CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-438

Correspondence

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-438

Reliant Pharmaceuticals, LLC
Attention: Mr. Robert J. Mandetta
110 Allen Road
Liberty, NJ 07938

Dear Mr. Mandetta:

We acknowledge receipt on November 27, 2002, of your November 26, 2002 resubmission to your new drug application for InnoPran XL (propranolol HCl) Extended Release 80 mg and 120 mg Capsules.

We consider this a complete, class 2 response to our August 30, 2002 action letter. Therefore, the user fee goal date is May 27, 2003.

If you have any questions, please call:

Ms. Melissa Robb
Regulatory Health Project Manager
(301) 594-5313

Sincerely,

{See appended electronic signature page}

/S/

Zelda McDonald
Chief, Regulatory Health Project Manager
Division of Cardio-Renal Drug Products
Office of Drug Evaluation 1
Center for Drug Evaluation and Research

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
1/3/03 01:48:28 PM

Reliant
PHARMACEUTICALS

Reliant Pharmaceuticals, LLC
110 Allen Road
Liberty Corner, NJ 07938
908-580-1200
Fax: 908-542-9405
www.ReliantRx.com

October 22, 2002

Via Federal Express

Douglas Throckmorton, MD
Director,
Division of Cardio-Renal Drug Products
Food and Drug Administration
Woodmont Office Complex 2
1451 Rockville Pike, 5th Floor (HFD-110)
Rockville, MD 20852

Re: Propranolol Hydrochloride Delayed Onset Controlled Release Capsules,
80 and 120 mg
NDA 21-438
Correspondence to Pending NDA – Reformatted Draft Labeling

Dear Dr. Throckmorton:

The purpose of his communication is to amend the above-mentioned pending application. This amendment consists of revised draft labeling. Ms. Melissa Robb called on October 17, 2002 to request we re-submit the draft labeling in a revised format. The draft labeling in the requested format is provided both electronically and paper.

Should there be any questions, comments or if additional information is needed, please contact me at (908) 542-4429, by email at rmandetta@reliantrx.com, or by telefax at (908) 542-4460.

Sincerely,

Robert J. Mandetta
Director,
Regulatory

RJM/mmc

cc: Melissa Robb

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: March 31, 2003
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Reliant Pharmaceuticals, LLC	October 22, 2002
TELEPHONE NO. (Include Area Code)	**FACSIMILE (FAX) Number (Include Area Code)**
908-542-4423	908-542-4460
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*: 110 Alien Road, Liberty Corner, NJ 07938	**AUTHORIZED U.S. AGENT NAME & ADDRESS** *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)* 21-438

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Propranolol Hydrochloride	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*	**CODE NAME** *(If any)*
(±)-1-(Isopropylamino)-3-(1-naphthyloxy)-2-propanol hydrochloride	—
DOSAGE FORM: Capsule Delayed Onset Controlled Release	**STRENGTHS:** 80, 120 mg
ROUTE OF ADMINISTRATION: Oral	

(PROPOSED) INDICATION(S) FOR USE: Hypertension.

APPLICATION INFORMATION

APPLICATION TYPE *(check one)*
☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b)(1) ☒ 505 (b)(2)

IF AN ANDA, or 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug Inderal LA Holder of Approved Application Wyeth - Ayerst

TYPE OF SUBMISSION *(check one)* ☐ ORIGINAL APPLICATION ☒ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT
☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

IF A SUBMISSION OR PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION Revised Draft Labeling

PROPOSED MARKETING STATUS *(check one)* ☒ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1 THIS APPLICATION IS ☐ PAPER ☒ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g., Final dosage form, Stability/testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

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IND [redacted]
For DMF letters, see Attachment 3.

This application contains the following items: *(Check all that apply)*

☐	1. Index		
☒	2. Labeling *(check one)*	☒ Draft Labeling	☐ Final Printed Labeling
☐	3. Summary (21 CFR 314.50(c))		
☐	4. Chemistry section		
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☐	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)		
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☐	14. A patent certification with respect to any patent which claims the drug (21 U.S.C.355(b)(2) or (j)(2)(A)		
☐	15. Establishment description (21 CFR Part 600, if applicable)		
☐	16. Debarment certification (FD&C Act 306(k)(1))		
☐	17. Field copy certification (21 CFR 314.50(l)(3))		
☐	18. User Fee Cover Sheet (Form FDA 3397)		
☐	19. Financial Information (21 CFR Part 54)		
☐	20. OTHER *(Specify)*		

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been review and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
R J Mandetta	Robert J. Mandetta Director, Regulatory	10/22/02

ADDRESS *(Street, City, State, and ZIP Code)*	TELEPHONE NUMBER
110 Allen Road, Liberty Corner, NJ 07938	908-542-4429

Public reporting burden for this collection of information is estimated to average 24 hours 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

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.

74 pages redacted from this section of the approval package consisted of draft labeling

Reliant Pharmaceuticals, LLC
110 Allen Road
Liberty Corner, NJ 07938
908-580-1200
Fax: 908-542-3405
www.ReliantRx.com

October 10, 2002

Via Federal Express

Douglas Throckmorton, MD
Director,
Division of Cardio-Renal Drug Products
Food and Drug Administration
Woodmont Office Complex 2
1451 Rockville Pike, 5th Floor (HFD-110)
Rockville, MD 20852

Re: Propranolol Hydrochloride Delayed Onset Controlled Release Capsules,
80 and 120 mg
NDA 21-438
Correspondence to Pending NDA – New Trade/Generic Name Consideration

Dear Dr. Throckmorton:

The purpose of his communication is to amend the above-mentioned pending NDA. Our submission of October 1, 2002 requested a new name for consideration by the Agency. We were informed that our current name, ——— would have to be withdrawn before the Agency will consider a new name. This amendment consists of providing new names for consideration by the Agency. We are therefore withdrawing our amendment of October 1, 2002 and the name ——— and submitting two new names. The names are:

First Choice	**Trade Name:**	InnoPran XL
	Generic Name:	Propranolol HCL Delayed Onset Controlled Release
Second Choice	**Trade Name:**	———
	Generic Name:	Propranolol HCL Delayed Onset Controlled Release

Should there be any questions, comments or if additional information is needed, please contact me at (908) 542-4429, by email at rmandetta@reliantrx.com, or by telefax at (908) 542-4460.

Sincerely,

Robert J. Mandetta
Director,
Regulatory

RJM/mmc

cc: Zelda McDonald

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: March 31, 2003
See OMB Statement on page 2.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Reliant Pharmaceuticals, LLC	October 10, 2002
TELEPHONE NO. (Include Area Code)	**FACSIMILE (FAX) Number (Include Area Code)**
908-542-4423	908-542-4460
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued):*	AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE
110 Allen Road Liberty Corner, NJ 07938	

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)* 21-438

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
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CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*
(±)-1-(Isopropylamino)-3-(1-naphthyloxy)-2-propanol hydrochloride

CODE NAME *(If any)*

DOSAGE FORM: Capsule Delayed Onset Controlled Release	STRENGTHS: 80, 120 mg	ROUTE OF ADMINISTRATION: Oral

(PROPOSED) INDICATION(S) FOR USE: Hypertension

APPLICATION INFORMATION

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Name of Drug Inderal LA Holder of Approved Application Wyeth - Ayerst

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REASON FOR SUBMISSION New Trade/Generic Name Consideration

PROPOSED MARKETING STATUS *(check one)* ☒ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

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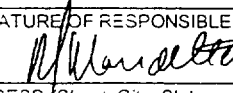	Robert J. Mandetta Director, Regulatory	10/10/02

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October 1, 2002

Via Federal Express

Douglas Throckmorton, MD
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Division of Cardio-Renal Drug Products
Food and Drug Administration
Woodmont Office Complex 2
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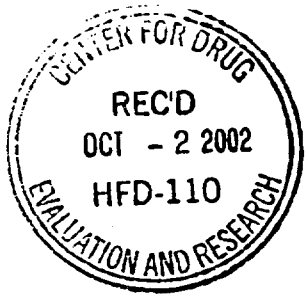
Rockville, MD 20852



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80 and 120 mg
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Generic Name: Propranolol HCL Delayed Onset Controlled Release

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cc: Zelda McDonald

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REASON FOR SUBMISSION Providing new name for consideration

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IND
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- ☐ 12. Case report forms (e.g., 21 CFR 314.50(f)(2); 21 CFR 601.2)
- ☐ 13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
- ☐ 14. A patent certification with respect to any patent which claims the drug (21 U.S.C.355(b)(2) or (j)(2)(A)
- ☐ 15. Establishment description (21 CFR Part 600, if applicable)
- ☐ 16. Debarment certification (FD&C Act 306(k)(1))
- ☐ 17. Field copy certification (21 CFR 314.50(l)(3))
- ☐ 18. User Fee Cover Sheet (Form FDA 3397)
- ☐ 19. Financial Information (21 CFR Part 54)
- ☒ 20. OTHER *(Specify)* Providing new name for consideration

CERTIFICATION

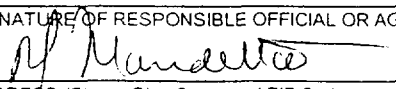
I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660 and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80 and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been review and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
	Robert J. Mandetta Director, Regulatory	10/01/02

ADDRESS *(Street, City, State, and ZIP Code)*	TELEPHONE NUMBER
110 Allen Road, Liberty Corner, NJ 07938	908-542-4429

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-438

Reliant Pharmaceuticals, LLC
Attention: Keith S. Rotenberg, Ph.D.
110 Allen Road
Liberty Corner, NJ 07938

Dear Dr. Rotenberg:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: [redacted] (propranolol HCl) ER Capsules

Review Priority Classification: Standard (S)

Date of Application: October 31, 2001

Date of Receipt: November 2, 2001

Our Reference Number: NDA 21-438

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on January 1, 2002 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be September 2, 2002 and the secondary user fee goal date will be November 2, 2002.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. All communications concerning this NDA should be addressed as follows:

U.S. Postal Service:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products, HFD-110
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products, HFD-110
Attention: Division Document Room
1451 Rockville Pike
Rockville, Maryland 20852-1420

If you have any questions, please call:

Ms. Zelda McDonald
Regulatory Health Project Manager
(301) 594-5333

Sincerely,

/S/

{See appended electronic signature page}

Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

/s/

Natalia Morgenstern
11/14/01 03:11:04 PM

EXTERNAL DISTRIBUTION: September 5, 2001

From: Robert Mandetta

Copies To:

FDA – Zelda McDonald, Project Manager DCRDP

Reliant Pharmaceuticals, LLC Regulatory File

Reliant Pharmaceuticals, LLC
110 Allen Road
Liberty Corner, NJ 07938
908-580-1200
Fax: 908-542-9405
www.ReliantRx.com

September 5, 2001

Raymond Lipicky, M.D.
Director,
Division of Cardio-Renal Drug Products
Woodmont Office Complex 2
1451 Rockville Pike – 5th Floor
Rockville, MD 20852

Re: IND [redacted] (propranolol hydrochloride) Extended Release
Serial No. 020
Meeting Minutes – August 1, 2001

Dear Dr. Lipicky:

The purpose of this communication is to provide the meeting minutes for the above-mentioned pre-NDA Teleconference, for August 1, 2001.

Please note two minor inconsistencies between the sponsor's minutes and the Division's minutes; specifically, comments to the proposed impurity specification and the presented executed batch record, points 5 and 7 respectively. For clarification and regarding point 5, the total impurities limit was reported as NMT % . For the other matter, Reliant proposed the incorporation of the executed manufacturing batch record of either the 80 mg or 120 mg strength drug product in lieu of the strength representation. The reason given was that capsule weight checking was performed on these other strength batches, and the Division said this would be acceptable.

If you require further assistance, please do not hesitate to call.

Sincerely,

Robert J. Mandetta
Director,
Regulatory Affairs
(908) 542-4429

RJM/mmc

cc: Reliant Pharmaceuticals, LLC Regulatory File

COPY

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

INVESTIGATIONAL NEW DRUG APPLICATION (IND)

(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)

Form Approved: OMB No. 0910-0014.
Expiration Date: September 30, 2002
See OMB Statement on Reverse.

NOTE: No drug may be shipped or clinical investigation begun until an IND for that investigation is in effect (21 CFR 312.40).

1. NAME OF SPONSOR
Reliant Pharmaceuticals, LLC

2. DATE OF SUBMISSION
05 September 2001

3. ADDRESS *(Number, Street, City, State and Zip Code)*
110 Allen Road
Liberty Corner, NJ 07938

4. TELEPHONE NUMBER *(Include Area Code)*
908.542.4429

5. NAME(S) OF DRUG *(Include all available names: Trade, Generic, Chemical, Code)*
Propranolol Hydrochloride

6. IND NUMBER *(If previously assigned)*

7. INDICATION(S) *(Covered by this submission)*
Hypertension

8. PHASE(S) OF CLINICAL INVESTIGATION TO BE CONDUCTED:
☐ PHASE 1 ☐ PHASE 2 ☐ PHASE 3 ☐ OTHER _____ *(Specify)*

9. LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS (21 CFR Part 312), NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, DRUG MASTER FILES *(21 CFR Part 314.420)*, AND PRODUCT LICENSE APPLICATIONS (21 CFR Part 601) REFERRED TO IN THIS APPLICATION.
DMF
DMF
DMF

10. ***IND submission should be consecutively numbered. The initial IND should be numbered "Serial number: 000." The next submission (e.g., amendment, report, or correspondence) should be numbered "Serial Number: 001." Subsequent submissions should be numbered consecutively in the order in which they are submitted.***

SERIAL NUMBER
0 2 0

11. THIS SUBMISSION CONTAINS THE FOLLOWING: *(Check all that apply)*

☐ INITIAL INVESTIGATIONAL NEW DRUG APPLICATION (IND)
☐ RESPONSE TO CLINICAL HOLD

PROTOCOL AMENDMENT(S):
☐ NEW PROTOCOL
☐ CHANGE IN PROTOCOL
☐ NEW INVESTIGATOR

INFORMATION AMENDMENT(S):
☐ CHEMISTRY/MICROBIOLOGY
☐ PHARMACOLOGY/TOXICOLOGY
☐ CLINICAL

IND SAFETY REPORT(S):
☐ INITIAL WRITTEN REPORT
☐ FOLLOW-UP TO A WRITTEN REPORT

☐ RESPONSE TO FDA REQUEST FOR INFORMATION
☐ ANNUAL REPORT
☒ GENERAL CORRESPONDENCE
☐ REQUEST FOR REINSTATEMENT OF IND THAT IS WITHDRAWN, INACTIVATED, TERMINATED OR DISCONTINUED
☐ OTHER Meeting Mins -8/1/01 Pre-NDA Teleconf. *(Specify)*

CHECK ONLY IF APPLICABLE

JUSTIFICATION STATEMENT MUST BE SUBMITTED WITH APPLICATION FOR ANY CHECKED BELOW. REFER TO THE CITED CFR SECTION(S) FOR FURTHER INFORMATION.

☐ PRE-IND MEETING (21 CFR 312.82(b)) ☐ FREQUENT PROTOCOL AMENDMENTS (21 CFR 312.30(b)(1)) ☐ CHARGE REQUEST (21 CFR 312.8(d))

FOR FDA USE ONLY

CDR/DBIND/DGD RECEIPT STAMP

DDR RECEIPT STAMP
CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
SEP - 6 2001
HFD-110

DIVISION ASSIGNMENT:

IND NUMBER ASSIGNED:

COPY

Redacted 3

pages of trade secret and/or confidential commercial information