CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-321

Correspondence

Redacted 19

pages of trade

secret and/or

confidential

commercial

information

Renal

Baxter Healthcare Corporation
1620 Waukegan Road
McGaw Park, Illinois 60085-6730
847.473.6030

Baxter

October 30, 2001

Raymond J. Lipicky, M.D.
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products
Attention: Document Control Room, HFD-110
1451 Rockville Pike
Rockville, MD 20852

RE: NDA 21-321
Extraneal™ (7.5% icodextrin) Peritoneal Dialysis Solution
Minor Amendment - 12
Proposed Draft Labeling

Dear Dr. Lipicky:

Baxter Healthcare Corporation acknowledges receipt of the Approvable Letter for NDA 21-321 by fax on October 22, 2001 and by mail on October 26, 2001. In response to this action letter and in accordance with 21 CFR 314.60, Baxter Healthcare Corporation is amending NDA 21-321 to include proposed draft labeling. This draft labeling is in response to the marked–up draft labeling included with the Approvable Letter.

Comments from the marked-up draft which were acceptable to Baxter or did not require or request sponsor input have been incorporated into the proposed labeling without highlighting. Those comments requesting sponsor input have been addressed as bolded, underlined text in the labeling and with a bolded reference or description in the right hand column. In addition, editorial/typographical comments have been identified in this same manner.

The amendment includes a version of the proposed label as described in the preceding paragraph, a version of text without sponsor comments, and electronic copies in pdf and Word.

Baxter Healthcare Corporation has accepted most of Dr. Temple's comments. There are two sections for which alternative proposals have been incorporated into the draft label:

1. The section "Clinical Studies – *Ultrafiltration, Urea and Creatinine Clearance, Negative Net Ultrafiltration*" (page 5-6) had been reorganized by Dr. Temple into CAPD data followed by APD data. The —— which had been a separate paragraph at the end of the section, was removed during the reorganization of this section. Baxter has included this integral and critical UF data by CAPD and APD to follow with Dr. Temple's organization of this section.

2. In the section "INDICATIONS AND USAGE" the second paragraph had been removed. Baxter proposes modifying this section by [redacted] described in a key section of the package insert for prescribing physicians.

Baxter would appreciate a response to the proposed draft labeling at the Division's earliest convenience. If the proposed labeling is acceptable, Baxter will submit final printed labeling and will not require the meeting with Dr. Temple scheduled for November 9, 2001 from 2:00 - 3:30pm EST.

Please do not hesitate to contact me at **847-473-6361** if you have any questions or comments.

Sincerely yours,

Mary Kay Rybicki

Mary Kay Rybicki
Associate Director, Regulatory Affairs

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

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

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

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

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Baxter Healthcare Corporation	October 30, 2001
TELEPHONE NO. *(Include Area Code)* 847-473-6361	FACSIMILE (FAX) Number *(Include Area Code)* 847-473-6952
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*: 1620 Waukegan Road, McGaw Park, IL 60085	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)* NDA 21-321

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
icodextrin	Extraneal

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)* alpha 1,4 polyglucopyranose

CODE NAME *(If any)*

DOSAGE FORM:	STRENGTHS:	ROUTE OF ADMINISTRATION:
PD Solution	7.5% w/v	Intraperitoneal

(PROPOSED) INDICATION(S) FOR USE:
Treatment of Chronic Renal Failure

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 — Holder of Approved Application

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 OF 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 Response to Requets for Information 9/6, 9/7, and 9/19, 2001

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.

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

IND ( ) NDA 17-512 NDA 20-163 NDA 20-183 DMF ( ) DMF ( ) DMF ( )

This application contains the following items: *(Check all that apply)*	
	1. Index
X	2. Labeling *(check one)* ☒ Draft Labeling ☐ Final Printed Labeling
	3. Summary (21 CFR 314.50 (c))
	4. Chemistry section
	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
	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 (k)(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, 211 or 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 Part 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 reviewed 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
Mary Kay Rybicki	**Mary Kay Rybicki, Assoc. Dir., Regulatory Affairs**	10/30/01

ADDRESS *(Street, City, State, and ZIP Code)*	Telephone Number
1620 Waukegan Road McGaw Park, IL 60085	**( ) 847-473-6361**

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

Food and Drug Administration
CDER, HFD-94
12420 Parklawn Dr., 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.

FORM FDA 356h (4/00)

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:	**(847) 473-6952**
Attention:	**Ms. Mary Kay Rybicki**
Company Name:	**Baxter Healthcare Corporation**
Phone:	(847) 473-6361
Subject:	**FDA Participants, November 9, 2001 Teleconference**
Date:	**November 16, 2001**
Pages including this sheet:	**2**
From:	**Quynh Nguyen, Pharm.D.**
Phone:	**(301) 594-5311**
Fax:	**(301) 594-5494**

Dear Mary Kay,

Per your request, please find attached a list of the FDA participants from the November 9, 2001 teleconference for NDA 21-321/Extraneal. If you have any questions, please do not hesitate to contact me at the above numbers.

Thanks.
Quynh

PLEASE LET ME KNOW YOU RECEIVED THIS. THANKS!

BAXTER HEALTHCARE CORPORATION
1620 Waukegan Road
McGaw Park, IL 60085

Fax Cover Sheet

DATE:	November 13, 2001	**TIME:**	1:16 PM
TO:	Quynh Nguyen, Pharm.D. FDA/CDER/DCRDP	**PHONE:** **FAX:**	301-594-5311 301-594-5494
FROM:	M.K. Rybicki Baxter Regulatory Affairs	**PHONE:** **FAX:**	847-473-6361 847-473-6952
RE:	NDA 21-321, Extraneal (7.55 icodextrin) PDS		
CC:			

Number of pages including cover sheet: 4

Message

Dear Quynh:

Please find attached the proposed Clinical Studies and Serum Electrolytes sections of the Extraneal Labeling. This information is being provided in follow-up to the teleconference held on November 9, 2001. The Baxter attendees for that teleconference were:

Richard Newman, PhD. VP Regulatory Affairs	Marsha Wolfson, M.D. VP Global Clinical Affairs

Please do not hesitate to contact me at **847-473-6361** if you have any questions.

Sincerely yours,

Mary Kay Rybicki

Mary Kay Rybicki
Associate Director, Regulatory Affairs

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

BAXTER HEALTHCARE CORPORATION
1620 Waukegan Road
McGaw Park, IL 60085

Fax Cover Sheet

DATE:	November 14, 2001	TIME:	9:41 AM
TO:	Quynh Nguyen, Pharm.D. FDA/CDER/DCRDP	PHONE: FAX:	301-594-5311 301-594-5494(5)
FROM:	Mary Kay Rybicki Baxter Regulatory Affairs	PHONE: FAX:	847-473-6361 847-473-6952
RE:	NDA 21-321, Extraneal (7.5% icodextrin) PDS		
CC:			

Number of pages including cover sheet: 17

Dear Quynh:

In follow-up to Baxter's conversation with Dr. Doug Throckmorton this morning, I am faxing to you a copy of draft labeling for Extraneal with changes discussed in the telephone conversation. Please note that the other changes requested at the November 9, 2001 teleconference have been incorporated except for the representation of the non-proprietary name and the statement requested at the end of the Carcinogenesis, Mutagensesis, Impairment of Fertility section. These two items are under discussion with the respective reviewers, with resolution expected later this week.

Thanks you for your help. Please do not hesitate to contact me at **847-473-6361** if you have any questions.

Mary Kay Mary Kay Rybecki

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

RENAL REG AFFAIRS Fax:8474736952

** Transmit Conf.Report **

P.1 Nov 14 2001 9:32

Fax/Phone Number	Mode	Start	Time	Page	Result	Note
93015945495	NORMAL	14, 9:32	6'01"	17	* O K	Manual

Mary Kay Rybicki
11/19/2001 08:48 AM

To: THROCKMORTON@CDER.FDA.GOV
cc: NGUYENQ@CDER.FDA.GOV
Subject: EXTRANEAL NDA 21-321

RE: Extraneal NDA 21-321, Draft Labeling - Serum Electrolytes- Change in Patient Numbers <125mmol/L for Control

Dear Dr. Throckmorton:

Per your voicemail, Baxter is providing via E-mail the change in numbers of control patients whom developed serum sodium values less than 125 mmol/L. In the fax of November 14, 2001 the numbers of patients were described as 4 Extraneal and 3 control. During annotation of the proposed labeling, it was noted that one of the control patients participated in study RD-97-CA-130 and experienced a serum sodium value of < 125mmol/L at the last visit (4 weeks). This patient then rolled over into study RD-97-CA-131. The 4 week value from the 130 study became the 4 week value for the 131 study. Thus, this was one patient who had a serum sodium value < 125mmol/L at only one time point, but was counted twice.

The patients with serum sodium <125mmol/L are described below:

CONTROL:

Study 130	Patient 26102	Value= 124 at Week 4 (originally counted twice as this patient rolled over into study 131)
Study 131	Patient 22301	Value= 124 at Week 39

EXTRANEAL:

Study 131	Patient 06201	Value= 124 at Week 13
Study 131	Patient 18302	Value= 119 at Week 39
Study 131	Patient 24301	Value= 124 at Week 39
Study 131	Patient 32501	Value= 123 at Week 13 and Value= 124 at Week 26

The proposed serum electrolyte section, with annotation to NDA 21-321, should read as follows:

Laboratory Tests	
Serum Electrolytes	
	Volume 1.31 Page 077 Volume 1.38 Page 088 Volume 1.54 Page 062 Volume 1.34 page 272 Volume 1.45 Page183 Volume 1.45 Page 214 Volume 1.45 Page 201 Volume 1.45 Page 218

Baxter will amend NDA 21-321 with the labeling changes provided by fax on November 13, 14 and the change described in this e-mail. In addition, disucssions are anticipated to conclude today (November 19, 2001) with the Pharmacologist, Dr. Jim Willard, regarding the pre-clinical statement requested in the

teleconference of November 9, 2001. Baxter has been in discusion with Dr. Willard reagarding his request to add the statment

to the Carcinogenesis, Mutagensesis, and Impairment of Fertility section. Baxter does not agree that data support this statment.

Please do not hesitate to contact me at 847-473-6361 if you have any questions of comments.

Mary Kay Rybicki

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-321

INFORMATION REQUEST LETTER

Baxter Health Care Corporation
Attention: Mary Kay Rybicki
Associate Director, Regulatory Affairs
1620 Waukegan Road
McGaw Park, IL 60885-6730

Dear Ms. Rybicki:

Please refer to your December 20, 2000 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Extraneal (7.5% Icodextrin) Peritoneal Dialysis Solution.

We also refer to your submissions dated March 20, 2001 May 16, 2001 May 23,2001 June 13, 2001.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

Regarding update of ML Laboratories DMF [redacted] for Icodextrin:

There are some issues related to DMF [redacted] which need to be resolved. The DMF holder has been informed to address these issues and update their DMF as per Lorna Clisby's e-mail of April 20, 2001.

Regarding Specifications of Icodextrin:

Please include % Mass in Range (Molecular Weight Distribution) in the drug substance icodextrin specifications. Weight Average Molecular Weight (Mw), Number Average Molecular Weight (Mn) and % Mass in range (Mw) specifications should all be similar to those included in ML Laboratories specifications of drug substance icodextrin.

Regarding . Method Validation of the drug product:

In the experimental design, please clearly describe the purpose of various control and test articles. For specificity, it was difficult to understand the purpose of test and control articles,

experimental design, and how the results proved the specificity of the method. Please clarify these issues.

To prove the ruggedness you have done re-assay of same solution after 24 hours which is not sufficient. Ruggedness is the ability of the procedure to provide analytical results of acceptable accuracy and precision under changed conditions of the test procedure. To prove the ruggedness please repeat the procedure taking into account the variations that may be expected when the same defined procedure of analysis is employed using different personnel, laboratories and equipment etc.

Regarding Regulatory Specification of the drug product Extraneal (7.5% icodextrin) PDS:

In addition to Number Average Molecular Weight and Weight Average Molecular Weight, please include % Mass in Range (Molecular Weight Distribution) in the regulatory and shelf-life specification of the drug product. Please also include an identification method in the product specification.

Extractables such as [redacted] should also be included in the regulatory specifications with limits.

Regarding [redacted] Method Validation for the drug product Extraneal (7.5% icodextrin) PDS:

Please provide a full method validation report for the [redacted] method for the parameters Number Average Molecular Weight, Weight Average Molecular Weight and % Mass in range (Mw).

Regarding stability protocols, stability data and expiration date of drug product:

The —— method alone cannot be considered stability indicating since breakdown of icodextrin to smaller units is also likely to contribute to overall specific ——. Therefore, the assay by —— will not properly reflect degradation products and cannot be considered a stability indicating method. Please revise all stability protocols to include testing of Number Average Molecular Weight, Weight Average Molecular Weight and % Mass in range (Molecular Weight Distribution).

The stability data and supporting clinical stability data provided and not sufficient to approve an expiration date of 24 months; instead an expiration date of— months can be granted at this time.

Regarding Extractable from containers:

The stability data provided in this NDA includes some tests for extractable —— —— items but you have not discussed the issue of extractables which is an important consideration for this product. The test for —— was removed from the stability protocol of first three production lots (Table III from Vol. 1.4, page 190) and no explanation was given. You have not discussed or monitored —— components in any of the stability studies. Please address these issues and provide full information about the possible extractable items and studies/tests for monitoring their levels in Extraneal. Please include all extractable products in the stability protocol of the first 3 post-approval production lots. Data from these studies will determine the extent to which further monitoring of annual commercial production batches will be necessary.

Regarding labeling of the final product:

Various –OH groups are missing but the bonds are still there which in standard organic chemistry terminology implies that there are CH_3 groups. The 1,4 linkage shown in the chemical structure of icodextrin in the package insert and various other places in the NDA represents the fragment "–CH_2OCH_2-" rather than "-O-". Please correct the icodextrin structure to remove the extra –CH_2 groups and to show all "-OH" groups. You may use the icodextrin structure similar to the one given in the USP Dictionary (2000) but including both 1,4 and 1,6 linkages.

The container labels (primary and secondary) have two different storage statements. Please revise the storage temperature statement on all labels including package insert to the following:

"Store at 20°C-25°C (68-77°F) [see USP Controlled Room Temperature]"

The adhesive labels provided have the container abbreviated as "CONT" which is confusing; please replace it with "CONTAINER". The adhesive labels also have too much information irrelevant to the actual label. Please provide copies of the adhesive labels with the final information, which will go on cardboard cartons and also submit a sample copy of the cardboard carton with adhesive label. The carton labels contain "7.5" in a rectangular box; please clarify its purpose and inform if this is the final format.

If you have any questions, call John Guzman, Regulatory Health Project Manager, at (301) 594-5312.

Sincerely,

/S/

Kasturi Srinivasachar, Ph.D.
Chemistry Team Leader, DNDC I for the
Division of Cardio-Renal Drug Products, HFD-110
DNDC 1, Office of New Drug Chemistry
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/

Kasturi Srinivasachar
9/7/01 05:12:11 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-321

Baxter Healthcare Corporation
Attention: Steven Engel, PharmD
1620 Waukegan Road
McGaw Park, IL 60085

Dear Dr. Engel:

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: Extraneal (icodextrin) 7.5% w/v PD Solution

Review Priority Classification: Standard (S)

Date of Application: December 22, 2000

Date of Receipt: December 22, 2000

Our Reference Number: NDA 21-321

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 February 20, 2001 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be October 22, 2001 and the secondary user fee goal date will be December 22, 2001.

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:

Mr. John Guzman
Regulatory Project Manager
(301) 594-5312

Sincerely,

/S/

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