CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

12-827/S024&S025

Trade Name: Robinul & Robinul Forte Tablets

Generic Name: (glycopyrrolate)

Sponsor: A.H. Robins Company

Approval Date: January 30, 1981

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

12-827/S024&S025

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Risk Assessment and Risk Mitigation Review(s)	
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 12-827/S024&S025

APPROVAL LETTER

15.1

NDA 12-827/S-024
S-025

JAN 30 1981

A.H. Robins Company
Attention: Frances Aaroe
1211 Sherwood Avenue
Richmond, Virginia 23220

Dear Mrs. Aaroe:

Please refer to your supplemental new drug applications of March 3, 1980 (S-024) and June 6, 1980 (S-025) submitted pursuant to section 505(b) of the Federal Food, Drug, and Cosmetic Act for Robinul and Robinul Forte (glycopyrrolate) Tablets.

We also acknowledge receipt of your additional communication dated July 3, 1980 amending S-024.

The supplemental applications provide for packaging the tablets in high density polyethylene containers (S-024) and [redacted] batch sizes (S-025). b(4) b(4)

We have completed the review of these supplemental applications and they are approved. Our letter of December 27, 1975, detailed the conditions relating the approval of this application.

Sincerely yours,

Stewart J. Ehrreich, Ph.D.
Deputy Director
Division of Cardio-Renal
Drug Products
Bureau of Drugs

cc:BALT-DO
Orig. NDA
HFD-616
HFD-110
HFD-110/CSO
HFD-110/Wolters/12/4/80/1/19/81/1/19/81/mbr/1/17/81/th/1/27/81/3418A
R/D init by:JLangston/12/4/80
RTemple/12/4/80
AThompson/1/19/81
SEhrreich/1/19/81

APPROVE SUPPLEMENT

1/29/81

1/29/81

1/29/81

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 12-827/S024&S025

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW
(If necessary, continue any item on 8" x 10½" paper. Key continuation to item by number.)

1. ORGANIZATION	2. NDA NUMBER
HFD-110	12-827

3. NAME AND ADDRESS OF APPLICANT *(City and State)*
A.H. Robins Company
1211 Sherwood Avenue
Richmond, Virginia 23220

4. AF NUMBER
16-375

5. SUPPLEMENT (S)

NUMBER(S)	DATE(S)
S-024	3-3-80
S-025	6-6-80

6. NAME OF DRUG	7. NONPROPRIETARY NAME
Robinul Robinul Forte	Glycopyrrolate

8. SUPPLEMENT(S) PROVIDES FOR:
S-024 Provides for packaging the tablets in HDPE containers.
S-025 Provides for [redacted] b(4) in the batch sizes.
Ammendment dated 7-3-80 submitted in response to our letter.

9. AMENDMENTS AND OTHER *(Reports, etc.)* DATES
7-3-80 b(4)

10. PHARMACOLOGICAL CATEGORY	11. HOW DISPENSED	12. RELATED IND/NDA/DMF(S)
Anticholinergic	☒ RX ☐ OTC	DMF [redacted] DMF [redacted] DMF [redacted]

13. DOSAGE FORM (S)	14. POTENCY *(ies)*
Tablets	1 mg and 2 mg (Forte)

15. CHEMICAL NAME AND STRUCTURE
USP XX

16. RECORDS AND REPORTS
CURRENT ☒ YES ☐ NO
REVIEWED ☒ YES ☐ NO

b(4)
COMMENTS S-024 [redacted] is being deleted as a source of the containers. Letters of authorization are included.
If additional suppliers are used an appropriate supplement will be submitted.
S-025- The [redacted] b(4) the batch sizes. These adjustments were slight.
b(4)

18. CONCLUSIONS AND RECOMMENDATIONS
Approve supplements

JAN 30 1981

19. REVIEWER

NAME	SIGNATURE	DATE COMPLETED
R.J. Wolters	RJWolters 1/29/81	12-4-80

DISTRIBUTION ☑ ORIGINAL JACKET ☐ REVIEWER ☐ DIVISION FILE

FORM FDH 2266 (7/75) PREVIOUS EDITION MAY BE USED UNTIL SUPPLY IS EXHAUSTED.

HFD-110/CSO

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 12-827/S024&S025

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

NDA 12-827

SEP 12 1980

A.H. Robins, C.
Attention: Ms. Frances Aaroe
1211 Sherwood Avenue
Richmond, Virginia 23220

Dear Ms. Aaroe:

We acknowledge receipt of your resubmitted supplemental application for the following:

Name of Drug: Robinul and Robinul Forte

NDA Number: 12-827

Supplement Number: S-024

Date of Resubmitted Supplement: July 3, 1980

Date of Receipt: July 8, 1980

All communications concerning this NDA should be addressed as follows:

Bureau of Drugs HFD-110
Attention: DOCUMENT CONTROL ROOM #16B-30
5600 Fishers Lane
Rockville, Maryland 20852

Sincerely yours,

9/12/80
Natalia A. Morgenstern
Supervisory Consumer Safety Officer
Division of Cardio-Renal
Drug Products
Bureau of Drugs

cc:BALT-DO
Orig. NDA
HFD-110
HFD-110/CSO
HFD-110/Gerding Gerding 9/10/80
HFD-110/Mathews/9/5/80/mbr/9/8/80/1960A

RESUBMITTED SUPPLEMENT
ACKNOWLEDGEMENT

15.1

NDA 12-827

A.H. Robins Company
Attention: Frances Aaroe
1211 Sherwood Avenue
Richmond, Virginia 23220

AUG 6 1980

Dear Ms. Aaroe:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Robinul & Robinul Forte

NDA Number: 12-827

Supplement Number: S-025

Date of Supplement: June 6, 1980

Date of Receipt: June 11, 1980

All communications concerning this NDA should be addressed as follows:

Bureau of Drugs HFD-110
Attention: DOCUMENT CONTROL ROOM #16B-30
5600 Fishers Lane
Rockville, Maryland 20857

Sincerely yours,

nam 8/4/80
Natalia A. Morgenstern
Supervisory Consumer Safety Officer
Division of Cardio-Renal
Drug Products
Bureau of Drugs

cc: Blt-Dist
NDA Orig. 12-827
HFD-110
HFD-110/CSO
HFD-616
HFD-110/ABrown/8/4/80/jj/8/4/80/1579A

SUPPLEMENT ACKNOWLEDGEMENT

Frances Aaroe, Manager
Domestic Regulatory Affairs

ORIGINAL

NDA No. 12-827 REF. NO. 5025
NDA SUPPL FOR Control

A. H. Robins Company
1211 Sherwood Avenue
Richmond, Virginia 23220
(804) 257-2502

CS

A·H·ROBINS

Division of Cardio-Renal Drug
Products
Bureau of Drugs, HFD #110
Document Control Room 16B-30
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

June 6, 1980

RE: NDA 12-827
Robinul and Robinul Forte
CFR 314.8(a)(5)(iv)

Gentlemen:

b(4) Reference is made to our updates of manufacturing procedures for [redacted] on May 20, 1977 for our New Drug Application for Robinul and Robinul Forte Tablets. These were approved on July 13, 1977.

b(4)

b(4) The [redacted] The [redacted] for
b(4) Robinul Tablets [redacted] smaller batch size [redacted] b(4)
and the [redacted] for Robinul-PH Tablets provides for a
b(4) [redacted] batch size [redacted]. The [redacted] the
manufacturing procedures have been amended to reflect the new batch
sizes. These new [redacted]

b(4)

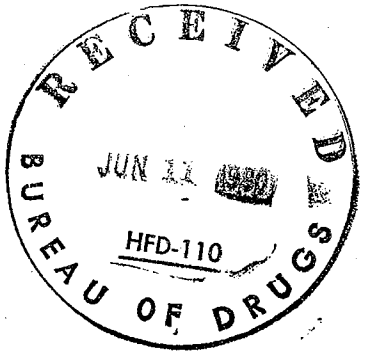
Copies of these are submitted in triplicate for inclusion in our NDA.

Sincerely,

Frances Aaroe

Frances Aaroe

FA/ps
Enclosure



13 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

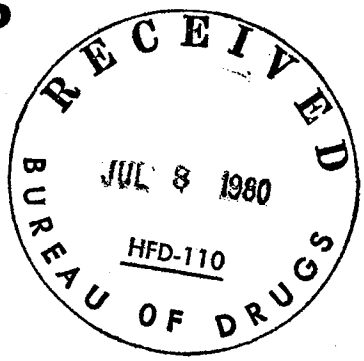
Withheld Track Number: Administrative- 12-827
5025

Frances Aaroe, Manager
Domestic Regulatory Affairs

A. H. Robins Company
1211 Sherwood Avenue
Richmond, Virginia 23220
(804) 257-2502

RESUBMISSION RS 024

A·H·ROBINS



Division of Cardio-Renal
Drug Products
Bureau of Drugs, HFD #110
Document Control Room 16B-30
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

July 3, 1980

ORIGINAL

Re: NDA 12-827/S-024
Robinul and Robinul Forte

Gentlemen:

Reference is made to your letter of April 30, 1980 regarding Supplement 024 to our New Drug Application for Robinul and Robinul Forte.

You requested letters authorizing the agency to refer to the drug master files of all containers. Attached are letters of reference from the following suppliers:

b(4)

(DMF —— b(4)
(DMF —— b(4)
(DMF —— b(4)

You requested that —— specify —— in the manufacture of all containers used —— b(4)
—— Please replace the packaging material specifications —— with the attached Code —— These specifications for the bottles —— indicate —— and other approved suppliers as the source. b(4)

If suppliers other than those listed above are to be used, an appropriate supplement will be made.

Since the bottles of 100 are not intended to be dispensed to consumers and will no longer have child-resistant closures, new labels will contain the statement, "Bulk Container - Not for Household Dispensing." This is in accordance with the CPSC's publication in the Federal Register of March 23, 1978 (copy attached) on interpretation of the Poison Prevention Act of 1970. Twelve copies of each label will be submitted as soon as available.

Sincerely,

Frances Aaroe

Frances Aaroe

dwm

4 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Administrative- 12-827
5024

01]

APTER II—CONSUMER PRODUCT SAFETY COMMISSION

SUBCHAPTER E—POISON PREVENTION PACKAGING ACT OF 1970 REGULATIONS

PART 1701—STATEMENTS OF POLICY AND INTERPRETATION

Prescription Drugs Distributed to Pharmacies

AGENCY: Consumer Product Safety Commission.

ACTION: Final rule.

SUMMARY: The Consumer Product Safety Commission is amending its regulations to add an interpretation under the Poison Prevention Packaging Act to require that all prescription drugs subject to a child-resistant packaging standard that are distributed to pharmacies shall be in child-resistant packaging if the immediate packages in which the drugs are distributed by the manufacturers are intended to be the packages in which the drugs are dispensed to the consumer. The regulation is necessary to insure that the pharmacist will actually dispense the drug in the proper package. The Commission has received inquiries that indicate that some manufacturers may not be aware of the proper interpretation of the act.

DATES: This statement of policy and interpretation is effective March 23, 1978.

FOR FURTHER INFORMATION CONTACT:

Wade Anderson, Directorate of Compliance and Enforcement, Consumer Product Safety Commission, Washington, D.C. 20207, 301-492-6760.

SUPPLEMENTARY INFORMATION: Section 3 of the Poison Prevention Packaging Act of 1970 ("the act"), 15 U.S.C. 1472, authorizes the establishment of standards requiring "special packaging" for certain household substances in order to protect children from serious personal injury or serious illness resulting from handling, using, or ingesting such substances. "Special packaging" is packaging that is designed or constructed to be: (1) Significantly difficult for children under 5 years of age to open or obtain a toxic or harmful amount of the substance contained therein within a reasonable time, and (2) not difficult for normal adults to use properly (15 U.S.C. 1471(4)). A "household substance" is one which is customarily produced or distributed for sale for consumption or use, or customarily stored, by individuals in or about the household.

In the FEDERAL REGISTER of April 16, 1973 (38 FR 9431, 9432), a regulation (now 16 CFR 1700.14(a)(10)) was issued that requires that all oral prescription human drugs be supplied in special packaging. In the preamble to that notice, the criterion for determining when a manufacturer has the obligation for providing special packaging for an item that will be dispensed pursuant to the order of a licensed medical practitioner was stated as follows:

> "• • • the person who *places* a household substance subject to these standards *into* a container must determine if that container is in fact a package in which the substance may be delivered to the consumer for use or storage in the household. If it is, these standards apply. The responsibility, however, for *repackaging* (bulk) prescription drugs in accordance with those standards rests with the individual dispensing such substances at the retail level" [emphasis supplied].

Manufacturers of prescription drugs generally package them in different types of packages, depending on whether the manufacturer intends that the original package will be the one in which the drug is ultimately given to the consumer or whether it is intended that the drug will be repackaged before it is dispensed to the consumer. If the drug is intended by the manufacturer to be repackaged (bulk package), the manufacturer need not utilize special packaging.

The policy of the Consumer Product Safety Commission and the Food and Drug Administration, which preceded the Commission in administering the Poison Prevention Packaging Act, has uniformly been that all prescription drugs subject to a special packaging standard that are distributed to pharmacies shall be in special packaging if the immediate package in which the drugs are distributed by the manufacturer is intended to be the package in which the drugs are dispensed to the consumer. Whether a manufacturer intends that a package will be the one in which the drugs are dispensed to the consumer can be determined from the type of package, whether the ancillary instructions provided on the package (such as for storage, handling, or use) are intended for consumers, and other factors. Bulk packages of drugs that are intended to be repackaged by the pharmacist for dispensing to consumers need not, of course, consist of special packaging. Such drugs must, however, be placed in special packaging by the pharmacy at the time of dispensing to the consumer unless, pursuant to section 4(b) of the act, the prescribing practitioner orders, or the purchaser requests, otherwise.

The Commission believes that this interpretation of the manufacturer's responsibility is necessary in order to insure that the pharmacist will actually dispense the drug in the proper package. If manufacturers were to place prescription drugs in packages that are intended for consumers but that do not comply with the standard, it is likely that these drugs would be distributed to consumers in such noncomplying packaging regardless of whether such packaging was ordered by the prescribing practitioner or requested by the consumer. The Commission believes such a likelihood exists because, unlike bulk-packaged drugs that must be repackaged, drugs placed in consumer packages by manufacturers in many instances cannot be repackaged without some inconvenience and ordinarily need only be labeled by the pharmacy before they can be dispensed to a consumer. The legislative history of the act shows that it was the intent of the act for special packaging to be the rule and not the exception.

The Commission has received inquiries that indicate that some manufacturers may not be aware of the proper interpretation of the act as expressed in this policy. Therefore, in order to assist manufacturers of prescription drugs in discharging their responsibilities under the act concerning such drugs that are distributed to pharmacies, the Consumer Product Safety Commission has codified (in § 1701.1) the following statement of its policy concerning which packages of prescription drugs must consist of "special" (child-resistant) packaging that complies with the standards in 16 CFR 1700.15.

Manufacturers should also note that section 4(a) of the act (which allows manufacturers to package a single size of a regulated product in noncomplying packaging under certain circumstances) does not apply to substances subject to section 4(b) of the act. Thus, since the section 4(a) single-size exemption for over-the-counter drugs and other household substances does not apply to prescription drugs, every unit of a prescription drug subject to a special packaging standard which is distributed by the manufacturer to a pharmacy in a package intended to be dispensed to a consumer shall be in special packaging. A pharmacy may, however, upon the request of a patient or an order of the medical practitioner prescribing the drug, convert the packaging to conventional (noncomplying) packaging or repackage it in such packaging.

This statement of policy and interpretation, which merely codifies a long-standing Commission policy, is being issued as § 1701.1 of a new Part 1701, which will also contain any future statements of policy and interpretation concerning the Poison Prevention Packaging Act of 1970. Since § 1701.1 is an interpretive rule and a statement of policy, the provisions of the Administrative Procedure Act (5 U.S.C. 553) relating to notice of proposed rulemaking, opportunity for

comment, and delayed effective date do not apply, and §1701.1 will become effective immediately.

Therefore, under provisions of the Poison Prevention Packaging Act of 1970 (secs. 2-4, Pub. L. 91-601, 84 Stat. 1670, 1671; 15 U.S.C. 1471-1473) and the Federal Food, Drug, and Cosmetic Act (sec. 701(a), 52 Stat. 1055, 21 U.S.C. 371(a)) and by the authority granted by the Consumer Product Safety Act (sec. 30(a), Pub. L. 92-573, 86 Stat. 1231; 15 U.S.C. 2079(a)), the Commission amends Title 16, Chapter II, of the Code of Federal Regulations by adding to Subchapter E a new Part 1701 reading as follows:

Sec.
1701.1 Special packaging for substances subject to a standard that are distributed to pharmacies to be dispensed pursuant to an order of a licensed medical practitioner.

AUTHORITY: Secs. 2-4, Pub. L. 91-601, 84 Stat. 1670, 1671 (15 U.S.C. 1471-1473); sec. 701(a), 52 Stat. 1055 (21 U.S.C. 371(a)).

§1701.1 Special packaging for substances subject to a standard that are distributed to pharmacies to be dispensed pursuant to an order of a licensed medical practitioner.

(a) In order to assist manufacturers of prescription drugs in discharging their responsibilities under the act concerning such drugs that are distributed to pharmacies, the Consumer Product Safety Commission has codified this statement of its policy concerning which prescription drug packages supplied by manufacturers to pharmacies must comply with the "special" (child-resistant) packaging requirements contained in 16 CFR 1700.15.

(b) Manufacturers of prescription drugs may package such drugs for distribution to pharmacies in different types of packages, depending on whether the manufacturer intends that the package will be the one in which the drug is ultimately given to the consumer or whether it is intended that the pharmacist will repackage the drug before it is dispensed to the consumer. If the drug is supplied in a bulk package from which individual prescriptions are intended to be repackaged by the pharmacist, the manufacturer need not utilize special packaging. However, the Commission interprets the provision of the act as requiring that all prescription drugs subject to a special packaging standard that are distributed to pharmacies shall be in special packaging if the immediate package in which the drugs are distributed by the manufacturer is intended to be the package in which the drugs are dispensed to the consumer. Examples of such packages include mnemonic dispensing devices; dropper bottles; packages with "tear off" labels; packages which incorporate ancillary instructions for consumer handling, storage, or use on permanently affixed portions of their labels; and products intended to be reconstituted in their original containers. The Commission believes that this interpretation is necessary in order to insure that the pharmacist will actually dispense the drug in the proper package. If the pharmacist receives a request from the consumer or an order from the prescribing medical practitioner for conventional (noncomplying) packaging, section 4(b) of the act permits the pharmacist to convert the package to conventional packaging or repackage the drug in conventional packaging.

(c) Manufacturers should also note that section 4(a) of the act (which allows a product to be marketed in noncomplying packaging of a single size under certain circumstances) does not apply to prescription drugs subject to section 4(b) of the act. Thus, since the section 4(a) single-size exemption for over-the-counter drugs and other household substances does not apply to prescription drugs, every unit of a prescription drug subject to a special packaging standard which is distributed to a pharmacy in a package intended by the manufacturer to be dispensed to a consumer shall be in special packaging.

(d) Nothing in this statement of policy and interpretation should be interpreted as relieving the pharmacist of the responsibility of insuring that all prescription drugs subject to a special packaging standard are dispensed to the consumer in special packaging unless otherwise ordered by the prescribing practitioner or otherwise requested by the consumer.

Effective date: This part is effective March 23, 1978.

Dated: March 16, 1978.

SADYE E. DUNN,

Acting Secretary, Consumer Product Safety Commission.

[FR Doc. 78-7690 Filed 3-22-78; 8:45 am]

[8010-01]

Title 17—Commodity and Securities Exchanges

CHAPTER II—SECURITIES AND EXCHANGE COMMISSION

[Release No. 34-14570]

PART 200—ORGANIZATION; CONDUCT AND ETHICS; AND INFORMATION AND REQUESTS

Delegation of Authority to the Director of the Division of Market Regulation

AGENCY: Securities and Exchange Commission.

ACTION: Final rule amendment.

SUMMARY: The Commission today announced the amendment of its Rules of Organization to delegate to the Director of the Division of Market Regulation limited authority to exempt SECO broker-dealers from the Commission's regulations governing the participation of a SECO broker-dealer in the public offering of its own securities or those of an affiliate. The delegation of authority will extend only to exemptions for public offerings of debt securities issued by an affiliate of a SECO broker-dealer.

EFFECTIVE DATE: March 16, 1978.

FOR FURTHER INFORMATION CONTACT:

Charles M. Horn, Esquire, Office of Chief Counsel, Division of Market Regulation, Securities and Exchange Commission, 500 North Capitol Street, Washington, D.C. 20549, 202-755-8747.

SUPPLEMENTARY INFORMATION: Securities Exchange Act Rule 15b10-9 (17 CFR 240.15b10-9) establishes standards for the participation by a broker-dealer which is not a member of a national securities association (a "SECO broker-dealer") in the public offering of its own or an affiliate's securities. Paragraph (d) of that Rule allows the Commission to grant exemptions from the provisions of the Rule if the proposed activities of the SECO broker-dealer do not fall within the intended meaning and purpose of the Rule. The Commission has granted conditional exemptions to SECO broker-dealers participating in the distribution of debt securities issued by affiliates of such broker-dealers and believes that those exemptions offer sufficiently clear guidance to warrant a delegation of its authority to the Director of the Division of Market Regulation. Moreover, by delegating its authority, the Commission also believes it will facilitate the processing, under the Securities Act of 1933, of registration statements for debt securities offered by a SECO broker-dealer affili-