CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-416

Chemistry Review(s)

CDER CHEMISTRY REVIEW

NDA 21-416

Rythmol SR (propafenone hydrochloride)
Capsules 225 mg, 325 mg, 425 mg

Abbott Laboratories Pharmaceutical Products
Division of Abbott Laboratories

Kathleen E. Jongedyk

Cardio-Renal Drug Products
HFD-110

Table of Contents

Chemistry Review Data Sheet

1. NDA 21-416

2. REVIEW #: 2

3. REVIEW DATE: December 23, 2002

4. REVIEWER Kathleen E. Jongedyk

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
NDA 21-416 Original Submission	15-Mar-2002

6. SUBMISSION (S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment NDA Submission	03-Dec- 2002 19-Dec-2002 20-Dec-2002

7. NAME & ADDRESS OF APPLICANT:

Name:	Abbott Laboratories
Address:	D-491/AP30-1E, 200 Abbott Park Road, Abbott Park, Illinois 60064-6157
Representative:	Marilou Reed
Telephone	(847) 937-6844

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Rythmol SR
b) Non-Proprietary Name (USAN): Propafenone Hydrochloride
c) Code Name/# (ONDC only):
d) Chem. Type/Submission Priority (ONDC only):
- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: N/A

10. PHARMACOL. CATEGORY: A Class 1C Antiarrythmic drug

11. DOSAGE FORM: Extended Release Capsules

12. STRENGTH/POTENCY: 225 mg, 325 mg, and 425 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: X Rx ___OTC

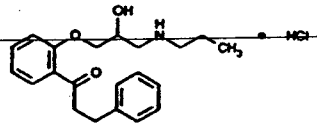
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product – Form Completed

__X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

USAN Name
1-Propanone, 1-[2-[2-hydroxy-3 –(propylamino)propoxylphenyl]-3-phenyl hydrochloride

Molecular Formula: $C_{21}H_{27}NO_3$ .HCl Molecular Weight: 377.91



17. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

Table 1 shows the packaging materials with their corresponding manufacturer names and references.

DMF	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
	III LOA 10/24/01			3	Adequate	09-01-99	N/A
	III LOA 10/24/01			3	Adequate	04-29-02	N/A
	III LOA 10-24-01			3	Adequate	05-22-00	N/A
	III LOA 10-26-01			3	Adequate	04-29-02	N/A
				4	Adequate	8-06-02	N/A
	III LOA 11-12-01			4	Adequate	03-30-99	N/A
	III LOA 10-31-01			3	Adequate	04-23-98	N/A
	III LOA 03-11-02			3	Adequate	06-16-00	N/A
	III			4	Adequate	04-29-02	N/A
	III			4	Adequate	8-14-02	N/A

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF

3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

Table 2 shows additional related documents that describe the drug substance and drug product..

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
New Drug Application	19-151	Immediate release tablets Rythmol (propafenone hydrochloride) Tablets 150 mg ,225 mg and 300 mg
IND	54,536	Propafenone SR Capsules
IND	17,189	Propafenone Hydrochloride Tablets

18. STATUS

ONDC
Table 3 shows the status of supportive reviewers, facility inspections, trade name acceptance and method validation.

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A	N/A	N/A
EES	Acceptable	12-Dec-02	S. Adams
Pharm/Tox.	N/A	N/A	N/A
Biopharm.	Acceptable with dissolution changes	23-Dec-02	Elena V. Mishina
LNC	N/A	N/A	N/A
Methods Validation	To be submitted pending finalization of dissolution.		Kathleen E. Jongedyk
OPDRA	Acceptable	13-May-02	Carol Holquist, RPh
EA	Granted a Categorical Exclusion from EA prep	30-Jul-02	Kathleen E. Jongedyk
Microbiology	N/A	N/A	N/A

The Chemistry Review for NDA 21-416

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Recommend that NDA 21-416 be approved from the standpoint of chemistry, manufacturing and controls.
All CMC deficiencies cited in review #1were satisfactorily resolved.

As per discussions with the medical officer, a statement in the labeling should include that patients should swallow the capsule as a whole and the capsule should not be opened and individual microtablets chewed.

The Office of Compliance has provided an overall acceptable Establishment Inspection Reports for the four analytical and manufacturing facilities.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Propafenone SR Capsules, a sustained release dosage form, are manufactured as 225 mg, 325 mg, and 425 mg capsules which are indicated for use in prolong the time of — recurrence of symptomatic — atrial fibrillation in — patients — without structural heart disease.

Propafeone SR Capsules consist of essentially identical microtablets filled into hard gelatin capsules. The microtablets control the dissolution rate release of Propafenone Hydrochloride by erosion. The microtablets 2 mm 2 mm, nearly spherical particles are — — hydroxypropylmethyl cellulose, and — magnesium stearate. There are no auxiliary controlled release excipients. The — hydroxypropylmethyl cellulose has no effect on the dissolution rate. Microtablets less then — do not give the desired dissolution release profile. Because Propafenone Hydrochloride is difficult to compress with other excipients, tablets can not be made with more than — which does not give the required dissolution rate for the desired pharmaceutical effect.. The dissolution rate is independent of the compression force in tableting and pH of dissolution medium.

Propafenone SR Capsules are available in white, opaque, hard gelatin capsules containing 225 mg, 325 mg, and 425 mg of propafenone hydrochloride and imprinted in red the corporate logo and color coded for dosage strengths: "225" mg capsule white, "325" mg capsules white with one red line ¾ around the circumference of capsule body and "425" mg white with three red lines ¾ around the circumference capsule body.

Propafenone SR Capsules are packaged in HDPE bottles of 100 count with child resistant closures, and induction seals, — blister hospital packages of HUD 100 in strips of 10, and physician samples — blister card of 7 capsules. The suitability of the container closure systems is supported by 21 CFR usage regulations for materials in contact with foods and acceptable stability data for — 25°C/60%RH using these container closure systems.

Propafenone SR Capsules manufacturing steps include

Propafenone SR Capsules in-process tests are adequate for tableting and encapsulation to ensure consistent reproducibility of essentially identical microtablets and desired strengths of each capsule.

Propafenone SR Capsules regulatory release methods are fully validated to ensure the strength, identity, and purity. The purity method HPLC control impurities at the [redacted] level. Dissolution method provides consistent values at the [redacted] 4 hour, [redacted] as shown by profile data. The dissolution method [redacted] although data provided shows rate release is independent of pH.

Propafenone SR Capsules exceptional chemical purity is supported by stability data for [redacted] stored at 25°C/60%RH and [redacted] at 40°C /75% RH.

Propafenone Hydrochloride [redacted] is a racemic mixture of (S) and (R) enantiomer is made by chemical synthesis and has USP monograph. Abbott Laboratories indicates they have modified the USP requirements and designates the drug substance as an in-house monograph with alternate methods. Abbott Laboratories provides the [redacted] specifications [redacted] to be used to make Propafenone SR Capsules. The complete drug substance manufacture and control information is referenced to NDA 19-151 Propafenone Immediate Release Tablets.

Propafenone Hydrochloride drug substance is chemical purity and the acceptance criteria are supported by [redacted] stored at 30°C/70%RH and [redacted] 40°C/75%RH as well as the assigned [redacted] expiration date and [redacted] retest date.

The proposed proprietary name for the drug product is Rythmol SR is acceptable by the Division of Medication Errors and Technical Support, Office of Drug Safety (DMET: HFD-420).

B. Description of How the Drug Product is Intended to be Used

"Dosage and Administration" section recommends dose therapy be initiated at 225 mg of Propafenone SR Capsules given every 12 hours. The dosage may be increased at a minimum of 5-day intervals to 325 mg, every 12 hours. If additional therapeutic effect is needed, the dose may be increased up to 425 mg given every 12 hours. Propafenone SR (propafenone hydrochloride) Capsules 225 mg, 325 mg, and 425 mg are available in bottles of 100 count and hospital blister of 100, in strips of 10, and physician samples in blister cards of 7 count.

Propafenone SR Capsules recommended storage statement is

"Storage: Store at 25°C (77° F); excursions permitted to 15-30°C (59-86°F) [See USP controlled room temperatures]. Dispense in tight container as defined in the USP."

Propafenone SR Capsules stability studies provide [redacted] acceptable stability that supports the 24 month expiration date stored at 25°C/60%RH and protected from moisture. The drug substance has [redacted] acceptable stability data stored at 30°C/60%RH with no increase in impurities reported. The drug product, [redacted] has acceptable stability data for [redacted] stored at 25°C/60% RH and for [redacted] at 40°C/75%RH with zero degradation products report.

C. Basis for Approvability or Not-Approval Recommendation

Recommend that NDA 21-416 be approved based on the Chemistry, Manufacturing, and Control information. The deficiencies identified in chemist review #1 were resolved. The Division of Biopharmaceuticals and Pharmaceutics has resolved the dissolution method issues.

Risk management steps taken N/A

III. Administrative

A. Reviewer's Signature

/S/

B. Endorsement Block

ChemistName/Date:	Kathleen E. Jongedyk, December 23, 2002
ChemistryTeamLeaderName:	Kasturi Srinivasachar Ph.D.
ProjectManagerName:	Russell Fortney

C. CC Block

Redacted 20

pages of trade

secret and/or

confidential

commercial

information

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Nallaperumal Chidambaram
12/27/02 11:28:09 AM
CHEMIST
This review is being placed into DFS on behalf
of Ms. Kathleen E. Jongedyk, Chemistry Reviewer.

John Simmons
12/27/02 12:14:33 PM
CHEMIST
for K Srinivasachar

CDER CHEMISTRY REVIEW CDER

NDA 21-416

Rythmol SR (propafenone hydrochloride)
Capsules 225 mg, 325 mg, 425 mg

Abbott Laboratories Pharmaceutical Products
Division of Abbott laboratories

Kathleen E. Jongedyk

Cardio-Renal Drug Products
HFD-110

Table of Contents

Chemistry Review Data Sheet

1. NDA 21-416

2. REVIEW #: 1

3. REVIEW DATE: August 31, 2002

4. REVIEWER: Kathleen E. Jongedyk

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
None	

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original NDA Submission	March 15, 2002

7. NAME & ADDRESS OF APPLICANT:

Name:	Abbott Laboratories
Address:	D-491/AP30-1E, 200 Abbott Park Road, Abbott Park, Illinois 60064-6157
Representative:	Marilou Reed
Telephone	(847) 937-6844

Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: Rythmol SR
b) Non-Proprietary Name (USAN): Propafenone Hydrochloride
c) Code Name/# (ONDC only):
d) Chem. Type/Submission Priority (ONDC only):
- Chem. Type 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: N/A

10. PHARMACOL. CATEGORY: A Class 1C Antiarrythmic drug

11. DOSAGE FORM: Extended Release Capsules

12. STRENGTH/POTENCY: 225 mg, 325 mg, and 425 mg

13. ROUTE OF ADMINISTRATION: Oral

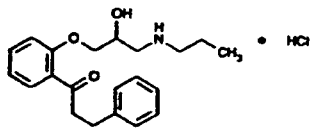
14. Rx/OTC DISPENSED: _X_Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
_____SPOTS product – Form Completed

__X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:
1-Propanone, 1-[2-[2-hydroxy-3 –(propylamino)propoxylphenyl]-3-phenyl hydrochloride

Molecular Formula C_{21} H_{27} $N0_3$ .HCl Molecular weight 377.92



17. RELATED/SUPPORTING DOCUMENTS:

18. **DMFs:**

Table 1 shows the packaging materials with their corresponding manufacturer names.

DMF	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS	DATE REVIEW COMPLETED	COMMENTS
	Adequate			3	Adequate	09-01-99	N/A
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	III LOA 10-24-01			3	Adequate	05-22-00	N/A
	III LOA 10-26-01			3	Adequate	04-29-02	N/A
	III			4	Adequate	8-06-02	N/A
	III LOA 11-12-01			4	Adequate	03-30-99	N/A
	III LOA 10-31-01			3	Adequate	04-23-98	N/A
	III LOA 03-11-02			3	Adequate	06-16-00	N/A
	III			4	Adequate	04-29-02	N/A
				4	Adequate	8-14-02	N/A

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
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6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

17. RELATED/SUPPORTING DOCUMENTS:

B. Other Documents:

Table 2 shows additional related documents that describe the drug substance and drug product.

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
New Drug Application	19-151	Immediate release tablets Rythmol (propafenone hydrochloride) Tablets 150 mg 225 mg and 300 mg
IND	54,536	Propafenone SR Capsules
IND	17,189	Propafenone Hydrochloride Tablets

19. STATUS:

Table 3 shows the status of supportive reviewers, facility inspections, trade name acceptance and method validation.

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics	N/A	N/A	N/A
EES	Pending	August 16, 2002	Shirnett Ferguson
Pharm/Tox.	N/A	N/A	N/A
Biopharm.	Pending	August, 16, 2002	Elena V. Mishina
LNC	N/A	N/A	N/A
Methods Validation	To be submitted	To be submitted	Kathleen E. Jongedyk
OPDRA	Rythmol Trade Name Acceptable	May 13, 2002	Carol Holquist, RPh
EA	Granted a Categorical Exclusion from EA prep	July 30, 2002	Kathleen E. Jongedyk
Microbiology	N/A	N/A	N/A

The Chemistry Review for NDA 21-416

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

Approvable from the standpoint of chemistry, manufacturing and controls information pending resolution of deficiencies and satisfactory completion of facilities evaluations. See VIII Draft Deficiency Letter. These informational requests will be sent to Abbott Laboratories

Methods validation will be submitted after the CMC deficiencies have been addressed .

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

Not applicable.

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

Propafenone SR Capsules a sustained release dosage form is manufactured as 225 mg, 325 mg, and 425 mg capsules which are indicated for use in prolonging the time of recurrence of symptomatic — for atrial fibrillation in — patients with — atrial arrhythmia without structural heart disease.

Propafeone SR Capsules consist of essentially identical microtablets filled into hard gelatin capsules. The microtablets control the dissolution rate release of Propafenone Hydrochloride by erosion. The microtablets 2 mm 2 mm nearly spherical particles are — hydroxypropylmethyl cellulose, and magnesium stearate. There are no auxiliary controlled release excipients. The hydroxypropylmethyl cellulose has no effect on the dissolution rate. Microtablets less then — do not give the desired dissolution release profile. Because Propafenone Hydrochloride is difficult to compress with other excipients, tablets can not be made with more than — , which does not give the required dissolution rate for the desired pharmaceutical effect.. The dissolution rate is independent of the compression force in tableting and pH of dissolution medium.

Propafenone SR Capsules are available in white, opaque, hard gelatin capsule containing 225 mg, 325 mg, and 425 mg of Propafenone hydrochloride and imprinted in red with the corporate logo and color coded for dosage strengths: "225" mg capsule white, "325" mg capsules white with one red line ¾ around the circumference of capsule body and "425" mg white with three red lines ¾ around the circumference capsule body.

Propafenone SR Capsules are packaged in HDPE bottles of 100 count with child resistant closures, and induction seals, — blister hospital packages of HUD 100 in strips of 10, and physician samples — blister card of 7 capsules. The suitability of the container closure systems is supported by 21 CFR usage regulations for materials in contact with foods and acceptable stability data for — stored at 25°C/60%RH using these container closure systems.

Propafenone SR Capsules manufacturing steps include: C

]

Propafenone SR Capsules in-process tests are adequate for tableting and encapsulation to ensure consistent reproducibility of essentially identical microtablets and desired strengths of each capsule and provide a final encapsulation step for —% weighing of each capsule.

Propafenone SR Capsules analytical methods are fully validated to ensure the strength, identity, and purity. The purity methods HPLC control impurities at the —% level. Dissolution method provides consistent values at the — 4 hours, and — as shown by profile data. These test intervals are to be revised; for example, 2 hour, 4 hour, and 12 hour. The dissolution method has —, although data provided shows rate release is independent of pH of the dissolution media.

Propafenone SR Capsules exceptional chemical purity is supported by stability data for — stored at 25°C/60%RH and — at 40°C /75% RH.

Propafenone Hydrochloride — a racemic mixture of (S) and (R) enantiomer, is made by chemical synthesis and has a USP monograph. Abbott Laboratories indicates they have modified the USP methods and designated the drug substance specification grade as an in-house monograph. Abbott Laboratories methods differ from the USP compendial methods, and therefore will be designated as alternate methods. Abbott Laboratories provides the — specifications — to be used to make Propafenone SR Capsules in NDA 21-416. The complete drug substance manufacture and control information is referenced to NDA 19-151 Propafenone Immediate Release Tablets.

Propafenone Hydrochloride drug substance is chemically pure and data on the drug substance (— stored at 30°C/70%RH and — 40°C/75%RH) support the assigned — expiration date and — retest date.

The proposed proprietary name for the drug product is Rythmol SR is acceptable by the Division of Medication Errors and Technical Support, Office of Drug Safety (DMET: HFD-420.)

B. Description of How the Drug Product is Intended to be Used

"Dosage and Administration" section recommends dose therapy be initiated at 225 mg of Propafenone SR Capsules given every 12 hours. The dosage may be increased at a minimum of 5-day intervals to 325 mg, every 12 hours. If additional therapeutic effect is needed, the dose may be increased up to 425 mg given every 12 hours. Propafenone SR (propafenone hydrochloride) Capsules 225 mg, 325 mg, and 425 mg are available in bottles of 100 count and hospital blister of 100, in strips of 10, and physician samples in

blister cards of 7 count. The extended release drug product is designated to release the active component over an extended period of time to maintain more consistent blood level to obtain the desired therapeutical effect. The immediate release Propafenone Tablets recommended dosing schedule is once every 8 hours.

Propafenone SR Capsule expiration date is 24 months when stored at the recommended storage conditions.

"Storage: Store at 25°C (77° F); excursions permitted to 15-30°C (59-86°F) [See USP controlled room temperatures]. Dispense in tight container as defined in the USP."

C. Basis for Approvability or Not-Approval Recommendation

NDA 21-416 is Approvable from the standpoint of chemistry, manufacturing and controls information. However, there are some relatively minor deficiencies that do not pose a significant risk for the drug product. These deficiencies that can be resolved in a relatively short time since they do not require additional studies. In addition the acceptable cGMP status of all facilities must be ascertained for the application can be approved.

III. Administrative

A. Reviewer's Signature

/S/

B. Endorsement Block

ChemistName/Date:	Kathleen E. Jongedyk August 31, 2002
ChemistryTeamLeaderName:	Kasturi Srinivasachar, Ph.D.
ProjectManagerName:	Russell Fortney

C. CC Block

Redacted 54

pages of trade secret and/or confidential commercial information

ESTABLISHMENT EVALUATION REQUEST

SUMMARY REPORT

Application : NDA 21416/000
Org Code : 110
Priority : 3S
Stamp Date : 15-MAR-2002
PDUFA Date : 15-JAN-2003
Action Goal :
District Goal: 16-NOV-2002

Sponsor: ABBOTT LABS
200 ABBOTT PARK RD DEPT 491 BLDG AP30
1E
ABBOTT PARK, IL 600646157

Brand Name : RYTHMOL SR (PROPAFENONE HCL)
CAPSULES
Estab. Name:
Generic Name: PROPAFENONE HCL
225MG/325MG/425MG
Dosage Form: (CONTROLLED RELEASE CAPSULE)
Strength : 225MG, 325MG, AND 425MG

FDA Contacts: K. JONGEDYK Review Chemist (HFD-110) 301-594-5300
K. SRINIVASACHAR Team Leader (HFD-110) 301-594-5376

--Overall Recommendation: ----------

Establishment : CFN : 9610142 FEI : 3002807401
ABBOTT GMBH & CO. KG
KNOLLSTRASSE
LUDWIGSHAFEN AM RHEIN, , GM

DMF No: AADA:

Responsibilities: DRUG SUBSTANCE RELEASE TESTER
FINISHED DOSAGE MANUFACTURER

Profile : CTL OAI Status: NONE
Last Milestone: INSPECTION SCHEDULED
Milestone Date: 29-OCT-02

:

:

Profile : CTR OAI Status: NONE

Last Milestone: INSPECTION PERFORMED

Milestone Date: 29-OCT-02

:

:

Establishment : CFN : 2211084 FEI : 2211084

ABBOTT LABORATORIES

30 NORTH JEFFERSON RD

WHIPPANY, NJ 07981

DMF No: AADA:

Responsibilities: FINISHED DOSAGE LABELER

FINISHED DOSAGE OTHER TESTER

FINISHED DOSAGE PACKAGER

Profile : CTR OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 03-MAY-02

Decision : ACCEPTABLE

Reason : DISTRICT RECOMMENDATION

ESTABLISHMENT EVALUATION REQUEST

SUMMARY REPORT

Establishment : CFN : [redacted] FEI : 1049418

DMF No: AADA:

Responsibilities:

Profile : CTL OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 02-APR-02

Decision : ACCEPTABLE

Reason : BASED ON PROFILE

Establishment : CFN : 9692017 FEI : 3002807399

KNOLL AG

P.O. BOX 631, CH 4410

LIESTAL, , SZ

DMF No: AADA:

Responsibilities: DRUG SUBSTANCE MANUFACTURER

DRUG SUBSTANCE RELEASE TESTER

Profile : CSN OAI Status: NONE

Last Milestone: OC RECOMMENDATION

Milestone Date: 07-OCT-02

Decision : ACCEPTABLE

Reason : DISTRICT RECOMMENDATION

IV. ENVIRONMENTAL ASSESSMENT (Acceptable)

Abbott Laboratories under 21 CFR 25.31 (a) claims a categorical exclusion from filing of an environmental assessment based on the approval of the application which does not increase that use of the Propafenone Hydrochloride activity moiety. NDA 21-416 Propafenone SR Capsules provides a new dosage form of an already approved drug Propafenone IR Tablets (propafenone hydrochloride) NDA 19-151. Propafenone SR Capsules, the new dosage form, can be used as an alternate to the already approved dosage form thereby not increasing the use of the Propafenone Hydrochloride active moiety.

V. METHODS VALIDATION (Acceptable)

The analytical methods for the drug substance were validated for NDA 19-151, Abbott Laboratories provides for the method validation package of the drug product that are ready to be sent to FDA laboratories to assess the validation information and suitability of the test methods to performs as described. Analytical methods for validation are identification, content, and related substance determined by the same HPLC method and the dissolution USP method.

VI. LABELING (Acceptable with Comment)

Vol. 1, pp. 2-1 through 3-43A

Draft labeling provided for:

1. DRAFT PACKAGE INSERT

2. DRAFT 100 -CAPSULE BOTTLE LABEL COPY

3. DRAFT SINGLE CAPSULE PRINT MAT COPY

4.. UNIT DOSE CARTON Draft Seven Capsule Sample print

The package insert meets the requirements of 21 CFR 201.57

The labels and labeling meet the requirements of 21 CFR 201.1

The same Recommend Storage Statement appears on all labeling.

> "Storage: Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F) [see USP controlled room temperatures]" "Dispense in a tight container as defined in the USP."

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Nallaperumal Chidambaram
12/27/02 11:25:51 AM
CHEMIST
This review is being placed into DFS on behalf
of Ms. Kathleen E. Jongedyk, Chemistry Reviewer.

John Simmons
12/27/02 12:11:48 PM
CHEMIST
for K Srinivasachar