

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

022372Orig1s000

CHEMISTRY REVIEW(S)

NDA 22-372

SUPREP[®] BOWEL PREP KIT (sodium sulfate, potassium sulfate and magnesium sulfate) Oral Solution

Braintree Laboratories

Tarun Mehta

Review Chemist

**Office of New Drug Quality Assessment
Division of Pre-Marketing Assessment II
Branch III**

**CMC REVIEW OF NDA 22-372
For the Division of Gastroenterology Products (HFD-180)**

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CMC Review Data Sheet

CMC Review Data Sheet

1. NDA 22-372
2. REVIEW #: 2
3. REVIEW DATE: 04-27-2009
4. REVIEWER: Tarun Mehta
5. PREVIOUS DOCUMENTS:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Original Submission	02-July-2008
Correspondence (C)	
Stability Update	26-Jan-2009
Amendment	27-Jan-2009
Amendment	26-Feb-2009
Stability update	18-Feb-2009
Letter of Authorization from K&S GmbH	03-April-2009
Revised Drug Product Specification	03-April-2009

6. SUBMISSION(S) BEING REVIEWED:

Labeling final revision was received on August 03, 2009

7. NAME & ADDRESS OF APPLICANT:

Name: Braintree Laboratories, Inc.
Address: 60 Columbian Street, West, PO Box: 850929
Braintree, MA 02185
Representative: Vivian A. Caballero, Director of Regulatory Affairs
Telephone: (781) – 843-2202

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: SUPREP[®] BOWEL PREP KIT
- b) Non-Proprietary Name: Sodium sulfate, potassium sulfate and magnesium sulfate
- c) Code Name/# (ONDQA only): None
- d) Chem. Type/Submission Priority (ONDQA only):
 - Chem. Type: 4

CMC Review Data Sheet

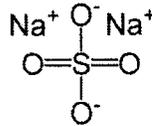
- Submission Priority: Standard

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)
10. PHARMACOL. CATEGORY: Osmotic bowel cleansing
11. DOSAGE FORM: Solution
12. STRENGTH/POTENCY: Each 6oz bottle contains: sodium sulfate 17.5g, potassium sulfate 3.13g, magnesium sulfate 1.6g.
13. ROUTE OF ADMINISTRATION: Oral
14. Rx/OTC DISPENSED: Rx OTC
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
 SPOTS product – Form Completed
 Not a SPOTS product

1. CHEMICAL NAME, MOLECULAR STRUCTURE, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: **Sodium Sulfate USP**

Molecular Formula: Na₂SO₄

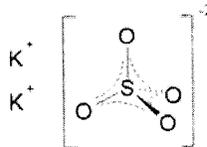


Molecular Structure:

Molecular Weight: 142.04

Chemical Name: **Potassium Sulfate, FCC**

Molecular Formula: K₂SO₄



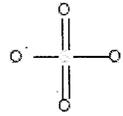
Molecular Structure:

Molecular Weight: 174.26

Chemical Name: **Magnesium Sulfate USP**

Molecular Formula: MgSO₄

CMC Review Data Sheet



Molecular Structure:
Molecular Weight: 120.37

CMC Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	(b) (4)	1	Adequate	16-DEC-2008	Reviewed by Tarun Mehta
	III			4	Adequate		
	III			4	Adequate		
	III			3	Adequate	Reviewed by Bertha Craig 9/24/07	No update since the last review

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 –Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

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

B. Other Documents: None

18. STATUS:

ONDQA:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EA	Adequate	4/07/2009	Categorical exclusion is acceptable as per 21CFR 25.31 (a)
EES	Overall Compliance	4/29/2009	E. Johnson (HFD-320)
Microbiology	Adequate	4/07/2009	Vinayak Pawar, Ph.D.

Executive Summary Section

The CMC Review for NDA 22-372

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This NDA has provided sufficient information to assure identity, strength, purity, and quality of the drug product. An “Acceptable” recommendation from the Office of Compliance has been made. The labels have adequate information as required. Therefore, from the CMC perspective, this NDA is now recommended for approval.

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

Not applicable

II. Summary of CMC Assessments

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

(1) Drug Substance

SuPrep® formulation contains three drug substances: sodium sulfate (USP), potassium sulfate (Ph.Eur., FCC) and magnesium sulfate (USP). All three drug substances are compendial grade materials. Adequate chemistry, manufacturing and controls information is provided either in the DMF or through the NDA. The drug substances are inorganic salts and freely soluble in water. The quality of the drug substances is controlled by the compendial (USP/FCC/Ph.Eur.) monographs. Based on the stability data, adequate re-test period are established by the manufacturers:

(b) (4)

(2) Drug Product

SuPrep® (sodium sulfate, potassium sulfate, magnesium sulfate) oral solution is a concentrated liquid (sodium sulfate 17.5g, potassium sulfate 3.13g, magnesium sulfate 1.6g in 6 oz) and supplied in a 6oz unit dose bottle, which is made of amber (b) (4) and capped with an induction seal and a child resistant HDPE cap. The composition and manufacturing process of the clinical batches and proposed commercial batches are identical. Except for sucralose, all other excipients used in the drug product are compendial (USP/FCC) grade. All the

Executive Summary Section

excipients are listed in the FDA inactive ingredient list and have been used in the previously drug products at or below the proposed concentration. The drug product is manufactured by (b) (4)

The identity, strength, purity and quality of the final drug product are assured by the specification: description, pH, content uniformity, deliverable volume, assay of APIs and benzoate and microbial limit assay Based on available stability data, the expiration dating period of 24 months is granted.

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

The drug product is indicated for cleansing the colon as a preparation for colonoscopy. The drug product can be dosed by (b) (4) overnight preparation (b) (4). The drug product is sold in single unit (6oz bottle) dose. Patient required to pour the drug product contents of one 6oz bottle into the (b) (4) mixing cup and dilute it with water to 16oz. The patient will drink entire volume of 16oz (b) (4) followed by two additional 16oz of water (b) (4). At certain time interval, (b) (4), the patient will prepare and drink the second dose (6oz bottle) in a similar manner.

C. Basis for Approvability or Not-Approval Recommendation

The sponsor has provided sufficient information on raw material controls, manufacturing process and process controls, and adequate specifications for assuring consistent product quality of the drug substance and drug product. The NDA has also provided sufficient stability information on the drug product to assure strength, purity, and quality of the drug product during the expiration dating period.

All facilities have an “Acceptable” recommendation from the office of compliance.
All labels have required information.

Executive Summary Section

III. Administrative**A. Reviewer's Signature:**

(See appended electronic signature page)

Tarun Mehta, M.Sc.

B. Endorsement Block:

(See appended electronic signature page)

Moo-Jhong Rhee, Ph.D. Branch Chief, Branch III, ONDQA

C. CC Block: entered electronically in DFS

11 Page(s) has been Withheld in Full as b4 (CCI/TS) immediately following this page

Linked Applications	Submission Type/Number	Sponsor Name	Drug Name / Subject
NDA 22372	ORIG 1	BRAINTREE LABORATORIES INC	SUPREP BOWEL PREP KIT
NDA 22372	ORIG 1	BRAINTREE LABORATORIES INC	SUPREP BOWEL PREP KIT

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

/s/

TARUN D MEHTA
08/06/2009

MOO JHONG RHEE
08/06/2009
Chief, Branch III

NDA 22-372

SUPREP[®] BOWEL PREP KIT (sodium sulfate, potassium sulfate and magnesium sulfate) Oral Solution

Braintree Laboratories

Tarun Mehta

Review Chemist

**Office of New Drug Quality Assessment
Division of Pre-Marketing Assessment II
Branch III**

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S.2 Manufacture	21
S.3 Characterization	23
S.4 Control of Drug Substance.....	23
S.5 Reference Standards or Materials	24
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CMC Review Data Sheet

1. NDA 22-372
2. REVIEW #: 1
3. REVIEW DATE: 04-27-2009
4. REVIEWER: Tarun Mehta
5. PREVIOUS DOCUMENTS: None
6. SUBMISSION(S) BEING REVIEWED:

<u>Submission(s) Reviewed</u>	<u>Document Date</u>
Original Submission	02-July-2008
Correspondence (C)	
Stability Update	26-Jan-2009
Amendment	27-Jan-2009
Amendment	26-Feb-2009
Stability update	18-Feb-2009
Letter of Authorization from K&S GmbH	03-April-2009
Revised Drug Product Specification	03-April-2009

7. NAME & ADDRESS OF APPLICANT:

Name: Braintree Laboratories, Inc.
Address: 60 Columbian Street, West, PO Box: 850929
Braintree, MA 02185
Representative: Vivian A. Caballero, Director of Regulatory Affairs
Telephone: (781) – 843-2202

8. DRUG PRODUCT NAME/CODE/TYPE:

- a) Proprietary Name: SUPREP[®] BOWEL PREP KIT
- b) Non-Proprietary Name: Sodium sulfate, potassium sulfate and magnesium sulfate
- c) Code Name/# (ONDQA only): None
- d) Chem. Type/Submission Priority (ONDQA only):
 - Chem. Type: 4
 - Submission Priority: Standard

9. LEGAL BASIS FOR SUBMISSION: 505(b)(1)

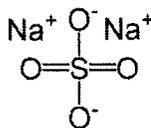
CMC Review Data Sheet

10. PHARMACOL. CATEGORY: Osmotic bowel cleansing
11. DOSAGE FORM: Solution
12. STRENGTH/POTENCY: Each 6oz bottle contains: sodium sulfate 17.5g, potassium sulfate 3.13g, magnesium sulfate 1.6g.
13. ROUTE OF ADMINISTRATION: Oral
14. Rx/OTC DISPENSED: Rx OTC
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):
 SPOTS product – Form Completed
 Not a SPOTS product

1. CHEMICAL NAME, MOLECULAR STRUCTURE, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: **Sodium Sulfate USP**

Molecular Formula: Na_2SO_4

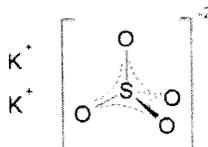


Molecular Structure:

Molecular Weight: 142.04

Chemical Name: **Potassium Sulfate, FCC**

Molecular Formula: K_2SO_4

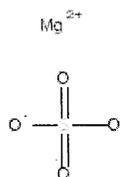


Molecular Structure:

Molecular Weight: 174.26

Chemical Name: **Magnesium Sulfate USP**

Molecular Formula: MgSO_4



Molecular Structure:

Molecular Weight: 120.37

CMC Review Data Sheet

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE ¹	STATUS ²	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	(b) (4)	1	Adequate	16-DEC-2008	Reviewed by Tarun Mehta
	III			4	Adequate		
	III			4	Adequate		
	III			3	Adequate	Reviewed by Bertha Craig 9/24/07	No update since the last review

¹ Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 –Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

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

B. Other Documents: None

18. STATUS:

ONDQA:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
EA	Adequate	4/07/2009	Categorical exclusion is acceptable as per 21CFR 25.31 (a)
EES	Overall Compliance	4/29/2009	E. Johnson (HFD-320)
Microbiology	Adequate	4/07/2009	Vinayak Pawar, Ph.D.

Executive Summary Section

The CMC Review for NDA 22-372

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

This NDA has provided sufficient information to assure identity, strength, purity, and quality of the drug product. An “Acceptable” recommendation from the Office of Compliance has been made. However, the labeling issues are still pending as of the date of this review. Therefore, from the CMC perspective, this NDA is not recommended for approval until labeling issues are resolved.

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

Not applicable

II. Summary of CMC Assessments

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

(1) Drug Substance

SuPrep® formulation contains three drug substances: sodium sulfate (USP), potassium sulfate (Ph.Eur., FCC) and magnesium sulfate (USP). All three drug substances are compendial grade materials. Adequate chemistry, manufacturing and controls information is provided either in the DMF or through the NDA. The drug substances are inorganic salts and freely soluble in water. The quality of the drug substances is controlled by the compendial (USP/FCC/Ph.Eur.) monographs. Based on the stability data, adequate re-test period are established by the manufacturers:

(b) (4)

(2) Drug Product

SuPrep® (sodium sulfate, potassium sulfate, magnesium sulfate) oral solution is a concentrated liquid (sodium sulfate 17.5g, potassium sulfate 3.13g, magnesium sulfate 1.6g in 6 oz) and supplied in a 6oz unit dose bottle, which is made of amber (b) (4) and capped with an induction seal and a child resistant HDPE cap. The composition and manufacturing process of the clinical batches and proposed commercial batches are identical. Except for sucralose, all

Executive Summary Section

other excipients used in the drug product are compendial (USP/FCC) grade. All the excipients are listed in the FDA inactive ingredient list and have been used in the previously drug products at or below the proposed concentration. The drug product is manufactured by (b) (4)

The identity, strength, purity and quality of the final drug product are assured by the specification: description, pH, content uniformity, deliverable volume, assay of APIs and benzoate and microbial limit assay. Based on available stability data, the expiration dating period of 24 months is granted.

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

The drug product is indicated for cleansing the colon as a preparation for colonoscopy. The drug product can be dosed by (b) (4) overnight preparation (b) (4). The drug product is sold in single unit (6oz bottle) dose. Patient required to pour the drug product contents of one 6oz bottle into the (b) (4) mixing cup and dilute it with water to 16oz. The patient will drink entire volume of 16oz (b) (4) followed by two additional 16oz of water (b) (4). At certain time interval, (b) (4) the patient will prepare and drink the second dose (6oz bottle) in a similar manner.

B. Basis for Approvability or Not-Approval Recommendation

The sponsor has provided sufficient information on raw material controls, manufacturing process and process controls, and adequate specifications for assuring consistent product quality of the drug substance and drug product. The NDA has also provided sufficient stability information on the drug product to assure strength, purity, and quality of the drug product during the expiration dating period.

All facilities have an “Acceptable” recommendation from the office of compliance.

However, review of labels is still pending .

Executive Summary Section

III. Administrative**A. Reviewer's Signature:**

(See appended electronic signature page)

Tarun Mehta, M.Sc.

B. Endorsement Block:

(See appended electronic signature page)

Moo-Jhong Rhee, Ph.D. Branch Chief, Branch III, ONDQA

C. CC Block: entered electronically in DFS

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this page is the manifestation of the electronic signature.**

/s/

Tarun Mehta
7/16/2009 01:54:31 PM
CHEMIST

Moo-Jhong Rhee
7/16/2009 03:01:53 PM
CHEMIST
Chief, Branch III

Initial Quality Assessment
Branch 3
Pre-Marketing Assessment Division 2

OND Division: Division of Gastroenterology Products
NDA: 22-372
Applicant: Braintree Laboratories, Inc.
Stamp Date: 7/2/2008
Received by PAL: 7/17/2008
Review Date: 8/23/2008
PDUFA Date: 5/2/2008
Filing Meeting: 8/21/2008
Proposed Trademark: SUPREP
Established Name: Sodium sulfate, potassium sulfate, and magnesium sulfate for oral solution
Dosage Form: solution
Route of Administration: oral
Indication: Bowel prep
P.A.L.: Marie Kowblansky, PhD

	YES	NO
ONDQA Fileability:	<input checked="" type="checkbox"/>	
Comments for 74-Day Letter	<input checked="" type="checkbox"/>	

A. Summary

SUPREP® BOWEL PREP KIT (sodium sulfate, potassium sulfate and magnesium sulfate for oral solution) is intended for bowel cleansing prior to colonoscopy. The product is supplied as a liquid concentrate in two 6 ounce bottles, along with a mixing cup which is used for diluting the product with water prior to drinking; dilution to 16 ounces is required, with instructions to drink the solution ^{(b) (4)}. The contents of each of the two bottles are to be taken at prescribed intervals prior to colonoscopy. This product, which was studied under IND 74,808, is being filed by Braintree as a 505(b)(1) application.

The proposed product contains three active ingredients: sodium sulfate and magnesium sulfate, which have been approved for use in other products, and potassium sulfate, which is a new active ingredient. However, it should be noted that both sulfate ions and potassium ions function as active moieties, as has been the case in other approved applications.

The applicant identifies sodium sulfate as the dominant osmotic agent, with the product requiring at least 250 mmoles of sulfate ion for acceptable efficacy. The role of the other ionic components in the formulation is not explicitly discussed in the application, but based on first principles it is a reasonable conclusion that all are osmotically active. The sponsor's statement that sodium sulfate is the dominant osmotic agent no doubt is based on the fact that it is the most abundant component in the formulation, not that sulfate is the primary active moiety in the formulation; all of the ions from the active ingredients (sodium, magnesium, potassium, and sulfate) are active moieties.

Based on the above considerations, this NDA should be classified as a Type 4 according to the Chemical Classification Code, MAPP 7500.3: *A new physical combination of two or more active ingredients combined into a single dosage form, or two or more active moieties packaged together...*

Drug Substances

Three active ingredients are included in the formulation:

1. Sodium sulfate, which will conform to USP requirements and will be supplied by (b) (4). DMF (b) (4) is referenced regarding all CMC information: synthesis, purification, characterization, and testing of this material.
2. Magnesium sulfate (anhydrous) will be manufactured by (b) (4) and will conform to USP requirements. The manufacturing process is (b) (4)
3. Potassium sulfate, FCC (Food Chemicals Codex) is supplied and release tested by (b) (4). It will be manufactured by (b) (4). The manufacturing process for preparing this material consists of (b) (4)

Drug Product

The proposed product, is a liquid concentrate of the following composition

Raw Material and Grade Quality	Method	Quantity per 6 oz bottle	Quantity per Dose (2-6 oz bottles)	Function
Sodium Sulfate, USP	USP	17.510 g	35.020 g	Active ingredient
Potassium Sulfate, FCC	FCC	3.130 g	6.260 g	Active ingredient
Magnesium Sulfate Anhydrous, USP	USP	1.600 g	3.200 g	Active ingredient
Sodium Benzoate, NF	NF	(b) (4)		
Sucralose (b) (4)	In-house method			
Malic Acid, FCC	FCC			
Citric Acid, USP (b) (4)	USP			
	FCC			
	FCC			
Purified Water, USP	USP			

* Note: the per bottle quantity is from the dose (2 bottle) which required rounding

The same formulation was used in the Phase 3 clinical studies. (b) (4)

The product will be packaged in two 6 oz. light amber bottles. (The amber container is for visual appeal, not for light protection.) A (b) (4) is used to allow for administration losses. A (b) (4) cup marked with a 16 oz fill line is copackaged with the product; it will be used for diluting the concentrate prior to administration.

A number of the excipients in the formulation are noncompendial: sucralose, (b) (4) and malic acid. Although malic acid will conform to FCC (Food Chemicals Codex) requirements, FCC is not a compendium that is recognized in the CFR. The specifications for these will need to be closely evaluated to determine if they are suitable for pharmaceutical use.

The product will be manufactured by Braintree Laboratories using the following process:

(b) (4)

The product specification includes evaluations of appearance, deliverable volume, microbial limits, assay for benzoate (b) (4), assay for sulfate (b) (4), assay for potassium (b) (4), assay for magnesium (b) (4) and weight (weight loss is monitored on stability testing). Preservative effectiveness testing was conducted to demonstrate the appropriateness of the (b) (4) lower limit that is part of the specification.

Two series of exhibit batches are presented in the submission. Three batches were prepared in April of 2007, for which six months of stability data are provided for product stored at 4°C and 40°C, in addition to 12 months of data for samples stored at 25°C. The data do not show any trends indicative of instability. Three additional batches were prepared in 2008, for which only initial data are provided. The additional batches were prepared after an inspection of the Braintree manufacturing facility in November of 2007 resulted “in several observations”, but according to the applicant the “observations” did not involve the current product. Based on the submitted data a 24-month expiration date is requested.

Braintree claims categorical exclusion from the requirement for submitting an environmental assessment on the basis of 21 CFR (c) i.e. the drug substances used in this application occur naturally in the environment and approval of this application will not significantly alter the concentration or distribution of the substance, its metabolites, or degradation products in the environment.

Inspection requests for the facilities involved in the manufacture of the drug substances and drug product have been entered into EES. (See appended list.)

B. Critical issues for review

Based on this initial assessment, the following issues should be considered during the full review of this NDA:

-- The applicant has not provided specifications for (b) (4). Consideration should be given to requesting a specification for (b) (4).

-- The potassium sulfate drug substance will conform to FCC requirements. Since FCC is not a compendium recognized by CFR, the proposed specification should be closely scrutinized to determine its adequacy.

-- A number of the excipients in the formulation are noncompendial: sucralose, (b) (4) and malic acid. The specifications for these will need to be closely evaluated to determine if they are suitable for pharmaceutical use. If necessary, the Clinical Pharmacology reviewer may need to be consulted.

-- The drug product specification does not include an identity test. This will need to be added to the specification.

-- The reason for manufacture of three additional exhibit batches following an inspection by FDA should be explored since stability data to support this application were submitted for only the pre-inspection batches.

C. Comments for 74-Day Letter –

The following comment should be transmitted to the applicant:

Potassium sulfate is not included in the USAN (U.S. Adopted Names) dictionary. Please file an application with the USAN Council for the established name of this drug substance..

D. Recommendation: From the CMC perspective, this application should be filed.

Marie Kowblansky, PhD
Pharmaceutical Assessment Lead

8/23/2008

Moo-Jhong Rhee, PhD
Branch Chief

8/23/2008

Drug Substance

Sodium Sulfate Manufacture

(b) (4)
[Redacted]

Potassium Sulfate Manufacture

(b) (4)
[Redacted]

Magnesium Sulfate Manufacture

(b) (4)
[Redacted]

Drug Product

Manufacturing and testing facility

Braintree Laboratories
270 Centre Street
Holbrook, MA

Contract testing facilities for components, product, and stability testing

(b) (4)
[Redacted]

[Redacted]

[Redacted]

[Redacted]

[Redacted]

Filing Checklists (NDA 22-372)

A. Administrative Checklists;

YES	NO		Comments
√		On its face, is the section organized adequately?	
√		Is the section indexed and paginated adequately?	
√		On its face, is the section legible?	
√		Are ALL of the facilities (including contract facilities and test laboratories) identified with full street addresses and CFNs?	
√		Has an environmental assessment report or categorical exclusion been provided?	

B. Technical Checklists;

1. Drug Substance

√		Does the section contain synthetic scheme with in-process parameters?	
		Does the section contain structural elucidation data?	
√		Does the section contain specifications?	
√		Does the section contain information on impurities?	
√		Does the section contain validation data for analytical methods?	
√		Does the section contain container and closure information?	
		Does the section contain stability data?	

2. Drug Product

√		Does the section contain manufacturing process with in-process controls?	
√		Does the section contain quality controls of excipients?	
√		Does the section contain information on composition?	
√		Does the section contain specifications?	
√		Does the section contain information on degradation products?	
√		Does the section contain validation data for analytical methods?	
√		Does the section contain information on container and closure systems?	
√		Does the section contain stability data with a proposed expiration date?	
√		Does the section contain information on labels of container and cartons?	
√		Does the section contain tradename and established name?	

C. Review Issues

√		Has all information requested during the IND phases, and at the pre-NDA meetings been included?	
	√	Is a team review recommended?	
√		Are DMFs adequately referenced?	

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/s/

Marie Kowblansky
8/25/2008 12:50:07 PM
CHEMIST

Moo-Jhong Rhee
8/25/2008 01:04:03 PM
CHEMIST
Chief, Branch III