CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 202511

Name: Sodium Sulfate, Potassium Sulfate, Magnesium Sulfate

Sponsor: Novel Labs Inc.

Approval Date: January 23, 2017

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 202511Orig1s000

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 202511

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 202511

ANDA APPROVAL

Lupin Inc.
400 Campus Drive
Somerset, NJ 08873
Attention: Scott Talbot
Vice President, Quality Assurance and Regulatory Affairs

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), for Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution, 17.5 g/3.13 g/1.6 g per 6 ounces.

Reference is made to our tentative approval letter issued on May 29, 2015, and to your amendments dated November 9, 2016; and January 13, 2017.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is **approved**, effective on the date of this letter. The Office of Bioequivalence has determined your Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution, 17.5 g/3.13 g/1.6 g per 6 ounces to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Suprep Bowel Prep Kit of Braintree Laboratories (Braintree).

The RLD upon which you have based your ANDA, Braintree's Suprep Bowel Prep Kit, is subject to a period of patent protection. As noted in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"), U.S. Patent No. 6,946,149 (the '149 patent), is scheduled to expire on March 7, 2023.

Your ANDA contains a paragraph IV certification to the '149 patent under section 505(j)(2)(A)(vii)(IV) of the FD&C Act stating that the patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution, 17.5 g/3.13 g/1.6 g per 6 ounces, under this ANDA. You have notified the agency that Lupin Inc. (Lupin) complied with the requirements of section 505(j)(2)(B) of the FD&C Act, and that litigation was initiated against Lupin for infringement of the '149 within the statutory 45-day period in the United States District Court for the District of New Jersey [Braintree Laboratories Inc., v. Lupin Atlantis Holdings SA, Civil Action No. 3:11-cv-01341PGS-LHG]. You have also notified the Agency that on September 19, 2016, a Final Consent Judgment and Order was entered by the Court.

With respect to 180-day generic drug exclusivity, we note that Lupin was the first ANDA applicant to submit a substantially complete ANDA with a paragraph IV certification. Therefore, with this approval, Lupin is eligible for 180 days of generic drug exclusivity for Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution, 17.5 g/3.13 g/1.6 g per 6 ounces. This exclusivity, which is provided for under section 505(j)(5)(B)(iv) of the FD&C Act, will begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). The agency notes that Lupin failed to obtain tentative approval of this ANDA within 40[1] months after the date on which the ANDA was filed. See section 505(j)(5)(D)(i)(IV) of the FD&C Act (forfeiture of exclusivity for failure to obtain tentative approval). Nevertheless, the agency has determined that the failure to obtain tentative approval within the 40-month period was caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application was filed. Please submit correspondence to this ANDA informing the agency of the date of commercial marketing.

Under section 506A of the FD&C Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Please note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the FD&C Act.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert(s) directly to:

Food and Drug Administration
Center for Drug Evaluation and Research

[1] For applications submitted between January 9, 2010, and July 9, 2012, containing a paragraph IV certification (or amended to first contain a paragraph IV certification during that period of time), and approved or tentatively approved during the period of time beginning on July 9, 2012, and ending on September 30, 2015, section 1133(a) of FDASIA extended this period to 40 months. For applications submitted between January 9, 2010, and July 9, 2012 (or amended to first contain a paragraph IV certification during that period of time), and approved or tentatively approved during the period of time beginning on October 1, 2015, and ending on September 30, 2016, section 1133(a) of FDASIA extended this period to 36 months. In addition, if an application was submitted between January 9, 2010, and July 9, 2012 containing a paragraph IV certification (or amended to first contain a paragraph IV certification during that period of time), and FDA had not approved or tentatively approved the application but must consider whether the applicant had forfeited exclusivity because a potentially blocked application is ready for approval, FDA applied the 36-month period if it made the forfeiture determination between the period of time beginning on October 1, 2015, and ending on September 30, 2016. For all other applications, the 30-month period set forth in section 505(j)(5)(D)(i)(IV) of the FD&C Act applies. This ANDA was submitted November 8, 2011, and tentatively approved on May 29, 2015.

Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Office of Prescription Drug Promotion with a completed Form FDA 2253 at the time of their initial use.

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1 of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the Federal Register notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL files using eLIST may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf. The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

Carol A. Holquist, RPh
Acting Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

Carol Holquist

Digitally signed by Carol Holquist
Date: 2/23/2017 02:21:35PM
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 202511

OTHER ACTION LETTER(S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

ANDA 202511

TENTATIVE APPROVAL

Novel Laboratories, Inc.
400 Campus Drive
Somerset, NJ 08873
Attention: Scott Talbot
Vice President, Quality Assurance and Regulatory Affairs

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated November 8, 2010, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution, 17.5 g/3.13 g/1.6 g per 6 ounces.

We have completed the review of this ANDA, and based upon the information you have presented to date we have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, we are unable to grant final approval to your ANDA at this time because of the patent issue noted below. Therefore, the ANDA is **tentatively approved**. This determination is based upon information available to the agency at this time (i.e., information in your ANDA and the status of current good manufacturing practice (cGMP) at the facilities used in the manufacturing and testing of the drug product) and is therefore subject to change on the basis of new information that may come to our attention. This letter does not address issues related to the 180-day exclusivity provisions under section 505(j)(5)(B)(iv) of the Act.

The reference listed drug (RLD) upon which you have based your ANDA, Suprep Bowel Prep Kit, of Braintree Laboratories (Braintree), is subject to a period of patent protection. As noted in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"), U.S. Patent No. 6,946,149 (the '149 patent), is scheduled to expire on March 7, 2023.

Your ANDA contains a paragraph IV certification under section 505(j)(2)(A)(vii)(IV) of the Act stating that the '149 patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Sodium Sulfate, Potassium Sulfate, Magnesium Sulfate Oral Solution, (17.5 g/3.13 g/1.6 g) per 6 ounces, under this ANDA. You notified the Agency that Novel Laboratories, Inc. (Novel) complied with the requirements of section 505(j)(2)(B) of the Act, and that litigation for infringement of the '149 patent was initiated against Novel within the statutory 45-day period in the United States District Court for the District of New Jersey [Braintree Laboratories, Inc. v. Novel Laboratories, Inc., Civil Action No. 3:11-cv-01341-PGS-LHG]. You also have notified the Agency that (a) the district court granted summary judgment in Braintree's favor and (b) that Novel appealed this decision and the United States Court of Appeals for the Federal Circuit remanded the case to the district court for further proceedings.

The district court's order of June 19, 2013, states that the effective date of any approval of this ANDA by the Agency shall be a date which is not earlier than the expiration date of the '149 patent, including any extension of the term of that patent or any exclusivity to which Braintree is or becomes entitled. In light of this order the agency may not approve your ANDA at this time.

Please note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the Act.

To reactivate your ANDA prior to final approval, please submit a "MINOR AMENDMENT – FINAL APPROVAL REQUESTED" 90 days prior to the date you believe that your ANDA will be eligible for final approval. This amendment should provide the legal/regulatory basis for your request for final approval and should include a copy of a court decision, or a settlement or licensing agreement, as appropriate. It should also identify changes, if any, in the conditions under which the ANDA was tentatively approved, i.e., updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. This amendment should be submitted even if none of these changes were made, and it should be designated clearly in your cover letter as a MINOR AMENDMENT – FINAL APPROVAL REQUESTED.

In addition to the amendment requested above, the agency may request at any time prior to the date of final approval that you submit an additional amendment containing the requested information. Failure to submit either or, if requested, both amendments may result in rescission of the tentative approval status of your ANDA, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this ANDA as well as changes in the status of the manufacturing and testing facilities' cGMPs are subject to agency review before final approval of the ANDA will be made. Such changes should be categorized as representing either "major" or "minor" changes, and they will be reviewed according to OGD policy in effect at the time of receipt. The submission of multiple amendments prior to final approval may also result in a delay in the issuance of the final approval letter.

This drug product may not be marketed without final agency approval under section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under section 301 of the Act. Also, until the agency issues the final approval letter, this drug product will not be deemed to be approved for marketing under section 505 of the Act, and will not be listed in the "Orange Book."

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1 of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the Federal Register notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded.

This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

In addition, we note that GDUFA requires that certain non-manufacturing sites and organizations listed in generic drug submissions comply with the self-identification requirement. The failure of any facility, site, or organization to comply with its obligation to self-identify and/or to pay fees when due may raise significant concerns about that site or organization and is a factor that may increase the likelihood of a site inspection prior to approval. FDA does not expect to give priority to completion of inspections that are required simply because facilities, sites, or organizations fail to comply with the law requiring self-identification or fee payment.

Additionally, we note that the failure of any facility referenced in the application to self-identify and pay applicable fees means that FDA will not consider the GDUFA application review goal dates to apply to that application.

For further information on the status of this ANDA, or prior to submitting additional amendments, please contact Nicole Carr, Regulatory Project Manager, at (240) 402-4741.

Sincerely yours,

Carol A. Holquist -S

Digitally signed by Carol A. Holquist -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300052464, cn=Carol A. Holquist -S
Date: 2015.05.29 14:06:28 -04'00'

Carol A. Holquist, RPh
Acting Deputy Director
Office of Regulatory Operations
Office of Generic Drugs
Center for Drug Evaluation and Research

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

ANDA 202511

COMPLETE RESPONSE

Novel Laboratories
Attention: Scott Talbot
Vice President, Quality Assurance and Regulatory Affairs
400 Campus Drive
Somerset, NJ 08873

Dear Sir:

Please refer to your Abbreviated New Drug Application (ANDA) dated November 8, 2010, received November 8, 2010, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act for Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution, (17.5 g/3.13 g/1.6 g) per 6 ounces.

We acknowledge receipt of your amendment dated July 25, 2011.

We have completed our review of this ANDA, as amended, and have determined that we cannot approve this ANDA in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

PRODUCT QUALITY

Drug Product: Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. Please provide compatibility of your proposed container closure system for the drug product with supporting leachables and extractables data. Such data is not able to be located in the current submission.
2. The drug product is diluted to 16 ounces using tap water before consumption by the user in a (b) (4) container. However, the developmental report does not indicate any evaluation of the (b) (4) container to establish its suitability of use with the drug product. Please comment.
3. (b) (4)

4. (b) (4)
5.
6.
7.
8.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. For future applications, it is critical that the answers to all QbR questions to be provided with supported data and other pertinent scientific information.
2. The Pharmaceutical Development Report is lacking studies that have been indicated in the Quality Overall Summary, (b) (4) (b) (4) For the reviewers to determine that a due process has been followed in development of the drug product, it is critical that all the pertinent developmental studies are reported methodically. Please ensue the studies performed in support of the development of the drug product are outlined in a progressive manner and presented in the submission accurately.
3. Please acknowledge that method verification studies for all compendia test methods following USP <1226> is recommended.
4. (b) (4).
5. (b) (4)
6.
7.

BIOEQUIVALENCE

The bioequivalence comments provided in this communication are comprehensive as of issuance. However, these comments are subject to revision if additional concerns raised by

chemistry, manufacturing and controls, microbiology, labeling, other scientific or regulatory issues or inspectional results arise in the future. Please be advised that these concerns may result in the need for additional bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

The Division of Bioequivalence I (DBI) has completed its review and the following deficiency has been identified:

Per the labeling of the reference listed drug product, Suprep® Bowel Prep Kit, the dose for colon cleansing requires administration of two bottles of the kit. (b) (4) (b) (4) (b) (4). Based on information available to the Agency, the maximum daily intake of sodium benzoate for your product (b) (4) those found in approved products. As a result, please justify the maximum daily intake of sodium benzoate with respect to the safety of your test product. Please provide evidence and documentation as necessary to support your justification.

LABELING

1. GENERAL COMMENTS:
   a. You state that your carton contains "one (b) (4) mixing container"; however, you did not submit information about the (b) (4) mixing container in the Section 3.2.P.7 Container Closure System. Please submit pertinent information about this (b) (4) mixing container to chemistry. Note that the container should have the 16-ounce line marked on the container.
   b. Before final approval of this drug product, you should submit the "patient booklet" stated on the carton for review.

2. CONTAINER:

   Revise to read "17.5 g/3.13 g/1.6 g per 6 ounces" [add a space between "17.5" and "g"].

3. CARTON:
   a. Side panel, Step 1, the six-ounce bottle depicted is (b) (4). Please verify that your six-ounce bottle is (b) (4).
   b. Side Panel, Step 2, the red "Fill Line" could not be read. Please revise.
   c. Please submit a depiction of the carton with all panels attached.
   d. Please refer to CONTAINER comment.

4. PATIENT INSTRUCTIONS
   Please submit patient instructions.

5. MEDICATION GUIDE
   Acceptable in draft.

6. REMS

Timetable for Submission of Assessments: revise to state "Not applicable".

7. INSERT
   a. Please submit the HIGHLIGHTS and FULL PRESCRIBING INFORMATION: CONTENTS* sections.
   b. (b) (4).
   c. Second footnote of Table 2, revise to read "... (≤ 21 mEq/L) and high anion gap (≥ 13 mEq/L)..."
   d. 11 DESCRIPTION
   (b) (4).

Submit final printed labeling electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – ANDA.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address – http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

To facilitate review of your next submission please provide a side-by-side comparison of your proposed labeling with your last labeling submission with all differences annotated and explained.

FACILITY INSPECTIONS

We have not yet completed inspection(s)/compliance evaluation of your manufacturing facility(s) named or referenced in this ANDA. We must perform a complete evaluation of the information associated with the inspection before determining that the site(s) are satisfactory and this ANDA may be approved.

OTHER

A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission:

RESUBMISSION
COMPLETE RESPONSE AMENDMENT
CHEMISTRY/BIOEQUIVALENCE /LABELING

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the ANDA under 21 CFR 314.65. You may also request

an extension of time in which to resubmit the ANDA. A resubmission response must fully address all the deficiencies listed.

The drug product may not be legally marketed until you have been notified in writing that this ANDA is approved.

The Generic Drug User Fee Amendments of 2012 (GDUFA) (Public Law 112-144, Title III) established certain provisions with respect to self-identification of facilities and payment of annual facility fees. Your ANDA identifies at least one facility that is subject to the self-identification requirement and payment of an annual facility fee. Self-identification must occur by June 1 of each year for the next fiscal year. Facility fees must be paid each year by the date specified in the Federal Register notice announcing facility fee amounts. All finished dosage forms (FDFs) or active pharmaceutical ingredients (APIs) manufactured in a facility that has not met its obligations to self-identify or to pay fees when they are due will be deemed misbranded. This means that it will be a violation of federal law to ship these products in interstate commerce or to import them into the United States. Such violations can result in prosecution of those responsible, injunctions, or seizures of misbranded products. Products misbranded because of failure to self-identify or pay facility fees are subject to being denied entry into the United States.

In addition, we note that GDUFA requires that certain non-manufacturing sites and organizations listed in generic drug submissions comply with the self-identification requirement. The failure of any facility, site, or organization to comply with its obligation to self-identify and/or to pay fees when due may raise significant concerns about that site or organization and is a factor that may increase the likelihood of a site inspection prior to approval. FDA does not expect to give priority to completion of inspections that are required simply because facilities, sites, or organizations fail to comply with the law requiring self identification or fee payment.

Additionally, we note that the failure of any facility referenced in the application to self-identify and pay applicable fees means that FDA will not consider the GDUFA application review goal dates to apply to that application.

If you have any questions, call Chinyelum Olele, Regulatory Project Manager, at (240) 276-9778.

Sincerely yours,

{See appended electronic signature page}

Kathleen Uhl, M.D.
Acting Director
Office of Generic Drugs
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/

ROBERT L WEST

03/04/2014

Deputy Director, Office of Generic Drugs, for
Kathleen Uhl, M.D.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 202511

LABELING

Instructions for Use

On the day before your procedure

- You may have a light breakfast or have clear liquids ONLY: please have nothing for dinner
- DO NOT drink milk
- DO NOT eat or drink anything colored red or purple
- DO NOT drink alcoholic beverages

Any of the following clear liquids are OK

- Water
- Strained fruit juices (without pulp) including apple, orange, white grape, or white cranberry
- Limeade or lemonade
- Coffee or teal (DO NOT use any dairy or non-dairy creamer)
- Chicken broth
- Gelatin desserts without added fruit or topping (NO RED OR PURPLE)

NOVEL LABORATORIES

Dispense the enclosed Medication Guide to each patient.

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution

17.5 g/3.13 g/1.6 g per 6 ounces

Patient Instructions for Use

Booklet Includes:

1. Patient Instructions
2. Full Prescribing Information
3. Medication Guide

40032-700-83

Your doctor has recommended split-dose Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution

Split-Dose (2-Day) Regimen

(Both 6-ounce bottles are required for a complete prep.)

- On the evening before procedure (or when your doctor tells you to begin) complete steps 1 through 4 using one (1) 6-ounce bottle before going to bed
- On the morning of your procedure, repeat steps 1 through 4 using the other 6-ounce bottle

Note: You must finish drinking the final glass of water at least 2 hours before your procedure or as directed by physician.

Note: Dilute the solution concentrate as directed prior to use.

Pour ONE (1) 6 ounce bottle of Sodium Sultate,Potassium Sulfate and Magnesium Sulfate Oral Solution liquid into the mixing container.

Add cool drinking water to the 16-ounce line on the container and mix.

Drink ALL the liquid in the container.

You must drink two (2) more 16-ounce containers of water over the next 1 hour.

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution safely and effectively. See full prescribing information for Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution
Initial U.S. Approval: 08/2010

----------RECENT MAJOR CHANGES----------

Dosage and Administration 11/2012

----------INDICATIONS AND USAGE----------

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution is an osmotic laxative indicated for cleansing of the colon in preparation for colonoscopy in adults (1)

----------DOSAGE AND ADMINISTRATION----------

Dilute the solution prior to use. See FULL PRESCRIBING INFORMATION for complete dosing and administration instructions (2)
Split Dose (2-Day) Regimen
- Evening before colonoscopy: dilute one bottle with water to a total volume of 16 ounces (up to the fill line) and drink the entire amount.
- Drink 32 ounces of water over the next hour.
- Next morning: repeat both steps using the second bottle.
- Complete preparation at least 2 hours before colonoscopy or as directed by physician.

----------DOSAGE FORMS AND STRENGTHS----------

- Two 6 ounce bottles of oral solution, each containing sodium sulfate 17.5 grams, potassium sulfate 3.13 grams, and magnesium sulfate 1.6 grams. (3)

----------CONTRAINDICATIONS----------

- Gastrointestinal obstruction (4, 5.6)
- Bowel perforation (4, 5.6)
- Gastric retention (4)
- Ileus (4)
- Toxic colitis or toxic megacolon (4)
- Known allergies to components of the kit (4, 11)

----------WARNINGS AND PRECAUTIONS----------

- Risk of fluid and electrolyte abnormalities, arrhythmias, seizures and renal impairment– assess concurrent medications and consider testing in some patients (5.1, 5.2, 5.3)
- Patients with renal insufficiency– use caution, ensure adequate hydration and consider testing (5.4)
- Suspected GI obstruction or perforation – rule out the diagnosis before administration (4, 5.6)
- Patients at risk for aspiration – observe during administration (5.7)
- Not for direct ingestion – dilute and take with additional water (5.8)

----------ADVERSE REACTIONS----------

Most common adverse reactions (≥3%) are: overall discomfort, abdominal fullness, nausea, abdominal cramping, and vomiting (6)

To report SUSPECTED ADVERSE REACTIONS, contact Novel Laboratories, Inc. at 1-866-403-7592 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

----------DRUG INTERACTIONS----------

- Some drugs increase risks due to fluid and electrolyte changes (7.1)
- Oral medication taken within 1 hour of start of each dose might not be absorbed properly (7.2)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 11/2014

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed

Medication Guide

Sodium Sulfate (soe' dee um sul' fate), Potassium Sulfate (poe tas' ee um sul' fate) and Magnesium Sulfate (mag nee' zee um sul' fate) Oral Solution

Read this Medication Guide before you start taking Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate oral solution. This information does not take the place of talking with your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution?

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution and other osmotic bowel preparations can cause serious side effects, including:

Serious loss of body fluid (dehydration) and changes in blood salts (electrolytes) in your blood.

These changes can cause:
- **abnormal heartbeats that can cause death**
- **seizures.** This can happen even if you have never had a seizure.
- **kidney problems**

Your chance of having fluid loss and changes in body salts with Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution is higher if you:
- have heart problems
- have kidney problems
- take water pills or non-steroidal anti-inflammatory drugs (NSAIDS)

Tell your healthcare provider right away if you have any of these symptoms of a loss of too much body fluid (dehydration) while taking Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution:
- vomiting that prevents you from keeping down the additional prescribed amount of water listed in the Instructions for Use in the Patient Instructions for Use Booklet
- dizziness
- urinating less often than normal
- headache

- A light breakfast may be consumed, or have only clear liquids on the day before colonoscopy. Avoid red and purple liquids, milk, and alcoholic beverages.
- Early in the evening prior to colonoscopy: pour the contents of one bottle of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution into the mixing container provided. Fill the container with water to the 16 ounce fill line, and drink the entire amount.
- Drink two additional containers filled to the 16 ounce line with water over the next hour.

Day of colonoscopy:
- Have only clear liquids until after the colonoscopy. Avoid red and purple liquids, milk, and alcoholic beverages.
- The morning of colonoscopy (10 to 12 hours after the evening dose): pour the contents of the second bottle of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution into the mixing container provided. Fill the container with water to the 16 ounce fill line, and drink the entire amount.
- Drink two additional containers filled to the 16 ounce line with water over the next hour.
- Complete all Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution and required water at least two hours prior to colonoscopy or as directed by physician.

3 DOSAGE FORMS AND STRENGTHS
Two 6 ounce bottles of oral solution.
Each 6 ounce bottle contains: sodium sulfate 17.5 grams, potassium sulfate 3.13 grams, magnesium sulfate 1.6 grams.

4 CONTRAINDICATIONS
- Gastrointestinal obstruction
- Bowel perforation
- Gastric retention
- Ileus
- Toxic colitis or toxic megacolon
- Known allergies to components of the kit [*see Description (11)*]

5 WARNINGS AND PRECAUTIONS

5.1 Serious Fluid and Serum Chemistry Abnormalities
Advise all patients to hydrate adequately before, during, and after the use of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution. If a patient develops significant vomiting or signs of dehydration after taking Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution, consider performing post-colonoscopy lab tests (electrolytes, creatinine, and BUN). Fluid and electrolyte disturbances can lead to serious adverse events including cardiac arrhythmias, seizures and renal impairment.

See Section "What are the possible side effects of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution?" for more information about side effects.

What is Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution?

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution is a prescription medicine used by adults to clean the colon before a colonoscopy. Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution cleans your colon by causing you to have diarrhea. Cleaning your colon helps your healthcare provider see the inside of your colon more clearly during your colonoscopy.

It is not known if Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution is safe and effective in children.

Who should not take Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution?

Do not take Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution if your healthcare provider has told you that you have:
- a blockage in your bowel (obstruction)
- an opening in the wall of your stomach or intestine (bowel perforation)
- problems with food and fluid emptying from your stomach (gastric retention)
- a very dilated intestine (bowel)
- an allergy to any of the ingredients in Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution. See the end of this leaflet for a complete list of ingredients in Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution.

What should I tell my healthcare provider before taking Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution?

Before you take Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution, tell your healthcare provider if you:
- have heart problems
- have stomach or bowel problems
- have ulcerative colitis
- have problems with swallowing or gastric reflux

Patients with electrolyte abnormalities should have them corrected before treatment with Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution. In addition, use caution when prescribing Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution for patients with conditions, or who are using medications, that increase the risk for fluid and electrolyte disturbances or may increase the risk of adverse events of seizure, arrhythmias, and renal impairment. [*See Drug Interactions (7.1)*]

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution can cause temporary elevations in uric acid. [*See Adverse Reactions (6.1)*]. Uric acid fluctuations in patients with gout may precipitate an acute flare. The potential for uric acid elevation should be considered before administering Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution to patients with gout or other disorders of uric acid metabolism.

5.2 Cardiac Arrhythmias
There have been rare reports of serious arrhythmias associated with the use of ionic osmotic laxative products for bowel preparation. Use caution when prescribing Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution for patients at increased risk of arrhythmias (e.g., patients with a history of prolonged QT, uncontrolled arrhythmias, recent myocardial infarction, unstable angina, congestive heart failure, or cardiomyopathy). Pre-dose and post-colonoscopy ECGs should be considered in patients at increased risk of serious cardiac arrhythmias.

5.3 Seizures
There have been reports of generalized tonic-clonic seizures and/or loss of consciousness associated with use of bowel preparation products in patients with no prior history of seizures. The seizure cases were associated with electrolyte abnormalities (e.g., hyponatremia, hypokalemia, hypocalcemia, and hypomagnesemia) and low serum osmolality. The neurologic abnormalities resolved with correction of fluid and electrolyte abnormalities.

Use caution when prescribing Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution for patients with a history of seizures and in patients at increased risk of seizure, such as patients taking medications that lower the seizure threshold (e.g., tricyclic antidepressants), patients withdrawing from alcohol or benzodiazepines, or patients with known or suspected hyponatremia.

5.4 Renal Impairment
Use caution when prescribing Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution for patients with impaired renal function or patients taking concomitant medications that may affect renal function (such as diuretics, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, or non-steroidal anti-inflammatory drugs). Advise these patients of the importance of adequate hydration, and consider performing baseline and post-colonoscopy laboratory tests (electrolytes, creatinine, and BUN) in these patients.

5.5 Colonic Mucosal Ulcerations and Ischemic Colitis
Administration of osmotic laxative products may produce colonic mucosal aphthous ulcerations, and there have been reports of more serious cases of ischemic colitis requiring hospitalization. Concurrent use of stimulant laxatives and Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution may increase these risks. The potential for mucosal ulcerations resulting from the bowel preparation should be considered when interpreting colonoscopy findings in patients with known or suspect inflammatory bowel disease (IBD).

5.6 Use in Patients with Significant Gastrointestinal Disease
If gastrointestinal obstruction or perforation is suspected, perform appropriate diagnostic studies to rule out these conditions before administering Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution.

Use with caution in patients with severe active ulcerative colitis.

5.7 Aspiration
Use with caution in patients with impaired gag reflex and patients prone to regurgitation or aspiration. Such patients should be observed during administration of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution.

5.8 Not for Direct Ingestion
Each bottle must be diluted with water to a final volume of 16 ounces and ingestion of additional water as recommended is important to patient tolerance. Direct ingestion of the undiluted solution may increase the risk of nausea, vomiting, dehydration, and electrolyte disturbances.

6 ADVERSE REACTIONS

6.1 Clinical Studies Experience
Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in clinical studies of another drug and may not reflect the rates observed in practice.

In a multicenter, controlled clinical trial comparing Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution with a bowel prep containing polyethylene glycol and electrolytes (PEG + E) that were administered in a split-dose (2-day) regimen, the most common adverse reactions after administration of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution were overall discomfort, abdominal distention, abdominal pain, nausea, vomiting, and headache; see Table 1, below. Less common Adverse Reactions occurring were AV Block (1 case) and CK increase. In this study, patients receiving Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution were limited to a light breakfast followed by clear liquids; patients receiving the PEG + E bowel prep were allowed to have a normal breakfast and a light lunch, followed by clear liquids.

Table 1: Treatment-Emergent Adverse Reactions Observed in at Least 2% of Patients on the Split-Dose (2-Day) Regimen

Symptom	Split-Dose (2-Day) Regimen	
	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution N=190	PEG + E product N=189
Overall Discomfort	54 %	67%
Abdominal Distension	40%	52%
Abdominal Pain	36%	43%
Nausea	36%	33%
Vomiting	8%	4%
Headache	1.1 %	0.5%

Table 2 shows the percentages of patients who developed new abnormalities of important electrolytes and uric acid after completing the bowel preparation with either Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution or PEG+E administered as a split-dose (2-day) regimen.

Table 2: Patients with Normal Baseline Serum Chemistry with A Shift to an Abnormal Value While on the Split-Dose (2-Day) Regimen

		Day of Colonoscopy n (%)*	Day 30 n (%)*
Anion gap (high)†	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution	14 (8.9)	3 (1.9)
	PEG + Electrolytes	12 (7.6)	2 (1.4)
Bicarbonate (low)	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution	20 (12.7)	7 (4.4)
	PEG + Electrolytes	24 (15.2)	4 (2.7)
Bilirubin, total (high)	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution	14 (8.5)	0 (0)
	PEG + Electrolytes	20 (11.7)	3 (1.9)

Continued

		Day of Colonoscopy n (%)*	Day 30 n (%)*
BUN (high)	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution	2 (1.6)	14 (11.2)
	PEG + Electrolytes	4 (2.9)	19 (14.5)
Calcium (high)	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution	16 (10.4)	8 (5.2)
	PEG + Electrolytes	6 (3.7)	6 (3.9)
Chloride (high)	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution	4 (2.4)	6 (3.7)
	PEG + Electrolytes	20 (12.2)	6 (3.8)
Creatinine (high)	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution	3 (1.9)	5 (3.2)
	PEG + Electrolytes	2 (1.2)	8 (5.2)
Osmolality (high)	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution	8 (5.8)	NA
	PEG + Electrolytes	19 (12.9)	NA
Osmolality (low)	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution	3 (2.2)	NA
	PEG + Electrolytes	2 (1.4)	NA
Potassium (high)	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution	3 (1.8)	6 (3.7)
	PEG + Electrolytes	5 (2.9)	8 (4.9)

Continued

- have gout
- have a history of seizures
- are withdrawing from drinking alcohol
- have a low blood salt (sodium) level
- have kidney problems
- any other medical conditions
- are pregnant. It is not known if Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution will harm your unborn baby. Talk to your doctor if you are pregnant or plan to become pregnant.
- are breastfeeding or plan to breastfeed. It is not known if Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution passes into your breast milk. You and your healthcare provider should decide if you will take Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution while breastfeeding.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution may affect how other medicines work. Medicines taken by mouth may not be absorbed properly when taken within 1 hour before the start of each dose of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution.

Especially tell your healthcare provider if you take:
- medicines for blood pressure or heart problems
- medicines for kidney problems
- medicines for seizures
- water pills (diuretics)
- non-steroidal anti-inflammatory medicines (NSAID) pain medicines
- laxatives

Ask your healthcare provider or pharmacist for a list of these medicines if you are not sure if you are taking any of the medicines listed above.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

		Day of Colonoscopy n (%)*	Day 30 n (%)*
Sodium (low)	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution	5 (3.1)	1 (0.6)
	PEG + Electrolytes	4 (2.3)	2 (1.2)
Uric acid (high)	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution	27 (23.5)	13 (11.5)
	PEG + Electrolytes	12 (9.5)	20 (16.7)

*Percent (n/N) of patients where N=number of patients with normal baseline who had abnormal values at the timepoint(s) of interest.
†Patients with normal bicarbonate at baseline who developed low bicarbonate (≤ 21 mEq/L) and high anion gap (≥ 13 mEq/L) on Day of Colonoscopy or Day 30.

There were also 408 patients who participated in a study in which either Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution or PEG+E were administered in an evening-only (1-day) regimen. Higher rates of overall discomfort, abdominal distention, and nausea were observed with the evening-only (1-day) regimen compared to the split-dose (2-day) regimen for both preparations. Patients treated with Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution had increased rates of vomiting with the evening-only (1-day) regimen. An evening-only (1-day) dosing regimen was associated with higher rates of abnormal values for some electrolytes when compared to the split-dose (2-day) regimen for both preparations. For Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution, the evening-only (1-day) regimen was associated with higher rates of total bilirubin (high), BUN (high), creatinine (high), osmolality (high), potassium (high) and uric acid (high) than the Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution split dose (2-day) regimen. Administration of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution in an evening-only (1-day) dosing regimen is *not* recommended.

7 DRUG INTERACTIONS

7.1 Drugs That May Increase Risks Due to Fluid and Electrolyte Abnormalities
Use caution when prescribing Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution for patients with conditions, or who are using medications, that increase the risk for fluid and electrolyte disturbances or may increase the risk of adverse events of seizure, arrhythmias, and prolonged QT in

the setting of fluid and electrolyte abnormalities. Consider additional patient evaluations as appropriate [*see Warnings (5)*] in patients taking these concomitant medications.

7.2 Potential for Altered Drug Absorption
Oral medication administered within one hour of the start of each Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution dose may be flushed from the gastrointestinal tract, and the medication may not be absorbed properly.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy
Teratogenic effects: Pregnancy Category C. Animal reproduction studies have not been conducted with Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution. It is also not known whether Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution should be given to a pregnant woman only if clearly needed.

8.3 Nursing Mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution is administered to a nursing woman.

8.4 Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use
Of the 375 patients who received Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution in clinical trials, 94 (25%) were 65 years of age or older, and 25 (7%) were 75 years of age or older. No overall differences in safety or effectiveness of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution administered as a split-dose (2-day) regimen were observed between geriatric patients and younger patients. Geriatric patients reported more vomiting when Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution was given as a one-day preparation.

11 DESCRIPTION

Each Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution contains two 6 ounce bottles of solution. Each 6 ounce bottle contains: sodium sulfate 17.5 grams, potassium sulfate 3.13 grams, magnesium sulfate 1.6 grams. Inactive ingredients include: sodium benzoate, sucralose, malic acid, citric acid, lemon flavor, purified water. The solution is a clear to slightly hazy liquid. The solution is clear and colorless when diluted to a final volume of 16 ounces with water.

How should I take Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution?

See the Instructions for Use in the Patient Instructions for Use Booklet for dosing instructions.

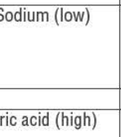
You must read, understand, and follow these instructions to take Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution the right way.

- Take Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution exactly as your healthcare provider tells you to take it.
- **Do not drink Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution that has not been mixed with water (diluted), it may increase your risk of nausea, vomiting and fluid loss (dehydration).**
- Each bottle of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution must be mixed with water (diluted) before drinking.
- It is important for you to drink the additional prescribed amount of water listed in the Instructions for Use to prevent fluid loss (dehydration).
- Do not take other laxatives while taking sodium sulfate, potassium sulfate and magnesium sulfate oral solution.
- Do not eat solid foods while taking Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution. Only clear liquids are allowed while taking Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution.

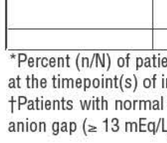
What are the possible side effects of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution?

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution can cause serious side effects, including:
- **See Section "What is the most important information I should know about Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution?"**
- **changes in certain blood tests.** Your healthcare provider may do blood tests after you take Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution to check your blood for changes. Tell your healthcare provider if you have any symptoms of too much fluid loss, including:
  - vomiting
  - nausea
  - bloating

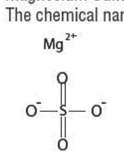
Sodium Sulfate, USP
The chemical name is Na_2SO_4. The average Molecular Weight is 142.04. The structural formula is:



Potassium Sulfate, FCC, Granular
The chemical name is K_2SO_4. The average Molecular Weight is 174.26. The structural formula is:



Magnesium Sulfate, USP
The chemical name is $MgSO_4$. The average Molecular Weight: 120.37. The structural formula is:



Each Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution package also contains a polypropylene mixing container.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
Sulfate salts provide sulfate anions, which are poorly absorbed. The osmotic effect of unabsorbed sulfate anions and the associated cations causes water to be retained within the gastrointestinal tract.

12.2 Pharmacodynamics
The osmotic effect of the unabsorbed ions, when ingested with a large volume of water, produces a copious watery diarrhea.

12.3 Pharmacokinetics
Fecal excretion was the primary route of sulfate elimination. After administration of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution in six healthy volunteers, the time at which serum sulfate reached its highest point (T_{max}) was approximately 17 hours after the first half dose or approximately 5 hours after the second dose, and then declined with a half-life of 8.5 hours.

The disposition of sulfate after Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution was also studied in patients (N=6) with mild-moderate hepatic impairment (Child-Pugh grades A and B) and in patients (N=6) with moderate renal impairment (creatinine clearance of 30 to 49 mL/min). The renal impairment group had the highest serum sulfate AUC and C_{max}, followed by the hepatic impairment group, and then by healthy subjects. Systemic exposure of serum sulfate (AUC and C_{max}) was similar between healthy subjects and hepatic impairment patients. Renal impairment resulted in 54% higher mean AUC and 44% higher mean C_{max} than healthy subjects. The mean sulfate levels of all three groups returned to their respective baseline levels by Day 6 after dose initiation. Urinary excretion of sulfate over 30 hours, starting after the first half dose, was similar between hepatic patients and normal volunteers, but was approximately 16% lower in moderate renal impairment patients than in healthy volunteers.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term studies in animals have not been performed to evaluate the carcinogenic potential of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution. Studies to evaluate the possible impairment of fertility or mutagenic potential of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution have not been performed.

13.2 Animal Toxicology and/or Pharmacology
The sulfate salts of sodium, potassium, and magnesium contained in Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution were administered orally (gavage) to rats and dogs up to 28 days up to a maximum daily dose of 5 grams/kg/day (approximately 0.9 and 3 times for rats and dogs, respectively, the recommended human dose of 44 grams/day or 0.89 grams/kg based on the body surface area). In rats, the sulfate salts caused diarrhea and electrolyte and metabolic changes, including hypochloremia, hypokalemia, hyponatremia, lower serum osmolality, and high serum bicarbonate. Significant renal changes included increased fractional sodium excretion, increased urinary sodium and potassium excretion, and alkaline urine in both males and females. In addition, creatinine clearance was significantly decreased in females at the highest dose. No microscopic renal changes were seen. In dogs, the sulfate salts caused emesis, excessive salivation, excessive drinking of water, and abnormal excreta (soft and/or mucoid feces and/or diarrhea) and increased urine pH and sodium excretion.

- dizziness
- stomach (abdominal) cramping
- headache
- urinate less than usual
- trouble drinking clear liquid
- **heart problems. Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution may cause irregular heartbeats.**
- **seizures**
- **ulcers of the bowel or bowel problems**
- **worsening gout**

The most common side effects of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution include:
- discomfort
- bloating
- stomach (abdominal) cramping
- nausea
- vomiting

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

These are not all the possible side effects of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution?
- Store Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution at room temperature, between 59ºF to 86°F (15ºC to 30°C).

Keep Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution and all medicines out of the reach of children.

14 CLINICAL STUDIES

The colon cleansing efficacy of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution was evaluated in a randomized, single-blind, active-controlled, multicenter study. In this study, 363 adult patients were included in the efficacy analysis. Patients ranged in age from 20 to 84 years (mean age 55 years) and 54% were female. Race distribution was 86% Caucasian, 9% African-American, and 5% other.

Patients were randomized to one of the following two colon preparation regimens: Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution or a marketed polyethylene glycol (PEG) bowel prep. In the Study Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution was administered according to a split-dose preparation regimen [*see Dosage and Administration (2.1)*]. The PEG bowel prep was also given as a split-dose preparation according to its labeled instructions. Patients receiving Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution were limited to a light breakfast followed by clear liquids on the day prior to the day of colonoscopy; patients receiving the PEG bowel prep were allowed to have a normal breakfast and a light lunch, followed by clear liquids.

The primary efficacy endpoint was the proportion of patients with successful colon cleansing as assessed by the colonoscopists, who were not informed about the type of preparation received. In the study, no clinically or statistically significant differences were seen between the group treated with Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution and the group treated with the PEG bowel prep. See Table 3 below.

Table 3: Colon Cleansing Response Rates

Treatment Group	Regimen	N	Responders[1] % (95% C. I.)	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution – PEG Difference (95% CI)
Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution (with light breakfast)	Split-Dose	180	**97**% (94%, 99%)	**2**%[2] (-2%, 5%)
PEG bowel prep (with normal breakfast & light lunch)	Split-Dose	183	**96**% (92%, 98%)	

[1] Responders were patients whose colon preparations were graded excellent (no more than small bits of adherent feces/fluid) or good (small amounts of feces or fluid not interfering with the exam) by the colonoscopist.
[2] Does not equal difference in tabled responder rates due to rounding effects.

16 HOW SUPPLIED/STORAGE AND HANDLING

Each Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution contains:
• Two (2) 6 ounce bottles of oral solution.
• One (1) 19 ounce mixing container with a 16 ounce fill line.

Storage:
Store at 20º to 25°C (68º to 77°F). Excursions permitted between 15º to 30°C (59º to 86°F). See USP controlled room temperature.

Keep out of reach of children.

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution package NDC 40032-700-83

17 PATIENT COUNSELING INFORMATION

See Medication Guide and FDA -Approved Patient Labeling

17.1 Patient Counseling
- Ask patients to let you know if they have trouble swallowing or are prone to regurgitation or aspiration.
- Instruct patients that each bottle needs to be diluted in water before ingestion and that they need to drink additional water according to the instructions. Direct ingestion of the undiluted solution may increase the risk of nausea, vomiting, and dehydration.
- Inform patients that oral medications may not be absorbed properly if they are taken within one hour of starting each dose of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution.
- Tell patients not to take other laxatives while they are taking Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution.

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Somerset, NJ 08873

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General information about the safe and effective use of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution.
Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution for a condition for which it was not prescribed. Do not give Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution to other people, even if they are going to have the same procedure you are. It may harm them.

This Medication Guide summarizes important information about Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information that is written for healthcare professionals.

For more information, call 1-866-403-7592

What are the ingredients in Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution?

Active ingredients: sodium sulfate, potassium sulfate and magnesium sulfate

Inactive ingredients: sodium benzoate, sucralose, malic acid, citric acid, lemon flavor, purified water

Novel Laboratories, Inc.
Somerset, NJ 08873

This Medication Guide has been approved by the U.S. Food and Drug Administration.

PI7000000104
Revised 12/2014

(b) (4)

Novel Pharmaceuticals 6oz. Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate OS

Flat Label

(b) (4)

(b) (4)

(b) (4)

NDC 40032-700-02

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution

17.5 g/3.13 g/1.6 g per 6 ounces

Dispense the enclosed Medication Guide to each patient.
This bottle contains 6 ounces (177 mL) of liquid bowel prep

Rx only

NOVEL LABORATORIES

Directions:
Dilute the solution concentrate prior to use.
See enclosed package insert for complete dosage and administration instructions. Both 6-ounce bottles are required for a complete prep.

KEEP THIS AND OTHER DRUGS
OUT OF REACH OF CHILDREN.

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

Manufactured by:
Novel Laboratories, Inc., Somerset, NJ 08873

LA7000200102 Rev. 07/2014

N 3 40032700002 9

Lot #
Exp:

(b) (4)

(b) (4)

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution

17.5 g/3.13 g/1.6 g per 6 ounces

Dispense the enclosed Medication Guide to each patient.

Read patient booklet contained in kit
at least 2 days before scheduled procedure.

Dilute the solution concentrate as directed prior to use.

Lot

Exp.

Instructions for use continued (refer to side panel)

Your doctor has recommended split-dose Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution

Split-Dose (2-Day) Regimen
(Both 6-ounce bottles are required for a complete prep.)

- On the evening before procedure (or when your doctor tells you to begin) complete steps 1 through 4 using one (1) 6-ounce bottle before going to bed
- On the morning of your procedure, repeat steps 1 through 4 using the other 6-ounce bottle

Note: You must finish drinking the final glass of water at least 2 hours before your procedure or as directed by physician

NOTE: Dilute the solution concentrate as directed prior to use.

STEP 1: Pour ONE (1) 6 ounce bottle of Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution liquid into the mixing container.

STEP 2: Add cool drinking water to the 16-ounce line on the container and mix.

STEP 3: Drink ALL the liquid in the container.

STEP 4: You must drink two (2) more 16-ounce containers of water over the next 1 hour.

Please read full prescribing information in this kit.

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution

17.5 g/3.13 g/1.6 g per 6 ounces

N 3 40032-700-83 8

Manufactured by:
Novel Laboratories, Inc.
Somerset, NJ 08873

CA7008300101
Rev. 11/2014

NDC 40032-700-83 **Rx Only**

Dispense the enclosed Medication Guide to each patient.

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution

17.5 g/3.13 g/1.6 g per 6 ounces

This carton contains:

- **2** 6-ounce (177 ml) bottles of liquid bowel prep
- **1** 16-ounce mixing container
- **1** Patient booklet. Booklet includes:
  1- Medication Guide
  2- Patient Instructions
  3- Full Prescribing Information

Dilute the solution concentrate as directed prior to use.

Both 6-ounce bottles are required for a complete prep.

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

NOVEL LABORATORIES

Instructions for Use Start Here

On the day before your procedure

- You may have a light breakfast or have clear liquids ONLY; please have nothing for dinner
- DO NOT drink milk
- DO NOT eat or drink anything colored red or purple
- DO NOT drink alcoholic beverages

Any of the following clear liquids are OK

- Water
- Strained fruit juices (without pulp) including apple, orange, white grape, or white cranberry
- Limeade or lemonade
- Coffee or tea (DO NOT use any dairy or non-dairy creamer)
- Chicken broth
- Gelatin desserts without added fruit or topping (NO RED OR PURPLE)

Continue

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 202511

LABELING REVIEWS

***** This document contains proprietary information that cannot be released to the public*****

LABELING REVIEW

Division of Labeling Review
Office of Regulatory Operations
Office of Generic Drugs (OGD)
Center for Drug Evaluation and Research (CDER)

Date of This Review	12/29/2014
ANDA Application Number	202511
Review Cycle Number	3
Applicant Name	Novel Laboratories Inc.
Established Name	Sodium Sulfate, Potassium Sulfate, Magnesium Sulfate Oral Solution
Strength(s)	(17.5 g/3.13 g/1.6 g) per 6 ounces
Proposed Proprietary Name	None
DARRTS Received Date	11/21/2014 and 12/18/2014
Labeling Reviewer	Charlie Hoppes
Labeling Team Leader	John Grace

Review Conclusion

☒ No Comments – The Labels and Labeling are ready for approval.

☐ Minor Deficiency* - Refer to Labeling Deficiencies and Comments for the Letter to Applicant

*Please Note: The Regulatory Project Manager (RPM) may change the recommendation from Minor Deficiency to Easily Correctable Deficiency if all other OGD reviews are acceptable. Otherwise the labeling minor deficiencies will be included in the Complete Response (CR) letter to the applicant.

LABELING DEFICIENCIES AND COMMENTS FOR LETTER TO APPLICANT

None

1. MODEL LABELING FOR ANDA

Our review is based on the following model labels and labeling used for comparison to the submitted ANDA labeling.

1.1 MODEL CONTAINER LABELS FOR ANDA

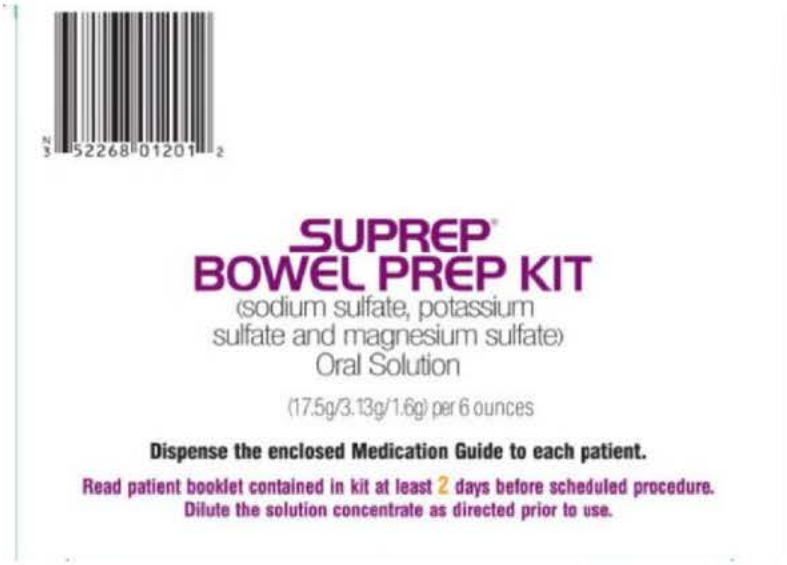
In Table 1 below, check all sources for Model container labels and carton labeling (secondary packaging) that applies.

Container labels are assessed in section 2.2.

Carton labeling (outer or secondary packaging) is assessed in section 2.3.

Table 1: Review Model Labeling for Container Label and Carton Labeling (Check all sources that apply)	
Source	**Date of source document (i.e. supplement approval date, annual report date)**
☐ drugs@fda	
☒ DARRTS	9/30/2013
☐ DailyMed	
☒ Annual Report Y-03	9/30/2013
☐ Other	

Model labels and carton labeling. [Insert or paste images below]



Instructions for use continued (refer to side panel)
Your doctor has recommended split-dose SUPREP

Split-Dose (2-Day) Regimen
(Both 6-ounce bottles are required for a complete prep.)

- On the evening before procedure (or when your doctor tells you to begin) complete steps 1 through 4 using one (1) 6-ounce bottle before going to bed
- On the morning of your procedure, repeat steps 1 through 4 using the other 6-ounce bottle

NOTE: You must finish drinking the final glass of water at **least 2 hours** before your procedure or as directed by physician

NOTE: Dilute the solution concentrate as directed prior to use.

Pour **ONE** (1) 6-ounce bottle of SUPREP liquid into the mixing container.

Add cool drinking water to the 16-ounce line on the container and mix.

Drink **ALL** the liquid in the container.

You **must** drink two (2) more 16-ounce containers of water over the next 1 hour.

Please read full prescribing information in this kit.

SUPREP® BOWEL PREP KIT

(sodium sulfate, potassium sulfate and magnesium sulfate) Oral Solution

(17.5g/3.13g/1.6g) per 6 ounces

NDC 52268-012-01

U.S. Patent 6,946,149

Dispense the enclosed Medication Guide to each patient.

SUPREP® BOWEL PREP KIT

(sodium sulfate, potassium sulfate and magnesium sulfate) Oral Solution

(17.5g/3.13g/1.6g) per 6 ounces

This carton contains:

2 6-ounce (177 mL) bottles of liquid bowel prep
1 16-ounce mixing container
1 Patient booklet. Booklet includes:
- 1- Medication Guide
- 2- Patient Instructions
- 3- Full Prescribing Information

Dilute the solution concentrate as directed prior to use.

Both 6-ounce bottles are required for a complete prep.

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

Rx only

Braintree Laboratories, Inc.

Instructions for Use Start Here

On the day before your procedure

- You may have a light breakfast or have clear liquids ONLY; please have nothing for dinner
- **DO NOT** drink milk
- **DO NOT** eat or drink anything colored red or purple
- **DO NOT** drink alcoholic beverages

Any of the following clear liquids are OK

- Water
- Strained fruit juices (without pulp) including apple, orange, white grape, or white cranberry
- Limeade or lemonade
- Coffee or tea (**DO NOT** use any dairy or non-dairy creamer)
- Chicken broth
- Gelatin desserts without added fruit or topping (**NO RED OR PURPLE**)

REV NOV 2012

Continue

1.2 PRESCRIBING INFORMATION MODEL LABELING

The review model labels and labeling used for comparison to the submitted ANDA labeling are described in Table 2.

Prescribing information is assessed in section 2.4.

Table 2: Review Model Labeling for Prescribing Information and Patient Labeling(Check all that apply)		
☐ MOST RECENTLY APPROVED REFERENCE LISTED DRUG		
NDA or ANDA: 022372	Proprietary Name: Suprep Bowel Prep Kit	Approval date: 11/1/2012
S- 004	Description of Supplement: Labeling revisions to the Dosage and Administration section.	
☐ BPCA or PREA TEMPLATE		
☐ OTHER (Describe):		

2. MATERIAL ANALYSIS

The results for each material reviewed in this section provide the basis for the labeling comments to the applicant (Page 2).

2.1 GENERAL

2.1.1 Established Name Assessment

We compared the established names of this ANDA, the Model Labeling and the USP to determine if the established name presented on the labeling is acceptable.

Table 3: Comparison of Established Names

Model Labeling:	Sodium Sulfate, Potassium Sulfate, Magnesium Sulfate Oral Solution
ANDA:	Sodium Sulfate, Potassium Sulfate, Magnesium Sulfate Oral Solution
USP:	No Monograph

Reviewer Assessment:

Is the established name for ANDA acceptable? **YES**
Is the established (and proprietary name) displayed in a manner consistent 21 CFR 201.10? **YES**
Is title case used in established name? **YES**
Is established name on list of name pairs that use Tall Man lettering found on FDA webpage? **NO**

- If yes does labeling comply with Tall Man lettering recommendations? **NA**

Reviewer Comments:

2.1.2 United States Pharmacopeia (USP) & Pharmacopeia Forum (PF)

We searched the USP and PF to determine if the drug product under review is the subject of a USP monograph or proposed USP monograph and determined how the monograph impacts the ANDA labeling with respect to packaging and storage. The results of this search are provided in Table 4.

Table 4: USP and PF Search Results

	Date Searched	Monograph? YES or NO	Labeling statements found NA if no monograph
USP	8/18/2014	**NO**	NA
PF	8/18/2014	**NO**	NA

Reviewer Assessment:

Does the ANDA labeling require revision or is clarification needed from other review disciplines based on the comparison of USP or PF label/labeling requirements? **NA**
Do required labeling statements appear on/in the ANDA labeling? **NA**
Are the USP packaging and storage recommendations reflected in the labels and labeling? **NA**

Reviewer Comments:

2.2 CONTAINER LABEL

We evaluated the container labels for the inclusion of all required statements and safety considerations.

2.2.1 Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors

We used the draft Guidance for Industry titled Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors for the following assessment.

Reviewer Assessment:

Does the following information appear as the most prominent information on the Principal Display Panel?
- Proprietary name? **NA**
- Established name? **YES**
- Product strength? **YES**
- Route(s) of administration (other than oral)? **NA**
- Warnings (if any) or cautionary statements (if any)? **YES**

Does the following information appear of lesser prominence on the Principal Display Panel?
- Rx-only statement? **YES**
- Net quantity statement? **YES**
- Manufacturer logo? **YES**

Are the requirements of 21 CFR 201.15 met for all required label statements? **YES**
Are the requirements of 21 CFR 201.100 met for all required label statements? **YES**

Reviewer Comments:

2.2.2 Other Container Label Considerations

Reviewer Assessment:

Does this container meet the "too small" exemption found in 21 CFR 201.10(i)? **NO**
Are all abbreviations acceptable? (i.e., mg, mcg, HCl)? **YES**
Are multiple strengths differentiated by use of different color or other acceptable means? **NA**
Does the net quantity statement appear separate from and less prominent than the statement of strength (e.g., not highlighted, boxed, or bolded)? **YES**
Are the rules governing leading and terminal zeroes, decimals, and commas followed? **YES**
If other than oral use, is the route of administration correctly described? **NA**
Are all required warning statements that appear on Model Label properly displayed? **YES**
Is space provided to display expiration date properly? **YES**
Is bar code properly displayed per 21 CFR 201.25(c)(2)? **YES**
Is NDC properly displayed? **YES**
Is controlled substance symbol properly displayed? **NA**
Is the "Usual Dosage" on side panel and is it acceptable? **YES**
Is a product strength equivalency statement on side panel? **NA**
Are the Medication Guide Pharmacist instructions included per 208.24(d)? **YES**

Reviewer Comments:

2.2.3 Container Label for Small Volume Parenteral Solutions:

Is container for small volume parenteral solution? **NO**
If YES go to Reviewer Assessment below, if NO go to section 2.2.4.

Reviewer Assessment:

Is the product strength expressed as total quantity per total volume followed by the concentration per milliliter (mL), as described in the USP, General Chapter <1> Injection? **NA**
If volume is less than 1 mL, is strength per fraction of a milliliter the only expression of strength?**NA**
Are inactive ingredients listed on label as required by regulations? **NA**

Reviewer Comments:

2.2.4 Container Label for Sterile Solid Injectable:

Is container for sterile solid injectable? **NO**
If YES go to Reviewer Assessment below, if NO go to section 2.2.5.

Reviewer Assessment:

Is the strength in terms of the total amount of drug per vial? **NA**
Are instructions for reconstituting the product and the resultant concentration if space permits? **NA**
Are inactive ingredients listed on label as required by regulations? **NA**

Reviewer Comments:

2.2.5 Container Label for Pharmacy Bulk Package:

Is container a Pharmacy Bulk Package? **NO**
If YES go to Reviewer Assessment below, if NO go to section 2.2.6.

Reviewer Assessment:

Is there a prominent, boxed declaration reading "Pharmacy Bulk Package – Not for Direct Infusion" on the principal display panel following the expression of strength? **NA**
Does the container label include graduation marks? **NA**
Does label contain the required information on proper aseptic technique including time frame in which the container may be used once it has been entered? **NA**
Are inactive ingredients listed on label as required by regulations? **NA**

Reviewer Comments:

2.2.6 Unit Dose Blister Labels

Is container a Unit Dose Blister Pack? **NO**
If YES go to Reviewer Assessment below, if NO go to section 2.2.7

Reviewer Assessment:

Does each blister include only one dosage unit (e.g., one tablet, one capsule)? **NA**
Do proprietary name, established name, strength, lot number, expiration date, bar code, and manufacturer appear on each blister cell? **NA**
Does the established name describe only one unit (e.g. "tablet" rather than "tablets")? **NA**

Reviewer Comments:

2.2.7 Over The Counter (OTC) Label

Is this label for an OTC product? **NO**
If YES go to Reviewer Assessment below, if NO go to section 2.2.8

Reviewer Assessment:

Is Drug Facts Labeling format acceptable per 21 CFR 201.66? **NA**
Does packaging meet the requirements for Special Packaging under the Poison Prevention Act and defined per 16 CFR 1700? **NA**
Does packaging meet the tamper-evident requirements 21 CFR 211.132? **NA**
Does "Questions?" have a toll-free number no less than size 6 pt. font per 21 CFR 201.66(c)(9) or "1-800-FDA-1088" [21 CFR 201.66 (c)(5)(vii)]? **NA**
Did firm submit a Labeling Format Information Table to evaluate the font size? **NA**

Reviewer Comments:

2.2.8 Presentation of Manufacturer/Distributor/Packer on Labeling

We compared the name and address of the manufacturer of this product to the name and address listed on the labels and labeling to determine if the labeling statements are consistent with the regulations (21 CFR 201.1). Table 5 provides a description of this comparison. [NOTE: This presentation/assessment may apply to other labeling submitted].

Table 5: Comparison of Manufacturer/Distributor/Packer Labeling Statements	
Name and Address of Facility ANDA Manufactured	Novel Laboratories Inc. 4000 Campus Drive Somerset NJ 08873
Name and Address on ANDA Labels	**Manufactured by:** **Novel Laboratories, Inc., Somerset, NJ 08873**
Name and Address on ANDA Labeling	Manufactured by: Novel Laboratories, Inc. Somerset, NJ 08873 **Insert:** Manufactured by Novel Laboratories, Inc. Somerset, NJ 08873, USA

Reviewer Assessment:

Does the labeling have the required qualifiers per 21 CFR 201.1? **YES**
For Foreign manufacturers, does the labeling have the country of origin? **NA**
For Foreign manufacturers, does the labeling have a US contact/distributor? **YES**

Reviewer Comments:

2.2.9 Description of the Container/Closure

We evaluated the container/closure system of this product to determine if special child-resistant packaging is required based on packaging configuration. Additionally, we evaluated other aspects of the container closure that relate to the dosage form, product formulation, and product class. Below is a description of the container/closure for the ANDA product.

Reviewer Assessment:

Does the container require a child-resistant closure (CRC) as described in the Poison Prevention Act and regulations? **YES**
Describe container closure in **Reviewer Comments** text box (e.g. 30s CRC, 100s non-CRC)
If the closure is not child-resistant, does the container or carton require a labeling statement warning the product is not child-resistant? **NA**
Are the tamper evident requirements met for OTC and Controlled Substances? **NA**
Does this ophthalmic products cap color match the American Academy of Ophthalmology (AAO) packaging color-coding scheme? **NA**
For parenteral products:
Is there text on the cap/ferrule overseal of this injectable product? **NA**
If YES, does text comply with the recommendations in USP General Chapter <1>? **NA**
What is the cap and ferrule color?
NOTE: Black closure system is prohibited, except for Potassium Chloride for Injection Concentrate.

Comment

Container closure description:

Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution is a stable product. SUPREP is available in 6 oz Amber colored (b) (4) Bottles. Novel's drug product is packaged in 200cc (b) (4) (HDPE) bottles with (b) (4) CRC Closure. The details of the container closure system are shown below.

Component	Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution
Container / Shape/ Type/ Color	200 cc (b) (4)
Closure	(b) (4) Child Resistance Closure (b) (4)
Seal	(b) (4)
Outsert	Yes

(b) (4)

(b) (4)

2.2.10 Storage and Dispensing Recommendations

We compared the storage and dispensing statements that appear on the ANDA labels to the model labeling and USP to confirm the statements do not conflict and the format is consistent with USP and OGD standards (see Table 6). [NOTE: This assessment may apply to other labeling submitted]

Table 6: Model Labeling and ANDA Storage/Dispensing Recommendations

Model Labeling
Insert – Storage: Store at 20° to 25°C (68° to 77°F). Excursions permitted between 15° to 30°C (59° to 86°F). See USP controlled room temperature.
Container – Keep this and other drugs out of reach of children. Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). **Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).** **Carton –**
ANDA
Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). **Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).**
USP
No monograph

Reviewer Assessment:

Is the storage or dispensing statement acceptable as compared to the Model Labeling? **YES**
Is the storage or dispensing statement acceptable as compared to the USP? **NA**
Are the storage temperature recommendations acceptable? **YES**
Does the temperature statement conform to the OGD format for controlled room temperature?**YES**

Reviewer Comments:

2.2.11 Related Applications Containing the Same Active Ingredient

We evaluated the following applications that contain the same active ingredient from the same applicant to determine if the labels and labeling are adequately differentiated from one another.

Reviewer Assessment:

Are the labels and labeling of these products differentiated to avoid selection errors? **NA**

Reviewer Comments:

2.2.12 Comparison of ANDA Inactive Ingredients that Require Special Labeling Statements to Model

We compared the list of inactive ingredients contained in this product to those contained in the Model Labeling. Specific inactive ingredients that require special warnings, precautions, or label/labeling statements are in Table 7.

NOTE: This section is for assessing required statements on container labels only for both prescription and OTC drug products. Required statements for prescribing information is assessed for Prescription drug products in Sections 2.4.2 and 2.4.3

Table 7: Inactive Ingredients contained in Model Product and ANDA that require special labeling statements

Model Labeling	ANDA

Reviewer Assessment:

Do any of the inactive ingredients need a label statement required by regulations? **NO**
If the labeling includes "Does not contain …" statements – Has this statement been verified by chemistry? **NA**

Reviewer Comments:

2.3 CARTON (OUTER OR SECONDARY PACKAGING) LABELING

Reviewer Assessment:

Do all required label statements and safety considerations assessed above for CONTAINER labels appear on the carton? YES
If container is too small or otherwise unable to accommodate a label with enough space to include all required information, is all required information present on the carton labeling? **NO**
For unit dose blister that are not child-resistant is there a statement indicating the package is not child-resistant. For example, "This package is not child-resistant. If dispensed for outpatient use, a child-resistant container should be used"? **NA**
If country of origin is not on Container, does appear on outer packaging labeling? **NA**

Reviewer Comments:

2.4 PRESCRIBING INFORMATION

Reviewer Assessment:

Are the labeling contained in the submission the same as the review model labeling? **YES**
Are the differences allowed under 21 CFR 314.94(a)(8)? **YES**
Are the specific requirements for format met under 21 CFR 201.57(new) or 201.80(old)? **YES**
Does the Model Labeling have combined insert labeling for multiple dosage forms? **NO**

Reviewer Comments:

2.4.1 Patents and Exclusivities

Are there any unexpired patents or marketing exclusivities for Model Labeling? **YES**

If YES go to the table and assessments below.
If NO go to section 2.4.2.
Table 8 describes how the applicant certified to the Orange Book patent(s) for the Model Labeling and how this

certification impacts the ANDA labels and labeling. For applications that have no patents N/A is entered in the patent number column.

Table 8: Impact of Model Labeling Patents on ANDA Labeling					
Patent Number	Patent Expiration	Patent Use Code	Patent Use Code Definition	How Applicant Filed	Labeling Impact
6946149	3/7/2023	U-837	GASTROINTESTINAL LAVAGE INDICATED FOR CLEANSING OF THE COLON AS A PREPARATION FOR COLONOSCOPY IN ADULTS	Paragraph IV	None

Reviewer Assessment:

Is the applicant's "patent carve out" acceptable? **NA**

Reviewer Comments:

Table 9 describes how the expiration of the Orange Book exclusivities for the Model Labeling impacts the ANDA labels and labeling. For applications that have no exclusivities N/A is entered in the Exclusivity Code column.

Table 9: Impact of Model Labeling Exclusivities on ANDA Labels and Labeling			
Exclusivity Code	Exclusivity Code Definition	Exclusivity Expiration	Labeling Impact
N/A			

Reviewer Assessment:

Is the applicant's "exclusivity carve out" acceptable? **NA**

Reviewer Comments:

2.4.2 Comparison of ANDA Inactive Ingredients to Model Labeling (Topical And Oral Products Only)

Is submitted labeling for a topical or oral product? **YES**

If YES, complete tables 10a, 10b, and 10c along with assessment below.
If NO, go to section 2.4.3.
We compared the list of inactive ingredients contained in this product to those contained in the Model Labeling.

In Table 10a we compared the lists of inactive ingredients in the DESCRIPTION sections of the Model labeling and the ANDA labeling.

Table 10a: Inactive Ingredients contained in Model Product and ANDA from Description section

Model Labeling Inactive Ingredients	ANDA Inactive Ingredients
Each SUPREP Bowel Prep Kit contains two 6 ounce bottles of solution. Each 6 ounce bottle contains: sodium sulfate 17.5 grams, potassium sulfate 3.13 grams, magnesium sulfate 1.6 grams. Inactive ingredients include: sodium benzoate, NF, sucralose, malic acid FCC, citric acid USP, flavoring ingredients, purified water, USP. The solution is a clear to slightly hazy liquid.	bottles of solution. Each 6 ounce bottle contains: sodium sulfate 17.5 grams, potassium sulfate 3.13 grams, magnesium sulfate 1.6 grams. Inactive ingredients include: sodium benzoate, sucralose, malic acid, citric acid, flavoring ingredients, purified water. The solution is a clear to slightly hazy

In Table 10b we compared the lists of inactive ingredients in the DESCRIPTION section and Components and Components statements in ANDA.

Table 10b: Comparison Inactive Ingredients contained in ANDA Description section and Components and Composition

Description Section	Components and Composition

Table 10b: Comparison Inactive Ingredients contained in ANDA Description section and Components and Composition

bottles of solution. Each 6 ounce bottle contains: sodium sulfate 17.5 grams, potassium sulfate 3.13 grams, magnesium sulfate 1.6 grams. Inactive ingredients include: sodium benzoate, sucralose, malic acid, citric acid, flavoring ingredients, purified water. The solution is a clear to slightly hazy	Components, composition and the function of excipient are given below: Name of the component / Composition (g) / Composition % (g/100 mL) / Function Sodium Sulfate Anhydrous, USP — 17.500 Potassium Sulfate — 3.130 Magnesium Sulfate USP — 1.600 Sodium Benzoate, NF Sucralose, NF Malic Acid, NF Citric Acid, Lemon Flavor (b) (4) Note: Product is diluted to 16 oz with water.

We noted any specific inactive ingredients that require special warnings, precautions, or label/labeling statements are listed in Table 10c.for Model and ANDA

Table 10c Specific inactive ingredients that require special warnings, precautions

Model Labeling Inactive Ingredients	ANDA Inactive Ingredients

Reviewer Assessment:

Is the DESCRIPTION section of the labeling consistent with the component and composition statement contained in the ANDA? **YES**
Are the required labeling statements present in the ANDA labeling? **YES**

Reviewer Comments:

2.4.3 Comparison of ANDA Inactive Ingredients to Model Labeling (Ophthalmic, Injectable, And Otic Products Only)

Is submitted labeling for an ophthalmic, injectable, or an otic product? **NA**

If YES, complete tables 11a, 11b, and 11c along with the assessment below.
If NO go to section 2.4.4.

We compared the list of inactive ingredients and the amount of the inactive ingredient contained in this product as to those contained in the Model Labeling to determine if all components and composition are the same and if they are listed accurately in the labeling.

In Table 11a we compared the lists of inactive ingredients in the DESCRIPTION sections of the Model labeling and the ANDA labeling.

Table 11a: Inactive Ingredients contained in Model Product and ANDA from Description section

Model Labeling Inactive Ingredients	ANDA Inactive Ingredients

In Table 11b we compared the lists of inactive ingredients in the DESCRIPTION section and Components and Components statements in ANDA.

Table 11b: Comparison Inactive Ingredients contained in ANDA Description section and Components and Composition

Description Section	Components and Composition

We noted any specific inactive ingredients that require special warnings, precautions, or label/labeling statements are listed in Table 11c.for Model and ANDA

Table 11c Specific inactive ingredients that require special warnings, precautions

Model Labeling Inactive Ingredients	ANDA Inactive Ingredients

Reviewer Assessment:

Is the DESCRIPTION section of the labeling consistent with the component and composition statement contained in the application? **NA**
Are the required labeling statements present in the ANDA labeling? **NA**
If the labeling includes "Does not contain …" statements – Has this statement been verified by chemistry? **NA**

Reviewer Comments:

2.4.4 How Supplied Section

We compared the descriptions of the model product to the ANDA finished product. Product differences, such as coring configuration, are highlighted in Table 12 and will be referred to the appropriate review discipline for evaluation. Additionally, we evaluated if the text contained in the HOW SUPPLIED section is accurate based on the ANDA finished product description.

Table 12: Comparison of Model Labeling to ANDA finished product

Model Labeling	**16 HOW SUPPLIED/STORAGE AND HANDLING** Each SUPREP Bowel Prep Kit contains: • Two (2) 6 ounce bottles of oral solution. • One (1) 19 ounce mixing container with a 16 ounce fill line.
ANDA	**16 HOW SUPPLIED/STORAGE AND HANDLING** Each Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution contains: • Two (2) 6 ounce bottles of oral solution. • One (1) 19 ounce mixing container with a 16 ounce fill line.

Reviewer Assessment:

Is the description (scoring, color, and imprint) of the finished product accurate in the HOW SUPPLIED section of the insert? **YES**
Are the packaging sizes acceptable as compared to the Model Labeling? **YES**
Does the packaging configuration require the addition or deletion of labeling statements based on the comparison to Model Labeling and/or stability data? **YES**

Reviewer Comments:

2.4.5 Previous Labeling Reviews for ANDA and/or Related Correspondence

Table 13 contains a listing of previously completed OGD labeling reviews and other correspondence relating to this application from DARRTS. We reviewed this information to determine if previous labeling comments were addressed by the applicant or if there is new information that may impact the labeling.

Table 13: Completed Labeling Reviews or Other Correspondence for Application Under Review

Search Date	Finalized Date of DARRTS Document	Were Previous Comments Addressed? (Yes/No/Explain)
12/29/2014	8/20/2014	Yes

2.5 MEDICATION GUIDE

We evaluated the medication guide to ensure the text is the same as the model labeling. We also ensured the directive appears on the container and carton labeling.

Reviewer Assessment:

Does the format meet the requirements of 21 CFR 208.20? **YES**
Are the dispensing and distributions requirements of 21 CFR 208.24 met? **YES**
Has the Applicant committed to provide a sufficient number of medication guides? **YES**
Is the phonetic spelling of the proprietary or established name present? **YES**
Is the dispensing directive present on the container and carton labeling? **YES**
Is FDA 1-800-FDA-1088 phone number included? **YES**

Reviewer Comments:

2.6 OTHER PATIENT LABELING

2.7 STRUCTURED PRODUCT LABELING (SPL) DATA ELEMENTS

We evaluated the SPL data elements to ensure they are consistent with the information submitted in the ANDA. Additionally, we compared the size of the model and ANDA tablet/capsule size to determine if the size of the ANDA tablet/capsule poses a safety risk or require a labeling statement (see Table 14).

Table 14: Comparison of Model and ANDA Tablet/Capsule Size

Model Labeling	
ANDA Labeling	

Reviewer Assessment:

Are the data elements consistent with the information submitted in the ANDA? **YES**
Is the tablet/capsule size similar to the RLD? **NA**

Reviewer Comments:

3. OVERALL ASSESSMENT OF MATERIALS REVIEWED

Tables 15 and 16 provide a summary of recommendations for each material analyzed in this review.

Table 15: Review Summary of Container Label and Carton Labeling			
	Packaging Sizes	**Submission Date**	**Recommendation**
Container ☐ Draft ☒ FPL		8/8/2014	☒ Satisfactory ☐ Revise
Blister ☐ Draft ☐ FPL			☐ Satisfactory ☐ Revise
Carton ☐ Draft ☒ FPL		11/21/2014	☒ Satisfactory ☐ Revise
Unit Dose Carton ☐ Draft ☐ FPL			☐ Satisfactory ☐ Revise
Table 16 Review Summary of Prescribing Information and Patient Labeling			
	Revision Date and/or code	**Submission Date**	**Recommendation**
Prescribing Info ☐ Draft ☒ FPL	12/14	12/18/2014	☒ Satisfactory ☐ Revise
Medication Guide ☐ Draft ☒ FPL	12/14	12/18/2014	☒ Satisfactory ☐ Revise
Patient Information ☐ Draft ☐ FPL		12/18/2014	☐ Satisfactory ☐ Revise
PPI ☐ Draft ☐ FPL			☐ Satisfactory ☐ Revise
SPL ☒		11/21/2014	☒ Satisfactory ☐ Revise

3.1 ANDA LABELS AND LABELING SUBMITTED

4. QUESTIONS AND COMMENTS FOR

During the course of this review, we sought clarification on the following issues to determine if a label or labeling revision is necessary.

Reviewer Assessment:

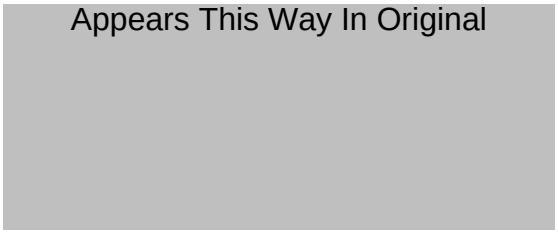
Does the response(s) received require a label and/or labeling revision? **NA**
Reviewer Comments:

5. SPECIAL CONSIDERATIONS

Please note that Reference Listed Drug (RLD) supplemental approval NDA 022372/S-003, approved on July 6, 2011, removes the REMS requirement. We ask that you request withdrawal of your REMS plan at this time consistent with the RLD.

Response:
Novel is requesting Agency to withdraw our REMS plan in consistent with RLD

6. POST APPROVAL REVISIONS



***** This document contains proprietary information that cannot be released to the public*****

LABELING REVIEW

Division of Labeling Review
Office of Regulatory Operations
Office of Generic Drugs (OGD)
Center for Drug Evaluation and Research (CDER)

Date of This Review	8/18/2014
ANDA Application Number	202511
Review Cycle Number	2
Applicant Name	Novel Laboratories Inc.
Established Name	Sodium Sulfate, Potassium Sulfate, Magnesium Sulfate Oral Solution
Strength(s)	(17.5 g/3.13 g/1.6 g) per 6 ounces
Proposed Proprietary Name	
DARRTS Received Date	8/8/2014
Labeling Reviewer	Charlie Hoppes
Labeling Team Leader	John Grace

Review Conclusion

☐ No Comments – The Labels and Labeling are ready for approval.

☒ Minor Deficiency* - Refer to Labeling Deficiencies and Comments for the Letter to Applicant

*Please Note: The Regulatory Project Manager (RPM) may change the recommendation from Minor Deficiency to Easily Correctable Deficiency if all other OGD reviews are acceptable. Otherwise the labeling minor deficiencies will be included in the Complete Response (CR) letter to the applicant.

LABELING DEFICIENCIES AND COMMENTS FOR LETTER TO APPLICANT

1. GENERAL COMMENTS

a. Please note that Reference Listed Drug (RLD) supplemental approval NDA 022372/S-003, approved on July 6, 2011, removes the REMS requirement. We ask that you request withdrawal of your REMS plan at this time consistent with the RLD.

b. We acknowledge comments regarding the INSTRUCTIONS FOR USE labeling piece. However, we believe that you should be the same as the RLD with regard to providing instructions for use.

2. CARTON LABELING

a. See applicable GENERAL COMMENT above and reference the INSTRUCTIONS FOR USE labeling piece on carton labeling as seen with RLD labeling.

b. Ensure that the conditions of 21 CFR 201.1(i) are met.

c. Revise "Note" to read, "…at least 2 hours…"

3. PHYSICIAN LABELING

a. See applicable GENERAL COMMENTS above.

b. The last approved RLD labeling is NDA 022372/S-004, approved on November 1, 2011. It appears that you have not made all the changes that were last approved for the RLD and we request that you do so at this time.

c. Add the missing row line to Table 2.

d. Include the type of flavoring in the DESCRIPTION section.

e. Add negative signs (b) (4) magnesium sulfate structural formula (see RLD labeling). Make the following revision to the last sentence in the DESCRIPTION section, "…package also contains…".

4. MEDICATION GUIDE

a. Provide the MEDICATION GUIDE as a separate labeling piece or, if providing it attached to the PHYSICIAN LABELING, format so that it can be removed from the physician labeling.

b. Ensure that the formatting requirements of 21 CFR 208.20 are met.

c. Provide the phonetic spelling of the product in the MEDICATION GUIDE title.

5. INSTRUCTIONS FOR USE

See second GENERAL COMMENT above.

Submit your revised labeling electronically in final print format.

To facilitate review of your next submission, please provide a side-by-side comparison of your proposed labeling with the last approved RLD labeling with all differences annotated and explained.

Prior to the submission of your amendment, please check labeling resources, including DRUGS@FDA, the electronic Orange Book and the NF-USP online, for recent updates and make any necessary revisions to your labels and labeling.

In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address –

http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

Apperas This Way In Original

1. MODEL LABELING FOR ANDA

Our review is based on the following model labels and labeling used for comparison to the submitted ANDA labeling.

1.1 MODEL CONTAINER LABELS FOR ANDA

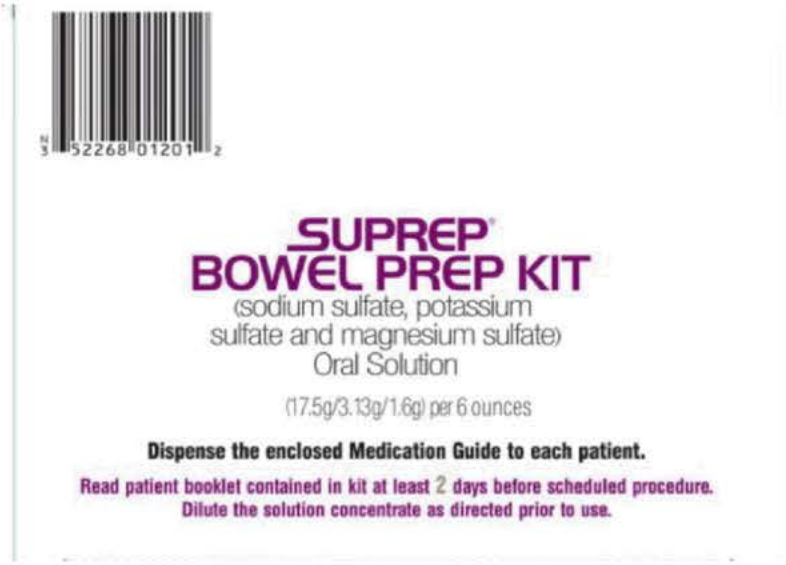
In Table 1 below, check all sources for Model container labels and carton labeling (secondary packaging) that applies.

Container labels are assessed in section 2.2.

Carton labeling (outer or secondary packaging) is assessed in section 2.3.

Table 1: Review Model Labeling for Container Label and Carton Labeling (Check all sources that apply)	
Source	**Date of source document (i.e. supplement approval date, annual report date)**
☐ drugs@fda	
☒ DARRTS	9/30/2013
☐ DailyMed	
☒ Annual Report Y-03	9/30/2013
☐ Other	

Model labels and carton labeling. [Insert or paste images below]



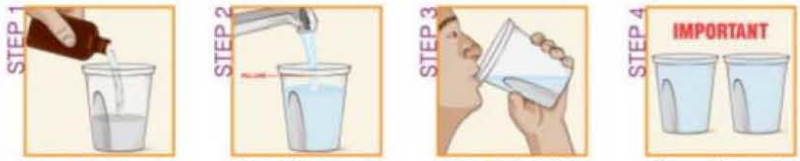
Instructions for use continued (refer to side panel)
Your doctor has recommended split-dose SUPREP

Split-Dose (2-Day) Regimen
(Both 6-ounce bottles are required for a complete prep.)

- On the evening before procedure (or when your doctor tells you to begin) complete steps 1 through 4 using one (1) 6-ounce bottle before going to bed
- On the morning of your procedure, repeat steps 1 through 4 using the other 6-ounce bottle

NOTE: You must finish drinking the final glass of water at **least 2 hours** before your procedure or as directed by physician

NOTE: Dilute the solution concentrate as directed prior to use.



Pour **ONE** (1) 6-ounce bottle of SUPREP liquid into the mixing container.

Add cool drinking water to the 16-ounce line on the container and mix.

Drink **ALL** the liquid in the container.

You **must** drink two (2) more 16-ounce containers of water over the next 1 hour.

Please read full prescribing information in this kit.

SUPREP® BOWEL PREP KIT

(sodium sulfate, potassium sulfate and magnesium sulfate) Oral Solution

(17.5g/3.13g/1.6g) per 6 ounces

NDC 52268-012-01

U.S. Patent 6,946,149

Dispense the enclosed Medication Guide to each patient.

SUPREP® BOWEL PREP KIT

(sodium sulfate, potassium sulfate and magnesium sulfate) Oral Solution

(17.5g/3.13g/1.6g) per 6 ounces

This carton contains:

2 6-ounce (177 mL) bottles of liquid bowel prep
1 16-ounce mixing container
1 Patient booklet. Booklet includes:
1- Medication Guide
2- Patient Instructions
3- Full Prescribing Information

Dilute the solution concentrate as directed prior to use.

Both 6-ounce bottles are required for a complete prep.

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

Rx only

Braintree

Instructions for Use Start Here

On the day before your procedure

- You may have a light breakfast or have clear liquids ONLY; please have nothing for dinner
- **DO NOT** drink milk
- **DO NOT** eat or drink anything colored red or purple
- **DO NOT** drink alcoholic beverages

Any of the following clear liquids are OK

- Water
- Strained fruit juices (without pulp) including apple, orange, white grape, or white cranberry
- Limeade or lemonade
- Coffee or tea (**DO NOT** use any dairy or non-dairy creamer)
- Chicken broth
- Gelatin desserts without added fruit or topping (**NO RED OR PURPLE**)

REV NOV 2012

Continue

1.2 PRESCRIBING INFORMATION MODEL LABELING

The review model labels and labeling used for comparison to the submitted ANDA labeling are described in Table 2.

Prescribing information is assessed in section 2.4.

Table 2: Review Model Labeling for Prescribing Information and Patient Labeling(Check all that apply)		
☐ MOST RECENTLY APPROVED REFERENCE LISTED DRUG		
NDA or ANDA: 022372	Proprietary Name: Suprep Bowel Prep Kit	Approval date: 11/1/2012
S- 004	Description of Supplement: Labeling revisions to the Dosage and Administration section.	
☐ BPCA or PREA TEMPLATE		
☐ OTHER (Describe):		

2. MATERIAL ANALYSIS

The results for each material reviewed in this section provide the basis for the labeling comments to the applicant (Page 2).

2.1 GENERAL

2.1.1 Established Name Assessment

We compared the established names of this ANDA, the Model Labeling and the USP to determine if the established name presented on the labeling is acceptable.

Table 3: Comparison of Established Names

Model Labeling:	Sodium Sulfate, Potassium Sulfate, Magnesium Sulfate Oral Solution
ANDA:	Sodium Sulfate, Potassium Sulfate, Magnesium Sulfate Oral Solution
USP:	No Monograph

Reviewer Assessment:

Is the established name for ANDA acceptable? **YES**
Is the established (and proprietary name) displayed in a manner consistent 21 CFR 201.10? **YES**
Is title case used in established name? **YES**
Is established name on list of name pairs that use Tall Man lettering found on FDA webpage? **NO**

- If yes does labeling comply with Tall Man lettering recommendations? **NA**

Reviewer Comments:

2.1.2 United States Pharmacopeia (USP) & Pharmacopeia Forum (PF)

We searched the USP and PF to determine if the drug product under review is the subject of a USP monograph or proposed USP monograph and determined how the monograph impacts the ANDA labeling with respect to packaging and storage. The results of this search are provided in Table 4.

Table 4: USP and PF Search Results

	Date Searched	Monograph? YES or NO	Labeling statements found NA if no monograph
USP	8/18/2014	**NO**	NA
PF	8/18/2014	**NO**	NA

Reviewer Assessment:

Does the ANDA labeling require revision or is clarification needed from other review disciplines based on the comparison of USP or PF label/labeling requirements? **NA**
Do required labeling statements appear on/in the ANDA labeling? **NA**
Are the USP packaging and storage recommendations reflected in the labels and labeling? **NA**

Reviewer Comments:

2.2 CONTAINER LABEL

We evaluated the container labels for the inclusion of all required statements and safety considerations.

2.2.1 Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors

We used the draft Guidance for Industry titled Safety Considerations for Container Labels and Carton Labeling

Design to Minimize Medication Errors for the following assessment.

Reviewer Assessment:

Does the following information appear as the most prominent information on the Principal Display Panel?
- Proprietary name? **NA**
- Established name? **YES**
- Product strength? **YES**
- Route(s) of administration (other than oral)? **NA**
- Warnings (if any) or cautionary statements (if any)? **YES**

Does the following information appear of lesser prominence on the Principal Display Panel?
- Rx-only statement? **YES**
- Net quantity statement? **YES**
- Manufacturer logo? **YES**

Are the requirements of 21 CFR 201.15 met for all required label statements? **YES**
Are the requirements of 21 CFR 201.100 met for all required label statements? **YES**

Reviewer Comments:

2.2.2 Other Container Label Considerations

Reviewer Assessment:

Does this container meet the "too small" exemption found in 21 CFR 201.10(i)? **NO**
Are all abbreviations acceptable? (i.e., mg, mcg, HCl)? **YES**
Are multiple strengths differentiated by use of different color or other acceptable means? **NA**
Does the net quantity statement appear separate from and less prominent than the statement of strength (e.g., not highlighted, boxed, or bolded)? **YES**
Are the rules governing leading and terminal zeroes, decimals, and commas followed? **YES**
If other than oral use, is the route of administration correctly described? **NA**
Are all required warning statements that appear on Model Label properly displayed? **YES**
Is space provided to display expiration date properly? **YES**
Is bar code properly displayed per 21 CFR 201.25(c)(2)? **YES**
Is NDC properly displayed? **YES**
Is controlled substance symbol properly displayed? **NA**
Is the "Usual Dosage" on side panel and is it acceptable? **YES**
Is a product strength equivalency statement on side panel? **NA**
Are the Medication Guide Pharmacist instructions included per 208.24(d)? **YES**

Reviewer Comments:

2.2.3 Container Label for Small Volume Parenteral Solutions:

Is container for small volume parenteral solution? **NO**
If YES go to Reviewer Assessment below, if NO go to section 2.2.4.

Reviewer Assessment:

Is the product strength expressed as total quantity per total volume followed by the concentration per milliliter (mL), as described in the USP, General Chapter <1> Injection? **NA**
If volume is less than 1 mL, is strength per fraction of a milliliter the only expression of strength?**NA**
Are inactive ingredients listed on label as required by regulations? **NA**

Reviewer Comments:

2.2.4 Container Label for Sterile Solid Injectable:

Is container for sterile solid injectable? **NO**
If YES go to Reviewer Assessment below, if NO go to section 2.2.5.

Reviewer Assessment:

Is the strength in terms of the total amount of drug per vial? **NA**
Are instructions for reconstituting the product and the resultant concentration if space permits? **NA**
Are inactive ingredients listed on label as required by regulations? **NA**

Reviewer Comments:

2.2.5 Container Label for Pharmacy Bulk Package:

Is container a Pharmacy Bulk Package? **NO**
If YES go to Reviewer Assessment below, if NO go to section 2.2.6.

Reviewer Assessment:

Is there a prominent, boxed declaration reading "Pharmacy Bulk Package – Not for Direct Infusion" on the principal display panel following the expression of strength? **NA**
Does the container label include graduation marks? **NA**
Does label contain the required information on proper aseptic technique including time frame in which the container may be used once it has been entered? **NA**
Are inactive ingredients listed on label as required by regulations? **NA**

Reviewer Comments:

2.2.6 Unit Dose Blister Labels

Is container a Unit Dose Blister Pack? **NO**
If YES go to Reviewer Assessment below, if NO go to section 2.2.7

Reviewer Assessment:

Does each blister include only one dosage unit (e.g., one tablet, one capsule)? **NA**
Do proprietary name, established name, strength, lot number, expiration date, bar code, and manufacturer appear on each blister cell? **NA**
Does the established name describe only one unit (e.g. "tablet" rather than "tablets")? **NA**

Reviewer Comments:

2.2.7 Over The Counter (OTC) Label

Is this label for an OTC product? **NO**
If YES go to Reviewer Assessment below, if NO go to section 2.2.8

Reviewer Assessment:

Is Drug Facts Labeling format acceptable per 21 CFR 201.66? **NA**
Does packaging meet the requirements for Special Packaging under the Poison Prevention Act and defined per 16 CFR 1700? **NA**
Does packaging meet the tamper-evident requirements 21 CFR 211.132? **NA**
Does "Questions?" have a toll-free number no less than size 6 pt. font per 21 CFR 201.66(c)(9) or "1-800-FDA-1088" [21 CFR 201.66 (c)(5)(vii)]? **NA**
Did firm submit a Labeling Format Information Table to evaluate the font size? **NA**

Reviewer Comments:

2.2.8 Presentation of Manufacturer/Distributor/Packer on Labeling

We compared the name and address of the manufacturer of this product to the name and address listed on the labels and labeling to determine if the labeling statements are consistent with the regulations (21 CFR 201.1). Table 5 provides a description of this comparison. [NOTE: This presentation/assessment may apply to other labeling submitted].

Table 5: Comparison of Manufacturer/Distributor/Packer Labeling Statements	
Name and Address of Facility ANDA Manufactured	Novel Laboratories Inc. 4000 Campus Drive Somerset NJ 08873
Name and Address on ANDA Labels	Manufactured by: Novel Laboratories, Inc., Somerset, NJ 08873
Name and Address on ANDA Labeling	 Manufactured by Novel Laboratories, Inc. Somerset, NJ 08873, USA

Reviewer Assessment:

Does the labeling have the required qualifiers per 21 CFR 201.1? **NO**
For Foreign manufacturers, does the labeling have the country of origin? **NA**
For Foreign manufacturers, does the labeling have a US contact/distributor? **YES**

Reviewer Comments: Carton: Ensure that the conditions of 21 CFR 201.1(i) are met.

2.2.9 Description of the Container/Closure

We evaluated the container/closure system of this product to determine if special child-resistant packaging is required based on packaging configuration. Additionally, we evaluated other aspects of the container closure that relate to the dosage form, product formulation, and product class. Below is a description of the container/closure for the ANDA product.

Reviewer Assessment:

Does the container require a child-resistant closure (CRC) as described in the Poison Prevention Act and regulations? **YES**
Describe container closure in **Reviewer Comments** text box (e.g. 30s CRC, 100s non-CRC)
If the closure is not child-resistant, does the container or carton require a labeling statement warning the product is not child-resistant? **NA**
Are the tamper evident requirements met for OTC and Controlled Substances? **NA**
Does this ophthalmic products cap color match the American Academy of Ophthalmology (AAO) packaging color-coding scheme? **NA**
For parenteral products:
Is there text on the cap/ferrule overseal of this injectable product? **NA**
If YES, does text comply with the recommendations in USP General Chapter <1>? **NA**
What is the cap and ferrule color?
NOTE: Black closure system is prohibited, except for Potassium Chloride for Injection Concentrate.

Comment

see page 24

Container closure description:

Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution is a stable product. SUPREP is available in 6 oz Amber colored (b) (4) Bottles. Novel's drug product is packaged in 200cc (b) (4) (HDPE) bottles with (b) (4) CRC Closure. The details of the container closure system are shown below.

Component	Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution
Container / Shape/ Type/ Color	200 cc (b) (4)
Closure	(b) (4) Child Resistance Closure (b) (4)
Seal	(b) (4)
Outsert	Yes

proprietary info, page 47

(b) (4)

[redacted]

2.2.10 Storage and Dispensing Recommendations

We compared the storage and dispensing statements that appear on the ANDA labels to the model labeling and USP to confirm the statements do not conflict and the format is consistent with USP and OGD standards (see Table 6). [NOTE: This assessment may apply to other labeling submitted]

Table 6: Model Labeling and ANDA Storage/Dispensing Recommendations
Model Labeling
Insert – Storage: Store at 20° to 25°C (68° to 77°F). Excursions permitted between 15° to 30°C (59° to 86°F). See USP controlled room temperature.
Container – Keep this and other drugs out of reach of children. Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). **Carton –** **Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).**
ANDA
Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). **Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).**
USP
No monograph

Reviewer Assessment:

Is the storage or dispensing statement acceptable as compared to the Model Labeling? **YES**
Is the storage or dispensing statement acceptable as compared to the USP? **NA**
Are the storage temperature recommendations acceptable? **YES**
Does the temperature statement conform to the OGD format for controlled room temperature?**YES**

Reviewer Comments:

2.2.11 Related Applications Containing the Same Active Ingredient

We evaluated the following applications that contain the same active ingredient from the same applicant to determine if the labels and labeling are adequately differentiated from one another.

Reviewer Assessment:

Are the labels and labeling of these products differentiated to avoid selection errors? **NA**

Reviewer Comments:

2.2.12 Comparison of ANDA Inactive Ingredients that Require Special Labeling Statements to Model

We compared the list of inactive ingredients contained in this product to those contained in the Model Labeling. Specific inactive ingredients that require special warnings, precautions, or label/labeling statements are in Table 7.

NOTE: This section is for assessing required statements on container labels only for both prescription and OTC drug products. Required statements for prescribing information is assessed for Prescription drug products in Sections 2.4.2 and 2.4.3

Table 7: Inactive Ingredients contained in Model Product and ANDA that require special labeling statements

Model Labeling	ANDA

Reviewer Assessment:

Do any of the inactive ingredients need a label statement required by regulations? **NO**
If the labeling includes "Does not contain …" statements – Has this statement been verified by chemistry? **NA**

Reviewer Comments:

2.3 CARTON (OUTER OR SECONDARY PACKAGING) LABELING

Reviewer Assessment:

Do all required label statements and safety considerations assessed above for CONTAINER labels appear on the carton? YES
If container is too small or otherwise unable to accommodate a label with enough space to include all required information, is all required information present on the carton labeling? **NO**
For unit dose blister that are not child-resistant is there a statement indicating the package is not child-resistant. For example, "This package is not child-resistant. If dispensed for outpatient use, a child-resistant container should be used"? **NA**
If country of origin is not on Container, does appear on outer packaging labeling? **NA**

Reviewer Comments:

2.4 PRESCRIBING INFORMATION

Reviewer Assessment:

Are the labeling contained in the submission the same as the review model labeling? **NO**
Are the differences allowed under 21 CFR 314.94(a)(8)? **YES**
Are the specific requirements for format met under 21 CFR 201.57(new) or 201.80(old)? **YES**
Does the Model Labeling have combined insert labeling for multiple dosage forms? **NO**

Reviewer Comments: The sponsor will be requested to be the same as last approved RLD labeling.

2.4.1 Patents and Exclusivities

Are there any unexpired patents or marketing exclusivities for Model Labeling? **YES**

If YES go to the table and assessments below.
If NO go to section 2.4.2.
Table 8 describes how the applicant certified to the Orange Book patent(s) for the Model Labeling and how this

certification impacts the ANDA labels and labeling. For applications that have no patents N/A is entered in the patent number column.

Table 8: Impact of Model Labeling Patents on ANDA Labeling					
Patent Number	Patent Expiration	Patent Use Code	Patent Use Code Definition	How Applicant Filed	Labeling Impact
6946149	3/7/2023	U-837	GASTROINTESTINAL LAVAGE INDICATED FOR CLEANSING OF THE COLON AS A PREPARATION FOR COLONOSCOPY IN ADULTS	Paragraph IV	None

Reviewer Assessment:

Is the applicant's "patent carve out" acceptable? **NA**

Reviewer Comments:

Table 9 describes how the expiration of the Orange Book exclusivities for the Model Labeling impacts the ANDA labels and labeling. For applications that have no exclusivities N/A is entered in the Exclusivity Code column.

Table 9: Impact of Model Labeling Exclusivities on ANDA Labels and Labeling			
Exclusivity Code	Exclusivity Code Definition	Exclusivity Expiration	Labeling Impact
N/A			

Reviewer Assessment:

Is the applicant's "exclusivity carve out" acceptable? **NA**

Reviewer Comments:

2.4.2 Comparison of ANDA Inactive Ingredients to Model Labeling (Topical And Oral Products Only)

Is submitted labeling for a topical or oral product? **YES**

If YES, complete tables 10a, 10b, and 10c along with assessment below.
If NO, go to section 2.4.3.
We compared the list of inactive ingredients contained in this product to those contained in the Model Labeling.

In Table 10a we compared the lists of inactive ingredients in the DESCRIPTION sections of the Model labeling and the ANDA labeling.

Table 10a: Inactive Ingredients contained in Model Product and ANDA from Description section

Model Labeling Inactive Ingredients	ANDA Inactive Ingredients
Each SUPREP Bowel Prep Kit contains two 6 ounce bottles of solution. Each 6 ounce bottle contains: sodium sulfate 17.5 grams, potassium sulfate 3.13 grams, magnesium sulfate 1.6 grams. Inactive ingredients include: sodium benzoate, NF, sucralose, malic acid FCC, citric acid USP, flavoring ingredients, purified water, USP. The solution is a clear to slightly hazy liquid.	bottles of solution. Each 6 ounce bottle contains: sodium sulfate 17.5 grams, potassium sulfate 3.13 grams, magnesium sulfate 1.6 grams. Inactive ingredients include: sodium benzoate, sucralose, malic acid, citric acid, flavoring ingredients, purified water. The solution is a clear to slightly hazy

In Table 10b we compared the lists of inactive ingredients in the DESCRIPTION section and Components and Components statements in ANDA.

Table 10b: Comparison Inactive Ingredients contained in ANDA Description section and Components and Composition

Description Section	Components and Composition

Table 10b: Comparison Inactive Ingredients contained in ANDA Description section and Components and Composition	
bottles of solution. Each 6 ounce bottle contains: sodium sulfate 17.5 grams, potassium sulfate 3.13 grams, magnesium sulfate 1.6 grams. Inactive ingredients include: sodium benzoate, sucralose, malic acid, citric acid, flavoring ingredients, purified water. The solution is a clear to slightly hazy	(b) (4) (b) (4) (b) (4) (b) (4) (b) (4) (b) (4) (b) (4)

We noted any specific inactive ingredients that require special warnings, precautions, or label/labeling statements are listed in Table 10c.for Model and ANDA

Table 10c Specific inactive ingredients that require special warnings, precautions	
Model Labeling Inactive Ingredients	ANDA Inactive Ingredients

Reviewer Assessment:

Is the DESCRIPTION section of the labeling consistent with the component and composition statement contained in the ANDA? **YES**
Are the required labeling statements present in the ANDA labeling? **YES**

Reviewer Comments: Include the type of flavor in the DESCRIPTION section.

2.4.3 Comparison of ANDA Inactive Ingredients to Model Labeling (Ophthalmic, Injectable, And Otic Products Only)

Is submitted labeling for an ophthalmic, injectable, or an otic product? **NA**

If YES, complete tables 11a, 11b, and 11c along with the assessment below.
If NO go to section 2.4.4.

We compared the list of inactive ingredients and the amount of the inactive ingredient contained in this product as to those contained in the Model Labeling to determine if all components and composition are the same and if they are listed accurately in the labeling.

In Table 11a we compared the lists of inactive ingredients in the DESCRIPTION sections of the Model labeling and the ANDA labeling.

Table 11a: Inactive Ingredients contained in Model Product and ANDA from Description section	
Model Labeling Inactive Ingredients	ANDA Inactive Ingredients

In Table 11b we compared the lists of inactive ingredients in the DESCRIPTION section and Components and Components statements in ANDA.

Table 11b: Comparison Inactive Ingredients contained in ANDA Description section and Components and Composition	
Description Section	Components and Composition

We noted any specific inactive ingredients that require special warnings, precautions, or label/labeling statements are listed in Table 11c.for Model and ANDA

Table 11c Specific inactive ingredients that require special warnings, precautions	
Model Labeling Inactive Ingredients	ANDA Inactive Ingredients

Reviewer Assessment:

Is the DESCRIPTION section of the labeling consistent with the component and composition statement contained in the application? **NA**
Are the required labeling statements present in the ANDA labeling? **NA**
If the labeling includes "Does not contain …" statements – Has this statement been verified by chemistry? **NA**

Reviewer Comments:

2.4.4 How Supplied Section

We compared the descriptions of the model product to the ANDA finished product. Product differences, such as coring configuration, are highlighted in Table 12 and will be referred to the appropriate review discipline for evaluation. Additionally, we evaluated if the text contained in the HOW SUPPLIED section is accurate based on the ANDA finished product description.

Table 12: Comparison of Model Labeling to ANDA finished product

Model Labeling	**16 HOW SUPPLIED/STORAGE AND HANDLING** Each SUPREP Bowel Prep Kit contains: • Two (2) 6 ounce bottles of oral solution. • One (1) 19 ounce mixing container with a 16 ounce fill line.
ANDA	**16 HOW SUPPLIED/STORAGE AND HANDLING** Each Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution contains: • Two (2) 6 ounce bottles of oral solution. • One (1) 19 ounce mixing container with a 16 ounce fill line.

Reviewer Assessment:

Is the description (scoring, color, and imprint) of the finished product accurate in the HOW SUPPLIED section of the insert? **YES**
Are the packaging sizes acceptable as compared to the Model Labeling? **YES**
Does the packaging configuration require the addition or deletion of labeling statements based on the comparison to Model Labeling and/or stability data? **YES**

Reviewer Comments:

2.4.5 Previous Labeling Reviews for ANDA and/or Related Correspondence

Table 13 contains a listing of previously completed OGD labeling reviews and other correspondence relating to this application from DARRTS. We reviewed this information to determine if previous labeling comments were addressed by the applicant or if there is new information that may impact the labeling.

Table 13: Completed Labeling Reviews or Other Correspondence for Application Under Review

Search Date	Finalized Date of DARRTS Document	Were Previous Comments Addressed? (Yes/No/Explain)
8/18/2014	3/31/2011	Yes

2.5 MEDICATION GUIDE

We evaluated the medication guide to ensure the text is the same as the model labeling. We also ensured the directive appears on the container and carton labeling.

Reviewer Assessment:

Does the format meet the requirements of 21 CFR 208.20? **NO**
Are the dispensing and distributions requirements of 21 CFR 208.24 met? **YES**
Has the Applicant committed to provide a sufficient number of medication guides? **YES**
Is the phonetic spelling of the proprietary or established name present? **NO**
Is the dispensing directive present on the container and carton labeling? **YES**
Is FDA 1-800-FDA-1088 phone number included? **YES**

Reviewer Comments: Provide the MEDICATION GUIDE as a separate labeling piece or, if providing it attached to the PHYSICIAN LABELING, format so that it can be removed from the physician labeling.

2.6 OTHER PATIENT LABELING

2.7 STRUCTURED PRODUCT LABELING (SPL) DATA ELEMENTS

We evaluated the SPL data elements to ensure they are consistent with the information submitted in the ANDA. Additionally, we compared the size of the model and ANDA tablet/capsule size to determine if the size of the ANDA tablet/capsule poses a safety risk or require a labeling statement (see Table 14).

Table 14: Comparison of Model and ANDA Tablet/Capsule Size

Model Labeling	
ANDA Labeling	

Reviewer Assessment:

Are the data elements consistent with the information submitted in the ANDA? **YES**
Is the tablet/capsule size similar to the RLD? **NA**

Reviewer Comments:

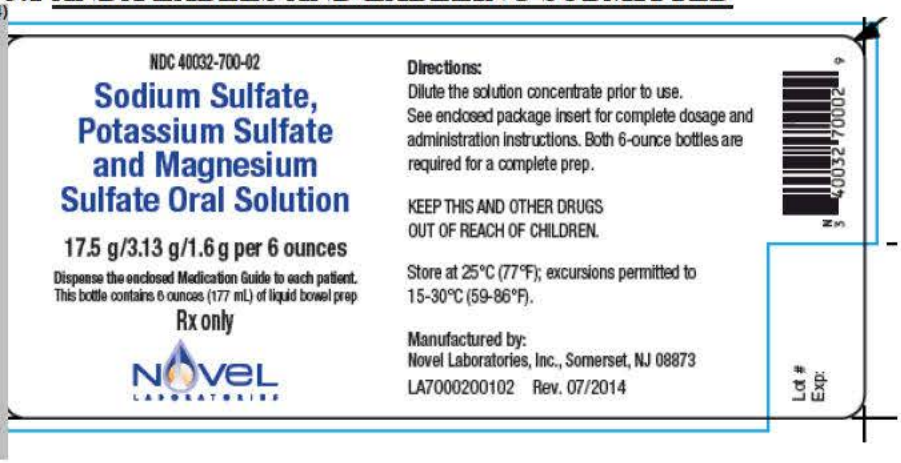
3. OVERALL ASSESSMENT OF MATERIALS REVIEWED

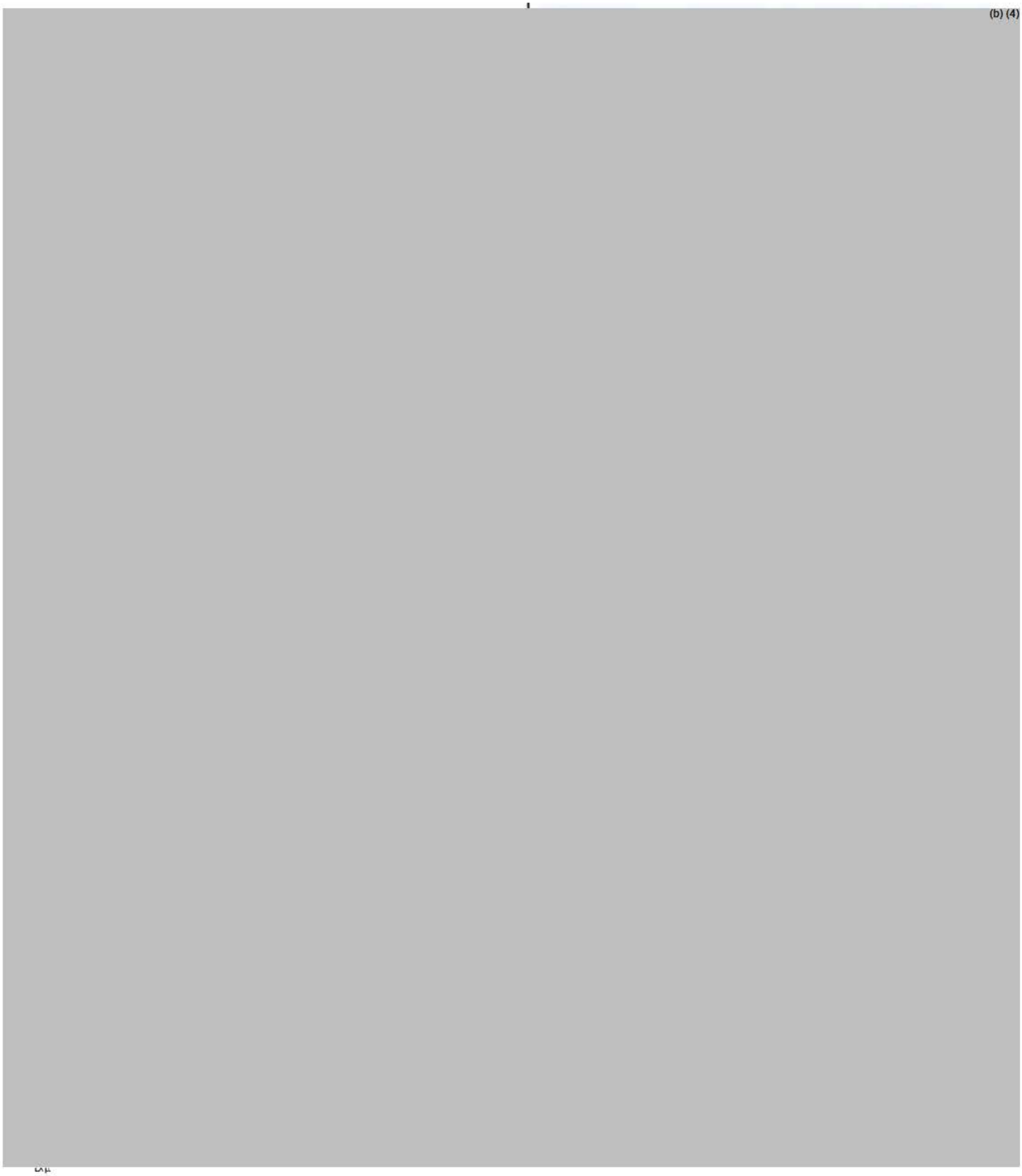
Tables 15 and 16 provide a summary of recommendations for each material analyzed in this review.

Table 15: Review Summary of Container Label and Carton Labeling			
	Packaging Sizes	Submission Date	Recommendation
Container ☐ Draft ☒ FPL		8/8/2014	☒ Satisfactory ☐ Revise
Blister ☐ Draft ☐ FPL			☐ Satisfactory ☐ Revise
Carton ☐ Draft ☒ FPL		8/8/2014	☐ Satisfactory ☒ Revise
Unit Dose Carton ☐ Draft ☐ FPL			☐ Satisfactory ☐ Revise
Table 16 Review Summary of Prescribing Information and Patient Labeling			
	Revision Date and/or code	Submission Date	Recommendation
Prescribing Info ☐ Draft ☒ FPL	3/14	8/8/2014	☐ Satisfactory ☒ Revise
Medication Guide ☐ Draft ☒ FPL	3/14	8/8/2014	☐ Satisfactory ☒ Revise
Patient Information ☐ Draft ☐ FPL			☐ Satisfactory ☐ Revise
PPI ☐ Draft ☐ FPL			☐ Satisfactory ☐ Revise
SPL ☒		8/8/2014	☐ Satisfactory ☒ Revise

3.1 ANDA LABELS AND LABELING SUBMITTED

(b) (4)




(b) (4)

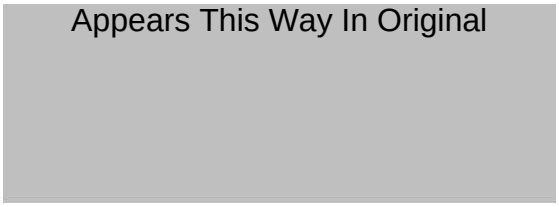
4. QUESTIONS AND COMMENTS FOR

During the course of this review, we sought clarification on the following issues to determine if a label or labeling revision is necessary.

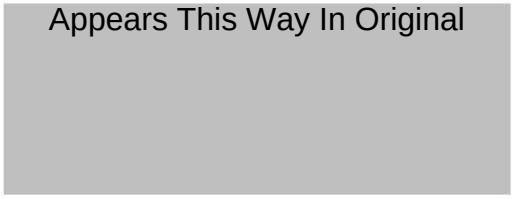
Reviewer Assessment:

Does the response(s) received require a label and/or labeling revision? **NA**
Reviewer Comments:

5. SPECIAL CONSIDERATIONS



6. POST APPROVAL REVISIONS



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

/s/

CHARLES V HOPPES
08/19/2014

JOHN F GRACE
08/20/2014

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: **202511** Date of Submission: **November 8, 2010**

Applicant's Name: **Novel Laboratories, Inc.**

Proposed Proprietary Name: **None**

Established Name: **Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution.**

Labeling Deficiencies:

1. GENERAL COMMENTS:

   a. You state that your carton contains "one (b) (4) mixing container"; however, you did not submit information about the (b) (4) mixing container in the Section 3.2.P.7 Container Closure System. Please submit pertinent information about this (b) (4) mixing container to chemistry. Note that the container should have the 16-ounce line marked on the container.

   b. Before final approval of this drug product, you should submit the "patient booklet" stated on the carton for review.

2. CONTAINER:

   Revise to read "17.5 g/3.13 g/1.6 g per 6 ounces" [add a space between "17.5" and "g"].

3. CARTON:

   a. Side panel, Step 1, the six-ounce bottle depicted is (b) (4). Please verify that your six-ounce bottle is (b) (4).

   b. Side Panel, Step 2, the red "Fill Line" could not be read. Please revise.

   c. Please submit a depiction of the carton with all panels attached.

   d. Please refer to CONTAINER comment.

4. PATIENT INSTRUCTIONS

   Please submit patient instructions.

5. MEDICATION GUIDE

   Acceptable in draft.

6. REMS

   Timetable for Submission of Assessments: revise to state "Not applicable".

7. INSERT

   a. Please submit the HIGHLIGHTS and FULL PRESCRIBING INFORMATION: CONTENTS* sections.

b. [redacted] (b) (4).

c. Second footnote of Table 2, revise to read "... (≤ 21 mEq/L) and high anion gap (≥ 13 mEq/L)..."

d. 11 DESCRIPTION

[redacted] (b) (4).

Submit final printed labeling electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – ANDA.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

To facilitate review of your next submission please provide a side-by-side comparison of your proposed labeling with your last labeling submission with all differences annotated and explained.

BASIS OF APPROVAL:

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):
Do you have 12 Final Printed Labels and Labeling? Yes No If no, list why:
Container Labels: 6 ounce bottles
Carton Labels:
Professional Package Insert Labeling:
Patient Instructions:
Medication Guide:
Revisions needed post-approval:

BASIS OF APPROVAL:
Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Suprep Bowel Prep Kit
NDA Number: 22372
NDA Drug Name: Suprep Bowel Prep Kit
NDA Firm: Braintree Labs
Date of Approval of NDA Insert and supplement #: NDA was approved 8/5/10- no supplements yet
Has this been verified by the MIS system for the NDA? Yes
Was this approval based upon an OGD labeling guidance? No
Basis of Approval for the Container & Carton Labels: side-by-sides
Other Comments

NOTES/QUESTIONS TO THE CHEMIST:

FOR THE RECORD:

1. Review based on the labeling of Braintree's Suprep Bowel Prep Kit (22372; application approved 8/5/10). This NDA is associated with a REMS and Med Guide.

2. Patent/ Exclusivities

Patent Data – 22372

No	Expiration	Use Code	Use	File
6945149	April 30, 2022	U-387	Gastrointestinal lavage indicated for cleansing of the colon as a preparation for colonoscopy in adults	IV

Exclusivity Data –22372

Code/sup	Expiration	Use Code	Description		Labeling Impact
NC	8/5/2013	NC	New Combination		No impact

On March 9, 2011Braintree sued Novel (Case 3:11-cv-01341-GEB-TJB) in U.S. District Court District of New Jersey.

Novel will not market until NC exclusivity expires on 8/5/2013.

3. Inactive Ingredients: [3.2.P.1-original submission]

Components, composition and the function of excipient are given below:

Name of the component	Composition (g)	Composition % (g/ 100 mL)	Function
Sodium Sulfate Anhydrous, USP	17.500	(b) (4)	
Potassium Sulfate (b) (4)	3.130		
Magnesium Sulfate, (b) (4) USP	1.600		
Sodium Benzoate, NF	(b) (4)		
Sucralose, NF			
Malic Acid, NF			
(b) (4) Citric Acid, (b) (4) USP			
Lemon Flavor (b) (4)			

Note: Product is diluted to 16 oz with water.

4. Drug Product Manufacturer: [3.2.P.3-original submission]

Novel Laboratories Inc.
4000 Campus Drive
Somerset NJ 08873

5. Finished Product Appearance: [3.2.P.5-original submission]

When reconstituted, clear to slightly hazy liquid with lemon flavor.

6. Container/Closure [3.2.P.7-original submission]

Container closure description:

Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution is a stable product. SUPREP is available in 6 oz Amber colored (b) (4) Bottles. Novel's drug product is packaged in 200cc (b) (4) HDPE) bottles with (b) (4) CRC Closure. The details of the container closure system are shown below.

Component	Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution
Container / Shape/ Type/ Color	200 cc (b) (4)
Closure	(b) (4) Child Resistance Closure (b) (4)
Seal	(b) (4)
Outsert	Yes

Novel is supposed to pack a (b) (4) mixing container in the carton but there's no container closure information for the (b) (4) mixing container. See comment to firm.

7. Storage Conditions:

NDA

PI: Store at 20 to 25C (68 to 77F). Excursions permitted between 15 to 30C (59 to 86F). See USP controlled room temperature.

Carton: Store at 25°C (77°F); excursions permitted to 15-30°C(59-86°F).

Container: (6 ounces bottle): Store at 25°C (77°F); excursions permitted to 15-30°C(59-86°F)

ANDA

PI: Store at 20 to 25°C (68 to 77°F). Excursions permitted between 15 to 30°C (59 to 86°F). See USP controlled room temperature.

Carton: Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

Container (6 ounces bottle): Store at 25°C (77°F); excursions permitted to 15-30°C(59-86°F).

8. Product Line:

RLD:
The carton contains: 2 six ounces bottles of liquid bowel prep, 1 (b) (4) mixing container, 1 patient booklet. Booklet includes: MED GUIDE, patient instructions, full PI.

Generic applicant: Two 6 ounces bottles.
The carton contains: 2 six ounces bottles of liquid bowel prep, 1 (b) (4) mixing container, 1 patient booklet. Booklet includes: MED GUIDE, patient instructions, full PI.

Primary Reviewer: Thuyanh Vu Date:

Team Leader: John Grace Date:

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

/s/

THUYANH VU
03/25/2011

JOHN F GRACE
03/31/2011

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 202511

CHEMISTRY REVIEWS

CHEMISTRY REVIEW

A. Check List

Solid IR/Oral Sol. RPN < 60 or Injection/Ophthalmic Q1/Q2 = RLD – 2 Tier	☐
First Generic – 3 Tier	☐
Other Criteria under "Exceptions List" for Table 1 of SOP – 3 Tier	☒

B. Approvability: – CMC Acceptable pending Labeling and EES

First Generic: Yes
Review cycle # 2: CMC Adequate
EES: Inadequate
Labeling: Inadequate
Bioequivalence: Adequate

ANDA 202511

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution (17.5 g/3.13 g/1.6 g per 6 oz)

Novel Laboratories, Inc.

Khalid M. Khan
Division of Chemistry III

Table of Contents

Chemistry Review Data Sheet

1. ANDA: 202511

2. REVIEW #: 2

3. REVIEW DATE: 09/16/2014

4. REVIEWER: Khalid M. Khan

5. PREVIOUS DOCUMENTS:

Submission(s) Reviewed	Document Date
Original	11/08/2010
Amendment – Patent & Exclusivity	02/02/2011
Amendment – Patent & Exclusivity	03/11/2011
Amendment – Patent & Exclusivity	03/16/2011
Amendment – Quality	07/25/2011

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	08/08/2014
Amendment	11/19/2014

7. NAME & ADDRESS OF APPLICANT:

Name:	Novel Laboratories
Address:	400 Campus Drive Somerset, NJ 08873 USA
Representative:	Scott Talbot, Vice President Quality Assurance and Regulatory Affairs stalbot@novellabs net
Telephone:	Phone: (908) 603-6000 Fax: (908) 603-6060

8. DRUG PRODUCT NAME/CODE/TYPE:

Proprietary Name:

Non-Proprietary Name (USAN): Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution: 17.5 g/3.13 g/1.6 g per 6 Ounces

9. LEGAL BASIS FOR SUBMISSION:

NDA # 022372

Ref Listed Drug: SUPREP Bowel Prep Kit

Firm: Braintree Laboratories, Inc.

1. Basis for Abbreviated New Drug Application
    a. The basis for Novel's proposed ANDA for Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution is the approved Reference Listed Drug, SUPREP Bowel Prep Kit, the subject of New Drug Application 022372, held by Braintree laboratories, Inc.

b. SUPREP Bowel Prep Kit is listed in the *Electronic Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the Electronic Orange Book) with one unexpired patent. The patent listed in the Electronic is Patent No. 6946149 which will expire on April 30, 2022.

2. Drug Substance
   a. The drug substances sodium sulfate, potassium sulfate and magnesium sulfate used in Novel's product are chemically the same as that in SUPREP Bowel Prep Kit.
   b. Refer to Novel's annotated draft labeling and to the currently approved labeling for SUPREP Bowel Prep Kit provided in Section 1.14.1 of this application.

3. Route of Administration, Dosage Form, and Strength
   a. The route of administration, dosage form, and strength of Novel's product is the same as that for SUPREP Bowel Prep Kit.
   b. Refer to Novel's annotated draft labeling and to the currently approved labeling for SUPREP Bowel Prep Kit provided in Section 1.14.3 of this application.

4. Bioavailability/Bioequivalence

Novel is requesting a Biowaiver for the drug product based on the fact that the drug product is a true solution, containing active ingredients sodium sulfate, potassium sulfate and magnesium sulfate in the same concentration and dosage form as that of reference listed drug product, SUPREP Bowel Prep Kit. Also, it contains the same inactive ingredients (sodium benzoate, sucralose, malic acid, (b) (4) citric acid and water) as that of the reference listed drug product, SUPREP Bowel Prep Kit.

10. PHARMACOL. CATEGORY:

Osmotic laxative. The product is used to cleanse colon and prepare adults for colonoscopy.

11. DOSAGE FORM: Clear liquid for oral administration

12. STRENGTH/POTENCY: 17.5 g/3.13 g/1.6 g per 6 oz

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: _X_ Rx __ OTC

15a. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

☐ SPOTS product – Form Completed

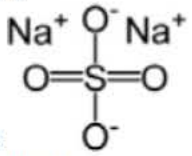
☒ Not a SPOTS product

15b. NANOTECHNOLOGY PRODUCT TRACKING:

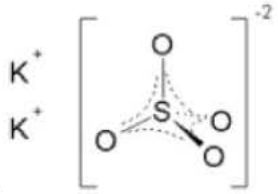
☐ NANO product – Form Completed (See Appendix A.4)

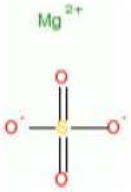
☒ Not a NANO product

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

Chemical Name(s)	: Sulfuric Acid Disodium Salt, Anhydrous. Disodium Sulfate, Anhydrous.
International Non-Proprietary Name(s)	: Sodium Sulfate Anhydrous
CAS Registry number	: 7757-82-6
Molecular Structure	: 
Molecular Formula	: Na_2SO_4
Molecular Weight	: 142.04

Chemical characteristics of the drug substance Potassium Sulfate are given below:

Chemical Name(s)	: Sulfuric acid dipotassium salt
International Non-Proprietary Name(s)	: Potassium Sulfate
CAS Registry number	: 7778-80-5
Molecular Structure	: 
Molecular Formula	: K_2SO_4
Molecular Weight	: 174.26

Chemical Name(s)	: (b) (4)
International Non-Proprietary Name(s)	: Magnesium Sulfate
CAS Registry number	: (b) (4)
Molecular Structure	: 
Molecular Formula	: $MgSO_4$
Molecular Weight	: (b) (4)

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	N/A		(b) (4)	6	N/A		†
	N/A			6	N/A		†
	N/A			6	N/A		†
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		

Updated based on amendment dated 08/08/2014.

† The drug substance is an inorganic salt, commonly used as excipient or food additive. DMF is not made available, however, the drug substance characterization and control are provided in the application.

[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:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
N/A		

18. STATUS

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
Methods Validation	N/A		
Labeling	Inadequate	08/20/2014	Hoppes, Charles
Bioequivalence	Adequate	09/19/2014	Bai, Tao
Toxicology/Clinical	N/A		
EA - Categorical exclusion requested	Adequate	12/09/2013	Khan, Khalid
Radiopharmaceutical	N/A		
Samples Requested	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt.

☒ Yes ☐ No If no, explain reason(s) below:

20. EES INFORMATION

Drug Substance
(b) (4)

Drug Product			
Function	**Site Information**	**FEI/CFN#**	**Status**
Drug Product Manufacturer	*Novel Laboratories, Inc.* *400 Campus Drive, Somerset NJ 08873* *Phone: (908) 603-6000*	*3006271438*	*Acceptable*
(b) (4)			

Chemistry Review for ANDA 202511

Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

CMC Acceptable

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

None

II. Summary of Chemistry Assessments

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

Drug substance: The drug product is an osmotic laxative which is composed of three osmotically active inorganic salts sodium sulfate, potassium sulfate and magnesium sulfate. Sodium sulfate and magnesium sulfate are USP/NF grade materials, whereas, potassium sulfate is (b) (4) grade materials. No DMFs have been referenced as the applicant claims that these materials are widely used as excipients in the pharmaceutical and food industries. The RLD uses magnesium sulfate (b) (4) whereas, the applicant uses magnesium (b) (4). They both meet the USP monograph requirements.

Drug Product: The drug product is marketed as a clear solution in two 6-ounces (b) (4) containers, with an additional larger container to dilute the solution to 16 ounces using tap water before consumption by the user. Each bottle contains solution of 17.5 grams of sodium sulfate anhydrous, 3.13 grams of potassium sulfate and 1.6 grams of magnesium sulfate on (b) (4) The drug product is a clear to slightly hazy solution of the three drug substances, (b) (4). Sucralose (b) (4) and sodium benzoate (b) (4). As per the labeling, the drug product from each 6 ounce bottle is diluted to 16 ounces and consumed by the adult user before colonoscopy.

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

The drug product is supplied as a kit and is indicated for cleansing of the colon as a preparation for colonoscopy in adults.

The dose for colon cleansing requires administration of two bottles of the solution; each bottle is administered as 16 oz of diluted drug product solution with an additional 1 quart of water taken orally. The total volume of liquid required for colon cleansing (using two bottles) is 3 quarts (approximately 2.8 L) taken orally prior to the colonoscopy.

C. Basis for Approvability or Not-Approval Recommendation

The CMC review is currently acceptable per the review team recommendations. ANDA approvability is pending Division review, other disciplines and/or EES. This CMC review may require an addendum based on recommendations made by other review disciplines.

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

ADMINISTRATIVE

A. Reviewer's Signature

B. Endorsement Block

K. M. Khan/ Reviewer/10/08/2014; 10/15/2014; 11/06/2014; 11/19/2014; 12/01/2014
L. Nagavelli, PhD/TL/10/14/2014; 10/30/2014/12/2/2014
D. Gill, PhD/DDD/RNguyen for/11/06/14/
L. A. Sears/PM/12/04/2014

File Name and Path:
M:\Desk TOP\202511\ANDA-202511-ORIG-1.doc

First Generic: Yes
CMC: Not Approvable – NA Minor
Labeling: Deficient
BE: Deficient

ANDA 202511

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution (17.5 g/3.13 g/1.6 g per 6 oz)

Novel Laboratories, Inc.

Khalid M. Khan
Division of Chemistry III

Table of Contents

Chemistry Review Data Sheet

1. ANDA: 202511

2. REVIEW #: 1

3. REVIEW DATE: 02/07/2014

4. REVIEWER: Khalid M. Khan

5. PREVIOUS DOCUMENTS:

Previous Document(s)	Document Date
None	N/A

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	11/08/2010
Amendment – Patent & Exclusivity	02/02/2011
Amendment – Patent & Exclusivity	03/11/2011
Amendment – Patent & Exclusivity	03/16/2011
Amendment – Quality	07/25/2011

7. NAME & ADDRESS OF APPLICANT:

Name:	Novel Laboratories
Address:	400 Campus Drive Somerset, NJ 08873 USA
Representative:	Scott Talbot, Vice President Quality Assurance and Regulatory Affairs stalbot@novellabs net
Telephone:	Phone: (908) 603-6000 Fax: (908) 603-6060

8. DRUG PRODUCT NAME/CODE/TYPE:

Proprietary Name:

Non-Proprietary Name (USAN): Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution: 17.5 g/3.13 g/1.6 g per 6 Ounces

9. LEGAL BASIS FOR SUBMISSION:

NDA # 022372
Ref Listed Drug: SUPREP Bowel Prep Kit
Firm: Braintree Labotatories, Inc.

1. Basis for Abbreviated New Drug Application
    a. The basis for Novel's proposed ANDA for Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution is the approved Reference Listed Drug, SUPREP Bowel Prep Kit, the subject of New Drug Application 022372, held by Braintree laboratories, Inc.

b. SUPREP Bowel Prep Kit is listed in the *Electronic Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the Electronic Orange Book) with one unexpired patent. The patent listed in the Electronic is Patent No. 6946149 which will expire on April 30, 2022.

2. Drug Substance
   a. The drug substances sodium sulfate, potassium sulfate and magnesium sulfate used in Novel's product are chemically the same as that in SUPREP Bowel Prep Kit.
   b. Refer to Novel's annotated draft labeling and to the currently approved labeling for SUPREP Bowel Prep Kit provided in Section 1.14.1 of this application.

3. Route of Administration, Dosage Form, and Strength
   a. The route of administration, dosage form, and strength of Novel's product is the same as that for SUPREP Bowel Prep Kit.
   b. Refer to Novel's annotated draft labeling and to the currently approved labeling for SUPREP Bowel Prep Kit provided in Section 1.14.3 of this application.

4. Bioavailability/Bioequivalence

Novel is requesting a Biowaiver for the drug product based on the fact that the drug product is a true solution, containing active ingredient s sodium sulfate, potassium sulfate and magnesium sulfate in the same concentration and dosage form as that of reference listed drug product, SUPREP Bowel Prep Kit. Also, it contains the same inactive ingredients (sodium benzoate, sucralose, malic acid, (b) (4) citric acid and water) as that of the reference listed drug product, SUPREP Bowel Prep Kit.

10. PHARMACOL. CATEGORY:

Osmotic laxative. The product is used to cleanse colon and prepare adults for colonoscopy.

11. DOSAGE FORM:

Clear liquid for oral administration

12. STRENGTH/POTENCY:

17.5 g/3.13 g/1.6 g per 6 oz

13. ROUTE OF ADMINISTRATION:

Oral

14. Rx/OTC DISPENSED: _X_ Rx __ OTC

15a. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

☐ SPOTS product – Form Completed

☒ Not a SPOTS product

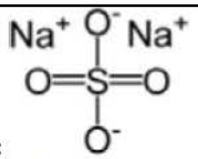
15b. NANOTECHNOLOGY PRODUCT TRACKING:

☐ NANO product – Form Completed (See Appendix A.4)

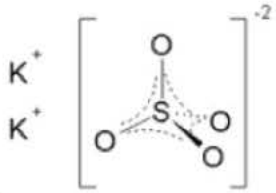
☒ Not a NANO product

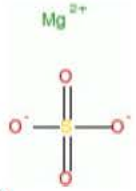
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name(s)	: Sulfuric Acid Disodium Salt, Anhydrous. Disodium Sulfate, Anhydrous.
International Non-Proprietary Name(s)	: Sodium Sulfate Anhydrous
CAS Registry number	: 7757-82-6

Molecular Structure	: 
Molecular Formula	: Na_2SO_4
Molecular Weight	: 142.04

Chemical characteristics of the drug substance Potassium Sulfate are given below:

Chemical Name(s)	: Sulfuric acid dipotassium salt
International Non-Proprietary Name(s)	: Potassium Sulfate
CAS Registry number	: 7778-80-5
Molecular Structure	: 
Molecular Formula	: K_2SO_4
Molecular Weight	: 174.26

Chemical Name(s)	: (b) (4)
International Non-Proprietary Name(s)	: Magnesium Sulfate
CAS Registry number	: (b) (4)
Molecular Structure	: 
Molecular Formula	: $MgSO_4$
Molecular Weight	: (b) (4)

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	III		(b) (4)	4	N/A		
	III			6	N/A		

[1] Action codes for DMF Table:

1 – DMF Reviewed.

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

2 –Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

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

(b) (4)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
N/A		

18. STATUS

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
Methods Validation	N/A		
Labeling	Inadequate	3/31/2011	Vu, Thuyanh
Bioequivalence	Inadequate	4/16/2013	Lerman, Bruce
Toxicology/Clinical	N/A		
EA - Categorical exclusion requested	Adequate	12/09/2013	Khan, Khalid
Radiopharmaceutical	N/A		
Samples Requested	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt.

☒ Yes ☐ No If no, explain reason(s) below:

20. EES INFORMATION

Drug Substance			
Function	**Site Information**	**FEI/CFN#**	**Status**
N/A			
Drug Product			
Function	**Site Information**	**FEI/CFN#**	**Status**
Drug Product Manufacturer	*Novel Laboratories, Inc.* *400 Campus Drive, Somerset NJ 08873* *Phone: (908) 603-6000*	3006271438	Pending

(b) (4)

Chemistry Review for ANDA 202511

Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

N/A - Minor

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

None

II. Summary of Chemistry Assessments

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

Drug substance: The drug product is an osmotic laxative which is composed of three osmotically active inorganic salts sodium sulfate, potassium sulfate and magnesium sulfate. Sodium sulfate and magnesium sulfate are USP/NF grade materials, whereas, potassium sulfate is (b) (4) grade materials. No DMFs have been referenced as the applicant claims that these materials are widely used as excipients in the pharmaceutical and food industries. The RLD uses magnesium sulfate (b) (4), whereas, the applicant uses magnesium (b) (4). They both meet the USP monograph requirements.

Drug Product: The drug product is marketed as a clear solution in two 6-ounces (b) (4) containers, with an additional larger container to dilute the solution to 16 ounces using tap water before consumption by the user. Each bottle contains solution of 17.5 grams of sodium sulfate anhydrous, 3.13 grams of potassium sulfate and 1.6 grams of magnesium sulfate on (b) (4). The drug product is a clear to slightly hazy solution of the three drug substances, (b) (4) (b) (4). Sucralose (b) (4) and sodium benzoate (b) (4). As per the labeling, the drug product from each 6 ounce bottle is diluted to 16 ounces and consumed by the adult user before colonoscopy.

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

The drug product is supplied as a kit and is indicated for cleansing of the colon as a preparation for colonoscopy in adults.

The dose for colon cleansing requires administration of two bottles of the solution; each bottle is administered as 16 oz of diluted drug product solution with an additional 1 quart of water taken orally. The total volume of liquid required for colon cleansing (using two bottles) is 3 quarts (approximately 2.8 L) taken orally prior to the colonoscopy.

Basis for Approvability or Not-Approval Recommendation

The application is not approvable due to CMC, BE and labeling deficiencies.

ADMINISTRATIVE

A. Reviewer's Signature

B. Endorsement Block

HFD-630/K. M. Khan/ Reviewer/01/25/2014; 02/07/2014; 02/19/2014
HFD-630/ L. Nagavelli, PhD/TL/1/28/2014; 2/10/2014; 2/20/2014
HFD-630/D. Gill, PhD/DDD/2/25/2014
HFD-617/ L. A. Sears/PM/2/26/2014

TYPE OF LETTER: Not Approvable – NA Minor

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

/s/

KHALID M KHAN
02/26/2014
202511 R01 - Quality Review NA-Minor

LEIGH A SEARS
02/26/2014

LAXMA R NAGAVELLI
02/26/2014

DEVINDER S GILL
02/28/2014

First Generic: Yes
CMC: Not Approvable – NA Minor
Labeling: Deficient
BE: Deficient

ANDA 202511

Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution (17.5 g/3.13 g/1.6 g per 6 oz)

Novel Laboratories, Inc.

Khalid M. Khan
Division of Chemistry III

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Chemistry Review Data Sheet

1. ANDA: 202511

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3. REVIEW DATE: 02/07/2014

4. REVIEWER: Khalid M. Khan

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Previous Document(s)	Document Date
None	N/A

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	11/08/2010
Amendment – Patent & Exclusivity	02/02/2011
Amendment – Patent & Exclusivity	03/11/2011
Amendment – Patent & Exclusivity	03/16/2011
Amendment – Quality	07/25/2011

7. NAME & ADDRESS OF APPLICANT:

Name:	Novel Laboratories
Address:	400 Campus Drive Somerset, NJ 08873 USA
Representative:	Scott Talbot, Vice President Quality Assurance and Regulatory Affairs stalbot@novellabs net
Telephone:	Phone: (908) 603-6000 Fax: (908) 603-6060

8. DRUG PRODUCT NAME/CODE/TYPE:

Proprietary Name:

Non-Proprietary Name (USAN): Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution: 17.5 g/3.13 g/1.6 g per 6 Ounces

9. LEGAL BASIS FOR SUBMISSION:

NDA # 022372
Ref Listed Drug: SUPREP Bowel Prep Kit
Firm: Braintree Labotatories, Inc.

1. Basis for Abbreviated New Drug Application
    a. The basis for Novel's proposed ANDA for Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution is the approved Reference Listed Drug, SUPREP Bowel Prep Kit, the subject of New Drug Application 022372, held by Braintree laboratories, Inc.

b. SUPREP Bowel Prep Kit is listed in the *Electronic Approved Drug Products with Therapeutic Equivalence Evaluations* (commonly known as the Electronic Orange Book) with one unexpired patent. The patent listed in the Electronic is Patent No. 6946149 which will expire on April 30, 2022.

2. Drug Substance
   a. The drug substances sodium sulfate, potassium sulfate and magnesium sulfate used in Novel's product are chemically the same as that in SUPREP Bowel Prep Kit.
   b. Refer to Novel's annotated draft labeling and to the currently approved labeling for SUPREP Bowel Prep Kit provided in Section 1.14.1 of this application.

3. Route of Administration, Dosage Form, and Strength
   a. The route of administration, dosage form, and strength of Novel's product is the same as that for SUPREP Bowel Prep Kit.
   b. Refer to Novel's annotated draft labeling and to the currently approved labeling for SUPREP Bowel Prep Kit provided in Section 1.14.3 of this application.

4. Bioavailability/Bioequivalence

Novel is requesting a Biowaiver for the drug product based on the fact that the drug product is a true solution, containing active ingredient s sodium sulfate, potassium sulfate and magnesium sulfate in the same concentration and dosage form as that of reference listed drug product, SUPREP Bowel Prep Kit. Also, it contains the same inactive ingredients (sodium benzoate, sucralose, malic acid, (b) (4) citric acid and water) as that of the reference listed drug product, SUPREP Bowel Prep Kit.

10. PHARMACOL. CATEGORY:

Osmotic laxative. The product is used to cleanse colon and prepare adults for colonoscopy.

11. DOSAGE FORM:

Clear liquid for oral administration

12. STRENGTH/POTENCY:

17.5 g/3.13 g/1.6 g per 6 oz

13. ROUTE OF ADMINISTRATION:

Oral

14. Rx/OTC DISPENSED: _X_ Rx __ OTC

15a. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

☐ SPOTS product – Form Completed

☒ Not a SPOTS product

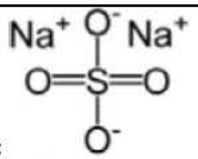
15b. NANOTECHNOLOGY PRODUCT TRACKING:

☐ NANO product – Form Completed (See Appendix A.4)

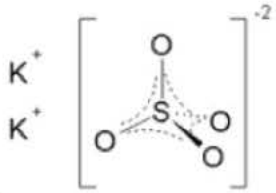
☒ Not a NANO product

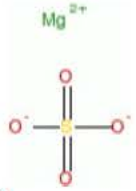
16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name(s)	: Sulfuric Acid Disodium Salt, Anhydrous. Disodium Sulfate, Anhydrous.
International Non-Proprietary Name(s)	: Sodium Sulfate Anhydrous
CAS Registry number	: 7757-82-6

Molecular Structure	: 
Molecular Formula	: Na_2SO_4
Molecular Weight	: 142.04

Chemical characteristics of the drug substance Potassium Sulfate are given below:

Chemical Name(s)	: Sulfuric acid dipotassium salt
International Non-Proprietary Name(s)	: Potassium Sulfate
CAS Registry number	: 7778-80-5
Molecular Structure	: 
Molecular Formula	: K_2SO_4
Molecular Weight	: 174.26

Chemical Name(s)	: (b) (4)
International Non-Proprietary Name(s)	: Magnesium Sulfate
CAS Registry number	: (b) (4)
Molecular Structure	: 
Molecular Formula	: $MgSO_4$
Molecular Weight	: (b) (4)

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	III		(b) (4)	4	N/A		
	III			6	N/A		

[1] Action codes for DMF Table:

1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

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

(b) (4)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
N/A		

18. STATUS

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
Methods Validation	N/A		
Labeling	Inadequate	3/31/2011	Vu, Thuyanh
Bioequivalence	Inadequate	4/16/2013	Lerman, Bruce
Toxicology/Clinical	N/A		
EA - Categorical exclusion requested	Adequate	12/09/2013	Khan, Khalid
Radiopharmaceutical	N/A		
Samples Requested	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt.

☒ Yes ☐ No If no, explain reason(s) below:

20. EES INFORMATION

Drug Substance			
Function	**Site Information**	**FEI/CFN#**	**Status**
N/A			
Drug Product			
Function	**Site Information**	**FEI/CFN#**	**Status**
Drug Product Manufacturer	*Novel Laboratories, Inc.* *400 Campus Drive, Somerset NJ 08873* *Phone: (908) 603-6000*	3006271438	Pending

(b) (4)

Chemistry Review for ANDA 202511

Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

N/A - Minor

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

None

II. Summary of Chemistry Assessments

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

Drug substance: The drug product is an osmotic laxative which is composed of three osmotically active inorganic salts sodium sulfate, potassium sulfate and magnesium sulfate. Sodium sulfate and magnesium sulfate are USP/NF grade materials, whereas, potassium sulfate is (b) (4) grade materials. No DMFs have been referenced as the applicant claims that these materials are widely used as excipients in the pharmaceutical and food industries. The RLD uses magnesium sulfate (b) (4), whereas, the applicant uses magnesium (b) (4). They both meet the USP monograph requirements.

Drug Product: The drug product is marketed as a clear solution in two 6-ounces (b) (4) containers, with an additional larger container to dilute the solution to 16 ounces using tap water before consumption by the user. Each bottle contains solution of 17.5 grams of sodium sulfate anhydrous, 3.13 grams of potassium sulfate and 1.6 grams of magnesium sulfate on (b) (4) The drug product is a clear to slightly hazy solution of the three drug substances, (b) (4) (b) (4). Sucralose (b) (4) and sodium benzoate (b) (4). As per the labeling, the drug product from each 6 ounce bottle is diluted to 16 ounces and consumed by the adult user before colonoscopy.

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

The drug product is supplied as a kit and is indicated for cleansing of the colon as a preparation for colonoscopy in adults.

The dose for colon cleansing requires administration of two bottles of the solution; each bottle is administered as 16 oz of diluted drug product solution with an additional 1 quart of water taken orally. The total volume of liquid required for colon cleansing (using two bottles) is 3 quarts (approximately 2.8 L) taken orally prior to the colonoscopy.

Basis for Approvability or Not-Approval Recommendation

The application is not approvable due to CMC, BE and labeling deficiencies.

ADMINISTRATIVE

A. Reviewer's Signature

B. Endorsement Block

HFD-630/K. M. Khan/ Reviewer/01/25/2014; 02/07/2014; 02/19/2014
HFD-630/ L. Nagavelli, PhD/TL/1/28/2014; 2/10/2014; 2/20/2014
HFD-630/D. Gill, PhD/DDD/2/25/2014
HFD-617/ L. A. Sears/PM/2/26/2014

TYPE OF LETTER: Not Approvable – NA Minor

File Name and Path:
V:\Chemistry Division III\Team 34\Final Version For DARRTS Folder\ANDA\14659-202511.doc

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

/s/

KHALID M KHAN
02/26/2014
202511 R01 - Quality Review NA-Minor

LEIGH A SEARS
02/26/2014

LAXMA R NAGAVELLI
02/26/2014

DEVINDER S GILL
02/28/2014

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 202511

BIOEQUIVALENCE REVIEWS

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	202511		
Drug Product Name	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution		
Strength(s)	17.5 g (Sodium Sulfate) / 3.13 g (Potassium Sulfate) / 1.6 g (Magnesium Sulfate) per 6 ounces		
Applicant Name	Novel Laboratories, Inc.		
Applicant Address	400 Campus Drive Somerset, NJ 08873		
US Agent Name and the Mailing Address	Mr. Scott Talbot, Vice President Quality Assurance and Regulatory Affairs 400 Campus Drive Somerset, NJ 08873		
US Agent's Telephone Number	908-603-6079		
US Agent's Fax Number	908-603-6060		
Original Submission Date(s)	11/8/2010 (Form 3674; New/ANDA)		
Submission Date(s) of Amendment(s) Under Review	8/8/2014 (Quality/Response To Information Request; Labeling/Other; Bioequivalence/Response to Information Request; Resubmission/After Action- Complete)		
First Generic (Yes or No)	No		
Reviewer	Tao Bai, Ph.D.		
OSI Status	**N/A**		
OVERALL REVIEW RESULT	**ADEQUATE**		
REVISED/NEW DRAFT GUIDANCE INCLUDED	**NO**		
BIOEQUIVALENCE STUDY TRACKING/SUPPORTING DOCUMENT #	**STUDY/TEST TYPE**	**STRENGTH**	**REVIEW RESULT**
1, 10	**Waiver**	**17.5 g (Sodium Sulfate) / 3.13 g (Potassium Sulfate) / 1.6 g (Magnesium Sulfate) per 6 ounces**	**ADEQUATE**

REVIEW OF AN AMENDMENT

I. EXECUTIVE SUMMARY

This is an amendment review.

In firm's original submission dated 11/8/2010, the firm has requested a waiver of *in vivo* bioequivalence (BE) study requirement under Section *21 Code of Federal Regulations (CFR) § 320.22 (b)(3)* for its product, Sodium Sulfate, Potassium Sulfate and Magnesium

Sulfate Oral Solution, 17.5 g / 3.13 g / 1.6 g per 6 ounces. The reference-listed drug (RLD) product is Suprep® Bowel Prep Kit (sodium sulfate, potassium sulfate, and magnesium sulfate) Oral Solution, 17.5 g / 3.13 g / 1.6 g per bottle (6 oz), by Braintree Labs under NDA 022372, which was approved on August 05, 2010[1]. However, the firm's waiver request was considered inadequate pending the firm's justification of the daily intake of sodium benzoate for its proposed test product[2].

In current amendment, the firm submitted a new formulation of its test product with (b) (4) of sodium benzoate. (b) (4) The amounts of active ingredients and other inactive ingredients in the newly submitted test formulation in current amendment are same as those in the original submission. Therefore, the firm's newly submitted formulation (b) (4) of sodium benzoate is acceptable. The firm's response to above deficiency is adequate.

The firm's waiver request under Section *21 CFR § 320.22 (b) (3)* is granted.

The application is **adequate**.

II. TABLE OF CONTENTS

[1] Electronic Orange Book: http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl_No=022372&TABLE1=OB_Rx (9/16/2014)
[2] DARRTS: ANDA 202511 REV-BIOEQ-21(Primary Review) 4/16/2013

III. SUBMISSION SUMMARY

3.1 Drug Product Information

Please refer to the original bioequivalence review, available at:

DARRTS: ANDA 202511 REV-BIOEQ-21(Primary Review) 4/16/2013.

3.2 Contents of Submission

Study Types	Yes/No?	How many?
Single-dose fasting	No	--
Single-dose fed	No	--
Steady-state	No	--
In vitro dissolution	No	--
Waiver requests	No	--
BCS Waivers	No	--
Clinical Endpoints	No	--
Failed Studies	No	--
Amendments	Yes	1

3.3 Review of Submission

Deficiency

Per the labeling of the reference listed drug product, Suprep® Bowel Prep Kit, the dose for colon cleansing requires administration of two bottles of the kit. Therefore, the maximum daily intake of the excipient sodium benzoate from your proposed product is (b) (4) *. Based on information available to the Agency, the maximum daily intake of sodium benzoate for your product* (b) (4) *than those found in approved products. As a result, please justify the maximum daily intake of sodium benzoate with respect to the safety of your test product. Please provide evidence and documentation as necessary to support your justification.*

Firm's Response:

Based on the agency's comment, Novel evaluated the sodium benzoate content in Suprep® Bowel Prep Kit and accordingly (b) (4) of sodium benzoate in the proposed generic product.

[redacted]

The amount of Sodium benzoate in the proposed composition is equivalent to the RLD; therefore, the maximum daily intake of sodium benzoate for Novel's drug product is same as that of the RLD and hence considered safe.

(b) (4)

[redacted]

Reviewer's Comments:

The following is excerpted from the original bio-review dated 4/16/2013 regarding the calculation of amount of sodium benzoate[4]:

(b) (4)

[redacted]

[3] The reviewer will not copy the details of the firm's submission here. For details see firm's complete response letter pages 7 and 8, Module 1.2, submission date in DARRTS: 8/8/2014
[4] DARRTS: ANDA 202511 REV-BIOEQ-21(Primary Review) 4/16/2013
[5] Drugs@FDA, search Suprep, label approved on 11/01/2012

3.5 Recommendations

1. The Division of Bioequivalence I (DBI) agrees that the information submitted by Novel Laboratories, Inc. demonstrates that Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution, 17.5 g/3.13 g/1.6 g per 6 ounces, meets the criteria specified in Section 21 CFR § 320.22 (b) (3). The DBI recommends the waiver of bioequivalence testing be granted.

2. The DBI deems the test product, Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution, 17.5 g/3.13 g/1.6 g per 6 ounces, manufactured by Novel Laboratories, Inc. to be bioequivalent to the reference product, Suprep® Bowel Prep Kit (sodium sulfate, potassium sulfate, and magnesium sulfate), 17.5 g/3.13 g/1.6 g per 6 ounce bottle, manufactured by Braintree Labs.

The firm should be informed of the above recommendations.

3.6 Comments for Other OGD Disciplines

Discipline	Comment
--	N/A

BIOEQUIVALENCE COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 202511

APPLICANT: Novel Laboratories Inc.

DRUG PRODUCT: Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution; 17.5g/3.13g/1.6g per 6 ounces

The Division of Bioequivalence I (DBI) has completed its review and has no further questions at this time.

The bioequivalence comments provided in this communication are comprehensive as of issuance. However, these comments are subject to revision if additional concerns raised by chemistry, manufacturing and controls, microbiology, labeling, other scientific or regulatory issues or inspectional results arise in the future. Please be advised that these concerns may result in the need for additional bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

{See appended electronic signature page}

Wayne DeHaven, Ph.D.
Acting Director, Division of Bioequivalence I
Office of Generic Drugs
Center for Drug Evaluation and Research

IV. OUTCOME PAGE

ANDA: 202511

COMPLETED ASSIGNMENT FOR 202511 ID: 24013

Reviewer: Bai, Tao **Date Completed:**

Verifier: **Date Verified:**

Division: Division of Bioequivalence

Description: Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution, (17.5g/3.13g/1.6g) per 6 ounces

---

Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
24013	8/8/2014	Other (REGULAR)	Waiver Oral Solution	1	1
				Total:	1

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

/s/

TAO BAI
09/19/2014

HEE S CHUNG
09/19/2014

UTPAL M MUNSHI on behalf of WAYNE I DEHAVEN
09/19/2014

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	202511		
Drug Product Name	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution		
Strength(s)	(17.5 g / 3.13 g / 1.6 g) per 6 ounces		
Applicant Name	Novel Laboratories, Inc		
Applicant Address	400 Campus Drive Somerset, NJ 08873		
US Agent Name and the mailing address	Hema Balachandra, Regulatory Affairs		
US agent's Telephone Number	908-603-6000		
US Agent's Fax Number	908-603-6060		
Original Submission Date(s)	11/8/2010		
Submission Date(s) of Amendment(s) Under Review	N/A		
First Generic (Yes or No)	No		
Reviewer	Bruce Lerman. Ph.D.		
OSI Status	**N/A**		
OVERALL REVIEW RESULT	**INADEQUATE**		
REVISED/NEW DRAFT GUIDANCE INCLUDED	**No**		
BIOEQUIVALENCE STUDY TRACKING/SUPPORTING DOCUMENT #	**STUDY/TEST TYPE**	**STRENGTH**	**REVIEW RESULT**
1	**Waiver**	(17.5 g / 3.13 g / 1.6 g) per 6 ounces	**INADEQUATE**

1 EXECUTIVE SUMMARY

The firm has requested a waiver of *in vivo* bioequivalence (BE) study requirement under Section *21 Code of Federal Regulations (CFR) § 320.22 (b)(3)* for its product, Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution, 17.5 g / 3.13 g / 1.6 g per 6 ounces. The reference-listed drug (RLD) product is Suprep Bowel Prep Kit (sodium sulfate, potassium sulfate, and magnesium sulfate) Oral Solution, 17.5 g / 3.13 g / 1.6 g per bottle (6 oz), by Braintree Labs under NDA 022372, which was approved on August 05, 2010.

The firm's waiver request is **inadequate** pending the firm's justification of the daily intake of sodium benzoate from the proposed product.

The application is **inadequate.**

2 TABLE OF CONTENTS

3 SUBMISSION SUMMARY

3.1 Drug Product Information[1]

Test Product	Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Anhydrous Oral Solution, (17.5g/3.13g/1.6g) per 6 ounces
Reference Product	Suprep® Bowel Prep Kit (magnesium sulfate anhydrous; potassium sulfate; sodium sulfate), 1.6g/3.13g/17.5g per 6 ounce bottle
RLD Manufacturer	Braintree Labs
NDA No.	022372
RLD Approval Date	August 5, 2010
Indication[2]	Suprep Bowel Prep Kit is an osmotic laxative indicated for cleansing of the colon in preparation for colonoscopy in adults.

3.2 PK/PD Information[3,4]

Bioavailability	Sulfate salts provide sulfate anions, which are poorly absorbed.
Food Effect	N/A
Tmax	17 hours after the first dose or approximately 5 hours after the second dose
Metabolism	(b) (4)
Excretion	Fecal excretion was the primary route of sulfate elimination
Half-life	8.5 hours
Dosage and Administration	SUPREP Bowel Prep Kit should be taken as a split-dose oral regimen. The dose for colon cleansing requires administration of two bottles of SUPREP Bowel Prep Kit. Each bottle is administered as 16 oz of diluted SUPREP solution with an additional 1 quart of water taken orally. The total volume of liquid required for colon cleansing (using two bottles) is 3 quarts (approximately 2.8 L) taken orally prior to the colonoscopy in the following way: Split-Dose (Two-Day) Regimen <u>Day prior to colonoscopy:</u> • A light breakfast may be consumed, or have only clear liquids on the day before colonoscopy. Avoid red and purple liquids, milk, and alcoholic beverages. • Early in the evening prior to colonoscopy: pour the contents of one

[1] Electronic Orange Book, last accessed date: 02/22/2013.
[2] Drugs@FDA, RLD Label approved on 11/01/2012, last accessed date: 03/27/2013.
http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022372s000lbl.pdf
[3] Drugs@FDA, RLD Label approved on 11/01/2012, last accessed date: 03/27/2013.
[4] Clinical Pharmacology, Keyword Search: Suprep; last accessed date: 02/22/2013
http://www.clinicalpharmacology-ip.com/Forms/drugoptions.aspx?cpnum=3702&aprid=52776

	bottle of SUPREP Bowel Prep Kit into the mixing container provided. Fill the container with water to the 16 oz fill line, and drink the entire amount. • Drink two additional containers filled to the 16 oz line with water over the next hour. Day of colonoscopy: • Have only clear liquids until after the colonoscopy. Avoid red and purple liquids, milk, and alcoholic beverages. • The morning of colonoscopy (10 to 12 hours after the evening dose): pour the contents of the second bottle of SUPREP Bowel Prep Kit into the mixing container provided. Fill the container with water to the 16 oz fill line, and drink the entire amount. • Drink two additional containers filled to the 16 oz line with water over the next hour. • Complete all SUPREP Bowel Prep Kit and required water at least one hour prior to colonoscopy.
Maximum Daily Dose	Two 6 oz bottles of solution
Drug Specific Issues (if any)	Suprep is contraindicated in patients with the following: Gastrointestinal obstruction Bowel perforation Gastric retention Ileus Toxic colitis or toxic megacolon Known allergies to components of the kit

3.3 OGD Recommendations for Drug Product

Number of studies recommended:	N/A – Waiver Request per the criteria for 21 CFR 320.22 (b) (3)
Analytes to measure (in plasma/serum/blood):	N/A
Bioequivalence based on:	According to 21 CFR 320.22 (b) (3), a waiver of the requirement for the submission of evidence measuring in vivo bioavailability or demonstrating bioequivalence may be granted to a drug product if 1) it is a solution for application to the skin, an oral solution, elixir, syrup, tincture, a solution for aerosolization or nebulization, a nasal solution, or similar other solubilized form. 2) contains an active drug ingredient in the same concentration and dosage form as a drug product that is the subject of an approved full new drug application or abbreviated new drug application. And 3) contains no inactive ingredient or other change in formulation from the drug product that is the subject of the approved full new drug application that may significantly affect absorption of the active drug ingredient or active moiety for products that are systemically absorbed, or that may significantly affect systemic or local availability for products intended to act locally.
Summary of OGD or DBE History	As per the Electronic Orange Book (last accessed date: 02/22/2013), there were no approved ANDAs for this drug product. The following are the ANDAs received by OGD for this drug product:

	ANDA # 204135; Firm: Cypress Pharmaceutical Inc. (b) (4) ANDA # 203102; Firm: Paddock Laboratories Inc. ANDA 202511; Firm: Novel Laboratories Inc (current ANDA). There are no control documents or protocols on this product[5].

3.4 Contents of Submission

Study Types	Yes/No?	How many?
Single-dose fasting	No	--
Single-dose fed	No	--
Steady-state	No	--
In vitro dissolution	No	--
Waiver requests	Yes	1
BCS Waivers	No	--
Clinical Endpoints	No	--
Failed Studies	No	--
Amendments	No	--

[5] Control document database and protocol tracking database. Search sodium sulfate. Last accessed date: 02/22/2013.

3.5 Waiver Request(s) For Immediate Release Dosage Forms

Strengths for which waivers are requested	17.5 g / 3.13 g / 1.6 g per 6 ounces
Proportional to strength tested in vivo?	N/A
Is dissolution acceptable?	N/A
Waivers granted?	**WAIVER DENIED**
If not then why?	Please see the Reviewer's Comments found in Section 4.2 of this review.

3.6 Deficiency Comment

The firm will be asked to justify the daily intake of Sodium Benzoate from its proposed product.

3.7 Recommendation

The Division of Bioequivalence I (DBI) finds the **waiver** request **inadequate** for the test product, Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution, 17.5 g/3.13 g/1.6 g per 6 ounces, under Section *21 CFR § 320.22 (b) (3)*.

3.8 Comments for Other OGD Disciplines

Discipline	Comment
None	

4 APPENDIX

4.1 Formulation Data

(NOT FOR RELEASE UNDER FOIA)

4.1.1 Formulation of the Test Product[6]

Name of the component	Composition (g)	Composition % (g/ 100 mL)	Function
Sodium Sulfate Anhydrous, USP	17.500	(b) (4)	
Potassium Sulfate (b) (4)	3.130		
Magnesium Sulfate, (b) (4) USP	1.600		
Sodium Benzoate, NF	(b) (4)		
Sucralose, NF			
Malic Acid, NF			
(b) (4) Citric Acid, (b) (4) USP			
Lemon Flavor (b) (4)			

Firm's Note: Product is diluted to 16 oz with water.

(b) (4)

[6] EDR: ANDA #202511 Section 3.2.P.1 Submit Date: 11/8/2010
[7] EDR: ANDA #202511 Section 3.2.P.1 Submit Date: 11/8/2010


(b) (4)

4.1.2 RLD Formulation Composition:[8]

As per a quality review of a currently accepted reformulation of the reference product, the RLD changed it formulation to include magnesium sulfate, (b) (4) to replace magnesium sulfate (b) (4). The most current RLD formulation is listed below[8].

Component and Grade	Method	Quantity per 6oz Bottle	Quantity per Dose (two 6oz bottles)	Function
Sodium Sulfate, USP	USP	17.510 g	35.020 g	(b) (4)
Potassium Sulfate, (b) (4)	(b) (4)	3.130 g	6.260 g	
Magnesium Sulfate, (b) (4) USP	USP	2.133 g	4.267 g	
Sodium Benzoate, NF	NF	(b) (4)		
Sucralose (b) (4)	(b) (4)			
Malic Acid, FCC	FCC			
Citric Acid, USP	USP			
(b) (4)				
Purified Water, USP	USP			

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

(b) (4)

[8] DARRTS, NDA 022372, REV-QUALITY-03 (General Review), 06/14/2012. This is the most updated formulation. No other new update on this formulation. Last accessed date: 3/27/2012.

4.1.3 Formulation Comparison of the Test Product versus RLD

	Test	RLD	Difference % [Test-RLD/RLD x 100]
Component	g/6-oz-bottle	g/6-oz-bottle	(b) (4)
Sodium Sulfate Anhydrous	17.50	17.510	
Potassium Sulfate (b) (4) (b) (4)	3.13	3.130	
Magnesium Sulfate, (b) (4) USP	1.60	(b) (4)	
		1.6 magnesium sulfate per 6 oz bottle***	
Sodium Benzoate, NF	(b) (4)		
Sucralose, NF			
Sucralose Liquid (25%)			
Malic Acid, NF			
Citric Acid (b) (4)			
(b) (4)			
Lemon Flavor (b) (4) (b) (4)			
			(b) (4)

Reviewer Comments[9]:

1. The API of Sodium Sulfate Anhydrous in the test product is (b) (4) than that in the RLD. However, the amount of this API in the Test product is the same as the target amount in the RLD labeling[10]. Other APIs in the test product have the same amounts as those in the RLD.

2. In the test product, the amount of Malic Acid , Citric Acid (b) (4), and Sucralose were found (b) (4) in the test product than that in the RLD. Therefore, these excipients meet IIG/MDI limits.

3. The test product does not have the following excipients which are present in the RLD: (b) (4).

4. The maximum daily intake of sodium benzoate in the Test product is calculated as follows:

(b) (4)

(b) (4)

[10] Drugs@FDA, RLD Label approved on 08/05/2010, last accessed date: 09/13/2012. http://www.accessdata.fda.gov/drugsatfda_docs/label/2010/022372s000lbl.pdf

[11] Drugs@FDA, search Suprep, label approved on 11/01/2012, last accessed date: 03/28/2013.
[12] DARRTS, NDA 020251, REV-QUALITY-03 (General Review), 12/11/2003, last accessed date: 03/22/2013.
[13] Clinical Pharmacology, search vioriconazole, Last accessed date: 03/22/2013.

5. Flavor Amounts:

- Lemon Flavor [redacted] (b) (4) in test product: The amount of Lemon Flavor [redacted] (b) (4) is not found in the RLD product. However, the amounts of each component in the Lemon Flavor [redacted] (b) (4) of the total test formulation and therefore will not likely pose a safety concern.
- [redacted] (b) (4)
- [redacted]

[redacted] (b) (4)

6. [redacted] (b) (4)

Is there an overage of the active pharmaceutical ingredient (API)?	No[20]
If the answer is yes, has the appropriate chemistry division been notified?	N/A
If it is necessary to reformulate to reduce the overage, will bioequivalence be impacted?	N/A
Comments on the drug product formulation	INADEQUATE

4.2 Consult Reviews

None at this time.

[20] EDR: ANDA #202511 Section 3.2.p.3.3 Description of Mnfg process Submit Date: 11/8/2010

4.3 Additional Attachments

(b) (4)

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BIOEQUIVALENCE DEFICIENCY TO BE COMMUNICATED TO THE APPLICANT

ANDA: 202511

APPLICANT: Novel Laboratories

DRUG PRODUCT: Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution, (17.5g/3.13g/1.6g) per 6 ounces

The Division of Bioequivalence I (DBI) has completed its review and the following deficiency has been identified:

Per the labeling of the reference listed drug product, Suprep® Bowel Prep Kit, the dose for colon cleansing requires administration of two bottles of the kit. Therefore, the (b) (4) (b) (4) Based on information available to the Agency, the maximum daily intake of sodium benzoate for your product (b) (4) those found in approved products. As a result, please justify the maximum daily intake of sodium benzoate with respect to the safety of your test product. Please provide evidence and documentation as necessary to support your justification.

Sincerely yours,

{See appended electronic signature page}

Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence I
Office of Generic Drugs
Center for Drug Evaluation and Research

4.4 Outcome Page

Completed Assignment for 202511 ID: 19186

Reviewer: Lerman, Bruce **Date Completed:**

Verifier: **Date Verified:**

Division: Division of Bioequivalence

Description: Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution

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Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
19186	11/8/2010	Other (REGULAR)	Waiver Oral Solution	1	1
				Total:	1

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/s/

BRUCE J LERMAN
04/01/2013

UTPAL M MUNSHI
04/01/2013

HOAINHON N CARAMENICO
04/03/2013

DALE P CONNER
04/16/2013

BIOEQUIVALENCE CHECKLIST for First Generic ANDA
FOR APPLICATION COMPLETENESS

ANDA# 202511 **FIRM NAME** Novel Laboratories Inc.

DRUG NAME Magnesium Sulfate [redacted (b) (4)], Potassium Sulfate and Sodium Sulfate, 1.6 g, 3.13 g and 17.5 g/bottle

DOSAGE FORM Oral Solution

SUBJ: Request for examination of: Bioequivalence Study

Requested by: _____ Date: _____
Chief, Regulatory Support Team, (HFD-615)

	Summary of Findings by Division of Bioequivalence
☐	**Study meets statutory requirements**
☐	**Study does NOT meet statutory requirements**
	Reason:
☒	**Waiver meets statutory requirements**
☐	**Waiver does NOT meet statutory requirements**
	Reason:

RECOMMENDATION: ☒ **COMPLETE** ☐ **INCOMPLETE**

Reviewed by:

_____ Date: _____
Hongling Zhang, Ph.D.
Reviewer

_____ Date: _____
Bing V. Li, Ph.D.
Team Leader

Item Verified:	YES	NO	Required Amount	Amount Sent	Comments
Protocol	☐	☐			
Assay Methodology	☐	☐			
Procedure SOP	☐	☐			
Methods Validation	☐	☐			
Study Results Ln/Lin	☐	☐			
Adverse Events	☐	☐			
IRB Approval	☐	☐			
Dissolution Data	☐	☐			
Pre-screening of Patients	☐	☐			
Chromatograms	☐	☐			
Consent Forms	☐	☐			
Composition	☒	☐			
Summary of Study	☐	☐			
Individual Data & Graphs, Linear & Ln	☐	☐			
PK/PD Data Disk Submitted)	☐	☐			
Randomization Schedule	☐	☐			
Protocol Deviations	☐	☐			
Clinical Site	☐	☐			
Analytical Site	☐	☐			
Study Investigators	☐	☐			

Medical Records	☐	☐			
Clinical Raw Data	☐	☐			
Test Article Inventory	☐	☐			
BIO Batch Size	☐	☐			
Assay of Active Content Drug	☐	☐			
Content Uniformity	☐	☐			
Date of Manufacture	☐	☐			
Exp. Date of RLD	☐	☐			
BioStudy Lot Numbers	☐	☐			
Statistics	☐	☐			
Summary results provided by the firm indicate studies pass BE criteria	☐	☐			
Waiver requests for other strengths / supporting data	☒	☐			

Additional Comments regarding the ANDA:

1. This is a *first generic* checklist. The reference listed drug (RLD) for Magnesium Sulfate (b) (4), Potassium Sulfate and Sodium Sulfate Oral Solution, 1.6 g, 3.13 g and 17.5 g/bottle is Suprep Bowel Prep Kit, NDA 022372, by Braintree Labs, approved on 08/05/2010.

2. Suprep® Bowel Prep Kit is an osmotic laxative indicated for cleansing of the colon in preparation for colonoscopy in adults[1].

3. The firm is requesting a biowaiver for the drug product based on the fact that the drug product is a true solution, containing active ingredients sodium sulfate, potassium sulfate and magnesium sulfate in the same concentration and dosage form as that of reference listed drug product, Suprep® Bowel Prep Kit. Also, it contains the same inactive ingredients (sodium benzoate, sucralose, malic acid, (b) (4) citric acid and water) as that of the reference listed

1 Drugs @ FDA, Drug labeling for Suprep® Bowel Prep Kit, approved 08/2010.

drug product, SUPREP Bowel Prep Kit. However, the excipients in the test formulation are not in the same amounts as those in the RLD product. The quantitative differences in the excipients are considered a review issue, and not a filing issue. They will be evaluated at the time of the waiver request review by the DBE.

4. The formulation of the firm's test product is as following[2]:

Name of the component	Composition (g)/ Dose	Composition g/ 100 mL	Function
Sodium Sulfate Anhydrous, USP	17.500	(b) (4)	
Potassium Sulfate (b) (4)	3.130		
Magnesium Sulfate, (b) (4) USP	1.600		
Sodium Benzoate, NF	(b) (4)		
Sucralose, NF			
Malic Acid, NF			
(b) (4) Citric Acid (b) (4) USP			
Lemon Flavor (b) (4)			

5. The formulation of the RLD product (Suprep® Bowel Prep Kit) is as following[3]:

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,		3.130 g	6.260 g	Active ingredient
Magnesium Sulfate (b) (4) USP	USP	1.600 g	3.200 g	Active ingredient
Sodium Benzoate, NF	NF	(b) (4)		
Sucralose (b) (4)				
Malic Acid, FCC	FCC			
Citric Acid, USP	USP			
(b) (4)				
Purified Water, USP	USP			

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

2 EDR, Module 2.3. P.1

3 DARRTS, NDA 022732, REV-QUALITY-03 (General Review), submitted 7/16/2009

6. Since the drug product is an oral solution, the firm has submitted the complete composition of the test formulation to support its waiver request. The firm's application for the waiver request is considered **acceptable** for filing.

ANDA 202511

Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
12798	11/8/2010	Paragraph 4	Paragraph 4 Checklist	1	1
				Bean Total:	1

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

/s/

HONGLING ZHANG
01/05/2011

BING V LI
01/05/2011

HOAINHON N CARAMENICO on behalf of DALE P CONNER
01/05/2011

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 202511

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

Approval Type: ✓ **FULL APPROVAL** ☐ **TENTATIVE APPROVAL** ☐ **SUPPLEMENTAL APPROVAL (NEW STRENGTH)**

RPM: Jeannettee Joyner Team: Mandy Kwong **Approval Date:** 2/23/2017

☐ **PI** ☐ **PII** ☐ **PIII** ✓ **PIV** (*eligible for 180 day exclusivity* ✓ **Yes** ☐ **No**) ☐ **MOU** ✓ **RX or** ☐ **OTC**

ANDA #: 202511 **Applicant:** Lupin Inc. **Established Product Name:** Sodium Sulfate, Potassium Sulfate, Magnesium Sulfate Oral Solution, (17.5 g/3.13 g/1.6 g) per 6 ounces

Basis of Submission (RLD): NDA 022372 Suprep Bowel Prep Kit

(Is ANDA based on an approved Suitability Petition? ☐ *Yes* ✓ *No)*

Does the ANDA contain REMS? ☐ **Yes** ✓ **No** *(If YES, initiate approval action 6 weeks prior to target action date)*

Regulatory Project Manager Evaluation: **Date:** 2/13/2017

✓ Previously reviewed and tentatively approved (if applicable) — Date 5/25/2015

Date of Application 11/8/2010	Original Received Date 11/8/2010	Date Acceptable for Filing 11/8/2010

YES	NO	
✓	☐	All submissions have been reviewed and relevant disciplines are adequate and finalized in the platform (Date or N/A) Date of Acceptable Quality 1/26/2017 Date of Acceptable Dissolution NA Date of Acceptable Bioequivalence 9/29/2014 Date of Acceptable Labeling 12/29/2014 If applicable: Date of Acceptable Microbiology NA Date of Acceptable Clinical Review NA Date of Acceptable REMS NA
✓	☐	Was a CR issued throughout the life of the ANDA? If Yes, date last CR letter was issued: 3/14/2014
☐	✓	Are consults pending for any discipline?
☐	✓	Has there been an amendment providing for a major change in formulation or new strength since filing? If YES→Verify a second filing review was completed and that all disciplines completed new reviews ☐
☐	✓	Is there a pending Citizen Petition (CP)?
✓	☐	Overall OC Recommendation is acceptable (EES is acceptable) Date Acceptable: 2/1/2017
✓	☐	OSI Clinical Endpoint and Bioequivalence Site Inspections are acceptable
☐	✓	Is ANDA a Priority Approval (First generic, drug shortage, PEPFAR, other OGD Communications priorities)? If YES → Email OGD Communications Staff (OGDREQUEST) 30 to 60 days prior to approval, Date emailed Enter Date
		Draft Approval/Tentative Approval Letter
✓	☐	Approval/Tentative Approval letter is drafted and uploaded to the Final Decision task
		Review Discipline/Division Endorsements
✓	☐	Division of Legal and Regulatory Support Endorsement completed, Date 2/17/2017
✓	☐	Paragraph IV Evaluation completed (if applicable), Date 2/21/2017
✓	☐	Quality Endorsement completed, Date 2/15/2017
✓	☐	Bioequivalence Endorsement completed, Date 2/14/2017
✓	☐	Labeling Endorsement completed, Date 2/14/2017
☐	✓	REMS Endorsement (if applicable), Date Enter Date
		RPM Team Leader Endorsement and Action Package Verification
✓	☐	RPM Team Leader Endorsement completed, Date 2/21/2017
		Final Decision and Letter Sign-off

✓	☐	Final Decision recommending approval/tentative approval completed, Date 2/23/2017
✓	☐	Approval/Tentative Approval letter electronically signed, Date: 2/23/2017
Project Close-Out		
✓	☐	Notify applicant of approval and provide a courtesy copy of the electronically signed letter
☐	✓	Is there a Post Marketing Agreement (PMA)? IF YES → Send email to PMA coordinator, Date emailed Enter Date
✓	☐	Email OGD Approval distribution list (CDER-OGDAPPROVALS) with approval information

This page to be completed by the RPM

ANDA APPROVAL ROUTING SUMMARY ENDORSEMENTS AND FINAL DECISION

I. Division of Legal and Regulatory Support Endorsement

Date: 2/17/2017
Name/Title: MHS

Contains GDEA certification: Yes ✓ No ☐	
(required if sub after 6/1/92)	Pediatric Exclusivity System
	RLD = _____ NDA# _____ Date Checked _____ Nothing Submitted ☐ Written request issued ☐ Study Submitted ☐
Patent/Exclusivity Certification: Yes ✓ No ☐ If Para. IV Certification- did applicant: Notify patent holder/NDA holder Yes ✓ No ☐ Was applicant sued w/in 45 days: Yes ✓ No ☐ Has case been settled: Yes ✓ No ☐ Date settled: 6/19/2016 Is applicant eligible for 180 day Yes Is a forfeiture memo needed: Yes ✓ No ☐ If yes, has it been completed	
Generic Drugs Exclusivity for each strength: Yes ✓ No ☐	
Date of latest Labeling Review/Approval Summary	
Any filing status changes requiring addition Labeling Review Yes ☐ No ✓	
Type of Letter: ✓ APPROVAL ☐ TENTATIVE APPROVAL ☐ SUPPLEMENTAL APPROVAL (NEW STRENGTH) ☐ OTHER:	
Comments:	

ANDA submitted on 11/8/2010, BOS=Suprep NDA 22372, PIV to '149. ANDA ack for filing with PIV on 11/8/2010(LO dated 1/10/2011).
Patent Amendment rec'd 2/2/2011-RR from Braintree Laboratories in Braintree MA signed and dated 1/28/2011.
Patent Amendment rec'd 3/14/2011-Letter from Wilmer Hale indicating that CA 11 CV 1341 was filed in the D of NJ on 3/9/2011 for infringement of the '149 patent.
Patent Amendment rec'd 3/16/2011- CA 11 CV 1341 filed in the D of NJ on 3/9/2011 for infringement of the '149 patent. As suit was brought within 45 days there is an automatic 30 month stay of approval that expired on 7/28/2013.
Patent Amendment rec'd 6/24/2013- Letter from Wilmer Hale-counsel for Braintree-indicating that an Opinion dated January 18, 2013 and Order dated January 18, and June 18, 2013 the Court found that Novel's product infringes multiple claims of the '149 patent, the Final Judgment dated June 18, 2013 contained 271(e)(4)(A) language setting the effective date of approval to a date not earlier than the expiration of the '149 patent.
Final Approval Request submitted 12/4/2013-in the request Novel acknowledges their loss in the DC but noted that the decision was appealed to the Federal Circuit and "a decision is expected soon". Novel notes that Braintree's NP exclusivity expired on 8/5/2013. Novel's request in this submission was that the Agency issue final approval for this application before Friday, March 7, 2014-the date that would permit Novel to retain eligibility for 180-day exclusivity. It is noted that at the time the letter was sent to OGD, Novel's application qualified for an extension of the 30 month to TA forfeiture provision with this extension being the 30 month was changed to 40 months. This 40 month provision had both a window of applicability with respect to when an ANDA was originally submitted and a window of applicability by which the sponsor needed to secure either TA or FA by the Agency. The window of applicability in which Novel needed to secure either TA or FA lapsed in September of 2016 so the relevant forfeiture timeframe as of today's date is the 30 month period which expired 30- months from Novel's date of submission-5/8/2013.
Expedited review was granted to this ANDA on 10/24/2013.
Patent Amendment rec'd 4/17/2015-Copy of decision from the CAFC 2013-1438 decided on 4/22/2014, with respect to the DC decision the CAFC Affirmed-in-part, Reversed-in-part, Vacated-in-part, and Remanded. The portion of this decision that is relevant from FDA's perspective is that the CAFC vacated the DC grant of summary judgment of infringement with this portion of the case remanded to the DC for further proceedings consistent with the CAFC opinion. The CAFC affirmed the DC finding that 'the asserted claims of the '149 patent are not anticipated, not obvious, and not indefinite.'
Tentative Approval issued on 5/29/2015-at the time the TA was issued the reason cited for TA was the DC order from June 19, 2013 which set the effective date of approval to a date not earlier than the expiration date of the '149 patent. The TA letter acknowledges that this decision had been appealed to the Federal Circuit which remanded the case back to the DC for further proceedings.
Patent Amendment rec'd 3/21/2016-Decision from D of NJ dated 6/2/2015 on remand from the CAFC. This decision id a Final Order of Judgment which only indicates two noteworthy items with respect to Novel's ANDA 1. Novel's equivalent of Suprep will, if marketed and sold infringe claims 15 and 18 and 2. Novel's equivalent Suprep will if marketed and sold will induce infringement of claims 19, 20, and 23 of the '149 Patent, which claims methods for using the compositions of claims 15 and 18 of the '149 patent.
Memo to file uploaded July 29, 2016-Memo to file documenting OGD's formal determination that Novel did NOT forfeit their exclusivity seat by virtue of not securing TA within 40 months of their submission date.
Patent Amendment rec'd 11/9/2016-Novel requests Final Approval in the cover letter of this amendment with the cover letter going on to recount the tortured litigation history of this ANDA. Importantly, Novel notes that after entry of the Final Order of Judgment on June 2, 2015(subsequently amended on June 25, 2015) they appealed the June 2015 Judgment to the CAFC in September of 2015 and that prior to any decision from the CAFC, Novel entered into a settlement agreement with Braintree. Braintree thus provided Novel with a license for Novel's product in relation to the '149 patent AND pursuant to the settlement agreement Novel and Braintree agreed to move to vacate all of the final judgments entered against Novel. This amendment contains Novel's 'licensing statement' pursuant to 21 CFR

314.94(a)(12)(v) and a copy of a Final Judgment and Order from the D of NJ dated September 19, 2016 in which it was Ordered and Adjudged that Final Orders from the District Court dated 6/1/2015(amended on 6/25/2015) as well as the original Final Judgment dated 6/18/2013 were 'hereby VACATED and shall be of no force or effect'. All rights to appeal this decision were waived by Novel and Braintree.

Patent Amendment rec'd 1/3/2017-copy of letter from Novel's counsel Bill Rakoczy. (b) (4)

As previously stated this ANDA has an extremely tortured litigation history that was ultimately resolved via settlement agreement between Novel and Braintree. This settlement agreement permits Novel to retain their PIV certification to the '149 patent which correspondingly allows them to retain eligibility for 180-day exclusivity. Rather than attempting to recite the tortuous litigation in the AP letter for this ANDA it is recommended that the AP letter focus on the District Court Judgment dated June 19, 2016. (b) (4)

ANDA is eligible for immediate Full AP with an award of 180-day exclusivity.

2. ***Paragraph IV Evaluation (for ANDAs with PIV certifications or other controversial regulatory issues)***
   Date: _____Name/Title: _____ Comments:

   Or see corresponding endorsement task under the ANDA project within the platform

3. ***Quality Endorsement by the Office of Pharmaceutical Science***
   Date: _____Name/Title: _____ Comments:

   Or see corresponding endorsement task under the ANDA project within the platform

4. ***Bioequivalence Endorsement***
   Date: _____Name/Title: _____ Comments:

   Or see corresponding endorsement task under the ANDA project within the platform

5. ***Labeling Endorsement***
   Date: _____Name/Title: _____ Comments:

   Or see corresponding endorsement task under the ANDA project within the platform

6. ***REMS Endorsement***
   Date: _____Name/Title: _____ Comments:

   Or see corresponding endorsement task under the ANDA project within the platform

7. ***RPM Team Leader Endorsement***
   Date: _____Name/Title: _____ Comments:

   Or see corresponding endorsement task under the ANDA project within the platform

8. Final Decision

Date: 2/23/2017
Name/Title: cah

Para.IV Patent Cert: Yes ✓ No ☐
Pending Legal Action: Yes ☐ No ✓
Petition: Yes ✓ No ☐
Entered to APTrack database ✓
GDUFA User Fee Obligation Status Met ✓ Unmet ☐
Press Release Acceptable ☐
First Generic Approval ☐
PD or Clinical for BE ☐
Special Scientific or Reg. Issue ☐

Date PETS checked for first generic drug _____

Comments:

ANDA received on 11/8/10 and TA issued on 5/29/15. The BOS=Suprep, NDA 022372, Braintree Laboratories Inc. The applicant provided a PIV certification to the '149 patent. The applicant was sued within 45 days for infringement of the '149 patent. See the extensive litigation history above from OGDP and the case was settled. The settlement agreement between Novel and Braintree permits Novel to retain their PIV certification to the '149 patent and according to OGDP allows them to retain eligibility for 180-day exclusivity. There are no new patents/exclusivities listed in the OB for this NDA (2/23/17). There is a pending CP on the OGD Policy Alert List for Suprep Bowel Prep Kit, FDA-2017-P-1104. Per OGDP Shimer (2/23/17 phone call) this CP does not impact OGD from taking an action on this ANDA. Also see memo dated 2/23/17 concerning 180 day exclusivity. Bio – waiver requested. Bio is adequate and waiver granted per Bai on 9/19/14. Bio endorsement completed by Liu on 2/14/17. Labeling is adequate per Hoppes/Grace on 12/29/14. Review confirms medication guide is adequate. Labeling endorsement completed by Vu on 2/14/17. No REMS required. Drug Product is adequate per Ruan/Tiwari on 1/26/17. (b) (4) QE checklist completed by Andrews/Tiwari on 2/15/17. This endorsement indicates OPQ reviews remain adequate including facilities. Quality endorsement completed by Andrews/Tiwari on 2/15/17. The overall manufacturing inspection recommendation is approve (see screen shots below – there are no visible alerts in the platform at the time of this action). ANDA is ready for Full Approval with an award of 180-day exclusivity.

(b) (4)

[redacted]

2 PAGES WERE REDACTED AS CCI/TS (B)(4) IMMEDIATELY FOLLOWING THIS PAGE

Orange Book Report:

Patent and Exclusivity for: N022372

Product: 001
MAGNESIUM SULFATE ANHYDROUS; POTASSIUM SULFATE; SODIUM SULFATE (SUPREP BOWEL PREP KIT) SOLUTION;1.6GM/BOT;3.13GM/BOT;17.5GM/BOT

Patent Data

Product No	Patent No	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Use Code	Delist Requested
001	8946149	Mar 7, 2023		DP	U-837	

Exclusivity Data

Product No	Exclusivity Code	Exclusivity Expiration

There is no unexpired exclusivity for this product in the Orange Book database.

REFERENCES / ASSOCIATED DOCUMENTS

4000-LPS-041 Processing Approval and Tentative Approval of an Original ANDA

REVISION HISTORY

Version	Effective date	Name	Role	Summary of changes
01	10/1/2014	Heather Strandberg	Author	New Form

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: July 29, 2016

FROM: Martin Shimer
Deputy Director, Division of Legal and Regulatory Support
Office of Generic Drug Policy

TO: ANDA 202511

SUBJECT: 180-day Exclusivity for Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution, 17.5 g/3.13 g/1.6 g per bottle

I. STATUTORY BACKGROUND

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) describes, among other things, certain events that can result in the forfeiture of a first applicant's[1] 180-day generic drug exclusivity as described in section 505(j)(5)(B)(iv) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act).

The forfeiture provisions of the MMA appear at section 505(j)(5)(D) of the FD&C Act. Included among these is section 505(j)(5)(D)(i)(IV), which states the following:

> FAILURE TO OBTAIN TENTATIVE APPROVAL.--The first applicant fails to obtain tentative approval of the application within 30 months[2] after the date on

[1] A "first applicant" is eligible for 180-day exclusivity by virtue of filing a substantially complete ANDA with a paragraph IV certification on the first day on which such an ANDA is received. Section 505(j)(5)(B)(iv)(II)(bb). If only one such ANDA is filed on the first day, there is only one first applicant; if two or more such ANDAs are filed on the first day, first applicant status is shared.

[2] For applications submitted between January 9, 2010, and July 9, 2012 containing a Paragraph IV certification (or amended to first contain a paragraph IV certification during that period of time), and approved or tentatively approved during the period of time beginning on July 9, 2012, and ending on September 30, 2015, section 1133 of the Food and Drug Administration Safety and Innovation Act (FDASIA) (P.L. 112-144) extends this period to 40 months. For applications submitted between January 9, 2010, and July 9, 2012 (or amended to first contain a paragraph IV certification during that period of time), and approved or tentatively approved during the period of time beginning on October 1, 2015, and ending on September 30, 2016, section 1133 of FDASIA extends this period to 36 months. In addition, if an application was submitted between January 9, 2010, and July 9, 2012 containing a Paragraph IV certification (or amended to first contain a paragraph IV certification during that period of time), and FDA has not approved or tentatively approved the application but must consider whether the applicant has forfeited exclusivity because a potentially blocked application is ready for approval, FDA will apply the 36-month period if it makes the forfeiture determination between the period of time beginning on October 1, 2015, and ending on September 30, 2016. For all other applications, the 30-month period set forth in FD&C Act section 505(j)(5)(D)(i)(IV) applies.

> which the application is filed, unless the failure is caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed.

The "failure to obtain tentative approval" forfeiture provision establishes a bright-line rule: If within 30 months of submission, an abbreviated new drug application (ANDA) has been determined by the agency to meet the statutory standards for approval and it is only patent and/or exclusivity protection that prevents full approval, then an applicant will be given a tentative approval and will maintain eligibility for 180-day exclusivity. If tentative approval or approval[3] is not obtained within 30 months, eligibility for 180-day exclusivity is generally forfeited unless "the failure [to obtain an approval] is caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application is filed." Under this provision, it is not sufficient to show that FDA's review of the ANDA (to determine that the ANDA has met the pre-existing approval requirements), caused a failure to obtain a tentative approval or approval at 30 months. Nor is it sufficient for an applicant to show that FDA changed or reviewed (i.e., considered whether to change) the requirements for approval while the application was under review. The applicant must also show that its failure to obtain a tentative approval at the 30 month date is **caused by** this change in or review of approval requirements. FDA generally will presume that the failure to obtain tentative approval or approval was caused by a change in or review of approval requirements if, at the 30 month date, the evidence demonstrates that the sponsor was actively addressing the change in or review of approval requirements (or FDA was considering such efforts), and these activities precluded tentative approval (or approval) at that time. Where the evidence fails to demonstrate that the sponsor was actively addressing the change in or review of approval requirements, and these activities precluded tentative approval (or approval) at the 30-month date, FDA generally does not presume that the failure was caused by a change in or review of approval requirements. If FDA were to hold otherwise, an applicant that receives one or more deficiencies resulting from a change in approval requirements could simply delay addressing those deficiencies and avoid forfeiture.

In addition, FDA has determined that if one of the causes of failure to get tentative approval or approval by the 30-month forfeiture date was a change in or review of the requirements for approval imposed after the application was filed, an applicant will not forfeit eligibility notwithstanding that there may have been other causes for failure to obtain tentative approval or approval by the 30-month forfeiture date. Thus, to avoid forfeiture, an applicant must show that acceptability of at least one aspect of the ANDA (e.g., chemistry) was delayed, and that this delay was caused at least in part, by a change in or review of the requirements for approval (which the sponsor or FDA is actively addressing), irrespective of what other elements may also have been outstanding at the 30-month date. In other words, "but-for" causation is not required in order to qualify for this exception. FDA has determined that this interpretation best effectuates the policy embodied in the exception. It does not penalize applicants for reviews of

[3] As explained below in note 4, FDA interprets this provision to also encompass the failure to obtain final approval, where applicable, within 30 months of filing.

or changes in approval requirements imposed on applicants after their ANDAs are filed that are a cause of the failure to obtain approvals or tentative approvals within 30 months (and presumes causation if, at the 30 month date, the sponsor was actively addressing those changes, and these changes precluded approval), and continues to incentivize applicants to challenge patents by preserving in many instances the opportunity to obtain 180-day exclusivity.

Under this provision, the 30-month timeframe is generally measured without regard to the length of time the ANDA was under review by the Agency. However, subsection 505(q)(1)(G) of the Act, enacted as part of the Food and Drug Administration Amendments Act of 2007 (Pub. Law 110-85) provides one exception. This subsection provides that:

> If the filing of an application resulted in first-applicant status under subsection (j)(5)(D)(i)(IV) and approval of the application was delayed because of a petition, the 30-month period under such subsection is deemed to be extended by a period of time equal to the period beginning on the date on which the Secretary received the petition and ending on the date of final agency action on the petition (inclusive of such beginning and ending dates), without regard to whether the Secretary grants, in whole or in part, or denies, in whole or in part, the petition.

Thus, pursuant to this provision, if approval was delayed because of a 505(q) petition such that the application was not ready to be approved at 30 months from the date of submission because of the time it took the Agency to respond to the 505(q) petition, the 30-month-period-from-initial-submission deadline for obtaining a tentative (or final) approval will be extended by the amount of time that the 505(q) petition was under review.[4]

II. DISCUSSION

Novel Laboratories, Inc. (Novel) submitted ANDA 202511 for Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution, 17.5 g/3.13 g/1.6 g per bottle, on November 8, 2010. Novel qualified as a "first applicant" and therefore is eligible for 180-day exclusivity for

[4] In addition to tolling the 30-month period described in 505(j)(5)(D)(i)(IV) in certain circumstances where a petition is under review, section 505(q)(1)(G) clarified the scope of section 505(j)(5)(D)(i)(IV). If the phrase "tentative approval" in section 505(j)(5)(D)(i)(IV) is viewed in isolation, it might be suggested that this section applies only when an ANDA is eligible for a tentative approval due to a patent, 30-month stay or exclusivity blocking final approval, and that this provision cannot serve as a basis for forfeiture when an ANDA would have otherwise been eligible only for a *final* approval because there is no blocking patent, 30-month stay or exclusivity. Although section 505(j)(5)(D)(i)(IV) refers to "tentative approvals," the terms of section 505(q)(1)(G) clearly describe a broader scope. Section 505(q)(1)(G) expressly states that if "approval" of the first applicant's application was delayed because of a petition, the 30-month period described in section 505(j)(5)(D)(i)(IV) will be extended. Thus, Congress contemplated that section 505(j)(5)(D)(i)(IV) establishes a 30-month period within which an ANDA generally must obtain either tentative approval or final approval. This interpretation squares both with the statutory language and with not permitting the 180-day exclusivity for a first applicant whose ANDA is deficient to delay approval of subsequent applications. Therefore, FDA interprets section 505(j)(5)(D)(i)(IV) as requiring that, unless the period is extended for one of the reasons described in section 1133 of FDASIA, a first applicant that fails to obtain either tentative approval or approval for its ANDA within 30 months will forfeit eligibility for 180-day exclusivity.

its generic Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution product absent forfeiture. Because Novel submitted its ANDA within the time period identified in Section 1133 of FDASIA, the company had 40 months to obtain tentative approval for the purposes of section 505(j)(5)(D)(i)(IV) of the FD&C Act.[5]

This memorandum addresses whether Novel has forfeited its eligibility for 180-day exclusivity due to its failure to obtain tentative approval by March 8, 2014.

On March 7, 2014, Novel submitted correspondence regarding its eligibility for 180-day exclusivity, in which it asserted that several changes in the requirements for approval occurred after ANDA 202511 was submitted, causing the company's failure to obtain tentative approval by the forfeiture date.[6] Novel submitted a second correspondence, supplementing the First Forfeiture Correspondence, on May 5, 2016, and requested a meeting with FDA.[7]

On June 14, 2016, staff from the Office of Chief Counsel and Office of Generic Drug Policy held a teleconference with Novel and its outside counsel in which outside counsel reiterated several points from the May 5, 2016 Second Forfeiture Correspondence.[8]

We must base our forfeiture analysis on the record before the agency. The following is a timeline of certain key submissions and actions regarding ANDA 202511:

11/08/2010	ANDA submitted
03/31/2011	Labeling review (deficient); labeling deficiencies faxed
07/06/2011	***Reference listed drug (RLD) labeling changes approved***
07/26/2011	Chemistry amendment
11/06/2012	***RLD labeling changes approved***
01/09/2013	***According to Novel's internal FDA communication log for ANDA 202511,[9] Novel asked an FDA employee whether it could submit a labeling amendment or should wait for a complete response letter, and the FDA employee responded via email that Novel should wait to receive a complete response letter***

[5] See note 2, above.
[6] See Letter to K. Uhl (OGD) fr. S. Talbot (Novel) re "General Correspondence: Preserving 180 day Exclusivity, ANDA # 202511: Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution (Sequence # 0005)" (Mar. 7, 2014) (First Forfeiture Correspondence). We note that ANDA applicants frequently submit correspondence related to forfeiture of 180-day exclusivity. Although FDA does not expect or require such correspondence, the agency will consider any submitted correspondence when making a forfeiture decision.
[7] Letter to K. Uhl (OGD) and E. Dickinson (Office of Chief Counsel (OCC)) fr. W. Rakoczy (Rakoczy Molino Mazzochi Siwik LLP, Outside Counsel for Novel) re "ANDA No. 202511: Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Oral Solution, 17.5 g/3.13g/1.6 g per bottle" (May 5, 2016) (Second Forfeiture Correspondence).
[8] FDA Public Calendar: June 12 – 18, 2016, available at: http://www.fda.gov/NewsEvents/MeetingsConferencesWorkshops/PastMeetingsWithFDAOfficials/ucm508875.htm
[9] Email to E. Dickinson (OCC) and M. Toufanian (OGDP) fr. L. FitzSimmons (Rakoczy Molino Mazzochi Siwik

04/16/2013	Bioequivalence review (deficient)
01/26/2014	***According to Novel's internal FDA communication log for ANDA 202511, Novel again asked an FDA employee whether it could submit a labeling amendment or should wait for a complete response letter, and the FDA employee again responded via email that Novel should wait to receive a complete response letter***
02/28/2014	Chemistry review #1 (deficient)
03/04/2014	Complete Response faxed (chemistry, bioequivalence, and labeling deficient; facilities pending inspection)
03/07/2014	Correspondence regarding 180-day exclusivity
03/08/2014	**11/08/2010 plus 40 months**
08/08/2014	Resubmission; chemistry, bioequivalence, and labeling amendment
08/20/2014	Labeling review (deficient)
09/19/2014	Bioequivalence review (acceptable)
11/07/2014	Chemistry ECD emailed and labeling ECD faxed
11/19/2014	Chemistry and facilities amendment
11/21/2014	Labeling amendment
12/04/2014	Chemistry review #2 (acceptable, pending facilities and labeling)
12/18/2014	Labeling amendment
12/29/2014	Labeling review (acceptable)
04/24/2015	"Checklist for Chemistry Review" (acceptable)
05/29/2015	ANDA tentatively approved

The tentative approval of Novel's ANDA was not delayed because of a citizen petition, such that the 40-month period would be extended past March 8, 2014, under section 505(q)(1)(G).

FDA Review of ANDA 202511

As the above timeline indicates, at the forfeiture date of March 8, 2014, chemistry, bioequivalence, and labeling were deficient. FDA has identified a change in the requirements for approval regarding labeling, as discussed below.

Labeling Review

As noted in the above timeline, two supplemental labeling changes were approved for the RLD, Suprep Bowel Prep Kit (sodium sulfate, potassium sulfate and magnesium sulfate) Oral Solution (Suprep) between the date ANDA 202511 was submitted and the 40-month forfeiture date: S-

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LLP, Outside Counsel for Novel) re "RE: Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution---HIGHLY CONFIDENTIAL" (June 17, 2016). A copy of the communication log is attached to this memorandum for reference.

003 was approved on July 6, 2011, which released the Risk Evaluation and Mitigation Strategy (REMS) that had been required for Suprep; and S-004 was approved on November 6, 2012 for revisions to the DOSAGE AND ADMINISTRATION section to increase the wait time between completion of ingestion and the start of a colonoscopy procedure from one hour to two hours. FDA previously has found that updates to the approved RLD labeling after an ANDA is submitted are a change in the requirements for approval;[10] therefore, the approval of these two labeling changes for the RLD constituted a change in the requirements for approval for ANDA 202511.

Novel asserts in its First Forfeiture Correspondence that FDA asked Novel not to respond to the March 31, 2011 labeling deficiencies until a complete response letter was issued.[11] Novel later provided a copy of its internal communication log for ANDA 202511, which indicates that Novel asked FDA staff on January 9, 2013 and January 26, 2014 whether a labeling amendment could be submitted, and, according to Novel's internal communication log, in both instances Novel was advised by an FDA employee to wait until receiving a complete response letter to submit the amendment. FDA issued a complete response letter on March 4, 2014, which repeated the March 31, 2011 labeling deficiencies that had been previously conveyed to Novel, including the suggestion to monitor FDA's website for any approved changes to the RLD labeling.[12] The complete response letter also contained chemistry and bioequivalence deficiencies and noted that "[a] partial response to this letter will not be processed as a resubmission and will not start a new review cycle."[13] Novel's resubmission was received on August 8, 2014, and the labeling provided did address the November 6, 2012 RLD labeling updates.[14]

As described above, an applicant must show that its failure to obtain a tentative approval is caused by a change in approval requirements. FDA generally will presume that the failure to obtain tentative approval was caused by a change in approval requirements if, at the forfeiture date, the evidence demonstrates that the applicant was actively addressing the change in approval requirements (or FDA was considering such efforts), and these activities precluded tentative approval at that time. Where the evidence fails to demonstrate that the applicant was actively addressing the change in approval requirements, and these activities precluded tentative approval, FDA generally does not presume that the failure was caused by a change in approval requirements. The rationale for this position is that, otherwise, an applicant who receives one or more deficiencies resulting from a change in approval requirements could simply delay

[10] See, e.g., Memorandum to ANDA 200828 re "180-day Exclusivity for Lamotrigine Orally Disintegrating Tablets, 25 mg, 50 mg, 100 mg, and 200 mg" (Oct. 29, 2014) and Memorandum to ANDA 201509 RE "180-day Exclusivity for Zolpidem Tartrate Sublingual Tablets, 5 mg and 10 mg" (June 2, 2016).
[11] First Forfeiture Correspondence, at 2.
[12] Letter to S. Talbot (Novel) fr. K. Uhl (OGD) re "ANDA 202511, COMPLETE RESPONSE" (Mar. 4, 2014), at 3-4.
[13] Id., at 4. This language is standard template language included in all OGD complete response letters.
[14] ANDA 202511, Sequence 0006, Section 1.14.3.1, *Side by side PI (PDF)* (Aug. 8, 2014). We note that the resubmission did not address the July 6, 2011 RLD labeling change; however, as described above, only one aspect of the ANDA must be delayed by a change in or review of the requirements for approval, irrespective of what other elements are also outstanding as of the forfeiture date.

addressing those deficiencies and avoid forfeiture.

In this case, changes to the RLD labeling required Novel to revise its labeling. The record indicates that Novel was actively attempting to address the deficiencies as of the forfeiture date, as evidenced by its communications of January 9, 2013 and January 26, 2014 inquiring whether it could submit a labeling amendment. FDA finds that the labeling changes were a cause of Novel's failure to obtain tentative approval by March 8, 2014. Specifically, Novel's efforts to address the labeling deficiencies, i.e., by inquiring whether it could submit an amendment prior to the forfeiture date, are evidence that Novel was actively addressing the deficiencies. In addition, there is no evidence that Novel sought to delay addressing the labeling deficiencies to avoid forfeiture. On the contrary, Novel actively inquired about submitting a labeling amendment to address these deficiencies, and an FDA employee instructed it not to. Therefore, FDA finds that the RLD labeling updates, which were approved after ANDA 202511 was submitted, constituted a change in the requirements for approval and these changes were a cause of Novel's failure to obtain tentative approval by March 8, 2014.

Novel's Correspondence regarding 180-day Exclusivity

As noted above, Novel submitted letters to FDA on March 7, 2014 and May 5, 2016 regarding its eligibility for 180-day exclusivity. Novel alleges that there were several changes in the requirements for approval date before the 40-month forfeiture date; however, as FDA has already found one change in the requirements for approval imposed after ANDA 202511 was submitted and has concluded that this change was a cause of Novel's failure to obtain tentative approval by March 8, 2014, it is unnecessary to determine whether any additional bases for non-forfeiture exist.

III. CONCLUSION

Novel's ANDA 202511 for Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution, 17.5 g/3.13 g/1.6 g per bottle, was submitted on November 8, 2010. The 40-month forfeiture date was March 8, 2014. Novel's ANDA was not tentatively approved within this period. FDA concludes that there was a change in the requirements for approval with respect to labeling, i.e., RLD labeling updates that were approved after Novel's ANDA was submitted, which was a cause of Novel's failure to obtain tentative approval by the forfeiture date. Therefore, Novel has not forfeited its eligibility for the 180-day exclusivity period described in section 505(j)(5)(B)(iv) of the FD&C Act for Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution, 17.5 g/3.13 g/1.6 g per bottle.

Martin H. Shimer Ii -S

Digitally signed by Martin H. Shimer Ii -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300157630, cn=Martin H. Shimer Ii -S
Date: 2016.07.29 12:56:28 -04'00'

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

/s/

MARTIN H Shimer
07/29/2016

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: **202511** Date of Submission: **November 8, 2010**

Applicant's Name: **Novel Laboratories, Inc.**

Proposed Proprietary Name: **None**

Established Name: **Sodium Sulfate, Potassium Sulfate, and Magnesium Sulfate Oral Solution.**

Labeling Deficiencies:

1. GENERAL COMMENTS:

   a. You state that your carton contains "one (b) (4) mixing container"; however, you did not submit information about the (b) (4) mixing container in the Section 3.2.P.7 Container Closure System. Please submit pertinent information about this (b) (4) mixing container to chemistry. Note that the container should have the 16-ounce line marked on the container.

   b. Before final approval of this drug product, you should submit the "patient booklet" stated on the carton for review.

2. CONTAINER:

   Revise to read "17.5 g/3.13 g/1.6 g per 6 ounces" [add a space between "17.5" and "g"].

3. CARTON:

   a. Side panel, Step 1, the six-ounce bottle depicted is (b) (4). Please verify that your six-ounce bottle is (b) (4).

   b. Side Panel, Step 2, the red "Fill Line" could not be read. Please revise.

   c. Please submit a depiction of the carton with all panels attached.

   d. Please refer to CONTAINER comment.

4. PATIENT INSTRUCTIONS

   Please submit patient instructions.

5. MEDICATION GUIDE

   Acceptable in draft.

6. REMS

   Timetable for Submission of Assessments: revise to state "Not applicable".

7. INSERT

a. Please submit the HIGHLIGHTS and FULL PRESCRIBING INFORMATION: CONTENTS* sections.

b. (b) (4)

c. Second footnote of Table 2, revise to read "... (≤ 21 mEq/L) and high anion gap (≥ 13 mEq/L)..."

d. 11 DESCRIPTION

(b) (4)

Submit labels and labeling electronically.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

To facilitate review of your next submission please provide a side-by-side comparison of your proposed labeling with your last labeling submission with all differences annotated and explained.

{See appended electronic signature page}

_____

Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
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/

JOHN F GRACE
03/31/2011
for Wm Peter Rickman

ANDA CHECKLIST FOR CTD or eCTD FORMAT
FOR COMPLETENESS and ACCEPTABILITY of an APPLICATION FOR FILING

For More Information on Submission of an ANDA in Electronic Common Technical Document (eCTD) Format please go to: http://www fda.gov/cder/regulatory/ersr/ectd.htm
***For a Comprehensive Table of Contents Headings and Hierarchy please go to:**
http://www fda.gov/cder/regulatory/ersr/5640CTOC-v1.2.pdf
**** For more** CTD and eCTD informational links **see the final page of the ANDA Checklist**
***** A model Quality Overall Summary for an immediate release tablet and an extended release capsule can be found on the OGD webpage** http://www.fda.gov/cder/ogd/ *****

ANDA #: 202511 **FIRM NAME**: NOVEL LABORATORIES, INC.

PIV: YES **Electronic or Paper Submission:** ELECTRONIC (GATEWAY)

RELATED APPLICATION(S): NA

First Generic Product Received? YES

DRUG NAME: MAGNESIUM SULFATE, POTASSIUM SULFATE, AND SODIUM SULFATE
DOSAGE FORM: ORAL SOLUTION, 1.6 G, 3.13 G, AND 17.5 G/BOTTLE

Review Team: (Bolded/Italicized & Checked indicate Assignment or DARRTS designation)

Quality Team: DC3 TM 34 ☒***Activity***	***Bio Team 6: Bing Li*** ☒***Activity***
ANDA/Quality RPM: Leigh Ann Bradford ☒ ***FYI***	Bio PM: Nam J. Chun (Esther) ☐ ***FYI***
Quality Team Leader: Nagavelli, Laxma No assignment needed in DARRTS	***Clinical Endpoint Team Assignment: (No)*** ☐***Activity***
Labeling Reviewer: Ann Vu ☒***Activity***	***Micro Review (No)*** ☐***Activity***

*****Document Room Note: for New Strength amendments and supplements, if specific reviewer(s) have already been assigned for the original, please assign to those reviewer(s) instead of the default random team(s). *****

Letter Date: NOVEMBER 8, 2010 **Received Date**: NOVEMBER 8, 2010

Comments: EC- 3 YES **On Cards:** YES
Therapeutic Code: 8015612 CATHARTICS AND LAXATIVES

Archival copy: ELECTRONIC (GATEWAY) **Sections** I
Review copy: NA E-Media Disposition: NA
Not applicable to electronic sections

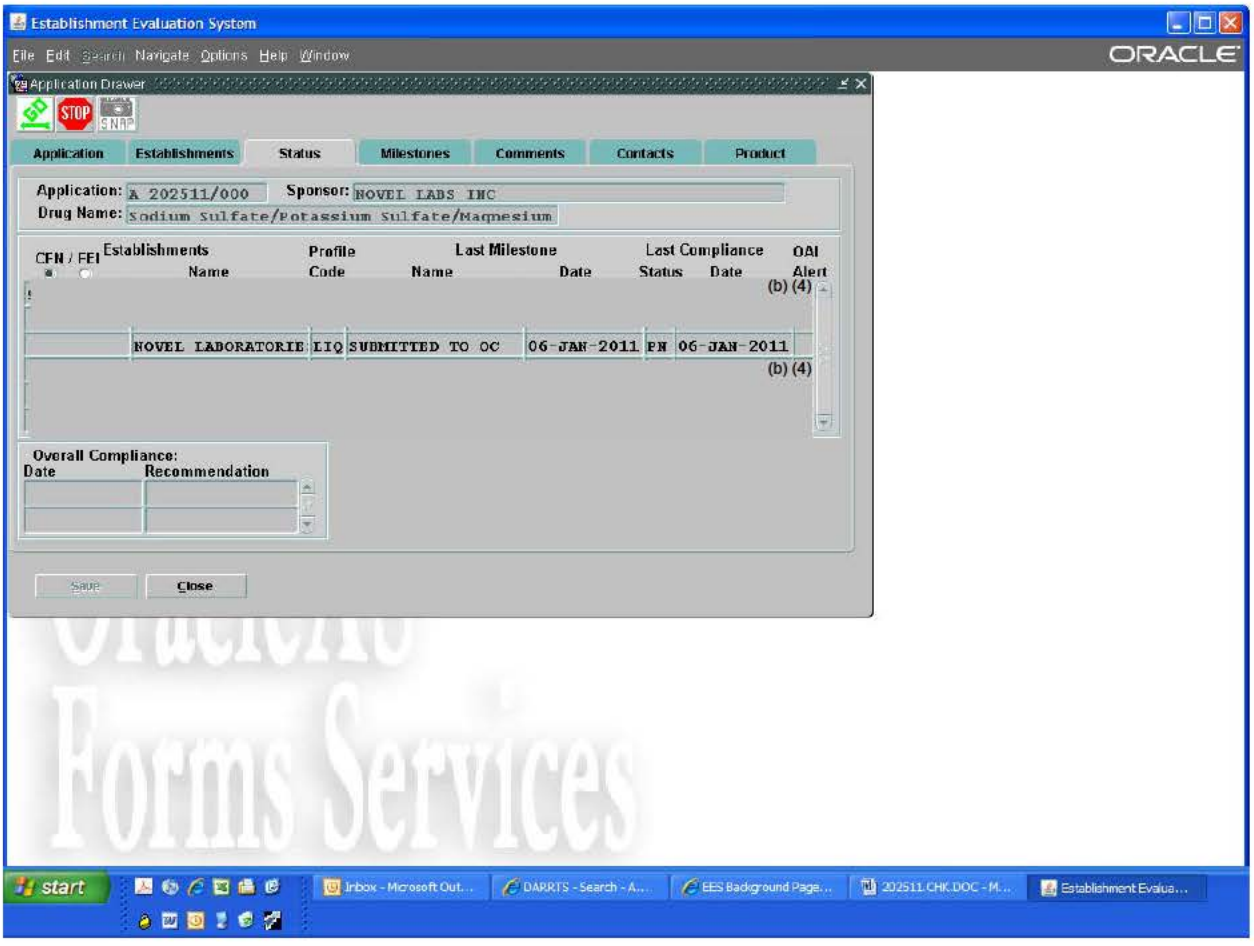
PART 3 Combination Product Category N Not a Part3 Combo Product
(Must be completed for ALL Original Applications) Refer to the Part 3 Combination Algorithm

Reviewing CSO/CST Ted Palat **Date 01/06/2011**	**Recommendation:** ☒ **FILE** ☐ **REFUSE to RECEIVE**
Supervisory Concurrence/Date: ____	**Date:** ____

1. Edit Application Property Type in DARRTS where applicable for
   a. First Generic Received
      ☒ Yes ☐ No
   b. Market Availability
      ☒ Rx ☐ OTC
   c. Pepfar
      ☐ Yes ☒ No
   d. Product Type
      ☐ Small Molecule Drug (usually for most ANDAs except protein drug products)
   e. USP Drug Product (at time of filing review)
      ☐ Yes ☒ No
2. Edit Submission Patent Records
   ☒ Yes
3. Edit Contacts Database with Bioequivalence Recordation where applicable
   ☒ Yes
4. Requested EER
   ☒ Yes

ADDITIONAL COMMENTS REGARDING THE ANDA: Hema Balachandra

1. waiting for 1st generic review. 1st generic review is acceptable.



BIOEQUIVALENCE CHECKLIST for First Generic ANDA
FOR APPLICATION COMPLETENESS

ANDA# 202511 **FIRM NAME** Novel Laboratories Inc.

DRUG NAME Magnesium Sulfate (b) (4) Potassium Sulfate and Sodium Sulfate, 1.6 g, 3.13 g and 17.5 g/bottle

DOSAGE FORM Oral Solution

SUBJ: Request for examination of: Bioequivalence Study

Requested by: _____ Date: _____
Chief, Regulatory Support Team, (HFD-615)

	Summary of Findings by Division of Bioequivalence
☐	**Study meets statutory requirements**
☐	**Study does NOT meet statutory requirements**
	Reason:
☒	**Waiver meets statutory requirements**
☐	**Waiver does NOT meet statutory requirements**
	Reason:

RECOMMENDATION: ☒ **COMPLETE** ☐ **INCOMPLETE**

Reviewed by:

_____ Date: _____
Hongling Zhang, Ph.D.
Reviewer

_____ Date: _____
Bing V. Li, Ph.D.
Team Leader

MODULE 1
ADMINISTRATIVE

		ACCEPTABLE
1.1	**1.1.2 Signed and Completed Application Form (356h) (original signature)** (Check Rx/OTC Status) RX YES	☒
1.2	**Cover Letter** Dated: NOVEMBER 8, 2010	☒

1.2.1	**Form FDA 3674 (PDF) YES**	☒
*	**Table of Contents (paper submission only)** YES	☒
1.3.2	**Field Copy Certification (original signature)** NA **(N/A for E-Submissions)**	☒
1.3.3	**Debarment Certification-GDEA (Generic Drug Enforcement Act)/Other:** 1. Debarment Certification (original signature) YES 2. List of Convictions statement (original signature) SAME	☒
1.3.4	**Financial Certifications** Bioavailability/Bioequivalence Financial Certification (Form FDA 3454) NA Disclosure Statement (Form FDA 3455, submit copy to Regulatory Branch Chief) NA	☒
1.3.5	**1.3.5.1 Patent Information** Patents listed for the RLD in the Electronic Orange Book Approved Drug Products with Therapeutic Equivalence Evaluations **1.3.5.2 Patent Certification** **PIV – '149** 1. Patent number(s) **Patent and Exclusivity Search Results from query on Appl No 022372 Product 001 in the OB_Rx list.**	☒

Appl No	Prod No	Patent No	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Use Code	Delist Requested
N022372	001	6946149	Apr 30, 2022		Y	U - 837	

Appl No	Prod No	Exclusivity Code	Exclusivity Expiration
N022372	001	NC	Aug 5, 2013

U - 837 GASTROINTESTINAL LAVAGE INDICATED FOR CLEANSING OF THE COLON AS A PREPARATION FOR COLONOSCOPY IN ADULTS

NC NEW COMBINATION

2. Paragraph: (Check all certifications that apply)
   MOU ☐ PI ☐ PII ☐ PIII ☐
   PIV ☒ (Statement of Notification) ☒
3. Expiration of Patent(s): 4/30/2022
   a. Pediatric exclusivity submitted?
   b. Expiration of Pediatric Exclusivity?
4. Exclusivity Statement: YES market after expiration.

1.4.1	**References** Letters of Authorization 1. DMF letters of authorization (b) (4) [redacted] Type III DMF authorization letter(s) for container closure YES 2. US Agent Letter of Authorization (U.S. Agent [if needed, countersignature on 356h]) NA	☒

1.12.11	**Basis for Submission OK** NDA# : 22-372 Ref Listed Drug: SUPREP BOWEL PREP KIT Firm: BRAINTREE LABORATORIES ANDA suitability petition required? NA If Yes, then is change subject to PREA (change in dosage form, route or active ingredient) see section 1.9.1	☒

MODULE 1 (Continued)
ADMINISTRATIVE

ACCEPTABLE

1.12.12	**Comparison between Generic Drug and RLD-505(j)(2)(A)** 1. Conditions of use SAME 2. Active ingredients SAME 3. Inactive ingredients SAME 4. Route of administration SAME 5. Dosage Form SAME 6. Strength SAME	☒
1.12.14	**Environmental Impact Analysis Statement** YES	☒
1.12.15	**Request for Waiver** Request for Waiver of In-Vivo BA/BE Study(ies): YES	☒
1.14.1	**Draft Labeling (Mult Copies N/A for E-Submissions)** **1.14.1.1** 4 copies of draft (each strength and container) YES **1.14.1.2** 1 side by side labeling comparison of containers and carton with all differences annotated and explained YES **1.14.1.3** 1 package insert (content of labeling) submitted electronically YES ***Was a proprietary name request submitted? NO (If yes, send email to Labeling Reviewer indicating such.)	☒
1.14.3	**Listed Drug Labeling** **1.14.3.1** 1 side by side labeling (package and patient insert) comparison with all differences annotated and explained YES **1.14.3.3** 1 RLD label and 1 RLD container label YES	☒

2.3	**Quality Overall Summary (QOS)** **E-Submission: PDF** YES **Word Processed e.g., MS Word** YES A model Quality Overall Summary for an immediate release tablet and an extended release capsule can be found on the OGD webpage http://www fda.gov/cder/ogd/ **Question based Review (QbR)** YES **2.3.S** **Drug Substance (Active Pharmaceutical Ingredient)** YES **2.3.S.1 General Information** **2.3.S.2 Manufacture** **2.3.S.3 Characterization** **2.3.S.4 Control of Drug Substance** **2.3.S.5 Reference Standards or Materials** **2.3.S.6 Container Closure System** **2.3.S.7 Stability** **2.3.P** **Drug Product** YES **2.3.P.1 Description and Composition of the Drug Product** **2.3.P.2 Pharmaceutical Development** **2.3.P.2.1 Components of the Drug Product** **2.3.P.2.1.1 Drug Substance** **2.3.P.2.1.2 Excipients** **2.3.P.2.2 Drug Product** **2.3.P.2.3 Manufacturing Process Development** **2.3.P.2.4 Container Closure System** **2.3.P.3 Manufacture** **2.3.P.4 Control of Excipients** **2.3.P.5 Control of Drug Product** **2.3.P.6 Reference Standards or Materials** **2.3.P.7 Container Closure System** **2.3.P.8 Stability**	☒
2.7	**Clinical Summary (Bioequivalence) NA** **Model Bioequivalence Data Summary Tables** **E-Submission: PDF** **Word Processed e.g., MS Word** **2.7.1 Summary of Biopharmaceutic Studies and Associated Analytical Methods** **2.7.1.1 Background and Overview** Table 1. Submission Summary Table 4. Bioanalytical Method Validation Table 6. Formulation Data **2.7.1.2 Summary of Results of Individual Studies** Table 5. Summary of In Vitro Dissolution **2.7.1.3 Comparison and Analyses of Results Across Studies** Table 2. Summary of Bioavailability (BA) Studies Table 3. Statistical Summary of the Comparative BA Data **2.7.1.4 Appendix** **2.7.4.1.3 Demographic and Other Characteristics of Study Population** Table 7. Demographic Profile of Subjects Completing the Bioequivalence Study **2.7.4.2.1.1 Common Adverse Events** Table 8. Incidence of Adverse Events in Individual Studies	☒

MODULE 3

3.2.S DRUG SUBSTANCE ACCEPTABLE

3.2.S.1	**General Information** **3.2.S.1.1 Nomenclature** **3.2.S.1.2 Structure** **3.2.S.1.3 General Properties**	☒
3.2.S.2	**Manufacturer** **3.2.S.2.1** **Manufacturer(s) (This section includes contract manufacturers and testing labs)** **Drug Substance (Active Pharmaceutical Ingredient)** 1. Name and Full Address(es)of the Facility(ies) (b) (4) [redacted] 2. F 3. (b) (4) [redacted] 4. CFN or FEI numbers YES	☒
3.2.S.3	**Characterization**	☒

3.2.S.4	**Control of Drug Substance (Active Pharmaceutical Ingredient)** **3.2.S.4.1 Specification** Testing specifications and data from drug substance manufacturer(s) YES **3.2.S.4.2 Analytical Procedures** YES **3.2.S.4.3 Validation of Analytical Procedures** : YES, Sodium Sulfate Anhydrous is described in the current USP/NF. The methods used for testing the drug substance are compendial methods. No in-house method has been used to test sodium sulfate. This is acceptable. **see ANDA 79-247**, CM C review #1, pg. 17. similar statements are made for the other drug substances. 1. Spectra and chromatograms for reference standards and test samples NO There is no IR Spectrum or chromatograms for the reference standard and the test samples. The identification of the raw material is performed as per USP/NF <191> and the assay of the raw material is determined by titration as per the current USP. Similar statements are made for the other drug substances. 2. Samples-Statement of Availability and Identification of: a. Drug Substance YES b. Same lot number(s) 0909000623, G24N15, ZE0270 **3.2.S.4.4 Batch Analysis** 1. COA(s) specifications and test results from drug substance mfgr(s) YES 2. Applicant certificate of analysis YES **3.2.S.4.5 Justification of Specification**	☒
3.2.S.5	**Reference Standards or Materials**	☒
3.2.S.6	**Container Closure Systems**	☒
3.2.S.7	**Stability**	☒

MODULE 3

3.2.P DRUG PRODUCT ACCEPTABLE

3.2.P.1 **Description and Composition of the Drug Product** ☒

1. Unit composition

11. What are the components and composition of the final drug product? What is the function of each excipient?

Components, composition and the function of excipient are given below:

Name of the component	Composition (g)/ Dose	Composition g/ 100 mL	Function
Sodium Sulfate Anhydrous, USP	17.500	(b) (4)	(b) (4)
Potassium Sulfate (b) (4)	3.130		
Magnesium Sulfate, (b) (4) USP	1.600		
Sodium Benzoate, NF			
Sucralose, NF			
Malic Acid, NF			
(b) (4) Citric Acid, (b) (4) USP			
Lemon Flavor (b) (4)			

Note: Product is diluted to 16 oz with water.

2. Inactive ingredients and amounts are appropriate per IIG YES

IIG Table:

(b) (4)

(b) (4)

Reference ID: 2888310

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

3.2.P.2	**Pharmaceutical Development** Pharmaceutical Development Report YES	☒
3.2.P.3	**Manufacture** **3.2.P.3.1 Manufacture(s)** (Finished Dosage Manufacturer and Outside Contract Testing Laboratories) 1. Name and Full Address(es)of the Facility(ies) **26. Who manufactures the drug product?** **Manufacturer:** Novel Laboratories, Inc. 400 Campus Drive, Somerset NJ 08873 Phone: (908) 603-6000 Contact Person: Ms. Anu Radha Subramanian, Esq. Head of Regulatory Affairs Direct Phone: (908) 603-6002 FDA Registration number: 3006271438 2. CGMP Certification: YES 3. Function or Responsibility YES 4. CFN or FEI numbers YES **3.2.P.3.2 Batch Formula** YES **3.2.P.3.3 Description of Manufacturing Process and Process Controls** 1. Description of the Manufacturing Process YES 2. Master Production Batch Record(s) for largest intended production runs (no more than 10x pilot batch) with equipment specified YES Batch Size of the Exhibit and the Proposed Commercial Scale-up Batch records are given below: **Batch** / **Batch Size** (b) (4) Exhibit (ANDA) Batch Proposed Scale-Up Batch 3. If sterile product: Aseptic fill / Terminal sterilization NA 4. Reprocessing Statement YES **3.2.P.3.4 Controls of Critical Steps and Intermediates** **3.2.P.3.5 Process Validation and/or Evaluation** 1. Microbiological sterilization validation NA 2. Filter validation (if aseptic fill) NA	☒
3.2.P.4	**Controls of Excipients (Inactive Ingredients)** Source of inactive ingredients identified YES **3.2.P.4.1 Specifications** 1. Testing specifications (including identification and characterization) YES 2. Suppliers' COA (specifications and test results) YES **3.2.P.4.2 Analytical Procedures** **3.2.P.4.3 Validation of Analytical Procedures** **3.2.P.4.4 Justification of Specifications** Applicant COA YES	☒

MODULE 3
3.2.P DRUG PRODUCT

ACCEPTABLE

3.2.P.5	**Controls of Drug Product** **3.2.P.5.1 Specification(s)** YES **3.2.P.5.2 Analytical Procedures** YES **3.2.P.5.3 Validation of Analytical Procedures** Samples - Statement of Availability and Identification of: 1. Finished Dosage Form YES 2. Same lot numbers **Statement of Availability and Identification of the Drug Product:** Novel Laboratories, Inc. agrees to have the following samples available upon request by FDA: **Drug product information:** Sodium Sulfate, Potassium Sulfate, Magnesium Sulfate Oral Solution Novel Product Code (b) (4) Exhibit Batch #: EB-151 **3.2.P.5.4 Batch Analysis** Certificate of Analysis for Finished Dosage Form YES **3.2.P.5.5 Characterization of Impurities** **3.2.P.5.6 Justification of Specifications**	☒
3.2.P.7	**Container Closure System** 1. Summary of Container/Closure System (if new resin, provide data) YES 2. Components Specification and Test Data YES 3. Packaging Configuration and Sizes **16 HOW SUPPLIED/STORAGE AND HANDLING** Each sodium sulfate, potassium sulfate and magnesium sulfate oral solution contains: • Two (2) 6 oz bottles of oral solution. • One (1) 19 oz mixing container with a 16 oz fill line. Storage: Store at 20° to 25°C (68° to 77°F). Excursions permitted between 15° to 30°C (59° to 86°F). See USP controlled room temperature. Keep out of reach of children. Sodium sulfate, potassium sulfate and magnesium sulfate oral solution NDC 40032-700-02 4. Container/Closure Testing YES 5. Source of supply and suppliers address YES	☒
3.2.P.8	**3.2.P.8.1 Stability (Finished Dosage Form)** 1. Stability Protocol submitted YES 2. Expiration Dating Period 24 months **3.2.P.8.2 Post-approval Stability and Conclusion** Post Approval Stability Protocol and Commitments YES **3.2.P.8.3 Stability Data** 1. 3 month accelerated stability data YES 2. Batch numbers on stability records the same as the test batch **YES**	☒

MODULE 3

3.2.R Regional Information

ACCEPTABLE

3.2.R (Drug Substance)	**3.2.R.1.S Executed Batch Records for drug substance (if available) NO** **3.2.R.2.S Comparability Protocols NO** **3.2.R.3.S Methods Validation Package YES** Methods Validation Package (3 copies) (Mult Copies N/A for E-Submissions) (Required for Non-USP drugs)	☒

3.2.R (Drug Product)	**3.2.R.1.P.1** **Executed Batch Records** Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures) Batch Reconciliation and Label Reconciliation YES	☒

	Sodium Sulfate (17.5g), Potassium Sulfate (3.13g), Magnesium Sulfate (1.6g) Oral Solution (6 ounces) **EB-151**	Sodium Sulfate (17.5g), Potassium Sulfate (3.13g), Magnesium Sulfate (1.6g) Oral Solution (6 ounces) **EB-155**
		(b) (4)

3.2.R.1.P.2 Information on Components YES

3.2.R.2.P Comparability Protocols NO

3.2.R.3.P Methods Validation Package YES

Methods Validation Package (3 copies) (Mult Copies N/A for E-Submissions)

(Required for Non-USP drugs)

MODULE 5

CLINICAL STUDY REPORTS NA

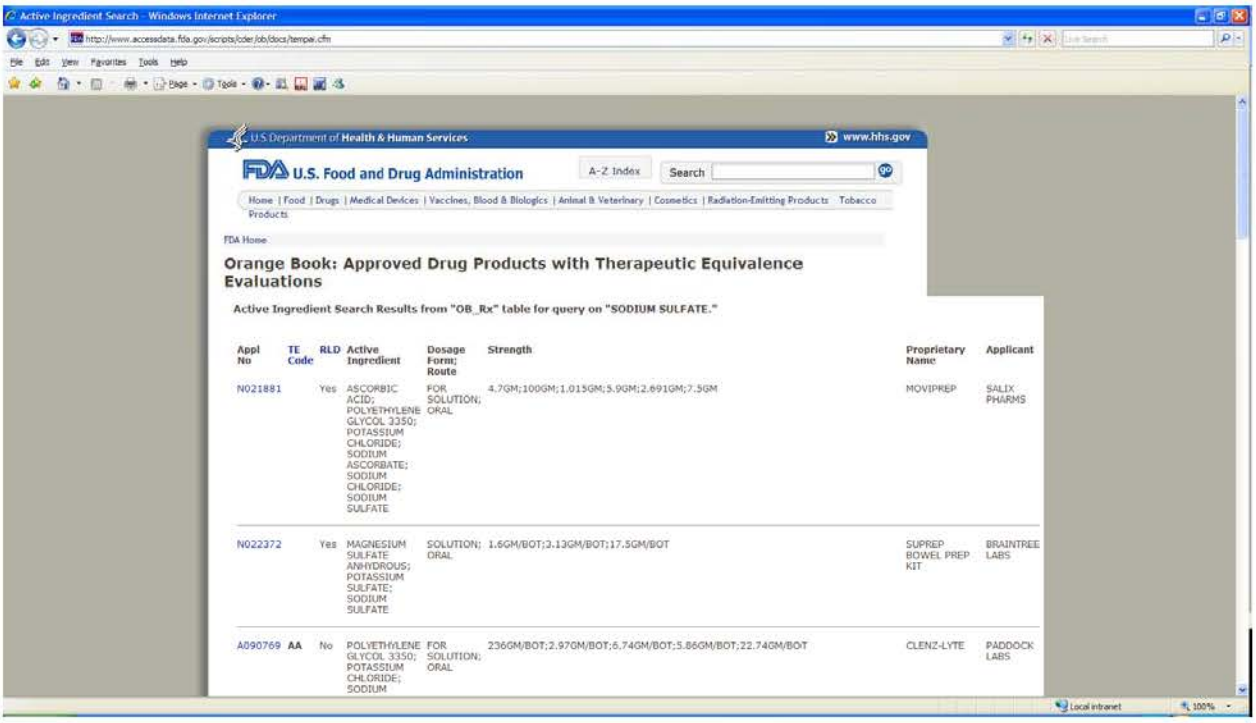
ACCEPTABLE

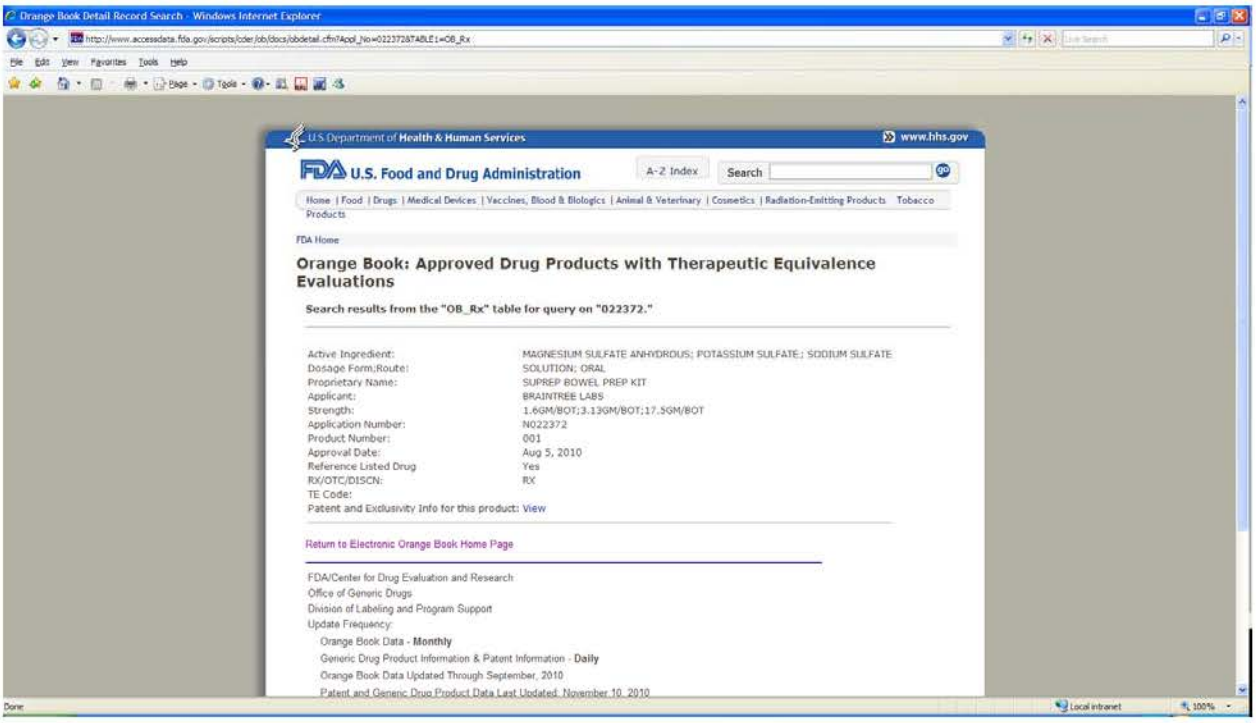
5.2	**Tabular Listing of Clinical Studies**	☐
5.3.1 (complete study data)	**Bioavailability/Bioequivalence** **1. Formulation data same?** a. Comparison of all Strengths (check proportionality of multiple strengths) b. Parenterals, Ophthalmics, Otics and Topicals per 21 CFR 314.94 (a)(9)(iii)-(v) **2. Lot Numbers of Products used in BE Study(ies):** **3. Study Type: IN-VIVO PK STUDY(IES)** (Continue with the appropriate study type box below)	☐

	5.3.1.2 Comparative BA/BE Study Reports 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) 2. Summary Bioequivalence tables: Table 10. Study Information Table 12. Dropout Information Table 13. Protocol Deviations **5.3.1.3** **In Vitro-In-Vivo Correlation Study Reports** 1. Summary Bioequivalence tables: Table 11. Product Information Table 16. Composition of Meal Used in Fed Bioequivalence Study **5.3.1.4** **Reports of Bioanalytical and Analytical Methods for Human Studies** 1. Summary Bioequivalence table: Table 9. Reanalysis of Study Samples Table 14. Summary of Standard Curve and QC Data for Bioequivalence Sample Analyses Table 15. SOPs Dealing with Bioanalytical Repeats of Study Samples **5.3.7** **Case Report Forms and Individual Patient Listing**	☐
5.4	**Literature References**	☐
	Possible Study Types:	
Study Type	**IN-VIVO BE STUDY(IES) with PK ENDPOINTS** (i.e., fasting/fed/sprinkle) NA 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) 2. EDR Email: Data Files Submitted: NA 3. In-Vitro Dissolution:	☐
Study Type	**IN-VIVO BE STUDY with CLINICAL ENDPOINTS** NO 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria: 90% CI of the proportional difference in success rate between test and reference must be within (-0.20, +0.20) for a binary/dichotomous endpoint. For a continuous endpoint, the test/reference ratio of the mean result must be within (0.80, 1.25). 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted	☐
Study Type	**IN-VITRO BE STUDY(IES)** (i.e., in vitro binding assays) NO 1. Study(ies) meets BE criteria (90% CI of 80-125) 2. EDR Email: Data Files Submitted: 3. In-Vitro Dissolution:	☐

Study Type	**NASALLY ADMINISTERED DRUG PRODUCTS** 1. Solutions (Q1/Q2 sameness): a. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming) 2. Suspensions (Q1/Q2 sameness): a. In-Vivo PK Study 1. Study(ies) meets BE Criteria (90% CI of 80-125, C max, AUC) 2. EDR Email: Data Files Submitted b. In-Vivo BE Study with Clinical End Points 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria (90% CI within +/- 20% of 80-125) 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted c. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming)	☐
Study Type	**IN-VIVO BE STUDY(IES) with PD ENDPOINTS** (e.g., topical corticosteroid vasoconstrictor studies) 1. Pilot Study (determination of ED50) 2. Pivotal Study (study meets BE criteria 90%CI of 80-125)	☐
Study Type	**TRANSDERMAL DELIVERY SYSTEMS** 1. In-Vivo PK Study 1. Study(ies) meet BE Criteria (90% CI of 80-125, C max, AUC) 2. In-Vitro Dissolution 3. EDR Email: Data Files Submitted 2. Adhesion Study 3. Skin Irritation/Sensitization Study	☐

Updated 10/19/2009


Active Ingredient Search - Windows Internet Explorer
http://www.accessdata.fda.gov/scripts/cder/ob/docs/tempai.cfm
File Edit View Favorites Tools Help
U.S. Department of Health & Human Services
www.hhs.gov
FDA U.S. Food and Drug Administration
A-Z Index
Search
go
Home | Food | Drugs | Medical Devices | Vaccines, Blood & Biologics | Animal & Veterinary | Cosmetics | Radiation-Emitting Products | Tobacco Products
FDA Home
Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations
Active Ingredient Search Results from "OB_Rx" table for query on "SODIUM SULFATE."
Appl No
TE Code
RLD
Active Ingredient
Dosage Form; Route
Strength
Proprietary Name
Applicant
N021881 Yes ASCORBIC ACID; POLYETHYLENE GLYCOL 3350; POTASSIUM CHLORIDE; SODIUM ASCORBATE; SODIUM CHLORIDE; SODIUM SULFATE FOR SOLUTION; ORAL 4.7GM;100GM;1.015GM;5.9GM;2.691GM;7.5GM MOVIPREP SALIX PHARMS
N022372 Yes MAGNESIUM SULFATE ANHYDROUS; POTASSIUM SULFATE; SODIUM SULFATE SOLUTION; ORAL 1.6GM/BOT;3.13GM/BOT;17.5GM/BOT SUPREP BOWEL PREP KIT BRAINTREE LABS
A090769 AA No POLYETHYLENE GLYCOL 3350; POTASSIUM CHLORIDE; SODIUM FOR SOLUTION; ORAL 236GM/BOT;2.97GM/BOT;6.74GM/BOT;5.86GM/BOT;22.74GM/BOT CLENZ-LYTE PADDOCK LABS
Local intranet
100%


Orange Book Detail Record Search - Windows Internet Explorer
U.S. Department of Health & Human Services
www.hhs.gov
U.S. Food and Drug Administration
A-Z Index
Search
Home | Food | Drugs | Medical Devices | Vaccines, Blood & Biologics | Animal & Veterinary | Cosmetics | Radiation-Emitting Products | Tobacco Products
FDA Home
Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations
Search results from the "OB_Rx" table for query on "022372."
Active Ingredient: MAGNESIUM SULFATE ANHYDROUS; POTASSIUM SULFATE; SODIUM SULFATE
Dosage Form;Route: SOLUTION; ORAL
Proprietary Name: SUPREP BOWEL PREP KIT
Applicant: BRAINTREE LABS
Strength: 1.6GM/BOT;3.13GM/BOT;17.5GM/BOT
Application Number: N022372
Product Number: 001
Approval Date: Aug 5, 2010
Reference Listed Drug: Yes
RX/OTC/DISCN: RX
TE Code:
Patent and Exclusivity Info for this product: View
Return to Electronic Orange Book Home Page
FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - Monthly
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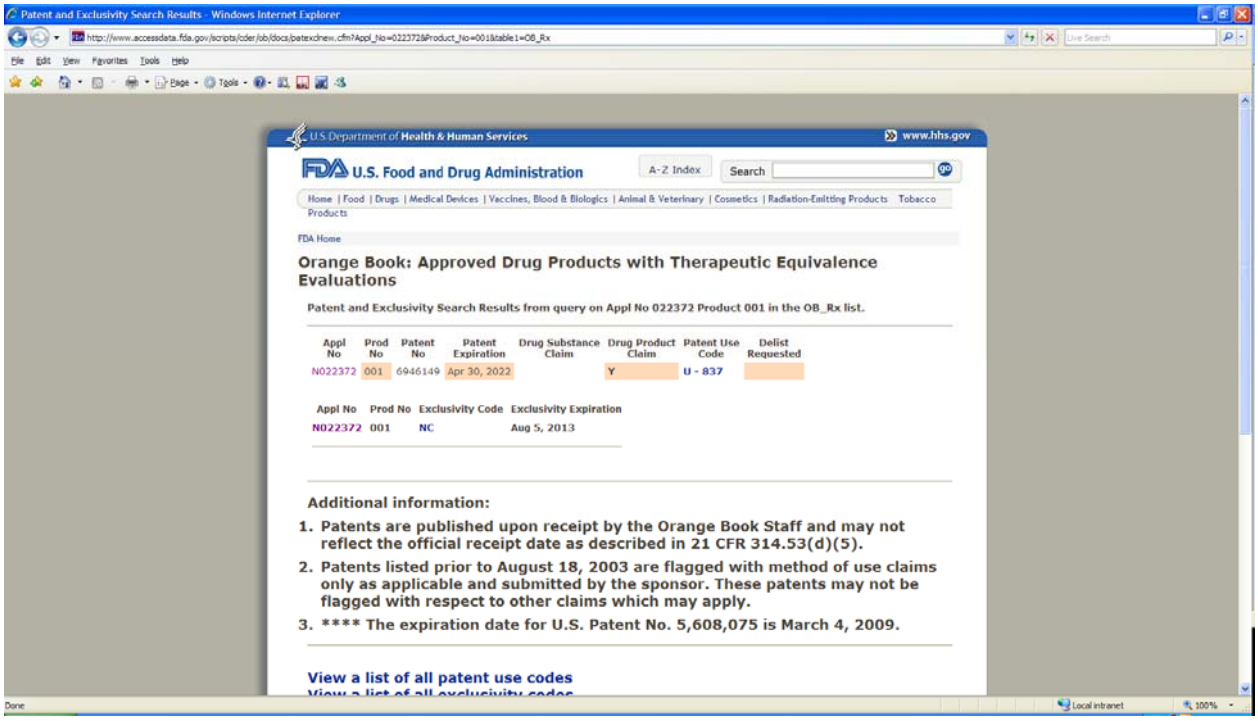
Patent and Exclusivity Search Results - Windows Internet Explorer
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U.S. Food and Drug Administration
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Search
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Patent and Exclusivity Search Results from query on Appl No 022372 Product 001 in the OB_Rx list.
Appl No | Prod No | Patent No | Patent Expiration | Drug Substance Claim | Drug Product Claim | Patent Use Code | Delist Requested
N022372 | 001 | 6946149 | Apr 30, 2022 | | Y | U - 837 |
Appl No | Prod No | Exclusivity Code | Exclusivity Expiration
N022372 | 001 | NC | Aug 5, 2013
Additional information:
1. Patents are published upon receipt by the Orange Book Staff and may not reflect the official receipt date as described in 21 CFR 314.53(d)(5).
2. Patents listed prior to August 18, 2003 are flagged with method of use claims only as applicable and submitted by the sponsor. These patents may not be flagged with respect to other claims which may apply.
3. **** The expiration date for U.S. Patent No. 5,608,075 is March 4, 2009.
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/s/

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01/07/2011

MARTIN H Shimer
01/10/2011

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE : November 10, 2010

TO : Director
Division of Bioequivalence (HFD-650)

FROM : Chief, Regulatory Support Branch
Office of Generic Drugs (HFD-615)

SUBJECT: Examination of the bioequivalence study submitted with an ANDA 202511 for Magnesium Sulfate, Potassium Sulfate and Sodium Sulfate, 1.6 g, 3.13 g and 17.5 g/bottle to determine if the application is substantially complete for filing and/or granting exclusivity pursuant to 21 USC 355(j)(5)(B)(iv).

Novel Laboratories Inc. has submitted ANDA 202511 for Magnesium Sulfate, Potassium Sulfate and Sodium Sulfate, 1.6 g, 3.13 g and 17.5 g/bottle. The ANDA contains a certification pursuant to 21 USC 355(j)(5)(B)(iv) stating that patent(s) for the reference listed drug will not be infringed by the manufacturing or sale of the proposed product. Also it is a first generic. In order to accept an ANDA that contains a first generic, the Agency must formally review and make a determination that the application is substantially complete. Included in this review is a determination that the bioequivalence study is complete, and could establish that the product is bioequivalent.

Please evaluate whether the request for study submitted by Novel Laboratories Inc. on November 08, 2010 for its Magnesium Sulfate, Potassium Sulfate and Sodium Sulfate product satisfies the statutory requirements of "completeness" so that the ANDA may be filed.

A "complete" bioavailability or bioequivalence study is defined as one that conforms with an appropriate FDA guidance or is reasonable in design and purports to demonstrate that the proposed drug is bioequivalent to the "listed drug".

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/s/

EDA E HOWARD
11/16/2010