 CFR 310.6 to file time written appearance and request for hearing as required by 21 CFR 314.200 constitutes an election by the person not to make use of the opportunity for a hearing concerning the action proposed with respect to the product and constitutes a waiver of any contentions concerning the legal status of any such drug product. Any such drug product may not thereafter lawfully be marketed, and the Food and Drug Administration will initiate appropriate regulatory action to remove such drug products from the market. Any new drug product marketed without an approved NDA is subject to regulatory action at any time.

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 data, information, and factual analyses in the request for the hearing that there is no genuine and substantial issue of fact which precludes the withdrawal of approval of the application, or when a 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(s) who requests the hearing, making findings and conclusions, denying a hearing.

All submissions under this notice 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 Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

(Sec. 505, 52 Stat. 1052-1053, as amended (21 U.S.C. 355)), and under the authority delegated to the Director of the Bureau of Drugs (21 CFR 5.82)

Dated: December 24, 1980.

J. Richard Crout,

Director, Bureau of Drugs.

[FR Doc. 81-1284 Filed 1-15-81; 8:45 am]

BILLING CODE 4110-03-M

[Docket No. 75N-0184; DESI Nos. 597, 3265, 9489 and 10837]

**Certain Anticholinergics or Antispasmodics in Combination With a Sedative, and Single-Entity Antispasmodics, in Conventional Dosage Form; Drug Efficacy Study Implementation; Revocation of Exemption**

**AGENCY:** Food and Drug Administration.  
**ACTION:** Notice.

**SUMMARY:** This notice revokes the temporary exemption for continued marketing of certain anticholinergics or antispasmodics in combination with a sedative, or single-entity antispasmodics. Under the exemption, the drugs have been allowed to remain on the market for continued study beyond the time limit scheduled for implementation of the Drug Efficacy Study.

**EFFECTIVE DATE:** January 16, 1981.

**FOR FURTHER INFORMATION CONTACT:** Suzanne O'Shea, Bureau of Drugs (HFD-32), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-3650.

**SUPPLEMENTARY INFORMATION:** In notices published in the *Federal Register* of June 22, 1971 (36 FR 11875) (DESI 10837), July 27, 1972 (37 FR 15026) (DESI 597), September 18, 1973 (38 FR 26138) (DESI 9489), and November 11, 1975 (40 FR 52649) (DESI 3265), the Food and Drug Administration (FDA) classified anticholinergic or antispasmodic drugs in combination with a sedative, and antispasmodic drugs alone, as possibly effective for various gastrointestinal diseases. In a notice published in the *Federal Register* of November 11, 1975 (40 FR 52644), conventional dosage forms of these products were permitted to remain in the market pending completion of clinical studies testing their effectiveness in treating gastrointestinal disease. That notice established a timetable for submission of protocols, for beginning studies, and for completion of the studies. In a notice published in the *Federal Register* of June 20, 1978 (43 FR 26490), the deadline for completion of the studies was extended for 1 year. The June 20, 1978 notice required abbreviated new drug applications for duplicative products covered by the exemption and stated that conditionally approved abbreviated new drug applications have the same legal status as "deemed approved" applications reviewed in the Drug Efficacy Study.

The data received for several completed studies are undergoing detailed FDA analysis. The drugs used