DIVISION OF CARDIO-RENAL DRUG PRODUCTS
FOOD AND DRUG ADMINISTRATION

US Mail address:
FDA/CDER/HFD-110
5600 Fishers Lane
Rockville, MD 20857

Woodmont II
1451 Rockville Pike
Rockville, MD 20852

Transmitted to FAX Number:	908-542-9405
Attention:	**Mr. Robert J. Mandetta**
Company Name:	Reliant Pharmaceuticals
Phone:	908-542-4429
Subject:	Minutes of 8/1/01 Telecon
Date:	8/27/01
Pages including this sheet:	7

From: **Zelda McDonald**
Phone: **301-594-5333**
Fax: **301-594-5494**

You are responsible for notifying us of any significant differences in understanding you may have regarding the meeting outcomes (as reflected in the minutes).

PLEASE LET ME KNOW YOU RECEIVED THIS. THANKS!

Minutes of a Meeting

Meeting Date:	June 4, 2001
Date Requested:	April 27, 2001
Date Confirmation Faxed:	May 7, 2001
Date Background Received:	May 18, 2001
Type:	Guidance
Classification:	C
IND:	[redacted] (propranolol hydrochloride)
Sponsor:	Reliant Pharmaceuticals, Inc.
Meeting Chair:	Kasturi Srinivasachar
Meeting Recorder:	Zelda McDonald
External Participant Lead:	Keith Rotenberg

FDA

Hasmukh Patel, Ph.D.	Deputy Director, Division of New Drug Chemistry I, HFD-810
Kasturi Srinivasachar, Ph.D.	Team Leader, HFD-810
Stuart Zimmerman, Ph.D.	Chemist, HFD-810
Angelica Dorantes, Ph.D.	Pharmacokineticist, HFD-86
Zelda McDonald	Regulatory Health Project Manager, HFD-110

Reliant

George Bobotas, Ph.D.	Vice President, Scientific Affairs
Keith Rotenberg, Ph.D.	Senior Advisor, Regulatory Affairs
Paulette Kosmoski	Director, Regulatory CMC
Goff Baker	Manager, Quality Assurance & Quality Control

Eurand America

Bhanu Balasubramaniam, RAC	Regulatory Specialist
Bela Nanavaty	Analytical Manager

Background:

— is a new formulation of propranolol (HCl). — oral capsule formulation is a combination of two types of release mechanism for spherical beads containing the active substance; one allows immediate release, and the other allows both a delayed and a sustained release of propranolol HCl. When taken in the evening around dinner time, the immediate and the delayed/sustained release of propranolol is intended to attenuate the early morning circadian increases in blood pressure and heart rate. The purpose of this meeting was to discuss the Chemistry, Manufacturing and Controls (CMC) development work of the sustained release drug product, — Capsules.

Meeting:

Reliant explained that Reliant is the sponsor of this application, ——— — that will put the NDA together, Eurand is in charge or research and development and . — ——— will do — studies. Following a brief presentation, Reliant's questions were discussed.

Discussion Points/Agreements Reached:

1. Are the release specifications and test methods for the drug product acceptable to FDA to support the NDA?

   - The Division stated that the test parameters were adequate but the acceptance criteria could not be commented on at this time. The Division requested that Reliant have a more specific identification test ——— The Division asked if any impurities/degradation products had been identified. Reliant stated that they were being monitored now and will be identified. Reliant will proposed suitable specifications for them in the NDA.

   - The Division stated the dissolution test methods, on their face, seemed acceptable. The Division could not specifically comment on dissolution specifications until the data were submitted.

   - When asked, Reliant stated that an in vivo/in vitro correlation had not been done.

2. Are the stability specifications and test methods for the drug product acceptable to FDA to support the NDA?

   - The Division stated that the test parameters seemed to be adequate, however, the acceptability of the methods and specification could only be determined by review of the NDA.

3. Is the Plan A design of the primary NDA stability study acceptable to FDA?

   - The Division was in favor of a combination of Plan A and Plan B as follows:

REDUCED STABILITY PROGRAM (MATRIX/BRACKETING DESIGN (Total of 33 batches))

Key (1) = not tested Blank spaces = not available presentation
——— - not placed on stability

4.

Additionally, 6 months supportive stability data under ICH conditions will be available for 2 batches of each strength of pilot scale drug product, at least 10% of full-scale production, in

capsules (total 6 batches). The batches were packaged in blister and plastic bottle, single configuration presentations.

The plan is to submit further accumulated data updates from the ongoing primary and supportive stability studies periodically during the NDA assessment period.

Assuming satisfactory data are generated, Reliant proposes —month expiration dating stored at 25°C. Is this stability database at submission time acceptable to FDA? Is this approach to post submission stability updating acceptable to FDA?

- The Division could not comment on the acceptability of the proposed expiration date before reviewing the data.

- The Division agreed that updating during the submission would be acceptable as long as the information needed was submitted before or up to six months into the review period and not toward the end. Reliant stated that they expected to have one year stability on full production (three batches of each strength) and six months accelerated stability (three batches of each strength) to submit by six months into the review period.

- Reliant asked if anything other than physical/chemical comparisons would be required if they obtained an alternate supplier. The Division stated that stability on the drug substance and the drug product would be needed, e.g., three months accelerated data from 3 batches manufactured with drug substance from the new source in a post-approval supplement.

Other Issues:

1. The Division noted that Reliant should be aware that there may be review issues regarding the Drug Master File. The Division had not reviewed it for purposes of this discussion.

2. It would be helpful if the Reliant provided a good set of specifications (USP) and definitions in the NDA for the packaging materials, e.g., were the CFR sanctions obeyed? This would help with equivalency issues.

3. Reliant should closely identify the critical process control variables involved where there is a change in parameters from the currently used —

Action Item:

Reliant will submit the modified Plan A as part of their minutes of this meeting.

Signature minutes preparer: /S/

Concurrence, Chair: _____

Drafted 4/5/01 Finaled 6/26/01
RD:
Dorantes 6/25/01
Srinivasachar 6/21/01
Zimmerman 6/8/01
Patel Did not respond

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

/s/

Zelda McDonald
6/27/01 02:21:28 PM
CSO
Dr. Srinivasachar signed off on these minutes on 6/27/01.

Redacted 77

pages of trade

secret and/or

confidential

commercial

information

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

Application Information			
NDA 21-438	Efficacy Supplement Type SE-	Supplement Number	
Drug: InnoPran XL (propranolol HCL) Extended Release Capsules		Applicant: Reliant Pharmaceuticals	
RPM: Melissa Robb		HFD-110	Phone # 594-5313
Application Type: ( ) 505(b)(1) **(X)** 505(b)(2)		Reference Listed Drug (NDA #, Drug name): NDA 18-553 Inderal LA (propranolol) Capsules	

❖ Application Classifications:	
• Review priority	**(X)** Standard ( ) Priority
• Chem class (NDAs only)	3
• Other (e.g., orphan, OTC)	NA
❖ User Fee Goal Dates	May 27, 2003
❖ Special programs (indicate all that apply)	**(X)** None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review
❖ User Fee Information	
• User Fee	**(X)** Paid
• User Fee waiver	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception	( ) Orphan designation ( ) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes **(X)** No
• This application is on the AIP	( ) Yes **(X)** No
• Exception for review (Center Director's memo)	NA
• OC clearance for approval	NA
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification and certifications from foreign applicants are co-signed by U.S. agent.	**(X)** Verified
❖ Patent	
• Information: Verify that patent information was submitted	**(X)** Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted	21 CFR 314.50(i)(1)(*i*)(A) ( ) I **(X)** II ( ) III ( ) IV 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	( ) Verified

❖ Exclusivity (approvals only)	
• Exclusivity summary	X
• Is there an existing orphan drug exclusivity protection for the active moiety for the proposed indication(s)? *Refer to 21 CFR 316.3(b)(13) for the definition of sameness for an orphan drug (i.e., active moiety). This definition is NOT the same as that used for NDA chemical classification!*	( ) Yes, Application #_____ **(X)** No
❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	8/29/02; 3/12/03
General Information	
❖ Actions	
• Proposed action	**(X)** AP ( ) TA ( ) AE ( ) NA
• Previous actions (specify type and date for each action taken)	AE, August 30, 2002
• Status of advertising (approvals only)	**(X)** Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	( ) Yes **(X)** Not applicable
• Indicate what types (if any) of information dissemination are anticipated	**(X)** None ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable)	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	
• Most recent applicant-proposed labeling	X
• Original applicant-proposed labeling	X
• Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	DMETS - 7/12/02 DMETS- 12/12/02
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	X – 2
❖ Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	
• Applicant proposed	X
• Reviews	DMETS – 7/12/02 DMETS – 12/12/02
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	NA
• Documentation of discussions and/or agreements relating to post-marketing commitments	NA
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	X
❖ Memoranda and Telecons	X
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	None Held
• Pre-NDA meeting (indicate date)	8/1/01
• Pre-Approval Safety Conference (indicate date; approvals only)	None Held
• Other	Telecons- 8/29/02; 12/12/02

❖ Advisory Committee Meeting	
• Date of Meeting	NA
• 48-hour alert	NA
❖ Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	NA
Summary Application Review	
❖ Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	Medical Team Leader- 8/29/02 Division Director- 8/30/02
Clinical Information	
❖ Clinical review(s) *(indicate date for each review)*	8/5/02; 5/1/02
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	NA
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	NA
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	X – Fully waived
❖ Statistical review(s) *(indicate date for each review)*	5/8/02
❖ Biopharmaceutical review(s) *(indicate date for each review)*	8/9/02
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	NA
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	NA
• Bioequivalence studies	NA
CMC Information	
❖ CMC review(s) *(indicate date for each review)*	8/16/02 (2), 8/30/02, 12/20/02
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	8/16/02
• Review & FONSI *(indicate date of review)*	NA
• Review & Environmental Impact Statement *(indicate date of each review)*	NA
❖ Micro (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	NA
❖ Facilities inspection (provide EER report)	Date completed: 8/29/02 **(X)** Acceptable **( )** Withhold recommendation
❖ Methods validation	**( )** Completed **( )** Requested **(X)** Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	11/22/02
❖ Nonclinical inspection review summary	NA
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	NA
❖ CAC/ECAC report	NA

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

/s/

Melissa Robb
3/18/03 01:37:45 PM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0297
Expiration Date: February 29, 2004

USER FEE COVER SHEET

See Instructions on Reverse Side Before Completing This Form

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on CDER's website: http://www.fda.gov/cder/pdufa/default.htm

1. APPLICANT'S NAME AND ADDRESS

Reliant Pharmaceuticals, LLC
110 Allen Road
Liberty Corner, New Jersey 07938

Att: Keith Rotenberg, Ph.D.

2. TELEPHONE NUMBER *(Include Area Code)*

(908) 542-4423

3. PRODUCT NAME

Propranolol hydrochloride Extended Release Capsules (80 mg, 120 mg)

4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER

21-438

5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?

☒ YES ☐ NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW:

☒ THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION.

☐ THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

_____
(APPLICATION NO. CONTAINING THE DATA).

6. USER FEE I.D. NUMBER

4209

7. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.

☐ A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 *(Self Explanatory)*

☐ A 505(b)(2) APPLICATION THAT DOES NOT REQUIRE A FEE *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(E) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS A PEDIATRIC SUPPLEMENT THAT QUALIFIES FOR THE EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act *(See item 7, reverse side before checking box.)*

☐ THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALLY *(Self Explanatory)*

8. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? ☐ YES ☒ NO

(See item 8, reverse side if answered YES)

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
CBER, HFM-99
1401 Rockville Pike
Rockville, MD 20852-1448

and

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Drive, Room 3046
Rockville, MD 20852

An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

SIGNATURE OF AUTHORIZED COMPANY REPRESENTATIVE	TITLE	DATE
Keith A. Rotenberg	Vice President, Regulatory Affairs	10/22/01

FORM FDA 3397 (4/01)

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COPY

DIVISION OF CARDIO-RENAL DRUG PRODUCTS
FOOD AND DRUG ADMINISTRATION

US Mail address:
FDA/CDER/HFD-110
5600 Fishers Lane
Rockville, MD 20857

Woodmont II
1451 Rockville Pike
Rockville, MD 20852

Transmitted to FAX Number:	908-542-4460
Attention:	**Bob Mandetta**
Company Name:	Reliant
Phone:	908-542-4429
Subject:	Action Letter
Date:	3/12/03
Pages including this sheet:	5

From: **Melissa Robb**
Phone: **301-594-5313**
Fax: **301-594-5494**

PLEASE LET ME KNOW YOU RECEIVED THIS. THANK YOU.

********** -COMM. JOURNAL- ********** DATE MAR-12-2003 ***** TIME 13:15 ********

MODE = MEMORY TRANSMISSION START=MAR-12 13:14 END=MAR-12 13:15

FILE NO.=745

STN NO.	COMM.	ONE-TOUCH/ ABBR NO.	STATION NAME/TEL NO.	PAGES	DURATION
001	OK	☎	919085424460	005/005	00:01:10

-FDA,CDER,OND,ODE1,DCRDP -

********** -CARDIO RENAL - ***** - 301 594 5494- **********

DIVISION OF CARDIO-RENAL DRUG PRODUCTS
FOOD AND DRUG ADMINISTRATION

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From: **Melissa Robb**
Phone: **301-594-5313**
Fax: **301-594-5494**

PLEASE LET ME KNOW YOU RECEIVED THIS. THANK YOU.

********** -COMM. JOURNAL- ********** DATE AUG-30-2002 ***** TIME 18:18 ********

MODE = MEMORY TRANSMISSION START=AUG-30 18:14 END=AUG-30 18:18

FILE NO.=729

STN NO.	COMM.	ONE-TOUCH/ ABBR NO.	STATION NAME/TEL NO.	PAGES	DURATION
001	OK	#	919085424460	011/011	00:03:22

-FDA,CDER,OND,ODEI,DCRDP -

********** -CARDIO RENAL - ***** - 301 594 5494- **********

DIVISION OF CARDIO-RENAL DRUG PRODUCTS
FOOD AND DRUG ADMINISTRATION

US Mail address:
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5600 Fishers Lane
Rockville, MD 20857

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Rockville, MD 20852

Transmitted to FAX Number:	908-542-4460
Attention:	**Dr. Keith Rotenberg**
Company Name:	**Reliant Pharmaceuticals**
Phone:	908-542-4423
Subject:	**AE Letter & Labeling**
Date:	8/30/02
Pages including this sheet:	1

From: **Zelda McDonald**
Phone: **301-594-5333**
Fax: **301-594-5494**

PLEASE LET ME KNOW YOU RECEIVED THIS. THANKS!

DIVISION OF CARDIO-RENAL DRUG PRODUCTS
FOOD AND DRUG ADMINISTRATION

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From: **Zelda McDonald**
Phone: **301-594-5333**
Fax: **301-594-5494**

PLEASE LET ME KNOW YOU RECEIVED THIS. THANKS!

McDonald, Zelda M

›m: McDonald, Zelda M
—nt: Wednesday, December 19, 2001 9:31 AM
ſo: El Hage, Antoine N; Butler, Earl H
Cc: Throckmorton, Douglas C
Subject: FW: — › NDA

Tony & Earl,
See below.
Z.

-----Original Message-----
From: Throckmorton, Douglas C
Sent: Wednesday, December 19, 2001 8:08 AM
To: McDonald, Zelda M
Subject: FW: — › NDA

fyi

-----Original Message-----
From: Throckmorton, Douglas C
Sent: Tuesday, December 18, 2001 4:51 PM
To: El Hage, Antoine N
Cc: Lipicky, Raymond J; Gordon, Maryann; Stockbridge, Norman L
Subject: —— NDA

I talked with Dr. Lipicky and he agrees that no inspections are needed for this NDA submission. Thanks, DCT

CONSULTATION RESPONSE
Division of Medication Errors and Technical Support
Office of Drug Safety
(DMETS; HFD-420)

DATE RECEIVED: October 17, 2002	**DUE DATE:** December 3, 2002	**ODS CONSULT #:** 02-0066-1

TO: Douglas Throckmorton
Director, Division of Cardio-Renal Drug Products
HFD-110

THROUGH: Melissa Robb
Regulatory Health Project Manager
HFD-110

PRODUCT NAME:	**NDA SPONSOR:**
InnoPran XL (Propranolol Hydrochloride Extended Release Capsules) 80 mg, 120 mg **NDA #** 21-438	Reliant Pharmaceuticals, LLC

SAFETY EVALUATOR: Scott Dallas, R.Ph.

SUMMARY: In response to a consult from the Division of Cardio-Renal Drug Products (HFD-110), the Division of Medication Errors and Technical Support (DMETS) conducted a review of the proposed proprietary name, "InnoPran XL", to determine the potential for confusion with approved proprietary and established names as well as pending names.

DMETS RECOMMENDATION: DMETS has no objections to the use of the proprietary name, "InnoPran XL". If the sponsor has not already addressed the safety comments in DMETS consult # 02-0066 concerning the proposed container labels, then DMETS recommends the comments outlined in section III of this review be forwarded to the sponsor.

This name must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.

/S/

Carol Holquist, RPh
Deputy Director
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: (301) 827-3242 Fax (301) 443-9664

/S/

Jerry Phillips, RPh
Associate Director
Office of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration

Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; Parklawn Building Room 6-34
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: **December 5, 2002**

NDA NUMBER: **21-438**

NAME OF DRUG: **InnoPran XL**
(Propranolol Hydrochloride Extended Release Capsules)

NDA SPONSOR: **Reliant Pharmaceuticals, LLC.**

I. INTRODUCTION:

This consult was written in response to a request from the Division of Cardio-Renal Drug Products (HFD-110) for an assessment of the proposed proprietary name, InnoPran XL. The proposed container labels and package insert labeling were previously reviewed in the initial DMETS consult for a proprietary name review on this application. Labeling comments found in the initial DMETS consult # 02-0066 have been included in section III of this review.

PRODUCT INFORMATION
InnoPran XL contains the active ingredient propranolol, which is a nonselective, beta-adrenergic receptor-blocking agent. InnoPran XL is formulated to provide an extended release of propranolol hydrochloride. InnoPran XL is seeking approval for the management of hypertension
— InnoPran XL will be available as an 80 mg, 120 mg — extended release oral capsule. For the treatment of hypertension, the initial dose is 80 mg once daily at bedtime. The usual maintenance dose is 120 mg to 160 mg once daily at bedtime. and in some instances the dose may be adjusted up to 640 mg once daily at bedtime.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[1, 2] as well as several FDA databases[3] for existing drug names which sound alike or look alike to "InnoPran XL" to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's trademark electronic

[1] MICROMEDEX Healthcare Intranet Series, 2002, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300. Englewood. Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Index Nominum, and PDR/Physician's Desk Reference (Medical Economics Company Inc, 2002).
[2] Facts and Comparisons, 2002, Facts and Comparisons, St. Louis, MO.
[3] The Drug Product Reference File [DPR], Established Evaluation System [EES], the DMETS database of proprietary name consultation requests, New Drug Approvals 98-02, and the electronic online version of the FDA Orange Book.

search system (TESS) was conducted[4]. The Saegis[5] Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted prescription analysis studies, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name "InnoPran XL". Potential concerns regarding drug marketing and promotion related to the proposed names were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

The Expert Panel identified four proprietary names and one established or generic name that were thought to have the potential for confusion with "InnoPran XL". These products are listed in Table 1, along with the dosage forms available and usual dosage.

DDMAC did not have any concerns with the promotional aspects of the name, "InnoPran XL".

TABLE 1

Product Name	**Generic name, Dosage form(s), and Strength (s)**	**Usual adult dose***	**Other****
InnoPran XL	Propranolol Hydrochloride Extended Release Capsule, 80 mg, 120 mg and 160 mg	Treatment of hypertension: Take one 80 mg capsule daily at bedtime.	
Imogam	Rabies Immune Globulin, Human (RIG) Injection, 150 IU/mL	Indicated for individuals suspected of exposure to rabies: Inject intra-muscularly 20 IU/kg as soon as possible after exposure, preferably with first dose of vaccine.	S A and L/A per DMETS
Innofem	Estradiol, Tablets, 0.5 mg, 1 mg, and 2 mg	Indicated for the treatment of moderate to severe vasomotor symptoms associated with the menopause: Take one tablet by mouth daily.	S A and L/A per DMETS
Tofranil, and Tofranil PM	**Imipramine** hydrochloride, Tablets. 10 mg, 25 mg and 50 mg **Imipramine** pamoate, Capsules, 75 mg, 100 mg, 125 mg, and 150 mg	Indicated for the treatment of symptoms of depression: Imipramine hydrochloride –Take one tablet by mouth daily. Imipramine pamoate – Take one capsule by mouth at bedtime.	L A per DMETS

[4]WWW location http://tess.uspto.gov/bin/gate.exe?f=tess&state=k0n826.1.1

[5] Data provided by Thomson & Thomson's SAEGIS(tm) Online Service, available at www.thomson-thomson.com.

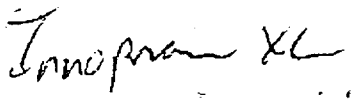
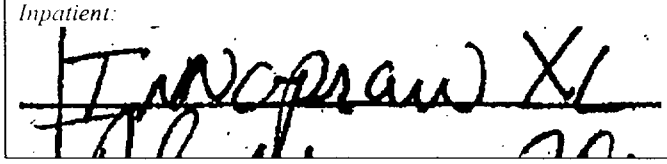
Ditropan XL	Oxybutynin Chloride, Extended Release Tablets, 5 mg, 10 mg and 15 mg	Indicated for the relief of symptoms of bladder instability: Take one 5 mg tablet one time a day. May increase up to a maximum of 30 mg/day.	S/A per DMETS
Imuran	Azathioprine, Tablets, 50 mg, Injection, 100 mg per vial	Indicated to prevent rejection of kidney in renal transplantation: Adults – Initial dose is usually 3 to 5 mg/kg/day, to a maintenance dose of 1 to 3 mg/kg/day.	S/A per DMETS

* Frequently used, not all-inclusive. ** L/A (look-alike), S/A (sound-alike)

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology

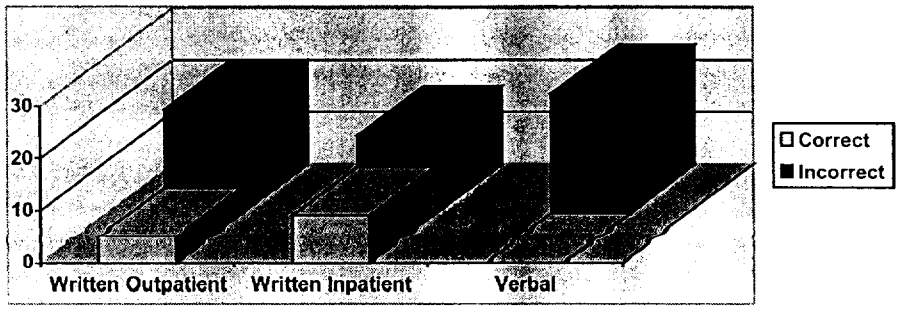
Three separate studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of InnoPran XL with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 106 health care professionals (nurses, pharmacists, and physicians). This exercise was conducted in an attempt to simulate the prescription ordering process. A DMETS staff member wrote an inpatient order and outpatient prescriptions, each consisting of a combination of marketed and unapproved drug products and prescriptions for InnoPran XL. These written prescriptions were optically scanned and one prescription was delivered via email to each study participant. In addition, one DMETS staff member recorded a verbal outpatient prescription that was then delivered to a group of study participants via telephone voicemail. Each reviewer was then requested to provide an interpretation of the prescription via email.

HANDWRITTEN PRESCRIPTIONS	VERBAL PRESCRIPTION
Outpatient: 	*Outpatient:* InnoPran XL 80 mg Take 1 at bedtime Dispense number 30
Inpatient: 	

2. Results

Results of the InnoPran XL exercises are summarized below:

Study	No. of participants	# of responses (%)	"InnoPran" response (%)	Other response (%)
Written: Outpatient	35	25 (71%)	5 (20%)	20 (80%)
Inpatient	39	24 (62%)	9 (38%)	15 (62%)
Verbal: Outpatient	32	23 (72%)	0 (0%)	23 (100%)
Total:	106	72 (68%)	14 (19%)	58 (81%)



Among participants in the written outpatient prescription study, 5 of 25 respondents (20%) interpreted the name correctly. Incorrect interpretations included Innoprain (1), and Innopram (19).

Among participants in the written inpatient prescription study, 9 of 24 respondents (38%) interpreted the name correctly. Incorrect interpretation included Ianopran (1), Inapran (1), Innopram (2), Innopraw (4), Inopram (1), Inopran (3), Inopraw (2) and Irnopran (1).

Among participants in the verbal outpatient prescription study, 0 of 23 respondents (0%) interpreted the name correctly. Incorrect interpretations included Anapren (1), Enapran (1), Enapren (2), Enaprin (7), Enepran (1), Eneprin (1), Enopran (3), Enopren (1), Enoprin (3), Iniprin (1), and Inopran (2).

None of the misinterpreted names in any of the studies is a currently marketed drug product.

C. SAFETY EVALUATOR RISK ASSESSMENT

1. The Proprietary Name Review

In reviewing the proprietary name, "InnoPran XL", the primary concerns raised were related to sound-alike and look-alike names that already exist in the U.S. marketplace. The products considered having the greatest potential for name confusion with InnoPran XL were Imogan, Innofem, Imipramine, Ditropan XL and Imuran.

DMETS also conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that InnoPran XL could be confused with proprietary or established names known in the U.S. marketplace. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to small sample size. The majority of the incorrect interpretations of the written and the verbal studies were misspelled/phonetic variations of the proposed name, InnoPran XL.

Imogan is a product containing rabies immune globulin, human. The complete name of Imogam is Imogam Rabies – HT^2. Rabies immune globulin is indicated for individuals with suspected exposure to rabies. Although Imogam may have look alike and sound alike qualities with InnoPran XL, the two products belong to different pharmacologic classes and are available in different dosage forms. Imogan is a product with limited distribution due to a very specific indication in a very limited patient population. The product would probably only be available in hospital or clinic with the administration of the medication in that facility. A hospital or clinic may also have to order the medication through an emergency requisition. The products have different strengths (150 IU/mL vs. 80 mg, 120 mg and 160 mg), units of measure (IU/mL vs. mg), and frequency of administration (one dose vs. daily). Although the names possess look alike and sound alike qualities, the risk of dispensing the wrong medication should be low based on the many differences between the medications.

Innofem contains the active ingredient estradiol. The Food and Drug Administration approved the application on November 19, 1999, however there is no evidence the product has ever been marketed. I contacted the customer service department (1-800-323-4204) of the sponsor Novo Nordisk Pharmaceutical concerning the distribution of Innofem. I was informed all hormonal products are marketed through Pharmacia Corporation. I contacted the product service department (908-801-8000) and was informed Pharmacia Corporation does have an agreement with Novo Nordisk to market hormone based products. However, the Pharmacia Corporation has never marketed Innofem. Innofem was not listed in the 2002 edition *of Drug Facts and Comparison* or the *Physician's Desk Reference* (PDR). Innofem is indicated for the treatment of moderate to severe vasomotor symptoms associated with the menopause. Innofem is approved as a 0.5 mg, 1 mg and 2 mg tablet. Innofem and InnoPran can sound similar when spoken and look similar when scripted. Both names begin with the same first 4 letters, "Inno", which results in the same sound when spoken or appearance when scripted. The "fem" sound can also sound similar to the "Pran" sound, especially if a short "a" sound is used to pronounce the "Pran". The last syllable in each name can also look similar if InnoPran is scripted without a capital letter "P" and the trailing letters are not clearly written. Innofem and InnoPran would have different strengths (0.5 mg, 1 mg, and 2 mg vs. 80 mg, 120 mg, and 160 mg), indication for use (vasomotor symptoms associated with menopause vs. hypertension), and time of administration (daytime vs. bedtime). Also a complete prescription

for InnoPran would also include the modifier, XL, which would aid in differentiating the medications. Although the names possess look alike and sound alike qualities, the risk of dispensing the wrong medication should be low based on the many differences between the medications.

Imipramine hydrochloride and imipramine pamoate are the established names for Tofranil and Tofranil PM, respectively. Imipramine hydrochloride and imipramine pamoate are indicated for the relief of symptoms of depression. Generic versions of Tofranil are also marketed in the United States, however there is no approved generic version of Tofranil PM. When scripted Imipramine and InnoPran can look similar. However when scripted the different distances between the letters "I" and "p" in the first part of the name and length of the names after the letters "pra" aid in differentiating the look of the names. Imipramine contains 10 letters, while InnoPran contains only 8 letters. If written correctly InnoPran XL should also be scripted with a capital letter "P" and the modifier "XL". Imipramine hydrochloride and InnoPran have different strengths (10 mg, 25 mg and 50 mg vs. 80 mg, 120 mg and 160 mg) and dosage formulations (tablets vs. capsules). The directions for use could be the same or different for these medications. Multiple tablets of imipramine hydrochloride could be administered at one time or at different time intervals, while multiple capsules of InnoPran should be administered at bedtime. It is also unlikely that multiple tablets of imipramine hydrochloride or multiple capsules of InnoPran would result in an overlapping dose. Imipramine pamoate and InnoPran also have different strengths (75 mg, 100 mg, 125 mg, and 150 mg vs. 80 mg, 120 mg, and 160 mg). Although the names possess some look alike qualities, the risk of dispensing the wrong medication should be low based on the scripted differences between imipramine and InnoPran, the addition of the "XL" modifier, and the differences in dosage strengths of the medications.

Ditropan XL is the proprietary name for oxybutynin chloride, extended release. It is indicated for the treatment of overactive bladder with symptoms of urinary incontinence, urgency, and frequency. Ditropan XL is available as a 5 mg, 10 mg and 15 mg tablet. When spoken Ditropan XL and InnoPran XL can sound similar. Both names contain 3 syllables and when spoken the "opan XL" and "oPran XL" produce a rhyming quality. However, these medications possess some different characteristics. Ditropan XL and InnoPran XL have different strengths (5 mg, 10 mg, and 15 mg vs. 80 mg, 120 mg, and 160 mg), dosage formulation (tablets vs. capsules), and indication for use (overactive bladder vs. hypertension). These medications would generally not be stored in close proximity to each other, due to the spelling of their names. Although the names possess some sound alike qualities due to the similarities in the last syllable and the "XL" modifier of each name, the risk of dispensing the wrong medication should be low based on the many differences between the medications.

Imuran is the proprietary name for azathioprine. It is indicated for the treatment of renal homotransplantation and rheumatoid arthritis. Imuran is available as a 50 mg tablet and 100 mg per vial injection. When spoken Imuran and InnoPran XL can sound similar. Both names contain 3 syllables. The names begin with a similar sound "Im vs. In" and end with exactly the same sound "an". However, these medications possess some different characteristics. Imuran and InnoPran XL have different strengths (50 mg or 100 mg per vial vs. 80 mg, 120 mg, and 160 mg), dosage formulation (tablet or injection vs. capsule), and indication for use (renal homotransplantation and rheumatoid arthritis vs. hypertension). Although the usual dose of both medications can be one tablet or capsule, it is also very common for an Imuran dose to be 1 ½ , 2 or 2 ½ tablets. Depending upon the indication, Imuran is dosed from 1 to 5 mg/kg/day with dosage adjustments in 25 mg or ½ tablet

increments. Although the names possess some sound alike qualities, the risk of dispensing the wrong medication should be low based on the many differences between the medications.

2. The Modifier "XL"

The addition of a modifier to a proprietary name is an accepted practice to designate a new dosage formulation for an existing product line. If approved InnoPran XL would establish a new product line, not an extension of an existing product line. However, InnoPran XL has been formulated as an extended release capsule. Therefore it would be acceptable to utilize a modifier to designate an extended release formulation. The modifier "XL" is currently utilized in seven product line extensions to indicate an extended release formulation with a once daily dosing. The use of the modifier "XL" in InnoPran XL would provide consistency, by interpreting the product as an extended release medication with a once daily dosing. Therefore, DMETS has no objections to the use of the modifier "XL" for this propranolol hydrochloride extended release capsule.

III. LABELING, PACKAGING AND SAFETY RELATED ISSUES:

We refer you to the labeling comments proposed in the original review for this product found in DMETS consult # 02-0066. These comments are being restated in this review, because revised labels and labeling were not submitted for re-review. All the comments pertain to the professional sample and 30 count container label, since these were the only two container labels available during the initial review.

1. In order to increase the prominence of the strength, we recommend increasing the font size. We also recommend relocating the strength to appear in close proximity to the proprietary and/or established name. ??
Relocate net qty. to bottom of container label & ↓ font size
2. We recommend relocating the net quantity to the bottom of the container label in order to prevent confusion with the strength. In addition, the font size of the net quantity statement should be decreased so that it appears smaller than the strength. ??

3. Revise the usual statement to read: "Usual dosage: One capsule daily at bedtime. See Package Insert" in accordance with 21 CFR 201.100(b)(2). ✓ Dose vs. Dosage

4. Please decrease the size and prominence of the manufacturer's name and logo. Currently, it appears more prominent than the proprietary name. ✓

5. In order to prevent medication errors due to the similarity in labeling among the strengths (80 mg, 120 mg we recommend differentiating the labels with the use of contrasting colors, boxing, or some other means.

80mg - Aquamarine PMS 109
120mg " PMS 534

IV. RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name InnoPran XL.

2. DMETS recommends implementation of labeling comments outlined in section III.

DMETS would appreciate feedback of the final outcome of this consult. We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Sammie Beam at 301-827-3242.

/S/

Scott Dallas, R.Ph.
Safety Evaluator
Office of Drug Safety (DMETS)

Concur: /S/

Denise Toyer, RPh
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

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/s/

Scott Dallas
12/12/02 02:57:50 PM
PHARMACIST

Carol Holquist
12/13/02 02:49:44 PM
PHARMACIST

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
Associate Director, Medication Error Prevention
Office of Drug Safety, HFD-400
(Rm. 15B-03, PKLN Bldg.)

FROM:
Regulatory Health Project Manager
Division of Cardio-Renal Drug Products, HFD-110
(Rm 5026, WOC2)

DATE	IND NO.	NDA NO.	TYPE OF DOCUMENT	DATE OF DOCUMENT
October 17, 2002		21-438	Correspondence	October 10, 2002

NAME OF DRUG	PRIORITY CONSIDERATION	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE
Propranolol Extended Release Capsules	3S		December 16, 2002

NAME OF FIRM: Reliant Pharmaceuticals

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE/ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE--NDA MEETING
- ☐ END OF PHASE II MEETING
- ☐ RESUBMISSION
- ☐ SAFETY/EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER *(SPECIFY BELOW)*: Trade name review

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR 3 NDA REVIEW ☐ END OF PHASE II MEETING ☐ CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER (SPECIFY BELOW):	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE IV STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL-BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

- ☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL	☐ PRECLINICAL

COMMENTS, CONCERNS and/or SPECIAL INSTRUCTIONS:
Although the tradename [redacted] was found acceptable to DMETS, the sponsor has withdrawn that name and submitted two new names for tradename review.
First choice: InnoPran XL [redacted]

SIGNATURE OF REQUESTER	METHOD OF DELIVERY (Check one)
Melissa Robb	X DFS ☐ HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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/s/

Melissa Robb
10/17/02 09:58:44 AM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

) *(Division/Office)*:
ssociate Director, Medication Error Prevention
Office of Drug Safety, HFD-400
(Rm. 15B-03, PKLN Bldg.)

FROM:
Regulatory Health Project Manager
Division of Cardio-Renal Drug Products, HFD-110
(Rm 5024 , WOC2)

DATE:	IND NO.:	NDA NO.:	TYPE OF DOCUMENT :	DATE OF DOCUMENT:
October 3, 2002		21-438	Correspondence	October 1, 2002

NAME OF DRUG:	PRIORITY CONSIDERATION:	CLASSIFICATION OF DRUG:	DESIRED COMPLETION DATE:
Propranolol Extended Release Capsules	3S		November 4, 2002

NAME OF FIRM: Reliant Pharmaceuticals

REASON FOR REQUEST

I. GENERAL

NEW PROTOCOL
☐ PROGRESS REPORT
☐ NEW CORRESPONDENCE
☐ DRUG ADVERTISING
☐ ADVERSE REACTION REPORT
☐ MANUFACTURING CHANGE/ADDITION
☐ MEETING PLANNED BY
☐ PRE--NDA MEETING
☐ END OF PHASE II MEETING
☐ RESUBMISSION
☐ SAFETY/EFFICACY
☐ PAPER NDA
☐ CONTROL SUPPLEMENT
☐ RESPONSE TO DEFICIENCY LETTER
☐ FINAL PRINTED LABELING
☐ LABELING REVISION
☐ ORIGINAL NEW CORRESPONDENCE
☐ FORMULATIVE REVIEW
X OTHER *(SPECIFY BELOW)*:
Trade name review

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW END OF PHASE II MEETING CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER:	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER:

III. BIOPHARMACEUTICS

☐ DISSOLUTION
☐ BIOAVAILABILTY STUDIES
☐ PHASE IV STUDIES
☐ DEFICIENCY LETTER RESPONSE
☐ PROTOCOL-BIOPHARMACEUTICS
☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
☐ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
☐ SUMMARY OF ADVERSE EXPERIENCE
☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:
Although the tradename [redacted] was found acceptable to DMETS, the sponsor has asked for review of another tradename:

No new labeling has been submitted. The WORD Files of the originally submitted labels and labeling can be found in the electronic document room.

SIGNATURE OF REQUESTER:	METHOD OF DELIVERY (Check one):
Zelda McDonald	Ξ DFS ☐ HAND
SIGNATURE OF RECEIVER:	SIGNATURE OF DELIVERER:

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

/s/

Zelda McDonald
10/3/02 01:55:37 PM

CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED: 04/10/02	**DUE DATE:** 07/10/02	**ODS CONSULT #:** 02-0066

TO:

Douglas Throckmorton, M.D.
Director, Division of Cardio-Renal Drug Products
HFD-110

THROUGH:

Zelda McDonald
Project Manager
HFD-110

PRODUCT NAME:	**NDA SPONSOR:** Reliant Pharmaceuticals, LLC
—— (Primary name) —— (Alternate name); (Propranolol Hydrochloride Extended Release Capsules) 80 mg, 120 mg, —— **NDA: 21-438**	

SAFETY EVALUATOR: Hye-Joo Kim, Pharm.D.

SUMMARY: In response to a consult from the Division of Cardio-Renal Drug Products (HFD-110), the Division of Medication Errors and Technical Support (DMETS) has performed a review of the proposed proprietary names —— " (primary) and ' —— (alternate) to determine the potential for confusion with approved proprietary and established names as well as pending names.

DMETS RECOMMENDATION: DMETS does not recommend the use of the primary name, —— ". However, DMETS has no objection to the use of the alternate name, —— In addition. DMETS recommends revising the labels and labeling as outlined in section IV of this review.

This name and its associated labels and labeling must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary and established names from the signature date of this document.

/S/

Carol Holquist, RPh
Deputy Director
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: (301) 827-3242 Fax: (301) 443-5161

/S/

Jerry Phillips, RPh
Associate Director
Office of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration

Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; Rm. 15B32
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: June 24, 2002

NDA: 21-438

NAME OF DRUG (S): ——— (Primary) and ——— (Alternate)
Propranolol Hydrochloride Extended Release Capsules
80 mg, 120 mg, ———

NDA HOLDER: Reliant Pharmaceuticals, LLC

I. INTRODUCTION:

This consult is written in response to a April 10, 2002 request from the Division of Cardio-Renal Drug Products (HFD-110) for an assessment of the proposed primary proprietary name, ——— " and the alternate name, ——— ' The container labels and package insert labeling were reviewed for possible interventions in minimizing medication errors.

PRODUCT INFORMATION

——— contains the active ingredient, propranolol, which is a nonselective, beta-adrenergic receptor-blocking agent. ——— is formulated to provide an extended release of propranolol hydrochloride. ——— is indicated in the management of hypertension ——— For the treatment of hypertension, the initial dose is 80 mg once daily at bedtime. The usual maintenance dosage is 120 mg ——— once daily at bedtime and in some instances, 640 mg once daily at bedtime may be required. ——— will be available as 80 mg, 120 mg. ——— extended-release capsules.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[1, 2] as well as several FDA databases[3] for existing drug names which sound-alike or look-alike to —— to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database[4] and the Saegis[5] Pharma-In-Use database were also conducted. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted six prescription analysis studies consisting of four written prescription studies, outpatient and inpatient for each name, and two verbal prescription studies, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary names, —— Potential concerns regarding drug marketing and promotion related to the proposed names were also discussed. The expert panel consists of members of DMETS Safety Evaluator Staff and a representative from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. The Expert Panel identified several names that were thought to have the potential for confusion with —— These products are listed in Table 1 and 2 (see page 4), along with the dosage forms available and usual FDA-approved dosage.

2. DDMAC has no objection to the proposed names, ——

[1] MICROMEDEX Healthcare Intranet Series, 2000, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Index Nominum, and PDR/Physician's Desk Reference (Medical Economics Company Inc, 2000).

[2] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

[3] The Established Evaluation System [EES], the Labeling and Nomenclature Committee [LNC] database of Proprietary name consultation requests, New Drug Approvals 98-00, and the electronic online version of the FDA Orange Book.

[4] WWW location http://www.uspto.gov/tmdb/index.html

[5] Data provided by Thomson and Thomson' SAEGIS™ Online Service, available at www.thomson-thomson.com.

Table 1

Product Name	Dosage form(s), Generic name	Usual Dose	Observation
[redacted]	Propranolol Hydrochloride Extended-Release Capsules; 80 mg, 120 mg	80 mg to po QD at bedtime.	
Betapace AF Betapace	Sotalol Hydrochloride; Tablets-80 mg, 120 mg and 160 mg Tablets-80 mg, 120 mg, 160 mg and 240 mg	80 mg to 160 mg QD or BID. 80 mg to 240 mg QD or BID.	LA/SA*
Betaderm	Betamethasone Valerate Cream, 0.1%	Apply to affected area QD to QID.	LA/SA*
Various Betadine products are available. For example, Betadine Solution Betadine Skin Cleaner	 Povidone-Iodine, 10% Povidone-Iodine, 7.5%	 Apply as often as needed as a paint, spray, or wet soak. Apply sufficient amount 2 to 3 times daily.	LA/SA*
Theo-Dur	Theophylline Extended-Release Tablets; 100 mg, 200 mg, 300 mg and 450 mg	100 mg to 450 mg BID.	SA*

*SA = Sound-alike
*LA = Look-alike

Table 2

Product Name	Dosage form(s), Generic name	Usual Dose	Observation
[redacted]	Propranolol Hydrochloride Extended-Release Capsules; 80 mg, 120 mg	80 mg to po QD at bedtime.	
Zofran Zofran ODT	Ondansetron Hydrochloride; Tablets-4 mg, 8 mg and 24 mg Oral Solution-4 mg/5 mL Injection-2 mg/mL Injection, premixed-32 mg/50 mL Ondansetron Hydrochloride Orally Disintegrating Tablets; 4 mg and 8 mg	Oral: 8 mg po BID to TID. A single 24 mg po 30 minutes before the chemotherapy. Injection: 4 mg IV or IM immediately before induction of anesthesia, or postoperatively. A single 32 mg intravenously infused over 15 minutes 30 minutes before the chemotherapy.	SA*
Pitressin Synthetic	**Vasopressin** Injection; 20 units/mL	5 units to 10 units IM or SC BID to QID prn.	LA/SA*
Vasotec Vasotec I.V.	Enalapril Maleate Tablets; 2.5 mg, 5 mg, 10 mg and 20 mg Enalaprilat Injection; 1.25 mg/mL	Hypertension: 5 mg to 40 mg per day (divided QD or BID) Heart Failure: 2.5 mg to 20 mg BID 1.25 mg IV q6h.	LA/SA*
Vasodilan	Isoxsuprine Hydrochloride Tablets; 10 mg and 20 mg	10 mg to 20 mg TID to QID	LA/SA*
Vasocine	Sulfacetamide Sodium and Prednisolone Acetate Ophthalmic Ointment, USP; 10%/0.5%	Apply a small amount to affected eye (s) TID to QID.	LA/SA*

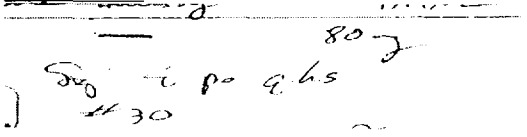
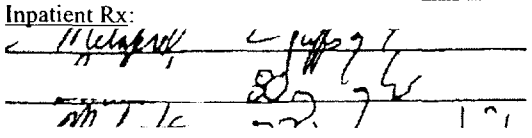
*SA = Sound-alike

B. PRESCRIPTION ANALYSIS STUDIES

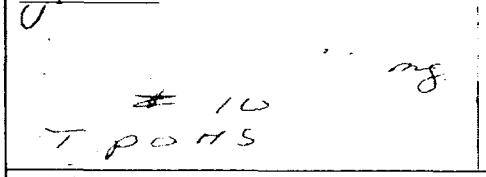
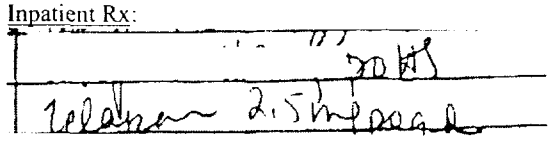
1. Methodology

Six separate studies were conducted within FDA for the proposed proprietary names to determine the degree of confusion of [redacted] with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 108 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. Inpatient and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for [redacted] (see below). These prescriptions were optically scanned and were delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

[redacted]

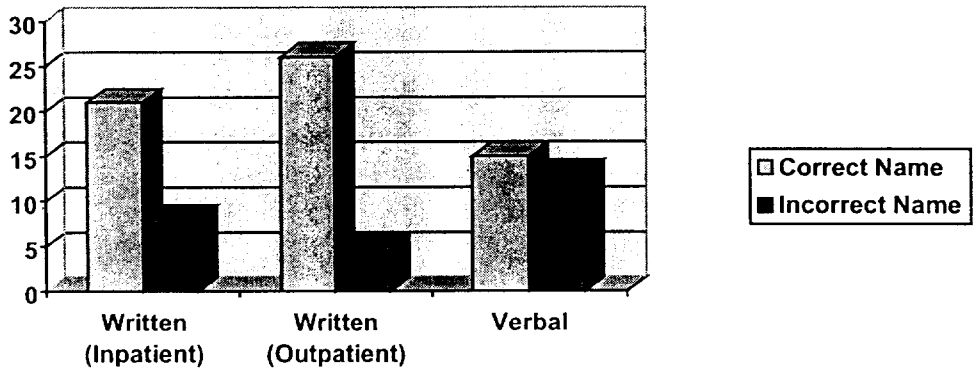
HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient Rx: 	Verbal Rx: [redacted]80 mg Take 1 capsule at bedtime. #30
Inpatient Rx: 	

[redacted]

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient Rx: 	Verbal Rx: [redacted] Take 1 capsule at bedtime. #10
Inpatient Rx: 	

2. Results for

Study	# of Participants	# of Responses (%)	Correctly Interpreted	Incorrectly Interpreted
Written Inpatient	33	29 (88%)	21 (72%)	8 (28%)
Written Outpatient	39	31 (79%)	26 (84%)	5 (16%)
Verbal	36	28 (78%)	15 (54%)	13 (46%)
Total	108	88 (81%)	62 (70%)	26 (30%)

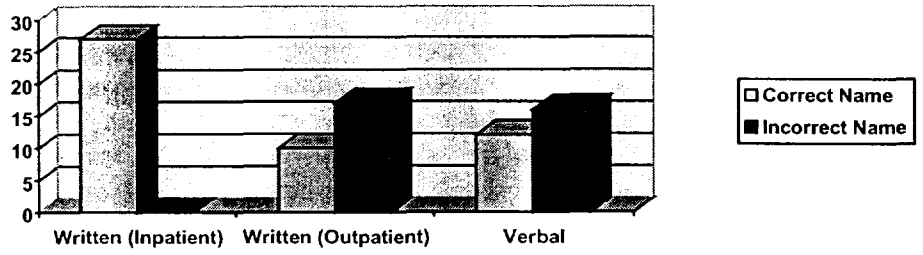


Among the verbal prescription study participants for —— 13 of 28 (46 %) participants interpreted the name incorrectly. The majority of the incorrect name interpretations were phonetic variations of —— " The incorrect responses were . *(4), Benadur (1), Medadur (1), Metador (1), Metadur (1), Bedadur (1), Bedudor (1), Venatdur (1), Benadori (1),* and *Bentadori (1).*

Among the written prescription study participants for —— 13 of 60 (22 %) participants interpreted the name incorrectly. *Two participants from the outpatient written study interpreted the name incorrectly as "Betadine," a marketed drug name.* Furthermore, one additional participant commented that the proposed name looks similar to Betadine. Lastly, two participants commented that the proposed name looks similar to *Betapace.* They also noted that both — and Betapace are available in 80 mg strength. Other incorrect responses were misspelled variations of ' —— · *Betadin (5), Betadurin (1), Betadium (1), Betzdin (1), Betadrin (2),* and *Betalin (1).*

3. Results for

Study	# of Participants	# of Responses (%)	Correctly Interpreted	Incorrectly Interpreted
Written Inpatient	33	23 (70%)	10 (43%)	13 (57%)
Written Outpatient	39	30 (77%)	13 (43%)	17 (57%)
Verbal	36	24 (67%)	9 (38%)	15 (63%)
Total	108	77 (71%)	32 (42%)	45 (58%)



Among the verbal prescription study participants for —— 15 of 24 (63 %) participants interpreted the name incorrectly. The majority of the responses were phonetic variations of —— The incorrect responses were *Vasopram (6), Vasoprim (6), Zasoprim (1),* and *Vasoprin (2).*

Among the written prescription study participants for ——, 30 of 53 (57 %) participants interpreted the name incorrectly. *Two participants from the inpatient written study interpreted the name incorrectly as "vasopressin," an approved established drug name.* Other incorrect responses were misspelled variations of —— : *Vasopram (18), Vasoprar (3), Vasoprai (1), Vasoprim (1), Vasopra (2), Vasoprex (1), Vasopr (1),* and *Vasogran (1).*

C. SAFETY EVALUATOR RISK ASSESSMENT

——

In reviewing the proprietary name —— ", the primary concerns raised were related to sound-alike and look-alike names that already exist in the U.S. marketplace. The products considered having the greatest potential for name confusion with —— were Betapace, Betaderm, Betadine, and Theo-Dur.

We conducted prescription studies to simulate the prescription ordering process. In this case, there was a suggestion that —— could be confused with **Betadine** and **Betapace**. Two participants from the outpatient written study interpreted the name incorrectly as *Betadine*, an approved drug name. Furthermore, one participant from the outpatient written study commented that the proposed name looks similar to "Betadine." Two participants from the outpatient written study commented that the proposed name looks similar to *Betapace,* an approved drug name. Additionally, they noted that both —— and Betapace are available in "80 mg" strength. Although there are limitations to the predictive value of these studies, primarily due to the small sample size, we have acquired safety concerns due to the positive interpretation with this drug product. A positive finding in a study with a small sample size may indicate a high risk and potential for medication errors when extrapolated to the general U.S. population.

Betapace and Betapace AF contain the active ingredient, sotalol hydrochloride. Betapace is indicated for the treatment of documented ventricular arrhythmias that are life-threatening. Betapace AF, on the other hand, is indicated for the maintenance of normal sinus rhythm in patients with symptomatic atrial fibrillation/atrial flutter who are currently in sinus rhythm. The risk of confusion between and Betapace is likely for several reasons. The proposed name, — and the currently available name, Betapace, look-alike when scripted (see below), because they share the same prefix "Beta." Our current post-marketing experience indicates that there is a potential risk of medication errors between names that share the same prefix. For instance, post-marketing experience with the drug products "Serzone" and "Seroquel" have demonstrated that having the same prefix may lead to medication errors. As of April 2002, the Agency has received **twenty-six (26)** medication error reports involving Serozone and Seroquel from the Adverse Event Reporting System (AERS) database. Furthermore, Serzone and Seroquel share an overlapping route of administration (oral), strengths (100 mg and 200 mg), and dosing interval (BID). These confounding factors were critical in causing unnecessary medication errors. Lastly, they are stored next to each other on pharmacy shelves, further increasing the risk of errors. Similarly, — and Betapace share the aforementioned commonalties. — and Betapace share an overlapping route of administration (oral), strengths (80 mg, 120 mg, and dosing interval (QD). Lastly, — will be placed in close proximity to Betapace on pharmacy shelves, further increasing the risk of errors. We acknowledge that — should be administered at bedtime; however, a provider may order it "QD" instead of "HS" on a prescription. Therefore, a prescription for — could be misinterpreted as "Betapace" or vice versa and lead to medication errors (see below).

Betapace 80mg po qd

— 80mg po QD

If a patient receives Betapace instead of — he or she may remain untreated for hypertension and may also experience the side effects associated with the use of Betapace, such as bradycardia, dyspnea, fatigue, proarrhythmia, and QT interval prolongation. If a patient receives — instead of Betapace, a patient could experience various adverse events associated with —, including hypotension, bradycardia, congestive heart failure, fatigue, light-headedness, and bronchospasm. Furthermore, since Betapace is administered to patients with life-threatening arrhythmias, the omission of Betapace could be fatal.

Betaderm contains the active ingredient, betamethasone and is indicated for relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses. Although — may have look-alike and sound-alike qualities with Betaderm, the two products belong to different pharmacologic classes and are available in different dosage forms. Betaderm is available as a topical cream while — will be available as 80 mg, 120 mg, and 160 mg capsules. Moreover, the route of administration is different. A small amount of Betaderm is applied topically while — is for oral administration.

Betadine products contain the active ingredients, povidone and iodine and are used as antiseptics and germicides. — and Betadine look alike when scripted and are phonetically similar as they share the same letter combination — " In fact, two participants from the outpatient written study interpreted — as Betadine. However, the risk of confusion between — and Betadine is minimal, because they belong to different pharmacologic classes and are available in different dosage forms. Betadine products are available as topical preparations, including ointment, solution, surgical scrub, and etc. — on the other hand, will be available as 80 mg, 120 mg, —

capsules. Lastly, since Betadine products are OTC agents and —— is a prescription only drug, these drug products will be stored in different areas, further decreasing the risk of medication errors.

Theo-Dur contains the active ingredient, theophylline and is indicated for the treatment of the symptoms and reversible airflow obstruction associated with chronic asthma and other chronic lung diseases, e.g., emphysema and chronic bronchitis. The names —— and Theo-Dur may sound alike as they share the same suffix "dur." However, there are distinguishing factors between —— and Theo-Dur, which may decrease the potential risk of medication errors. First, they do not share overlapping strengths. Theo-Dur is available as 100 mg, 200 mg, 300 mg, and 450 mg tablets while —— will be available as 80 mg, 120 mg, and 160 mg capsules. Second, Theo-Dur is dosed twice daily while —— will be dosed once daily. Lastly, the risk of confusion between —— and Theo-Dur is minimal because the prefixes "Beta" and "Theo" are different enough to distinguish one name from the other.

——

In reviewing the proprietary name ——", the primary concerns raised were related to sound-alike and look-alike names that already exist in the U.S. marketplace. The products considered having the greatest potential for name confusion with —— were Zofran, vasopressin, Vasotec, Vasodilan, and Vasocine.

We conducted prescription studies to simulate the prescription ordering process. In this case, there was a suggestion that —— could be confused with **vasopressin.** Two participants from the inpatient written study interpreted the name as *vasopressin,* an established name for Pitressin. Although there are limitations to the predictive value of these studies, primarily due to the small sample size, we have acquired safety concerns due to the positive interpretation with this drug product. A positive finding in a study with a small sample size may indicate a high risk and potential for medication errors when extrapolated to the general U.S. population.

Vasopressin is an established name for Pitressin. Pitressin (vasopressin) is indicated for the treatment of diabetes insipidus. Vasopressin is also used for the prevention and treatment of postoperative abdominal distention and to dispel interfering gas shadows in abdominal roentgenography. —— sounds and looks similar to vasopressin as they share the same letter combination —— " In fact, two participants from the inpatient written study provided "vasopressin" as an interpretation. However the risk of confusion between —— and vaspopressin is minimal, because the two products share no commonalties except similar names. —— and vasopressin belong to different pharmacologic classes and are available in different dosage forms. Vasopressin, an antidiuretic hormone, is available in 0.5 mL and 1 mL ampules that contain 20 units/mL. —— an antihypertensive agent, on the other hand, will be available as 80 mg, 120 mg, —— capsules. Moreover, the dosing regimen is different. For the treatment of diabetes insipidus, 5 units to 10 units of vasopressin is administered subcutaneously or intramuscularly two to four times daily. —— on the other hand, is for oral administration and is dosed once daily.

Vasocine contains the active ingredients, prednisolone acetate and sodium sulfacetamide and is indicated for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists. —— may sound and look similar to Vasocine as they share the same prefix "Vaso." However, —— and Vasocine belong to different pharmacologic classes and are available in different dosage forms. Vasocine is available as an ophthalmic ointment while —— will be available as 80 mg, 120 mg, —— capsules. Moreover, the dosing regimen is different. A small amount of Vasocine is applied to affected

eye (s) three to four times daily while —— is orally administered once daily. Lastly, the suffixes "cine" and "pran" differ enough to distinguish one name from the other.

Vasodilan contains the active ingredient, ixosuprine hydrochloride and is indicated for the relief of symptoms associated with cerebral vascular insufficiency; peripheral vascular disease of arteriosclerosis obliterans, thromboangitis obliterans (Buerger's disease) and Raynaud's disease. The names and Vasodilan sound and look similar as they share the same prefix "Vaso" and ending "an." However, there would not be a great risk of potential confusion between —— and Vasodilan, because they differ in strength and dosing interval. Vasodilan is available as 10 mg and 20 mg tablets while —— will be available as 80 mg, 120 mg, capsules. Furthermore, Vasodilan is dosed three to four times daily while —— is dosed once daily.

Vasotec contains the active ingredient, enalapril. Vasotec is indicated for the treatment of hypertension, Symptomatic Congestive Heart Failure, and Asymptomatic Left Venticular Dysfunction. —— and Vasotec may sound and look similar as they share the same prefix, "Vaso". Although —— can look and sound similar to Vasotec, there are distinguishing factors between —— and Vasotec, which may decrease the potential risk of medication errors. —— and Vasotec do not share overlapping strengths. Vasotec is available as 2.5 mg, 5 mg, 10 mg, and 20 mg tablets as well as 1.25 mg/mL injection. —— on the other hand, will be available as 80 mg, 120 mg, capsules. Furthermore, the suffixes "tec" and " look and sound different enough to distinguish one name from the other.

Zofran contains the active ingredient, ondansetron hydrochloride and is used to prevent nausea and vomiting relating to chemotherapy, radiotherapy, and operation. —— and Zofran may sound similar as they share the phonetically similar letter combinations "sopran" and "Zofran". Although —— sounds similar to Zofran, there are distinguishing factors between —— and Zofran, which may decrease the potential risk of medication errors. Zofran products are available in many formulations and are supplied in numerous strengths. For example, Zofran tablets are available in 4 mg, 8 mg, and 24 mg strengths and Zofran oral solution is available in 4 mg/5 mL strength. Zofran is also available as 2 mg/mL injection and 32 mg/50 mL premixed injection. —— on the other hand is available only in 80 mg, 120 mg, capsules. We acknowledge that —— and Zofran share numerically similar strength (8 mg vs. 80 mg), however, they differ in dosing interval. Zofran tablets are dosed twice to three times daily while —— is dosed once daily. Lastly, the prefix "Va" of —— helps to distinguish one name from the other.

III. COMMENTS TO BE SUPPLIED TO THE SPONSOR

DMETS does not recommend the use of the primary proprietary name, —— However, DMETS has no objection to the use of the alternate name, —— In reviewing the proprietary name, ——, the primary concerns were related to one sound-alike and/or look-alike name that already exists in the U.S., namely Betapace.

Betapace and Betapace AF contain the active ingredient, sotalol hydrochloride. Betapace is indicated for the treatment of documented ventricular arrhythmias that are life-threatening. Betapace AF, on the other hand, is indicated for the maintenance of normal sinus rhythm in patients with symptomatic atrial fibrillation/atrial flutter who are currently in sinus rhythm. The risk of confusion between —— and Betapace is likely for several reasons. The proposed name, —— and the currently available name, Betapace, look-alike when scripted (see below), because they share the same prefix "Beta." Our current post-marketing experience indicates that there is a potential risk of medication errors between names that share the same prefix. For instance, post-marketing experience with the drug products "Serzone" and

"Seroquel" have demonstrated that having the same prefix may lead to medication errors. As of April 2002, the Agency has received **twenty-six (26)** medication error reports involving Serozone and Seroquel from the Adverse Event Reporting System (AERS) database. Furthermore, Serzone and Seroquel share an overlapping route of administration (oral), strengths (100 mg and 200 mg), and dosing interval (BID). These confounding factors were critical in causing unnecessary medication errors. Lastly, they are stored next to each other on pharmacy shelves, further increasing the risk of errors. Similarly, — and Betapace share the aforementioned commonalties. — and Betapace share an overlapping route of administration (oral), strengths (80 mg, 120 mg, and 160 mg) and dosing interval (QD). Lastly, — will be placed in close proximity to Betapace on pharmacy shelves, further increasing the risk of errors. We acknowledge that — should be administered at bedtime; however, a provider may order it "QD" instead of "HS" on a prescription. Therefore, a prescription for — could be misinterpreted as "Betapace" or vice versa and lead to medication errors (see below).

Betapace 80mg po QD

— 80mg po QD

If a patient receives Betapace instead of — he or she may remain untreated for hypertension and may also experience the side effects associated with the use of Betapace, such as bradycardia, dyspnea, fatigue, proarrhythmia, and QT interval prolongation. If a patient receives — instead of Betapace, a patient could experience various adverse events associated with — including hypotension, bradycardia, congestive heart failure, fatigue, light-headedness, and bronchospasm. Furthermore, since Betapace is administered to patients with life-threatening arrhythmias, the omission of Betapace could be fatal.

IV. LABELING, PACKAGING AND SAFETY RELATED ISSUES

In the review of the container labels and insert labeling of — DMETS has focused on safety issues relating to possible medication errors. DMETS has identified several areas of possible improvement, which might minimize potential user error.

A. CONTAINER LABEL (Professional sample and 30 count)

1. In order to increase the prominence of the strength, we recommend increasing the font size. We also recommend relocating the strength to appear in close proximity to the proprietary and/or established name.

2. We recommend relocating the net quantity to the bottom the container label in order to prevent confusion with the strength. In addition, the font size of the net quantity statement should be decreased so that it appears smaller than the strength.

3. Revise the usual statement to read: "Usual dosage: One capsule daily at bedtime. See Package Insert" in accordance with 21 CFR 201.100(b)(2).

4. Please decrease the size and prominence of the manufacturer's name and logo. Currently, it appears more prominent than the proprietary name.

5. In order to prevent medication errors due to the similarity in labeling among the strengths (80 mg, 120 mg), we recommend differentiating the labels with the use of contrasting color, boxing, or some other means.

B. INSERT LABELING

No Comments at this time.

V. RECOMMENDATIONS

1. DMETS does not recommend the use of the primary proprietary name, — However, DMETS has no objection to the use of the alternate proprietary name, —

2. DMETS recommends implementation of the labels and labeling as outlined in section IV of this review.

We would appreciate feedback of the final outcome of this consult. We would also be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarification, please contact Sammie Beam at 301-827-3242.

/S/

Hye-Joo Kim Pharm.D.
Safety Evaluator
Office of Drug Safety

Concur:

/S/

Alina R. Mahmud, R.Ph.
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

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

/s/

Hye-Joo Kim
7/12/02 08:10:43 AM
PHARMACIST

Alina Mahmud
7/12/02 08:16:09 AM
PHARMACIST

Carol Holquist
7/12/02 08:42:12 AM
PHARMACIST

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Division/Office)*:
ssociate Director, Medication Error Prevention
Office of Drug Safety, HFD-400
(Rm. 15B-03, PKLN Bldg.)

FROM:
Regulatory Health Project Manager
Division of Cardio-Renal Drug Products, HFD-110
(Rm 5024 , WOC2)

DATE:	IND NO.:	NDA NO.:	TYPE OF DOCUMENT :	DATE OF DOCUMENT:
April 10, 2002		21-438	Correspondence	April 5, 2002

NAME OF DRUG:	PRIORITY CONSIDERATION:	CLASSIFICATION OF DRUG:	DESIRED COMPLETION DATE:
Propranolol Extended Release Capsules	3S		August 1, 2002

NAME OF FIRM:

REASON FOR REQUEST

I. GENERAL

NEW PROTOCOL
☐ PROGRESS REPORT
☐ NEW CORRESPONDENCE
☐ DRUG ADVERTISING
☐ ADVERSE REACTION REPORT
☐ MANUFACTURING CHANGE/ADDITION
☐ MEETING PLANNED BY
☐ PRE--NDA MEETING
☐ END OF PHASE II MEETING
☐ RESUBMISSION
☐ SAFETY/EFFICACY
☐ PAPER NDA
☐ CONTROL SUPPLEMENT
☐ RESPONSE TO DEFICIENCY LETTER
☐ FINAL PRINTED LABELING
☐ LABELING REVISION
☐ ORIGINAL NEW CORRESPONDENCE
☐ FORMULATIVE REVIEW
X OTHER *(SPECIFY BELOW)*:
Trade name review

II. BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
☐ TYPE A OR B NDA REVIEW END OF PHASE II MEETING CONTROLLED STUDIES ☐ PROTOCOL REVIEW ☐ OTHER:	☐ CHEMISTRY REVIEW ☐ PHARMACOLOGY ☐ BIOPHARMACEUTICS ☐ OTHER:

III. BIOPHARMACEUTICS

☐ DISSOLUTION
☐ BIOAVAILABILTY STUDIES
☐ PHASE IV STUDIES
☐ DEFICIENCY LETTER RESPONSE
☐ PROTOCOL-BIOPHARMACEUTICS
☐ IN-VIVO WAIVER REQUEST

IV. DRUG EXPERIENCE

☐ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
☐ DRUG USE e.g. POPULATION EXPOSURE,
ASSOCIATED DIAGNOSES
☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
☐ REVIEW OF MARKETING EXPERIENCE. DRUG USE AND SAFETY
☐ SUMMARY OF ADVERSE EXPERIENCE
☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

☐ CLINICAL ☐ PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:
The sponsor submitted the following product trade names:
First Choice: —
Second Choice: —
The WORD Files of the labels and labeling can be found in the electronic document room.

SIGNATURE OF REQUESTER:	METHOD OF DELIVERY (Check one):
Zelda McDonald	DFS ☐ HAND
SIGNATURE OF RECEIVER:	SIGNATURE OF DELIVERER:

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

/s/

Zelda McDonald
4/10/02 12:56:05 PM

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FILE NO.=746

STN NO.	COMM.	ONE-TOUCH/ ABBR NO.	STATION NAME/TEL NO.	PAGES	DURATION
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-FDA,CDER,OND,ODEI,DCRDP -

********** -CARDIO RENAL - ***** - 301 594 5494- **********

DIVISION OF CARDIO-RENAL DRUG PRODUCTS
FOOD AND DRUG ADMINISTRATION

US Mail address:
FDA/CDER/HFD-110
5600 Fishers Lane
Rockville, MD 20857

Woodmont II
1451 Rockville Pike
Rockville, MD 20852

Transmitted to FAX Number:	7-4576
Attention:	**Roy Castle**
Company Name:	FOI
Phone:	
Subject:	NDA 21-438 AP Letter and draft labeling
Date:	3/12/03
Pages including this sheet:	10

From: **Melissa Robb**
Phone: **301-594-5313**
Fax: **301-594-5494**

PLEASE LET ME KNOW YOU RECEIVED THIS. THANK YOU.

DIVISION OF CARDIO-RENAL DRUG PRODUCTS
FOOD AND DRUG ADMINISTRATION

US Mail address:
FDA/CDER/HFD-110
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Rockville, MD 20857

Woodmont II
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Fax: **301-594-5494**

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